SOP: secondary studies and subsequent publications

Version	Author(s)	Date	Changes	Approved by
1.0	Mathias Lühr Hansen	06.09.21	Initial version	Trial Steering Committee

1.0 Approval of secondary studies and publication plan

All principal investigators are allowed to plan and conduct secondary studies and subsequent publications based on SafeBoosC-III trial data. However, the study must be approved by the steering committee 'up-front'.

If a single or a group of principal investigators or members of the steering committee intend to do so, a description of the study must be sent to mathias.luehr.hansen@regionh.dk before 17th of March 2022.

The description of the study shall, as a minimum, include

1) A specific, well-defined quantified hypothesis
2) A power calculation (see openepi.com for an online power calculation tool)

The investigator(s) shall then present the study at an online meeting on secondary publications, held on the 24th of March 2022 at 20:00 CET.

After the online meeting, the steering committee will discuss the suggested studies and develop and decide on a 'secondary study and publication plan'.

The secondary study publication plan must, for each study, include the following information:

1) Title
2) Hypothesis
3) Expected data of registration of the study protocol on clinicaltrials.gov
4) Expected date of manuscript submission
5) First author (investigator responsible for the study and publication)
6) Additional authors

2.0 Authorship and collaborative investigators

Authorship and collaborative investigators on secondary publications, shall be determined as below:

1) If the principal investigators only use data from participants within their own NICUs, they are not obliged to invite other principal investigators to collaborate/co-author the publications and can do as they decide.
2) If the principal investigators use data from other NICUs, principal investigators from such NICUs shall be invited to participate as non-author collaborators or co-authors.

The non-author collaborators will not participate in the working process of the secondary study nor in writing the manuscript, but will be mentioned by name in the publication as part of the "SafeBoosC-III investigator group" and traceable on PubMed. Thus, these investigators will be recognised for contributing with data.

The name of co-authors will appear in the byline. However, adherent to the Vancouver criteria, a co-authorship requires significant contribution and active involvement in all aspects of the secondary study.

3.0 Data management and publication

If a copy of a larger dataset is required for the analysis for a secondary study as approved by the steering committee, data will be anonymized (i.e. trial study numbers are removed) before the transfer from Copenhagen to the responsible investigator. To reduce the risk of re-identification of children, NICU identification numbers are also removed, gestational age and birth weight is recoded into binary variables, and twin status is removed. This is necessary to honour parental consent and the trial protocol.

If analysis can be done without transfer of data, the original dataset can be used.

Publication
Manuscripts based on secondary studies should not be submitted for publication before the SafeBoosC-III trial's primary outcome results are published.

4.0 Data points available for secondary studies

On the next couple of pages you will find screen dumps of all data entry modules in the eCRF, which provides an overview of the available data points.

Randomisation

R01 Birth date (dd-mm-yyyy)

R02 Birth time (hh:mm) [info]

R02a Singleton or multiple birth? ○ Singleton ○ Multiple birth

R02b Number of babies to include in trial ○ 1 ○ 2 ○ 3 ○ 4 [info]

Inclusion criteria

R03 Neonate born more than 12 weeks preterm (GA up to 27+6) ○ Yes ○ No [info]

R04 Which consent method has been used

- Please select...
- Prior informed consent
- Deferred consent
- Opt-out
- None

Exclusion criteria

R05 Decision not to conduct full life support ○ Yes ○ No

R06 Not possible to place cerebral NIRS oximeter within six hours of birth ○ Yes ○ No

Stratification and allocation

Patient is eligible for inclusion.
Fill in Gestational age at randomisation
and click 'Perform randomisation' button.

R07 Gestational age at randomisation

○ Less than 26 weeks
○ 26 weeks or more

R08 Site

Perform randomisation

End of monitoring (72 hours of age)

E01 Gestational age _____ (weeks+days) [info]

E02 Birth weight _____ (grams)

E03 Apgar score after **one minute** ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 ○ N/A

E04 Apgar score after **five minutes** ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 ○ N/A

E05 Sex ○ Male ○ Female

NIRS monitoring (experimental group)

E06 Age in full hours when cerebral oximetry was started _____ (hours)

E07 Did cerebral oximetry monitoring stop prematurely? ○ Yes ○ No [info]

E07a What caused premature monitoring stop? _____

E08 Did clinical staff change the medical management due to cerebral hypoxia? ○ Yes ○ No

E09 Did the baby receive cardiovascular support at any time during the first 72 hours? ○ Yes ○ No

E10 Which NIRS device did you use to monitor the baby?

- ○ INVOS
- ○ NIRO
- ○ Fore-Sight
- ○ Sensmart
- ○ O3 / Masimo
- ○ Egos
- ○ Oxyprem
- ○ Other

E10a Please write the name of the NIRS device _____

NIRS monitoring (control group)

E11 Had the baby cerebral NIRS monitoring despite being in the control group? ○ Yes ○ No

E11a Was information on cerebral oxygenation available for clinical staff? ○ Yes ○ No

E11b Did the baby receive cardiovascular support at any time during the first 72 hours? ○ Yes ○ No

Parental withdrawal

E12 Did the parents withdraw consent? ○ Yes ○ No

E12a What reason did the parents give? _____

E12b Did the parents withdraw permission to use data from the baby's future clinical course? ○ Yes ○ No

Deferred consent

E12D Did the parents decline the baby's continuation in the trial? ○ Yes ○ No

E12Da What reason did the parents give? _____

E12Db Did the parents decline permission to use data from the baby's future clinical course? ○ Yes ○ No

E12Dc Did the parents decline permission to use data up until time of exclusion? ○ Yes ○ No

Treatment

E13 Did the baby receive surfactant therapy? ○ Yes ○ No

Severe Adverse Reactions

(1) Date of severe adverse reaction (SAR)	(2) SAR specification	(2a) Specification of mismanagement	(3) Comment	
	Severe skin damage = 0			X
	Critical displacement of endotracheal tube threatening the life of the baby = 1			X
	Critical displacement of endovascular line threatening the life of the baby = 2			X
	Mismanagement while trying to improve respiratory status = 3			X
	Mismanagement while trying to improve cardiovascular status = 4			X
	Clinical mismanagement while trying to improve oxygen transport = 5			X

Add

Follow-up form
(36 weeks PMA or discharge to home)

F01 Follow-up date

F02 Did the baby suffer from any major congenital anomaly? ○ Yes ○ No [info]

F03 Did the baby receive mechanical ventilation? ○ Yes ○ No

F03a How many days did the baby receive mechanical ventilation in total during admission? (days)

F04 Did the baby receive treatment for patent ductus arteriosus (medical or surgical)? ○ Yes ○ No

F05 What was the last registered weight of the baby before follow-up? (grams)

F06 Date of last weighing

Cranial ultrasound

F07 When has cranial ultrasound been performed? [info]

- ○ Early cUS
- ○ Late cUS
- ○ Both early and late cUS
- ○ The baby was never scanned

Bronchopulmonary dysplasia

F08 Did the baby require any respiratory support and/or supplementary oxygen at 36 weeks postmenstrual age or discharge to home? ○ Yes ○ No [info]

Necrotising enterocolitis (NEC)

F09 Was necrotising enterocolitis Bells stage 2 or 3 diagnosed before 36 weeks postmenstrual age? ○ Yes ○ No [info]

Retinopathy of prematurity (ROP)

F10 Was retinopathy of prematurity grade 3 or more diagnosed before 36 weeks postmenstrual age? ○ Yes ○ No

Sepsis

F11 Did the baby receive antibiotics for 5 consecutive days or more before 36 weeks postmenstrual age (prophylactic use excluded)? ○ Yes ○ No [info]

Death

F12 Did the baby die before discharge or 36 weeks? ○ Yes ○ No

F12a Cause of death [info]

- ○ Congenital anomaly
- ○ Respiratory distress syndrome
- ○ Bronchopulmonal dysplasia
- ○ Infection
- ○ NEC
- ○ CNS injury
- ○ Immaturity
- ○ Other
- ○ Unknown

F12b Please specify cause of death

Blinded follow-up form
(36 weeks PMA or discharge to home)

BF01	Did the infant suffer from Intraventricular haemorrhage grade 3 or 4 up until 36 weeks postmenstrual age, death or discharge to home?	○ Yes ○ No [info]
BF02	Did the infant suffer from cystic periventricular leukomalacia up until 36 weeks postmenstrual age, death or discharge to home?	○ Yes ○ No
BF03	Did the infant suffer from post-haemorrhagic ventricular dilatation up until 36 weeks postmenstrual age, death or discharge to home?	○ Yes ○ No
BF04	Did the infant suffer from cerebellar haemorrhage up until 36 weeks postmenstrual age or discharge to home?	○ Yes ○ No
BF05	Did the infant suffer from cerebral atrophy up until 36 weeks postmenstrual age or discharge to home?	○ Yes ○ No
BF06	The baby was never scanned	☐ The baby was never scanned