



**LEBANESE MINISTRY OF HEALTH DIRECTIVE**

**LAYING DOWN DETAILED GUIDELINES  
FOR SPONSORS OF CLINICAL TRIALS**

March 2012

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*F-MRI Confidential Draft*



## GUIDELINES FOR SPONSORS OF CLINICAL TRIALS

### A) FIELD OF APPLICATION

The guidelines presented herein apply to all clinical trials conducted in Lebanon on human subjects, including non interventional trials, eg epidemiological trials, observational trials, post-marketing surveillance trials and registries trials.

Interventional trials are concerned by these regulations whenever they are conducted with one of the following investigational product (IP):

- A medicinal product bearing a market authorisation
- A medicinal product under clinical development, whatever its origin or its components. This includes medicinal products with specific characteristics, such as
  - Medicinal products the active ingredient of which is of human or animal origin, or contains biological components of human or animal origin, or the manufacturing of which requires such components.
  - Medicinal products for gene therapy, somatic cell therapy including xenogenic cell therapy and all medicinal products containing genetically modified organisms
- A medical device, whatever its nature or its composition

### B) GENERAL CONSIDERATIONS

Clinical trials should be conducted in authorized university hospitals and clinics, in accordance with the applicable good clinical practice and with the ethical principles stated in the declaration of Helsinki.

Clinical trials may be undertaken on minors only where such research is justified.

No gene therapy trials may be carried out which result in modifications to the subject's genetic identity.

All kinds of non commercial trials should have a named sponsor.

The sponsor of a clinical trial may transfer any or all of the sponsor's trial related duties and functions to a Contract Research Organisation or to other third party, but the ultimate responsibility for the trial resides and remains with the sponsor.

Prior to a subject's participation in the trial, a written informed consent should be read, understood, signed and dated by the subject, or by the subject's legal representative. An impartial witness should sign and date the informed consent in order to attest that the consent information was accurately explained, understood and accepted by the subject or his legal representative, in case the latter is unable to read or write.

Trial's data recorded by the investigator should be consistent with the subjects' medical source documents.

The Foundation-Medical Research Institutes (F-MRI) may inspect the modalities under which clinical trials are performed and recorded, and trials subjects' safety is followed up. The investigator should make available for direct access by the inspector all requested trial's related records and source documents.

### **C) TRIAL'S SUBMISSION FOR F-MRI OPINION**

Before starting a clinical trial the sponsor should first request F-MRI opinion on the trial's dossier, after which he applies for trial's approval from each hospital Institutional review Board (IRB), or Ethics Committee (EC), where the trial is planned to be performed.

For submission to the F-MRI, the sponsor should fill a Clinical Trial Application form, and transmit it with the requested documents, as per appendix 1.

If the submitted dossier is complete, F-MRI will return electronically to the sponsor an acknowledgement of receipt, and will assign a trial registration number, to be specified in any further formality or correspondence with the F-MRI

Three weeks after acknowledgement of receipt of the complete dossier, the F-MRI will transmit to the sponsor its opinion.

F-MRI opinion should be included with the documents submitted to the IRB/EC.

Where F-MRI has issued critical questions or requests, the sponsor should first provide the requested answers or documents to the F-MRI, and submit to the IRB/EC only after F-MRI has released its opinion.

An electronic copy of all IRB/EC approvals or non approvals should be transmitted to the F-MRI, within one month after their issue.

### **D) VALIDITY OF F-MRI OPINION**

F-MRI opinion is valid for 8 months as of its date of issue.

A trial that has not recruited patients during this 8 months period should be re-submitted.

If modifications to the submitted documents have been introduced since first submission, the amended documents should be submitted, together with a list of the changes made, indicating their section, the initial wordings and the amended wordings, as per appendix 2.

Otherwise, the sponsor may just inform the F-MRI that no changes were made to the previously submitted dossier. In both cases, F-MRI will release its opinion within two weeks after receipt of the re-submitted dossier.

### **E) PROTOCOL AMENDMENTS AND CHANGES IN THE TRIAL CONDUCT**

During the course of the trial, any protocol amendment or change in the trial conduct, including amendments related to other participating countries, should be transmitted at the same time to the IRB/EC and to the F-MRI together with an explanation letter.

If the amendment or change relates to the trial global conduct or methodology, or if it relates to the trial organisation in Lebanon, it should not be implemented inasmuch as the F-MRI has not informed the sponsor of any ground for objection, within 15 days, and until the IRB/EC has issued its approval.

Details for transmission to the F-MRI are provided in appendix 2

If an additional university hospital in Lebanon is to participate after the trial has started, the F-MRI should be informed and provided as soon as possible with an electronic copy of the Hospital IRB/EC trial's approval.

### **F) INFORMATION ON TRIAL'S START**

When first patient first trial visit to any of the participating Lebanese trial's hospitals has been performed, the information should be transmitted to the F-MRI within 15 days, as per appendix 3.

## G) INTERVENTIONAL TRIALS SUBJECTS' SAFETY

The clinical trial design should consider minimization and close monitoring of any foreseeable risk or discomfort to the subjects, in relation to the IP, to the disease or to the trial's procedures. The F-MRI should be informed on trial subjects' safety aspects as per the following basis:

Information per subject/patient basis

Unexpected serious adverse reaction to the tested product(s) should be documented on a CIOMS form and notified to the F-MRI.

Fatal or life-threatening cases should be transmitted within 7 calendar days, and other cases should be transmitted within 15 calendar days.

Time clock starts as of first knowledge of the reaction or finding by the sponsor or its representative.

Further relevant follow-up information should be given within an additional eight calendar days for fatal or life-threatening cases and as soon as possible for other cases.

Information per product basis

- If a foreign sponsor of a clinical trial is requested by its local regulations to provide regular safety information on the IP, such as Development Safety Update Reports (DSUR) or Annual Safety Reports (ASR) or any other kind of safety data information included in regular periodic reports, the reports should also be transmitted to the F-MRI at similar timelines. Applicable reports and their expected timelines will be indicated by the sponsor in the Clinical Trial Application form.
- If the trial is conducted by a sponsor located in Lebanon, safety annual information should be included in the yearly progress report (refer to next section), presenting a comprehensive summary analysis and listing of all unexpected adverse reactions and of relevant safety findings, as well as a conclusive update of the benefit/risk ratio to the trial's subjects.

## H) INTERVENTIONAL TRIALS YEARLY PROGRESS REPORT

A yearly progress report should be transmitted to the F-MRI, containing the following trial information:

- Number of centres in each participating country
- Number and name of newly opened or closed country or centre, in the concerned year of reporting
- Reason for country or centre opening or closure
- Cumulative number of patients in each centre in Lebanon:
  - Treated (having received the IP)
  - Dropped out for safety reason - specify the reason
  - Dropped out for inefficacy reason
  - Terminated trial
- Cumulative total number of patients in the trial:
  - Treated (having received the IP)
  - Dropped out for safety reason - specify the reason
  - Dropped out for inefficacy reason
  - Terminated trial

### Timelines for foreign sponsors

Foreign sponsors will be asked in the Clinical Trial Application form to indicate a yearly date on which they commit to transmit the progress report to the F-MRI.

This may be of particular interest to foreign sponsors for the following reasons:

- They can indicate a unique date for transmission of both safety and progress reports
- If all information requested by the annual progress report are anticipated to be included in the safety report (DSUR, ASR,..), for as much as this report is prepared on a yearly basis, and only in this case, then this must be specified and a unique report may be submitted to the F-MRI.

### **Timelines for sponsors located in Lebanon**

When the trial's sponsor is located in Lebanon, safety information should be included in the yearly progress report as per section g). Time clock starts as of the release of F-MRI opinion following CTA submission. The report should be transmitted within 2 months after the annual cut-off date. The last final report in the last trial year period should be transmitted within 2 months after trial termination, ie after last centre closure.

### **I) NON-INTERVENTIONAL TRIALS YEARLY PROGRESS REPORT**

There is no requirement for a yearly progress report. However, such report may be requested by the F-MRI for specific trials. This will be indicated then in the F-MRI opinion release.

### **J) TRIAL'S TERMINATION**

The F-MRI should be informed, as per appendix 3

- Of the trial's termination in Lebanon, within one month after last centre closure. If the trial in Lebanon has to be terminated prematurely, this period should be reduced to 15 days and the reasons clearly explained.
- And of the global trial termination in all participating countries, if any, within 2 months after last centre closure. If the global trial has to be terminated prematurely, this period should be reduced to 15 days and the reasons clearly explained.

A summary of the trial's results should be transmitted to the F-MRI within one year after the trial has ended in Lebanon and in all other participating countries, if any.

All remaining used or unused trial medicinal product should be shipped and recuperated by the sponsor out of Lebanon.

### **K) F-MRI COMMUNICATION WITH TRIALS SPONSORS**

**Hard copies** submissions and notification to F-MRI should be provided to:

Foundation-Medical Research Institutes office:  
Faculty of Medicine.  
Lebanese University.  
Haddath. Lebanon.

**Electronic copy** should be transmitted to: [clinicaltrials@f-mri.org](mailto:clinicaltrials@f-mri.org)

F-MRI will release its opinion, request or any other kind of communication to the sponsors by electronic transfer. Original hard copies can be retrieved, on demand, at the F-MRI office

## L) F-MRI FEES

The following charges apply:

- Fees for submission of CTA: 1500 USD  
To be paid upon submission of the CTA
- Fees for following submissions, including re-submission of CTA, protocol amendments, trial reports and results: 500 USD  
To be paid upon information on trial's start

Payments should be performed by bank transfer, to the following account:

Beneficiary:	Foundation-Medical Research Institutes.
Name of the Bank:	Audi – Saradar Group
Address of the Bank:	Sin El Fil, Hojeily Street
SWIFT n°:	AUDBLBBX
Account n°:	085670
IBAN n°:	LB93 0056 0000 8567 0461 0020 2502

## M) INFRINGEMENT OF THE PRESENT DIRECTIVE

If a sponsor fails to fulfill any of the provisions of this Directive, the F-MRI reserves the right to inform the administrative supervision, in particular the Ministry Of Health, and undertake jointly adequate or legal actions that may lead to the trial's suspension or interruption in Lebanon.

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