Procedures for Reporting Serious Adverse Events (SAEs)

This guidance sheet outlines the type of events that need reporting; in what timeframe these must be reported; and how to report them. For more information on safety and incident reporting, please refer to the BASE Protocol.

The safety reporting window for this trial for each participant will be from **randomisation until discharge from neonatal care or reaching 40 weeks' postmenstrual age** (whichever is sooner).

- Any member of staff can report a safety event or incident
- The causality assessment of the safety event must be undertaken by a delegated medically qualified doctor.

Definitions

ADVERSE EVENT (AE) is any untoward medical occurrence in a participant, which does not necessarily have a causal relationship with the trial intervention.

ADVERSE REACTION (AR) is an untoward and unintended response in a participant to an investigational medicinal product that is related to any dose administered to that participant.

SERIOUS ADVERSE EVENT (SAE) is any untoward medical occurrence that:

- Results in death
- Is life-threatening
- Requires inpatient hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity
- Consists of a congenital anomaly or birth defect
- Other important medical events

Other 'important medical events' may also be considered as a SAE when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

The term 'life-threatening' refers to an event in which 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.

SERIOUS ADVERSE REACTION (SAR) is an adverse event that is both serious and, in the opinion of the reporting Investigator, believed with reasonable probability to be due to one of the trial treatments, based on the information provided.

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SUSPECTED UNEXPECTED SERIOUS ADVERSE EVENT (SUSAR) is a serious adverse reaction, the nature and severity of which is not consistent with the information about the medicinal product in question set out:

- In the case of a product with a marketing authorisation, in the Summary of Product Characteristics (SmPC) for that product
- In the case of any other investigational medicinal product, in the investigator's brochure (IB) relating to the trial question.

Reporting of Adverse Events

In this trial population we anticipate day-to-day fluctuations of pre-existing conditions. As a result, many AEs are foreseeable due to the nature of the participant population and their routine care/treatment. Consequently, only those AEs identified as serious will be reported for the trial.

Reporting procedures for Serious Adverse Events

As the use of sodium bicarbonate represents standard clinical practice in neonatal units in the UK, **only SAEs deemed causally related to the IMP** (as assessed by delegated medically trained doctor) **will be reported expeditiously as an SAE.**

SAEs that are deemed causally related to the IMP must be reported as soon as possible and within 24-hours of the site becoming aware of the event. Anyone can report an SAE. **No personal identifiers should be included in the report.** There are three ways of reporting the SAE:

1) Complete online:

Complete the BASE SAE Form online on OpenClinica

2) Complete paper form:

Copies of the paper BASE SAE Form can be found in the Site Document Box. Once complete, inform the BASE study team by using the TADA document upload tool or via email.

3) Report via phone:

Call the BASE study team using the details at the bottom of the guidance sheet during office hours in order to report the SAE verbally. Once you have made the team aware of the event, you must still complete a SAE form as detailed above.

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A copy of the SAE form along with any follow up information should be filed in the infant's medical notes and also in the Electronic Investigator Site File (e-ISF).

Completing Causality Assessment

The relationship of each adverse event to the trial medication must be determined by a medically trained doctor according to the following definitions:

- **Unrelated:** Where an event is not considered to be related to the IMP
- **Possibly:** Although a relationship to the IMP cannot be completely ruled out, the nature of the event, the underlying disease, concomitant medication or temporal relationship make other explanations possible
- **Probably:** The temporal relationship and absence of a more likely explanation suggest the event could be related to the IMP
- **Definitely:** The known effects of the IMP, its therapeutic class or based on challenge testing suggest that the IMP is the most likely cause.

All SAEs labelled possibly, probably, or definitely will be considered as related to the IMP.

Do not delay SAE reporting whilst awaiting a causality assessment.

Expectedness Assessment

For SAEs that require reporting, expectedness will be determined by NPEU CTU.

Procedures for Recording and Reporting Incidents

Incident Reporting

Any deviations from the protocol, trial procedures, Good Clinical Practice (GCP) or regulatory requirements must be reported as incidents to the BASE study team, using the BASE Incident and Deviation Reporting Form. Any member of the team can report incidents.

Incidents should be reported as soon as practical and can be reported by either:

1. **Completing the Incident & Deviation Reporting Form** (available as editable PDFs and as hard copies in BASE Documents Box).

   Paper version: Please fill in all documentation clearly and legibly. If you make a mistake, please cross through this with a single line and put your initials and date next to it. Once completed, scan and send to BASE study team by email (base@npeu.ox.ac.uk) or via the study upload tool

   PDF version: Enter data onto editable PDF, save, and email to BASE study team.

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If applicable, for the purpose of anonymity, all paperwork should have the Study number only and no further identifiable information.

OR

2. **Verbally via phone.** However, this must be followed up in writing.

If you are unable to complete the 'resolution' section of the form in the first instance, send the partially completed form and re-send the form with 'resolutions' at a later date.

Copies of all incident reports should be kept in the ISF.

Serious Breaches

Incidents and protocol deviations may be defined as a serious breach if there is a breach of GCP or trial protocol which is likely to affect to a significant degree either:

- The safety, physical or mental integrity of the subjects of the trial.
- The scientific value of the trial.

The BASE study team will conduct an assessment of all reported incidents to determine if they could be classified as a serious breach.

Emergency Queries Contact Details

During office hours

Any queries whether urgent or not should be directed to the BASE study team during office hours (i.e. between 09:00 – 17:00, Monday to Friday) on 01865 289716
** **Important** ** Please DO NOT send patient identifiable information to base@npeu.ox.ac.uk instead please use Document Upload tool.

Out-of-Hours

In the case of urgent out-of-hours queries, please phone **0800 1385 451**.
Please see **Guidance sheet: Emergency Queries** for further information.

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