Table of Contents

No.	Content	Page No.
1.	**PURPOSE**	**2**
2.	**SCOPE**	**2**
3.	**RESPONSIBILITY**	**2**
4.	**FLOW CHART**	**2**
5.	**DETAILED INSTRUCTIONS**	**3**
5.1.	BEFORE EACH IRB MEETING	3
5.1.1	*Review and determine the review channel*	*3*
5.1.2	*Criteria for the review*	*3*
5.2.	DURING THE IRB MEETING	3
5.2.1	*Review and discuss*	*3*
5.2.2	*Decide what action should be taken.*	*3*
5.2.3	*Inform investigator or clinical trial office*	*4*
6.	**GLOSSARY**	**4**
7.	**REFERENCES**	**6**
8.	**ANNEX**	**6**
ANNEX 1:	SERIOUS ADVERSE EVENT REPORT	7
ANNEX 2:	UNEXPECTED ADVERSE EVENT SUMMARY REPORT	8

1. Purpose

The purpose of this SOP is to describe the procedures for the review of initial and follow-up reports of serious adverse events and unexpected events for any active study reported to IRB for any study approved by the IRB.

2. Scope

This SOP applies to the review of SAE and unexpected events reports submitted by investigators, Data Safety Monitoring Board (DSMB), sponsor, local safety monitor, IRB members or other concerned parties.

3. Responsibility

It is the responsibility of the IRB to review all SAEs and unexpected event reported to the IRB in a timely manner.

4. Flow Chart

No.	Activity	Responsibility
	Before an IRB meeting	
1	SAE related activities	IRB/Secretariat Office/SERO
	↓	
2	Review and determine the review channel	IRB/Secretariat Office/SERO
	↓	
3	**CRITERIA FOR THE REVIEW**	IRB/Secretariat Office/SERO
	↓	
4	During the IRB meeting	IRB
	↓	
5	Review and discuss	IRB / Chairperson
	↓	
6	Decide what action should be taken.	IRB /Chairperson
	↓	
7	Inform investigator or clinical trial office	SERO/Chairperson

5. Detailed instructions

5.1. Before each IRB meeting

5.1.1 Review and determine the review channel

- IRB Secretariat or members review the reporter's assessment to determine whether the report requires review by full Board or; expedited by the chairperson or other qualified IRB member(s) or reviewer

5.1.2 Criteria for the review

- The **review criteria** are as follows:
  - Assessment of adverse experience is unknown or unlikely
  - Report is forwarded to the Chairperson for review and determination if report should be reviewed at the convened meeting by full Board
- Assessment of adverse experience is possibly caused by, or probably caused by the investigational product
  - The report is added to the agenda for review at a convened meeting by full Board
- An adverse experience/IND Safety Report has been previously seen by full Board but being resubmitted by another investigator participating in the multi-study site (as part of a multi-center/site study), or is offsite
  - This notification does not require full Board review
  - Reviewed by the Chairperson or other qualified IRB members and secretariat

5.2. During the IRB meeting

5.2.1 Review and discuss

- After reading and reviewing the report, the Chairperson or designee entertains discussion on the study and similar adverse experiences or advisories.
- If appropriate to the discussions, the Chairperson or another Board member may call for a consensus on whether to:
- No Further Action Required,
- Request Information,
- Recommend Further Action

5.2.2 Decide what action should be taken.

- If any of the above actions are taken, the IRB Secretariat or designee notifies the investigator of the action taken.

- If the IRB *takes no action*, a notation is made in the minutes and the study is allowed to continue.

5.2.3 Inform investigator or clinical trial office

- The IRB secretariat member drafts a formal letter to the investigators or the clinical trial office to notify them of the action they should take according to the IRB decision.
- Get the Chairperson to approve, sign and date the letter.
- Send the letter and record the delivery date.

6. Glossary

Adverse Drug Reaction	In the pre-clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not established all noxious or unintended responses to the product related to any dose should be considered adverse drug reactions. The phrase "responses to a medicinal product" means that a causal relationship between the product and the adverse event is at least a reasonable possibility, i.e., the relationship can not be ruled out. Regarding marketed products, a response to a product which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of diseases or for modification of physiological function.
Adverse Event	Any untoward medical occurrence in a patient or clinical investigation participant administered an investigational product and which does not necessarily have a causal relationship with this treatment. The adverse event can therefore be any unfavorable or unintended sign or experience associated with the use of the investigational product, whether or not related to the product.
IND	Investigational New Drugs means substances with potential therapeutic actions during the process of scientific studies in human in order to verify their potential effects and safety for human use and to get approval for marketing.
SAE (SERIOUS ADVERSE	The adverse event is SERIOUS and should be reported when the patient outcome is: **Death** - Report if the patient's death is suspected as being a

EVENT)

direct outcome of the adverse event.

Life-Threatening: Report if the patient was at substantial risk of dying at the time of the adverse event or it is suspected that the use or continued use of the product would result in the patient's death.

Examples: Pacemaker failure; gastrointestinal hemorrhage; bone marrow suppression; infusion pump failure which permits uncontrolled free flow resulting in excessive drug dosing.

Hospitalization (initial or prolonged): Report if admission to the hospital or prolongation of a hospital stay results because of the adverse event.

Examples: Anaphylaxis; pseudomembranous colitis; or bleeding causing or prolonging hospitalization.

Disability: Report if the adverse event resulted in a significant, persistent, or permanent change, impairment, damage or disruption in the patient's body function/structure, physical activities or quality of life.

Examples: Cerebrovascular accident due to drug-induced hypercoagulability; toxicity; peripheral neuropathy.

Congenital Anomaly: Report if there are suspicions that exposure to a medical product prior to conception or during pregnancy resulted in an adverse outcome in the child.

Examples: Vaginal cancer in female offspring from diethylstilbestrol during pregnancy; malformation in the offspring caused by thalidomide.

Requires Intervention to Prevent Permanent Impairment or Damage: Report if suspect that the use of a medical product may result in a condition which required medical or surgical intervention to preclude permanent impairment or damage to a patient.

Examples: Acetaminophen overdose-induced hepatotoxicity requiring treatment with acetylcysteine to prevent permanent damage; burns from radiation equipment requiring drug therapy; breakage of a screw requiring replacement of hardware to prevent malunion of a fractured long bone.

Unexpected ADR	Unexpected Adverse Drug Reaction is an adverse reaction, the nature or severity of which is not consistent with the informed consent / information sheets or the applicable product information (e.g., investigator's brochure for the unapproved investigational product or package insert / summary of product characteristics for an approved product.

7. References

1. World Health Organization, Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participant, 2011.
2. International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use Guidance for Good Clinical Practice (ICH GCP) E6(R2), 2016.

8. Annex

Annex 1: Serious Adverse Event Report
(EPHI-IRB AF 01-020/02.0)

Principal Investigator:……..

Study Title:……

Protocol No.: EPHI-IRB-☐☐☐-☐☐☐☐

Name of the study medicine/device……. ……. Sponsor/Host institution: …… …….	Report Date : …… ☐ initial ☐ follow-up Onset date:…… Date of first use: ……..

Study participant's initial/number:	Age:	☐ Male ☐ Female

Study participant's history:	Laboratory findings:
SAE:	Treatment: Outcome: ☐ resolved ☐ on-going

Seriousness: ☐ Death ☐ **LIFE THREATENING** ☐ Hospitalization –○ initial ○ prolong ☐ Disability / Incapacity ☐ Congenital Anomaly ☐ Other……	Relation to ○ Drug ○ Device ○ study ☐ Not related ☐ Possibly ☐ Probably ☐ Definitely related ☐ Unknown

Changes to the protocol recommended?	☐ No ☐ Yes , attach proposal
Changes to the informed consent form recommended?	☐ No ☐ Yes , attach proposal

Decision	☐ No Further Action Required
	☐ Request Information
	☐ Recommend Further Action

Reviewed by:……..	Date:……
Comment:……	Action:……

Annex 2: Unexpected Adverse Event Summary Report
EPHI-IRB AF 02-020/02.0

Principal Investigator:…….

Study Title:……... Protocol No.: EPHI-IRB-☐☐☐-☐☐☐☐

Name of the studied medicine/device……..…….. This report covers the period :

Sponsor:……... From……To…….

#	Description of Unexpected Adverse Events	Date of Event (D/M/Y)	Date start and end of Tx (D/M/Y)	F or M	Initial	Age (Y)	Serious Yes	Serious No	Related to Study Yes	Related to Study No	Concomitant medication	Intervention
							☐	☐	☐	☐		
							☐	☐	☐	☐		
							☐	☐	☐	☐		

							☐ ☐	☐ ☐		
							☐ ☐	☐ ☐		
							☐ ☐	☐ ☐		
							☐ ☐	☐ ☐		
							☐ ☐	☐ ☐		

Comment: ……

Reviewed by:…… Date (D/M/Y):……