ADVERSE EVENTS REPORTING

All Adverse Events (AE), Serious Adverse Events (SAE), Adverse Drug Reactions (ADR), Serious Adverse Drug Reactions (Serious ADR) and Suspected and Unsuspected Serious Adverse Reactions (SUSARS) must be reported to MNTRH-IREC for review.

It is the responsibility of the Principal Investigator on site as well as off site for multicentre studies to report the occurrence of all the aforementioned to MNTRH-IREC, Data Safety Monitoring Board, and Sponsor.

i) **Adverse Event** is defined as 'any untoward medical occurrence in a participant in a research investigation participant administered a pharmaceutical product and that does not necessarily have a casual relationship with this treatment'. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding). Symptom or disease temporarily associated with the use of a medicinal/investigations product, whether or not related to the medicinal (investigational) product.

ii) **Serious Adverse Event** is defined as 'any untoward medical occurrence that at any dose results into death, is life threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect'.

iii) **Adverse Drug Reaction (ADR)** is defined as any noxious and unintended response associated with the use of a drug in human or animals.

iv) **Serious Adverse Event (AE) or Serious Adverse Drug Reaction (Serious ADR)** is an AE or ADR that is associated with death, hospitalisation, and prolongation of hospitalisation, persistent or significant disability or incapacity, or a congenital anomaly or birth defect or is otherwise life threatening.

v) **Suspected Unexpected Serious Adverse Reactions (SUSARS);** An Unexpected Adverse Reaction (UAR) is an adverse reaction that is not consistent with the product information in summary of product characteristics. A Suspected Unexpected Serious Adverse Reaction (SUSARS is any UAR that at any dose results in death, is life threatening (i.e. the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe); requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect'.

11.1 REPORTING PROCEDURE

i) All AEs must be reported to MNTRH-IREC via the prompt reporting form and a cover letter by the Principal Investigator via email within a maximum of 72 hours.

ii) If the AE is considered by the PI to have implications to other research participants and upon assessment suggests further risk or possible adverse events the PI is required to report the AE and its potential implications to MNTRH-IREC immediately followed by the formal completion and submission of the prompt report from within 72 hours of occurrence.

iii) All SAEs and Serious ADRs must be reported to MNTRH-ISEC immediately by the PI followed by the formal completion and submission of the prompt report form within 72 hours of occurrence.

iv) All ADRs and SUSARS must be reported to MNTRH-ISEC immediately by the PI followed by the formal completion and submission of the prompt report form within 72 hours of occurrence.

11.2 REVIEW AND DECISSIONS ON SAE REPORTS

i) The Secretariat will receive the documentation within the specified time frame.

ii) The Secretariat will verify that the report is complete and has been received within the specified time frame. If the time frame is surpassed, it shall be considered a deviation.

iii) The Secretariat will forward the report to the Secretary within **2 calendar days.**

iv) The Secretary will review the SAE and in liaison with the Human Participant Administrator, the report will be included into the agenda of the Monitoring and Evaluation Sub-Committee.

v) The reports will be reviewed by the Monitoring and Evaluation Sub-Committee during the monthly meetings. The Monitoring and Evaluation Sub-Committee meeting with special focus on relatedness on the clinical trial, medical management and financial compensation to be given to research participants.

vi) The Monitoring and Evaluation Sub-Committee will refer the issue to the full board during the monthly meetings, for further action or for ratification of the decision taken by the Sub-Committee.

vii) Upon receiving the report from the Monitoring and Evaluation Sub-Committee, the Full Board Committee during the meeting shall determine and recommend appropriate intervention(s) which may include review of the research protocol in light of the event, call for further investigation, suspend the study till review is complete, suspend the study till changes requested are completed, suspend enrolment of new participants, terminate the study or recommend any other appropriate action.

viii) The decision of the Full Board Committee will be communicated to the PI within **2 calendar days.**

ix) The PI will be requested to respond if there are further clarifications needed **within 7 calendar days.**