Monitoring plan, SafeBoosC Phase III Trial

Version	Author(s)	Date	Changes	Approved by
1.0	Mathias Lühr Hansen	04/12-18	Initial version	Gorm Greisen
2.0	Mathias Lühr Hansen	16/01-19	• Removal of document in TMF • Editing in 'check of delegation and training log' • Removal of source data verification for severe brain injury • Addition of 'issues for follow-up' • Addition of 'check of patient inclusion list'	Gorm Greisen
2.1	Mathias Lühr Hansen	28/07-19	• Addition that first monitoring visit should take place after follow-up data have been entered for the first participant	Gorm Greisen
2.2	Mathias Lühr Hansen	11/12-19	• Removal of "login information for eCRF" since this is personal information	Gorm Greisen
2.3	Mathias Lühr Hansen	28/1-20	• Elaboration of Mortality definition	Gorm Greisen

Initiation visit

The initiation visit must take place at each site before inclusion of trial participants.

Check of Trial Master File

The Trial Master File (TMF) should be checked to make sure it includes the following documents:

- Patient inclusion list
- Parental information sheets
- Consent forms
- Local procedure description for enrollment and randomisation
- Local procedure description for blinding of cranial ultrasound readings and data entry
- SOP: NIRS device and sensor handling
- SOP: treatment guideline
- Copy of delegation and training log
- Newest protocol version including amendments
- List of data needed and where to find them
- Approval from Research Ethics Committee

- Any other approvals needed according to local regulations/laws
- Copy of GCP monitoring plan
- Copies of GCP monitoring reports.
- Any contracts between investigator and sponsor

The principal investigators must present the TMF to the GCP person.

Check of delegation and training log

The GCP person must register 1) the total number of clinical staff members on the delegation and training log, and 2), the number of clinical staff members that have signed for being informed about the SafeBoosC III trial, their tasks as written in the delegation and training log, and the existence of the web-based training and certification program.

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 GCP person therefore does not have to check for curricula vitae on staff members.

Check of blinding procedure in the diagnostics of cranial ultrasound readings and data entry

In order to ensure proper blinding of cranial ultrasound readings and data entry, the PI must have established a procedure for this. A written description of this procedure has been sent to the sponsor, who must approve this.

In order to ensure that these procedures are realistic, the PI must demonstrate to the GCP monitor how this will be done practically.

Initiation visit report

A copy of the signed initiation visit report must be stored in the TMF after the visit and the original should be sent to the Sponsor.

A template for this report can be found on www.safeboosc.eu under “GCP”.

Monitoring visits during the trial

The first visit should take place as soon as possible after follow-up data for the first enrolled participant have been entered, in order to ensure that trial procedures were successfully implemented. The following visits should be approximately after every fifth patient or every third month, and also after the last participant.

Existence of clinical file/records and signed consent

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

- Existence of the participant's clinical file and documentation of trial inclusion in the participant's clinical file (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 file of trial participation, that parents have been informed and their response. If prior consent is used, the date should not be after the date of enrollment.

The PI must show the GCP person where to find this information and give access to the eCFR

Source verification

The following data in the eCRF must be verified against the clinical file

- Group allocation (experimental or control group)
- GA < 28 weeks gestational age at birth
- Whether the participant is dead or alive at 36+0 weeks postmenstrual age*

*Please recall that the babies should only be registered as "dead" if the event occurred before 36+0 weeks PMA. If death occurs later than that, babies should be registered as "alive" in the eCRF.

Check of delegation and training log

At each monitoring visit, the GCP person must check and document 1) the total number of clinical staff members on the delegation and training log, and 2), the number of clinical staff members that have signed the delegation and training log, documenting that they have been informed about the SafeBoosC III trial, their tasks as written in the delegation and training log, and the existence of the web-based training and certification program..

Check of patient inclusion list

During monitoring visits, the GCP person must check if 1) all patients on the patient inclusion list are registered both with a study-ID and personal identifiers and 2) whether the study ID's on the patient inclusion list match the study ID's in the eCRF.

Issues for follow-up

It is important that the GCP person 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 GCP monitoring reports.

Monitoring reports

Monitoring reports must be made after each visit, signed by GCP-monitor and principal investigator and sent to the Sponsor Investigator, and a copy filed in the trial master file.