ADVERSE EVENT REPORTING FLOWCHART

CRASH-19

Adverse Event (AE)

"Any untoward medical occurrence affecting a trial participant during the course of a clinical trial".

Does the event fulfil any of the following seriousness criteria?

- *results in death*
- *is life threatening*
- *requires in-patient hospitalisation or prolongation of existing hospitalisation*
- *results in persistent or significant disability/incapacity*
- *other, medically important*

NO → **Adverse Event (AE)**

Event does **not** need reporting. Only Serious Adverse Reactions need to be reported for CRASH-19.

YES

CAUSALITY

Does the investigator suspect that the SAE is possibly **linked** to the trial drug?

NO → **Serious Adverse Event (SAE)**

Event does **not** need reporting. Only Serious Adverse Reactions need to be reported for CRASH-19.

YES

Serious Adverse Reaction (SAR)

- Report this to the CTU by entering into the CRASH-19 database within **24 hours**

YES

Is the SAR expected?

- CTU to assess against Reference Safety Information

NO

Suspected Unexpected Serious Adverse drug Reaction (SUSAR)

"An unexpected occurrence of a SAR; there need only be an index of suspicion that the event is a previously unreported reaction to a trial drug, or a previously reported but exaggerated or unexpectedly frequent adverse drug reaction."

If fatal or life threatening CTU must ensure:

- Report to:
  - Regulatory authorities of all countries where the trial is being conducted, and
  - the relevant ethics committees

  WITHIN 7 DAYS OF LEARNING OF THE SUSAR
- Follow-up information must be provided within a further eight days
- **If not fatal or life threatening** **CTU will report to the above bodies within 15 days of learning of the SUSAR**
- CTU also informs all investigators and LSHTM Quality Assurance Manager and presents the data for Data Monitoring Committee review

All SARs and SUSARs are reported through an annual report to the relevant Regulatory Authorities and Ethics Committees.

Report includes:

- list of SARs and SUSARs
- Data Monitoring Committee report

Reported annually on the anniversary of the first Regulatory agency approval.

The Electronic Investigator Site File (e-ISF) contains:

- Guidance on AE Reporting for the CRASH-19 trial (Section 6: Training Materials)
- Copies of blank SAR report forms (Section 7: Blank Forms & Logs)
- Completed SAR report forms should be filed, together with any CRFs for the participant in Section 9: Completed forms and Logs

CTU will coordinate the reporting to all relevant Ethics Committees, Regulatory Authorities and other investigators.