SCOPE: To describe the procedure for submission of clinical trials protocols for evaluation by the Ethics Committee.	**DOMAIN OF APPLICATION:** This SOP applies to all interventional and non-interventional clinical trials intended to be conducted at Mount Lebanon Hospital. A clinical trial cannot be started, and trial related procedures cannot be initiated at MLH, before the trial has obtained approval from MLH Ethics Committee. **ANNEXES:** - MA-F-35: Clinical Trial Application Form in Human Subjects - MA-F-32: Ethics' committee interventional trial annual progress report - MA-F-36: Curriculum vitae for participation in a clinical trial
- **REFERENCE DOCUMENTS:** Declaration of Helsinki, adopted in 1964, first revised in 1975 and updated in 2013. - Guidance for Industry: E6 Good Clinical Practice- International Conference on Harmonisation- ICH- April 1996; www.fda.gov. Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research, Report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research; published in 1979. - Standards and operational guidance for ethics review of health-related research with human participants - Guidance document; http://www.who.int/ethics/publications/9789241502948/en/	**DEFINITIONS AND ABBREVIATIONS:** - Clinical Trial/study is an experiment done in clinical research. - Investigational Medicinal Product: A pharmaceutical form of an active substance or placebo being tested, or to be tested, or used, or to be used, as a reference in a Clinical Trial. - Informed Consent Form: Informed consent is a process for getting permission before conducting a healthcare intervention on a person. - CV: Curriculum Vitae - CRF: Case Report Form - CRA: Clinical Research Assistant - SOP: Standard Operating Procedure - CRO: Contract Research Organisation - CTA: Clinical Trial Application - SUSAR: Suspected Unexpected Serious Adverse Reaction - SADR: Serious Adverse Drug Reaction - IB: Investigator's Brochure - EC: Ethics Committee - MLH: Mount Lebanon Hospital - SPC: Summary of Product characteristics - GCP: Good Clinical Practice - CSR: Clinical Study Report - ECRF: Electronic Case Report Form - ePRO: Electronic Patient Reported Out Comes - ISF: Investigator Site File
POLICY: MA-PO-47 : Before initiating a trial, the investigator must have written and dated approval or favorable opinion from the EC for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures and any other written information to be provided to the subjects.	

I- Interventional trials

1. Clinical trial approval process
   - Clinical trial application form (CTA)

The sponsor/CRO should fill and submit a CTA form (MA-F-35) together with the trial documents to be submitted as listed below.

- TRIAL Documents to be SUBMITTED FOR ETHICS COMMITTEE APPROVAL
  - Investigator's submission letter
  - Trial CTA form
  - Trial Protocol (Most updated version) *
  - Subject information and consent form **
  - Case report form *
  - Patient card ***
  - Other patient document (diary...)
  - Recruitement advertisement
  - Investigator Brochure or Summary of Product Characteristics (If study drug is marketed and used according to the terms and conditions of its SPC) *
  - Trial insurance
  - Principal investigator updated CV (MA-F-36, unless sponsor's or CRO's template used)
  - Co-investigators updated CV (MA-F-36, unless sponsor's or CRO's template used)
  - And any other document pertinent to the study conduct

  *: English or French
  **: Arabic + English or French
  ***: Arabic
- Trial submission recipient

  The submission package (trial CTA and submission documents) should be transmitted as follow**:**
  - To the Asssitant Medical Director (Dr. Marie Merheb, Ground Floor/MLH, marie.merheb@mlh.com.lb):
    - One full hard copy and one full electronic copy of the submission package.
- Acknowledgement of receipt

  The Assitant Medical Director or the EC secretary will complete the last page of the CTA form and will communicate with the applicant (sponsor or CRO) in order to certify acknowledgement of receipt of the submitted documents. He/she will coordinate with the applicant (sponsor or CRO) until the dossier is completed.
- Meetings and approval timelines

  The following timelines apply
  - Trial dossier submitted before the 13th of month M
  - Trial dossier evaluation by Ethics Committee on the first Tuesday of month M+1
  - The secretary of the Ethics Committee will transmit, within one week after the meeting:
    - To the principal investigator: the original copy of the Ethics Committee decision's letter
  - Timelines may be delayed for submissions performed within holidays period, or in exceptional circumstances, of which the sponsor or CRO will be informed by the assistant medical director
- Approval validity
  - A trial approval by Ethics Committee is valid till the trial's end.
  - A trial that has not recruited patients within 6 months after Ethics Committee's approval should be re-submitted for evaluation.
  - If modifications to the submitted documents have been introduced since first submission, the amended documents should be submitted, together with a list of changes made, indicating their section, the initial wordings and the amended wordings.
  - The Ethics Committee reserves the right to interrupt a trial (temporary or definitely), at any time, for ethical or safety concerns.
  - The close out visit report should be submitted only when all activities related to the study are finished (such as payment for all parties, soft or hard copy of the ECRF, ePRO, pharmacy and laboratory files collected and archived with the ISF,...). A clearance from the study team of MLH must be taken before proceeding with the close out visit report.

2. Information to be submitted during the trial

The following should be transmitted hard copy to the Assistant Medical Director/EC secretary at: marie.merheb@mlh.com.lb, for submission to the Ethics Committee:

- Any interruption and the reason of interruption of the trial in any participating centre/country, within 7 calendar days after sponsor's decision.
- Investigator notifications (INs) about SUSAR and safety: these should be submitted at least once per year, either in the Investigator Brochure or during the continuing review submission.
- Serious Adverse Events (SAE):
  - If this has lead to patient death, these should be initially submitted within 48 hours after investigator awareness. And an updated report within 7 working days.
  - If this has not lead to death, these should be initially submitted within 48 hours after investigator awareness. And an updated report within 7 working days.
- Protocol Deviations and non compliance reports:
  - If affecting patients' safety, these should be submitted within 7 working days.
  - Other protocols deviations and non compliance reports should be submitted within 6 months of investigator's awareness.
- Blinded Suspected Unexpected Adverse Reaction (SUSARS): these should be reported quarterly or every 6 months based on the sponsor procedure.
- Annual progress report (MA-F-32): such report is submitted on a yearly basis after Ethics' Committee approval and a final report at the study closure.
- The CSR once released by the sponsor or the CRO.

3. Ethics committee statement

At sponsor's/CRO's request, the Ethics Committee can deliver a statement indicating names and function of its members as well as the regulations and process applied.

4. Clinical trial agreement process:

The study agreement with the sponsor or the CRO should include and be signed by the three following parties:

- The investigator(s) and co investigator(s)
- The hospital site (MLH medical director), for hospital services (lab, radiology, pharmacy...)

An initial draft of the agreement including study budget should be transmitted for comments to:

- The investigator(s) and co inversigator(s)
- The Assistant Medical Director at marie.merheb@mlh.com.lb

II- Non-interventional trials

1. Clinical trial approval process

- Clinical trial application form (CTA)
  The sponsor/CRO should fill and submit a CTA form (MA-F-35) together with the trial documents to be submitted as listed below.
- Trial documents to be submitted for ethics committee approval
  - Investigator's submission letter
  - Trial CTA form
  - Trial Protocol (Most updated version) *
  - Subject information and consent form **
  - Case report form *
  - Patient documents (diary...) ***
  - Recruitement advertisement
  - Principal investigator updated CV (MA-F-36)
  - Co-investigators updated CV (MA-F-36)
  - And any other document pertinent to the study conduct

*: English or French

**: Arabic + English or French
***: Arabic

- Trial submission receipient
  One full hard copy and one full electronic copy of the submission package.
  (trial CTA and submission documents) should be transmitted to the Asssitant Medical Director (Dr. Marie Merheb, Ground Floor/MLH , marie.merheb@mlh.com.lb).
- Acknowledgement of receipt
  The Assitant Medical Director or the EC secretary will complete the last page of the CTA form and will communicate with the applicant (sponsor or CRO) in order to certify acknowledgement of receipt of the submitted documents. He/she will coordinate with the applicant (sponosr or CRO) until the dossier is completed.
- Meetings and approval timelines
  The following timelines apply
  - Trial dossier submitted before the 13th of month M
  - Trial dossier evaluation by Ethics Committee on the first Tuesday of month M+1
  - The secretary of the Ethics Committee will transmit, within one week after the meeting:
    - To the principal investigator: the original copy of the Ethics Committee decision's letter
  - Timelines may be delayed for submissions performed within holidays period, or in exceptional circumstances, of which the sponsor or CRO will be informed by the assistant medical director.
  - Approval of such non-interventional trials can be done in an ***expedited manner***, at the discretion of the EC chariperson.
- Approval validity
  - A trial approval by Ethics Committee is valid till the trial's end.
  - A trial that has not recruited patients within 6 month after Ethics Committee's approval should be re-submitted for evaluation.
  - If modifications to the submitted documents have been introduced since first submission, the amended documents should be submitted, together with a list of changes made, indicating their section, the initial wordings and the amended wordings.
  - The Ethics Committee reserves the right to interrupt a trial (temporary or definitely), at any time, for ethical or safety concerns.
  - The close out visit report should be submitted only when all activities related to the study are finished (such as payment for all parties, soft or hard copy of the ECRF, ePRO, pharmacy and laboratory files collected and archived with the ISF,...). A clearance from the study team of MLH must be taken before proceeding with the close out visit report.

2. Ethics committee statement

At sponsor's/CRO's request, the Ethics Committee can deliver a statement indicating names and function of its members as well as the regulations and process applied.

3. Clinical trial agreement process:

The study agreement with the sponsor or the CRA should include and be signed by the two following parties:
- The investigator(s) and co investigator(s)
- The hospital site (MLH medical director).

An initial draft of the agreement including study budget should be transmitted for comments to:
- The investigator(s) and co investigator(s)
- The Assistant Medical Director at marie.merheb@mlh.com.lb.

III- Types of review

All clinical trial protocols are reviewed by the EC, either as a full, an exempt or an expedited review.
- Full review, which is applicable to all interventional and non-interventional trials.

Specific attention is additionnally paid to the following trials where research involves greater than minimal risk to participants and/or involves sensible data collection:

- research involving vulnerable groups – for example, children and young people, those with a learning disability or cognitive impairment, or individuals in a dependent or unequal relationship
- research involving sensitive topics – for example participants' sexual behaviour, their illegal or political behaviour, their experience of violence, their abuse or exploitation, their mental health, or their gender or ethnic status
- research involving groups where permission of a gatekeeper is normally required for initial access to members – for example, ethnic or cultural groups, native peoples or indigenous communities
- research involving deception or which is conducted without participants' full and informed consent at the time the study is carried out
- research involving access to genetic or other biological records or information, concerning identifiable individuals
- research which would induce psychological stress, anxiety or humiliation or cause more than minimal pain
- research involving intrusive interventions – for example, vigorous physical exercise, or techniques such as hypnotherapy. Participants would not encounter such interventions, which may cause them to reveal information which causes concern, in the course of their everyday life

- Exempt review: it applies to research with "minimal risk":
  - Education research
  - Surveys, interviews, educational tests, public observations (that do not involve children)
  - Studies of public officials
  - Analysis of previously – collected, anonymous data
  - Public benefit or service program
  - Consumer acceptances, taste, and food quality studies
- Expedited Review: It can be done by the EC chairperson or one of its designee:
  - Applicable to non-interventional research projects that have a short lead time and are commissioned in response to a demand of a justified pressing importance.
  - Applicable to all trials for minor changes in previously approved research during the period for which approval is authorized.
    - Clinical studies of drugs and medical devices only when certain conditions are met
    - Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture in certain populations and within certain amounts
    - Prospective collection of biological specimens for research purposes by noninvasive means.
    - Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves.
    - Reserch involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non – research purposes
    - Collection of data from voice, video, digital, or image recordings made for research purposes
    - Research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.