8. SAE & Incident Reporting

Procedures for Recording Adverse Events (AEs) and Reporting Serious Adverse Events (SAEs)

This guidance sheet outlines the different types 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 **neoGASTRIC Study Protocol.**

Key notes and definitions

Due to the nature of the patient population, neonates in intensive care, a high incidence of adverse events is foreseeable during their routine care and treatment. Consequently, **only those adverse events identified as serious will be recorded for the trial.**

The **safety reporting window** for this trial will be from the time the infant is randomised until the end of trial follow-up (discharge home or 44^{+0} gestational $weeks^{+days}$, whichever is sooner).

Any staff member can report a safety event or incident and events can be defined as:

- Adverse Events or Reactions (AE/AR)
- Serious Adverse Events or Reactions (SAE/SAR)

Definitions

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

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
- is a congenital anomaly or birth defect (not relevant in this trial)

Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.

NOTE: The term "life-threatening" in the definition of "serious" 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.

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Events exempt from immediate reporting

Foreseeable SAEs that do not require expedited reporting via an SAE Form:

Outcomes

The following events are expected in the population, and information will be collected by recruiting sites during the intervention period as outcomes, therefore do not require reporting as SAEs. Data pertaining to these events will be reviewed by the DMC at a frequency to be determined by the DMC (at least annually).

- Death (unless cause not anticipated in this population)
- Necrotising enterocolitis or gastrointestinal perforation
- Bronchopulmonary dysplasia or chronic lung disease
- Late-onset infection
- Intraventricular haemorrhage (grade 3 or 4)

Known complication(s) of prematurity

Any event that is deemed by the investigator to be a known complication of prematurity at that gestational age should not be reported as an SAE but should be recorded in the infant's medical notes, as per usual practice. They do not require reporting by trial centres as SAEs unless considered that they may be causally related to the allocated pathway of care, in which case they must be reported as detailed in Section 8.2.4

All other serious adverse events are classed as unforeseeable SAEs and must be reported.

1. Causality assessment

Do not delay SAE reporting whilst awaiting a causality assessment.

A medically qualified individual, according to the following definitions, must determine the relationship of each adverse event to the allocated pathway of care:

Not related – where an event is not considered to be related to the trial allocation pathway.

Possibly – although a relationship to the trial allocation pathway cannot be completely ruled out, the nature of the event, the underlying condition, concomitant medication or temporal relationship make other explanations possible.

Probably – the temporal relationship and absence of a more likely explanation suggest event could be related to the trial allocation pathway.

Definitely – the trial allocation pathway is the most likely cause.

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All SAEs labelled possibly, probably or definitely **will be** considered as related to the allocated pathway of care.

If an appropriate delegated individual is not available to make the causality assessment, send in the SAE Reporting Form without this information and re-send the form as soon as this assessment has been made.

A Physician who is not a member of the study team may offer an opinion as to whether the event was related to the investigational intervention(s) and this opinion should be documented in the infant's medical records.

2. Reporting Serious Adverse Events

All unforeseeable SAEs, and foreseeable SAEs deemed causally related to the allocated pathway of care must be reported on the **SAE Report Form** to the relevant coordinating centre (UK or AU) as soon as possible after the site becomes aware of the event being defined as serious.

Use one of the following SAE reporting methods:

1. Staff with access to the study electronic database on OpenClinica **should complete the SAE form online**. For sign off, please add signature directly onto OpenClinica. An automatic email notification to the coordinating centre staff will be triggered for SAEs reported electronically.

2. The e-ISF contains **editable PDF** versions of the forms. Once the PDF has been completed and saved, it must be printed and signed (a signature cannot be added through the PDF). A scan of the signed copy should be sent **via the TADA document upload tool or via email to the relevant coordinating centre**.

3. **Paper forms**, with instructions, are provided in the neoGASTRIC Document Box. The completed SAE form **must be scanned and emailed to the relevant coordinating centre** (NPEU CTU for UK SAEs neogastric@npeu.ox.ac.uk.

4. Where the above routes are not possible, then the SAE may be reported **by telephone** to the local coordinating centre and the SAE form will be completed. Please see emergency queries and key contacts guidance sheets.

Please file the completed SAE Reporting Form in your eISF.

(If printing from OpenClinica, click on the SAE form, then click through every SAE page before printing)

Ensure **ALL** details of the SAE are documented in the infant's medical records (if applicable), including the assessment of causality, which must be documented in the medical records.

Follow-up SAE information should be reported by filling out a new SAE form and stating that it is a follow-up report in the relevant question.

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Procedure for Recording and Reporting Incidents

Incident Reporting

Any deviations from the neoGASTRIC Study Protocol, study specific procedures, Good Clinical Practice (GCP) or regulatory requirements must be reported as incidents to the neoGASTRIC study team, using the **neoGASTRIC Incident and Deviation Reporting Form**. Any member of the team included on the neoGASTRIC Site Delegation Log can report incidents.

> Examples of incidents in this context might be a study activity performed by an individual not listed on the delegation log or who is listed on the delegation log but not delegated for that specific activity; forms not amended in accordance with GCP; consent forms not signed and dated correctly; and use of a superseded form.

Sites can complete the form either as an editable electronic (PDF) form (provided as part of the neoGASTRIC electronic Investigator Site File (e-ISF) or paper forms (provided in the neoGASTRIC Document Box) can be completed and scanned copies sent to neogastric@npeu.ox.ac.uk

Please complete all documentation clearly and legibly in **black ink.** If an error is made whilst completing the form, cross through the error with a single line with the initials of the person completing the form and date next to it.

PLEASE DO NOT SEND PATIENT IDENTIFIABLE INFORMATION.

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 completed **neoGASTRIC Incident & Deviation Reporting Forms (Incident Form)** relevant to the site should be filed in the e-ISF.

Serious Breaches

Incidents and protocol deviations will be defined as a serious breach if there is a breach of GCP or study 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 neoGASTRIC study team will assess all reported incidents to determine if they should be classified as a serious breach.

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