Local data monitoring plan, SafeBoosC-IIIv trial

Version	Author(s)	Date	Changes	Approved by
1.0	Johanne Juul Petersen Mathias Lühr Hansen Caroline Kamp	9/12-24	Initial version	Steering Committee

Initiation visit

The initiation visit must take place at each site before inclusion of the first trial participant.

Check of Investigator Site File

The Investigator Site File (ISF) should be checked to make sure it includes the following documents:

- Sponsor contact list
- Participant inclusion list
- Parental information sheets
- Consent forms (empty forms for hand-out to parents and signed consent forms for included participants)
- SOP: Screening and randomisation
- Approved local blinding procedure for primary outcome assessment ("SOP: Blinding of primary outcome assessment" or alternative method)
- SOP: NIRS device and sensor handling
- SOP: Treatment guideline
- Delegation log
- Primary outcome log
- Newest protocol version including amendments
- List of data needed for eCRF data entry
- Approval from Research Ethics Committee
- Any other approvals needed according to local regulations/laws
- Copy of local data monitoring plan
- Copies of local monitoring reports
- Signed Clinical Trial Agreement
- Any other signed contracts between investigator and sponsor

The principal investigators must present the ISF to the local monitor.

Check of delegation log

The local monitor must register 1) the total number of clinical staff members on the delegation log, and 2), the number of clinical staff members that have signed for being informed about the SafeBoosC-IIIv trial, their tasks as written in the delegation log, and that they have received sufficient training to conduct their trial related tasks (e.g. individual web-based training, group training, read-through of education material and cases). The type of education must be documented on the delegation log.

We trust that all staff members involved in the care of infants in the trial, are clinically qualified and that the individual hospitals have procedures to ensure this. The local monitor therefore does not have to check for curricula vitae on staff members.

Check of blinding procedure for primary outcome assessment

In order to ensure proper blinding of assessment and data entry of hospital-free days, the principal investigator must establish a procedure for this. Suggested methods for blinded assessment are provided in the SOP: Blinding of the primary outcome assessment. The investigator may choose a different method described. However, this must be approved by the trial manager.

In order to ensure that these procedures are realistic, the principal investigator must demonstrate to the local monitor how the blinded assessment will be done, and the local monitor person must confirm its feasibility.

Initiation visit report

The signed initiation visit report must be stored in the ISF after the visit and a copy must be sent to the Sponsor.

A template for this report can be found on http://www.safeboosc.eu/ under ‘Data monitoring’.

Monitoring visits

Frequency of monitoring visits

The first monitoring visit should take place as soon as possible after the first participant has reached 90-day follow-up, to ensure that trial procedures were successfully implemented. Further visits should take place after every fifth participant has reached 90-days follow-up or every third month, whichever occurs first, and also after the last participant has reached 90-day follow-up.

Only participants that have reached 90-days follow up should be included in the monitoring visits.

Existence of clinical records and signed consent

For all participants enrolled in the trial, the following must be verified:

- Existence of the participant's clinical records and documentation of trial inclusion in the participant's clinical records (unless it is not allowed by local regulations).
- Existence of signed and dated consent form (single or both parents as required by local regulations) or if 'opt-out' method is used, documentation in clinical records of trial participation, that parents have been informed and their response. If prior consent is used, the date on the signed consent form should be before the date of enrolment.

The principal investigator must show the local monitor where to find this information and give access to the eCRF.

Source verification

The following data in the eCRF must be verified against the clinical records and/or the primary outcome log:

- Group allocation (experimental or control group) (clinical records: as stated in the 'SOP: screening and randomisation', a note on group allocation should be available in the clinical records from the day of randomisation)
- GA > 28 weeks gestational age at birth (clinical records)
- Whether the participant is dead or alive at 90 days after randomisation (clinical records or primary outcome log, details below)
- Number of hospital-free days within 90 days of randomisation (clinical records and primary outcome log, details below)

In the primary outcome log, data on hospital-free days and survival status are collected through review of clinical records and contact to parents. Information from clinical records will be prioritised for source verification when available, while information from the parents will be used as supporting information, e.g., readmissions at other hospitals, as this information might not be registered in the clinical records. Details on source verification for survival status and hospital-free days follows below.

Source verification on survival status

If clinical records include up-to-date information on survival status (e.g., in countries where clinical records are linked directly to national registries and automatically updated), the local monitor person must verify survival status in the eCRF against mortality status in the clinical records.

If clinical records do not include up-to-date information about survival status, the local monitor person must verify survival status in the eCRF against survival status in the primary outcome log.

It is the principal investigators responsibility to determine whether clinical records include up-to-date information on survival status or not and inform the local monitor person accordingly.

Source verification on hospital-free days

Data on hospital-free days within 90 days from randomisation are split into three data entry points:

- 'Hospital-free days according to clinical records' (F07 data entry point in eCRF): Must be verified against the clinical records.
- 'Information from parents on additional hospitalisation not reported in clinical records' (F08 data entry point in eCRF): Must be verified against the primary outcome log (column 6).
- 'Total number of hospital-free days' (F09 data entry point in eCRF): Must be verified against the primary outcome log (column 7)

Check of delegation log

At each monitoring visit, the local monitor must check and document: 1) the total number of clinical staff members on the delegation log, and 2), the number of clinical staff members that have signed the delegation log, documenting that they have received information on a) the SafeBoosC-IIIv trial, b) trial tasks related to their clinical position, and c) that they have received sufficient training to conduct these tasks. The type of training must be documented on the delegation log.

Check of participant inclusion list

During monitoring visits, the local monitor must check if 1) all patients on the participant inclusion list are registered with randomisation date, national identification number, and participant ID and 2) whether the participant IDs on the participant inclusion list and eCRF are identical.

Issues for follow-up

It is important that the local monitor register issues for follow-up at each monitoring visit, i.e. problems that need to be solved until the next monitoring visit, and follow-up on whether this has been done at the next monitoring visit. This process must be documented in the local monitoring reports.

Monitoring reports

Monitoring reports must be made after each visit, signed by the local monitor and principal investigator and filed in the Investigator Site File. A copy must be sent to the Sponsor.

Templates for all reports can be found on http://www.safeboosc.eu/ under ‘Data monitoring’.