GUIDANCE SHEET 6: Safety & Incident Reporting

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 NeoCLEAR Protocol.

Safety Reporting

Safety events are defined as Adverse Events (AE) or Serious Adverse Events (SAE). For NeoCLEAR, only SAEs require reporting and must be reported from randomisation until discharge from hospital.

Adverse Event (AE): An adverse event is any untoward medical occurrence in a participant, which does not necessarily have a causal relationship with the trial intervention.
Due to the high incidence of adverse events routinely expected in the study population, only those adverse events identified as **serious** will be reported for NeoCLEAR.

Serious Adverse Event (SAE): A serious adverse event is any untoward medical occurrence which:

- Results in death
- Is life-threatening
- Requires participant hospitalisation or prolongation of existing hospitalisation
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Is an important medical event

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. Medical and scientific judgement should be exercised in deciding whether an adverse event is serious.

The term ‘severe’ is often used to describe the intensity (severity) of a specific event; the event itself, however, may be of relatively minor medical significance. This is not the same

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as 'serious', which is based on participant/event outcome or action criteria usually associated with events that pose a threat to a participant's life or functioning.

Reportable Serious Adverse Events

The following events are known, but rare, complications of LP. If they occur before discharge home following a NeoCLEAR LP, they must be **reported as SAEs**:

- Iatrogenic meningitis
- Iatrogenic haemorrhage: spinal haematoma (symptomatic), intraventricular, intracerebral and subarachnoid haemorrhage
- Cerebral herniation
- Nerve damage

Expected SAEs

The following are serious events which could be expected to occur in this population of infants during the course of the trial, or form part of outcome data. They do not need to be reported as SAEs unless they have been thought to be causally related to the lumbar puncture:

- Anaemia
- Clinically significant intracranial abnormality on cranial ultrasound scan – intracranial haemorrhage or white matter injury
- Chronic lung disease / Broncho pulmonary dysplasia
- Coagulopathy requiring treatment
- Death (unless related to LP technique)
- Difficulty establishing enteral feeding
- Failed LP resulting in prolonged hospitalisation
- Hyperbilirubinemia (jaundice)
- Hypoglycaemia
- Hypotension
- Hypoxic ischaemic encephalopathy
- Low sodium level/hyponatremia
- Non-iatrogenic meningitis
- Necrotising enterocolitis

- Patent ductus arteriosus
- Pneumothorax or air leaks
- Pneumonia
- Pulmonary haemorrhage
- Pulmonary hypertension requiring treatment
- Respiratory failure
- Retinopathy of prematurity
- Seizures
- Sepsis / infection
- Thrombocytopenia

If there is uncertainty regarding whether an event is related to the procedure and/or requires reporting, please discuss with the infant's Consultant, Principal Investigator or Research Nurse. If uncertainty remains, please report the event as detailed below.

Unforeseeable Serious Adverse Events

An unforeseeable SAE is any event that meets the definition of a SAE and is not detailed in the list above as expected. All unforeseeable SAEs that occur after consent until discharge home must be reported, as soon as study staff become aware of the event (as detailed below).

Reporting Serious Adverse Events

SAEs must be reported as soon as possible after becoming aware of the event. Anyone can report an SAE.

There are three ways of reporting SAEs:

1. Electronic form on OpenClinica
    - Complete form and inform NPEU Clinical Trials Unit (CTU) by:
        - Email to neoclear@npeu.ox.ac.uk (use study ID, do not send patient identifiable information) OR
        - **Print and fax** to the NeoCLEAR Coordinating Centre on **01865 289740** OR
        - Call the NeoCLEAR Coordinating Centre on **01865 289278** (within office hours)

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2. Complete Paper SAE form located in Site Document Box and:
   - Email from an nhs.net account to orh-tr.NeoCLEAR@nhs.net OR
   - Fax to the NeoCLEAR Coordinating Centre on **01865 289740**.

3. By telephone direct to NeoCLEAR Coordinating Centre on **01865 289278** (within office hours) or **0800 138 5451** (out of hours).

Do not delay SAE reporting whilst awaiting a causality assessment. The causality assessment must be completed by a medically qualified practitioner with delegated duty. The SAE form may be faxed or emailed without the causality assessment; an updated form must be sent when the causality assessment is complete.

If faxed or emailed, the person reporting the SAE must ensure the NeoCLEAR Coordinating Centre is aware of the SAE and check that they have received the form by telephoning the NeoCLEAR Coordinating Centre on 01865 289278 within office hours. The NeoCLEAR Coordinating Centre will confirm receipt of the SAE via telephone or email on the next working day.

A copy of the SAE form must be filed in the Investigator Site File.

Updates or corrections to the initial SAE form should be reported on a new SAE form. This should then be forwarded to the NeoCLEAR Coordinating Centre by fax or email as soon as possible.

Incident Reporting

Any deviations from the protocol, trial procedures, Good Clinical Practice or regulatory requirements must be reported as incidents to the NeoCLEAR Coordinating Centre, using the Incident Form.

Examples of incidents in this context might be a trial activity performed by a practitioner not listed on the delegation log; forms not amended in accordance with GCP; and use of a superseded form.

Incidents should be reported to the NeoCLEAR Coordinating Centre as soon as practical and can be reported by either:

- Completing the NeoCLEAR Incident Form (kept in the NeoCLEAR Document Box). Written forms must be faxed to the NeoCLEAR Coordinating Centre on **01865 289740**, or emailed to neoclear@npeu.ox.ac.uk as soon as practical (using Study ID only)
    - Ensure the NeoCLEAR Coordinating Centre confirms receipt of the incident.
    - Send the original Incident Form to the NeoCLEAR Coordinating Centre (using the Freepost Envelopes provided) and retain a copy in the Investigator Site File.
- Calling the NeoCLEAR Coordinating Centre on **01865 289278**, where a member of the trial team will record the incident using the Incident Form.

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.

Serious Breaches

The NeoCLEAR Coordinating Centre will carry out an assessment of all incident reports, some of which will be classified as serious breaches. Incidents will be defined as a Serious Breach if there is a breach of Good Clinical Practice (GCP) or the trial protocol, which is likely to significantly affect either:

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