Monitoring of Clinical Studies

1- Definitions / Key Terms:*

1-1 **Amendments** - A research study is considered to have commenced when the first participant or patient gives written informed consent to participate. Occasionally, the PI (Sponsor) may revise the terms of the EC application, the protocol or other supporting documentation after approval has been given or after the study has Commenced. This revision may be considered a minor, substantial or major amendment.

1-2 **Inspection**: The act by a regulatory authority (ies) of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority (ies) to be related to the clinical trial and that may be located at the site of the trial.

2- Purpose:

2-1 To provide guidance on monitoring of the research study to the Investigators and other stake holders involved in research.

3- Scope of application

3-1 This applies to the Investigators and other stake holders involved in research planned at the institutions governed by DHA; or institutions that are within the jurisdiction of DHA in the Emirates of Dubai. It does apply to interventional, non-interventional studies including medical devices.

4- Applicable To:

4-1 Investigators and other stake holders involved in research.

5- Responsibilities

5-1 DHA/DG/MERD/SOP/001

6- Operational Resources:*

6-1 DHA/DG/MERD/SOP/001

7- Policy:

7-1 NA

8- Procedure/Steps:

8-1 **Subsequent Submissions and Extensions to Approved Projects:**

- **Definition of Amendments**

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- **Types of Amendment**
  - **Minor:** of relatively little importance and therefore not considered as substantial.
  - **Substantial:** the following changes should normally be regarded as substantial:
    - ✓ Changes to the design or methodology of the study, or to background information affecting its scientific value.
    - ✓ Changes to the procedures undertaken by participants
    - ✓ Any change relating to the safety or physical or mental integrity of participants, or to the risk/benefit assessment for the study.
    - ✓ Changes to study documentation such as participant information sheets, consent forms, questionnaires, letters of invitation, letters to GPs or other clinicians, information sheets for relatives or caregivers.
    - ✓ Change in the use of biological samples.
    - ✓ A change of sponsor(s) or sponsor's legal representative.
    - ✓ Appointment of a new PI or key collaborator.
    - ✓ A change to the responsibility and liability insurance coverage for the study.
    - ✓ A significant change to the definition of a research site.
    - ✓ A change to the definition of the end of the study.
    - ✓ Any other significant change to the protocol or the terms of the original.
    - ✓ EC application.
  - **Major:** whatever procedural changes alter the risk, which participants are exposed to, or the potential benefit, constitutes a major amendment.

Examples include:

- ✓ A change in the primary purpose or objective of the research, such as Introduction of additional genetic studies.
- ✓ A substantial change in research methodology.
- ✓ Introduction of new classes of investigations or other interventions (rather than simply re-scheduling or modifying those already approved).
- ✓ Recruitment of a new type of participant (especially if these would be regarded as being from vulnerable groups).

For minor amendments- A Notification letter addressed to the DSREC enlisting the changes done to the document along with the reason for the same should be sent. The committee shall acknowledge the receipt of the same.

For major and substantial amendments – Submission of a cover letter addressed to the DSREC informing a major/substantial changes made in a below tabular format. Please attach the amended documents with the required track changes.

Previous Text	Amended Text	Reason for change

- All amended submitted documents must have the changes highlighted and contain revised version numbers and dates, where applicable.
- Expedited review of requests for minor amendments and extensions may be undertaken by the Chairperson between scheduled meetings at the discretion of the Chairperson and in accordance, on the condition that it is ratified at the next DSREC meeting. Where an urgent protocol amendment is required for safety reasons, the Chairperson may review and approve the request. In such circumstances, the DSREC will review the decision at its next available meeting.
- All other requests for amendments shall be reviewed by the DSREC at its next available meeting, provided the request has been received by the Coordinator by the agenda closing date.

- The DSREC will report in writing to the principal investigator, advising of the ethical approval of the proposed amendment and/or request for extension, within 7 working days of the meeting at which the request was considered (this may be the full DSREC meeting or the Executive meeting), or determines if further information, clarification or modification is needed to support the approval process.

8-2 **Monitoring of approved research projects:**

1. The DSREC will monitor approved projects to ensure compliance with its ethical approval. In doing so it may request and discuss information on any relevant aspects of the project with the investigators at any time.
2. Monitoring of approved projects by the DSREC will be through the following:
   - Annual Progress Reports submitted by the Principal Investigator.
   - Notification of study completion at the end of the study.
   - Clinical Study Report, when available.
   - Ongoing Reporting of safety Information, if any (Refer to Handling of Adverse Events Section).
   - Major Protocol deviations affecting patients' safety, if any, should be informed with adequate justifications.
   - Random inspections by DSREC of research sites, data and signed consent forms;
   - Interview, with their prior consent, of research participants.

Progress Reports should include, as a minimum, the following information:

- Dates of Site Initiations

- Number of patients recruited at the time of writing the report
- Targeted Number of patients on site
- Expected End of Recruitment
- Any major safety events
- Any other important information
- Final Investigational Product reconciliation and destruction, applies only to End of study Report.

3. The DSREC shall require, as a condition of approval of each project, that investigators immediately report anything which might warrant review of ethical approval of the protocol, including:
    - Proposed changes in the protocol;
    - Any unforeseen events that might affect continued ethical acceptability of the project; and
    - New information from other published or unpublished studies which may have an impact on the continued ethical acceptability of the trial, or which may indicate the need for amendments to the trial protocol.
    - The DSREC shall require, as a condition of approval of each project, that investigators inform the DSREC, giving reasons, if the research project is discontinued before the expected date of completion.
    - Where the DSREC is satisfied that circumstances have arisen such that a research project is not being or cannot be conducted in accordance with the approved project, the DSREC may withdraw approval. In such circumstances, the DSREC shall inform the principal investigator and the institution of such withdrawal of approval in writing, and recommend

to the institution that the research project be discontinued, suspended, or that other necessary steps be taken.

- In determining the frequency and type of monitoring required for approved projects, the DSREC will give consideration to the degree of risk to participants in the research project.

8-3 **Handling of adverse events:**

1. Reporting guidelines for both National and Foreign adverse drug reactions:

	EVENT	TIMELINE	SUBMISSION TYPE
National	All Local Serious Adverse Events (Reported from institutions falling under DHA or other participating Institutions within UAE)	• 1st Notification within 48 hours (Initial Report) of Investigator's awareness. • Follow up Report, if any, should be completed and submitted with 14 days.	Using Study specific Reporting form OR DHA form Appendix 3.1 To be sent via email OR handed to DHA as hardcopy.
Foreign	ONLY Suspected, Unexpected, Serious Adverse Drug reactions(SUSARs) should be submitted	Quarterly	CIOMS reports OR sponsor's listings To be sent via email OR handed over as hardcopy.
	Serious Expected ADRs/ Unrelated Unexpected SAEs/ Unrelated expected SAEs		Not required

2. The procedures and format for notification of adverse events to the DSREC shall be readily available to investigators.

Monitoring of Clinical Studies

Adverse events may be reviewed by the Chairperson, which shall determine the appropriate course of action. This may include:

- Notation on file of the occurrence;
- increased monitoring of the project;
- Request for an amendment to the protocol and/or Patient Information Sheet/Consent Form;
- Suspension of ethical approval; or
- Termination of ethical approval

Any such adverse events and actions taken by the Chairperson shall be reported to the DSREC at the next available meeting.

The Chairperson may take the appropriate course of action for those adverse events deemed serious and requiring immediate attention. This may include:

- Referral to scientific/technical expertise;
- Immediate request for additional information;
- Immediate suspension of ethical approval;
- Immediate termination of ethical approval.

The DSREC shall provide notice to the investigator that it has received notification of the serious or unexpected adverse event, and the course of action it has deemed necessary to take

Appendix 3.1

Study Site Progress/Annual Report Template

DATE of the Report:

Monitoring of Clinical Studies

Covering Period of Report:	From:			To:	
Report Number:					
Sponsor Name:					
Principal Investigator:					
Study Site:					
Project Full Title:					
Protocol Number/Study Phase:					
DSREC Last Approval Date with reference code:					
Site Name	Site Initiation Date	Patient Number till Date			
		Screened Patients	Enrolled Patients	Completed Treatment	Discontinued Treatment
Expected Date for End of Recruitment:					
Expected Date for End of Study:					
Number of Serious Adverse Events Reported within the Report coverage period:					
All Serious Adverse Events reported to DSREC: Yes No* *If No, please make sure a completed Serious Adverse Event Reporting Form is attached to the Progress Report.					
Number of Violations/Deviations Reported within the Report coverage period: Yes No* *If No, please make to report the same to the Committee along with this document.					
Notes:					

Principal Investigator/designee Signature: _____

Date: _____

Appendix 3.2

Serious Adverse Events reporting form

Full title of study – _____

Sponsor protocol No: (If applicable) – _____

Name of Principal Investigator – _____

Monitoring of Clinical Studies

Report No. and date	Description of event	Start date of the event	Stop date of the event (indicate if ongoing)	Frequency of event in relation to total number of participants on site	*Relationship of the event to the study drug/device	Impact on study drug(study drug/device put on hold, No impact, permanently discontinued)

*Unlikely/possible/probable/definite

Narrative /outcome:

Signature of the Principal investigator/Delegate: _____

Date: _____

9- Deployment of Monitoring of Clinical Studies: (Check all that apply)

☒Announcement
☒Awareness
☐Training
☐On Job Training

10- Measures of Monitoring of Clinical Studies

10-1 Refer DHA/DG/MERD/SOP/001 | Target/Threshold

11- List of Risks of Monitoring of Clinical Studies:

11-1 Refer DHA/DG/MERD/SOP/001 | Risk Level

12-Audit, Improvement & Development of Monitoring of Clinical Studies:

12-1 Internal audit for compliance with the document content

12-2 Corrective actions for non-conformities with the document content

13- Records of Monitoring of Clinical Studies :

13-1 Cover letter and Study Progress Report

13-2 Inspection checklist-Reference - CP_7.1.08 Inspect Approved Research Studies

14- Annexes of Monitoring of Clinical Studies:

14-1 Reference - CP_7.1.08 Inspect Approved Research Studies

N.B.: "*" Put "N/A" if there is nothing to write.
(the document) to be replaced by document title