F.No. CT/SAE-MISC-001/2014

Office of Drugs Controller General (India)

SAE Division

Subject: System of Pre-screening for submission of reports of SAEs to CDSCO

The Drugs & Cosmetics Rules have been amended vide GSR no 53 (E) dated 30-01-2013 inserting a Rule 122DAB, and a new Appendix-XII in Schedule "Y" along with other amendments. The amendments specifies the detail procedures for analysis of Serious Adverse Events (SAEs) including deaths occurring during clinical trial to arrive at the cause of death / injury to the subject, as the case may be, and to determine the quantum of compensation, if any to be paid by the sponsor or his representative whosoever have obtained permission from CDSCO in a time bound manner.

As per the provisions, each SAE including death is required to be examined and decision regarding causality of death and quantum of compensation, if any, is required to be taken by CDSCO in a time bound manner as per the procedure specified in Appendix XII of Schedule Y.

As per Appendix XII the Investigator shall report all serious and unexpected adverse events to the CDSCO, the Sponsor or his representative whosoever had obtained permission from the CDSCO for conduct of the clinical trial and the Ethics Committee, within twenty four hours of their occurrence.

The Sponsor or his representative, whosoever had obtained permission from the Licensing Authority for Conducting the Clinical Trial and the Investigator shall forward their reports on Serious Adverse Event, after due analysis to the Licensing Authority as Defined under rule 21(b), within ten calendar days of occurrence of the Serious Adverse Event.

The Ethics Committee shall forward its report on the Serious Adverse Event, after due analysis, along with its opinion regarding the financial compensation, if any, to be paid by the sponsor or his representative, whosoever had obtained permission from the Licensing Authority within twenty one calendar days of occurrence of the serious adverse event.

In case of serious adverse events of death, the reports shall be examined by an independent Expert Committee constituted by DCG(I) to determine if the cause of death is due to following reasons, which are considered as clinical trial related death and gives its recommendation to CDSCO. In case of clinical trial related death the committee shall also recommend the quantum of compensation to be paid by the sponsor or his representative, to CDSCO.

a) adverse effect of investigational product(s);
b) violation of the approved protocol, scientific misconduct or negligence by the Sponsor or his representative or the investigator;

c) failure of investigational product to provide intended therapeutic effect;
d) use of placebo in a placebo-controlled trial;
e) adverse effects due to concomitant medication excluding standard care, necessitated as part of approved protocol;
f) for injury to a child in–utero because of the participation of parent in clinical trial;
g) any clinical trial procedures involved in the study

CDSCO shall consider the recommendations of the Expert Committee and shall determine the cause of death and also the quantum of compensation in case of clinical trial related death within three months of receiving the report of SAE of death.

In cases of serious adverse event other than death, CDSCO shall determine the cause of injury, if any, due to any of the reasons mentioned above as in the case of death, which is considered as clinical trial related injury. However CDSCO has option to constitute an independent Expert Committee, wherever considered necessary, to examine such serious adverse event. In case of clinical trial related injury, CDSCO shall also determine the quantum of compensation within three months of receiving of the SAE

In case of clinical trial related injury or death, the Sponsor or his representative concerned shall pay the compensation as per the order of CDSCO within thirty days of the receipt of such order.

In order to streamline the submission of reports of SAEs, a system of pre-screening of reports of SAEs at the time of receiving these reports is being introduced in CDSCO.

The pre-screening system will be as under:
The preliminary scrutiny of the SAE reports will be done by CDSCO officer(s) based on laid down checklist which is attached herewith. During the preliminary examination, the CDSCO officer(s) will scrutinize the SAE reports to ensure that it contains all the required administrative as well as technical information in proper manner as per the checklist. If SAE reports are not submitted in accordance with the format and the checklist, it will not be accepted by CDSCO for further examination.

Once a report of SAE is accepted, the information in the report will be reviewed by CDSCO as per the specified procedures.

I. The sponsor or his representative conducting clinical trials in India are requested to prepare the SAE reports for submission to CDSCO as per appendix-XI of Schedule-Y of D&C Rules and the checklist enclosed.

II. The Ethics Committees are requested to forward the causality assessment / due analysis report of serious adverse event(s) within 21 days of occurrence of the SAE (SL No. 23 of the Checklist-Annexure A)

III. The SAE reports must be submitted with proper binding, indexing and page number. Without indexing of page number, no SAE report will be accepted.

IV. The reports of SAEs of deaths should be prepared and submitted in red cover.

V. The reports of SAE of injury other than deaths should be prepared and submitted in blue cover.

VI. The SAE report other than that mentioned at (a) & (b) above is to be prepared and submitted in white cover.

VII. Clear and unequivocal information should be provided in the SAE report.

VIII. Text and tables should be prepared using margins that allow the document to be printed clearly without losing any information and the left-hand margin should be sufficiently large so that information is not obscured by the method of binding. The documents printed on both sides of a page, can be submitted. However, one should take care that the information is not obscured when the page is placed in a binder.

IX. While submitting reply to a query, the applicant should always enclose with the reply, a copy of query letter issued by CDSCO.

X. All items mentioned in the checklist may not be applicable in all the case of SAE"s. The items not relevant to a particular SAE should be marked with "Not Applicable (NA)".

The checklist for submission of Serious Adverse Event Report (SAE) occurring in clinical trial is at **Annexure -A**:

Effective from 22 /04 /2014

CHECKLIST FOR SUBMISSION OF SERIOUS ADVERSE EVENT REPORT (SAE) OCCURRING IN CLINICAL TRIAL/BIO-EQUIVALENCE STUDY.

ANNEXURE-A

S.No.	Details		
1.	**Country (Name of the country should be specified)**		
2.	**SAE report of death or other than death, Please tick (✓)**	Death ☐	Other Than Death ☐
		Yes/No	**Page No.**
3.	**In case of Serious Adverse Event(SAE), please specify if there is any injury to the subject (Please specify Yes/No) in the box**		
4.	Protocol Title		
5.	Protocol Study No./ ID /Code		
6.	Copy of Clinical Trial permission/ BE-NOC obtained from CDSCO		
7.	CTRI Registration No. (Mandatory for Clinical Trial Permitted after 15/06/09)		
8.	Sponsor(Address with contact no and Email)		
9.	CRO (Address with contact no and Email)		
10.	Clinical Trial Site address and site number.		
11.	Initial / Follow-up (FU)		
12.	In case of follow-up: Date & Diary no of initial or recently submitted report information		
13.	**Patient/Subject Details**		
a.	Initials & other relevant identifier (Hospital/OPD record number etc.)		
b.	Gender		
c.	Age, Date of birth, Weight & Height		
14.	**Suspected Drug(s)/Medical Device**		
a.	Generic name of the Drug(s)/Device.		
b.	Indication(s) for which suspect/study drug was prescribed or tested.		
c.	Dosage form and strength / Dosage regimen		
d.	Route of administration.		
e.	Starting date and time of day.		
f.	Stopping date and time & duration of treatment		
g.	Baseline values of investigations prior to administration of Suspected Drug(s)/ Medical Device.		
15.	**Other Treatment(s) / Concomitant Drug History**		
	Provide the same information for concomitant drugs (including non-prescription/OTC Drugs) and non-drug therapies, as for the suspected drug(s).		
a.	Generic name of the Drug(s)/Device.		
b.	Indication(s) for which suspect/study drug was prescribed or tested.		
c.	Dosage form and strength / Dosage regimen		
d.	Route of administration.		
e.	Starting date and time of day.		
f.	Stopping date and time & duration of treatment		
16.	**Details of the events**		
a.	Full description of event (s) including body site and severity, as well as the criterion (or criteria) for regarding the report as serious. In addition to a description of the reported signs and symptoms, whenever possible, describe a specific diagnosis for the reaction.		
b.	Start date (and time) of onset of reaction.		
c.	Stop date (and time) or duration of reaction.		

d.	Dechallenge and rechallenge information.		
e.	Setting (e.g., hospital, out-patient clinic, home, nursing home).		
f.	Expectedness of SAE (Expected / Unexpected) as per IB		
17.	**Outcome**		
a.	Information on recovery and any sequelae; results of specific tests and/or treatment that may have been conducted.		
b.	For a fatal outcome, cause of death and a comment on its possible relationship to the suspected reaction; any post-mortem findings.		
c.	Other information: anything relevant to facilitate assessment of the case, such as medical history with date including allergy, drug or alcohol abuse; family history; findings from special investigations etc.		
18.	**Details about the Investigator**		
a.	Name		
b.	Address		
c.	Telephone/Mobile Number & Email		
d.	Profession (speciality)		
e.	Date of reporting the event to Licensing Authority:		
f.	Date of reporting the event to Ethics Committee overseeing the site:		
g.	Date of reporting the event to Sponsor/CRO		
h.	Signature of the Investigator		
19.	**Details about the Ethics Committee**		
a.	Name & Address		
b.	Name of Chairman & Address		
c.	Telephone/Mobile Number		
d.	Email		
20.	Adverse Event Term / Details of SAE		
21.	Causality Assessment by Investigator with reasoning for Relatedness/Un-relatedness along with supporting investigational documents. For SAE-Death the name(s) of the suspected drug(s) must be provided after Unblinding.		
22.	Causality Assessment by Sponsor/CRO with reasoning for Relatedness/Un-relatedness. For SAE-Death the name(s) of the suspected drug(s) must be provided after Unblinding.		
23.	Causality Assessment by Ethics Committee with reasoning for Relatedness/Un-relatedness. For SAE-Death the name(s) of the suspected drug(s) must be provided after Unblinding.		
24.	Details of compensation provided for injury or death. In case no compensation has been paid, reason for the same.		
25.	Duly filled SAE Form as per Appendix XI of Schedule Y		
26.	Laboratory investigations report /Discharge summary during the time of SAE.		
27.	Post-mortem report & Medical death certificate (if applicable)		
28.	Copy of Signed Informed Consent Form of the Subject/Patient along with English version. (To be forwarded in case of death)		
29.	Filled copy of CRF. (To be forwarded in case of Death)		
30.	Socioeconomic background of subject/patient viz. Qualification, Occupation, Monthly income.		
31.	Copy of latest amended version of Protocol approved by CDSCO.		
32.	Copy of Investigator's Brochure (In case of SAE-death)		

Note: SL.No. 23 (to be submitted by EC within 21 days of Occurrence of SAE)
SL.No. 28 (Hard Copy/Soft Copy)
SL. No. 29 (e-CRF/Hard Copy)
SL. No. 31 & 32 (Soft Copy to be submitted in case of SAE-death)