SOP: Screening and randomisation

Version	Author(s)	Date	Changes	Approved by
1.0	Mathias Lühr Hansen Caroline Kamp Johanne Juul Petersen	27.01.25	Initial version	Janus Christian Jakobsen

Content

Introduction

Infants fulfilling the following eligibility criteria should undergo screening:

a. gestational age ≥28+0
b. postnatal age less than 28 days
c. expected to receive mechanical ventilation for ≥24 hours
d. no suspicion of or confirmed brain injury or disorder
e. no suspicion or diagnosis of congenital heart disease likely to require surgery

Screening is important since it enables assessment of the external validity of the SafeBoosC-IIIv trial.

In this Standard Operation Procedure (SOP), the process of screening infants followed by either randomisation or no randomisation is described.

Screening followed by randomisation

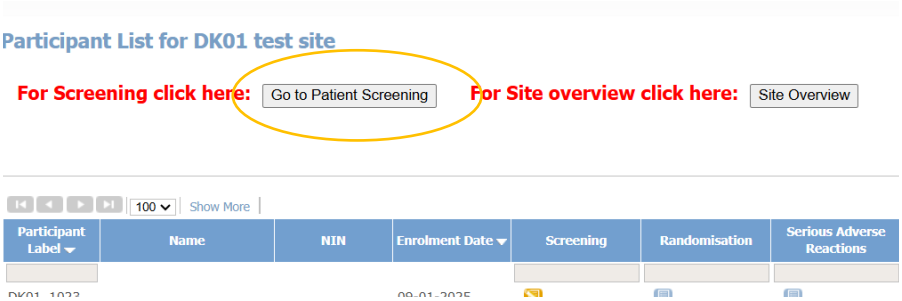
1. Identify infants fulfilling the eligibility criteria described above.
2. Check that an oximeter is available, and that cerebral oximetry monitoring can be initiated within six hours from initiation of mechanical ventilation.
3. If using prior consent, approach the parents, inform them of the study, and hand out the appropriate *parental information sheet** and *consent form*. These can be found in the Investigator Site File (ISF).
4. Once the parents have signed the consent form, place it in the ISF.

Infants fulfilling the eligibility criteria, who will not be randomised e.g., due to lack of parental consent or no cerebral oximeter available, please see 'Screening not followed by randomisation'.

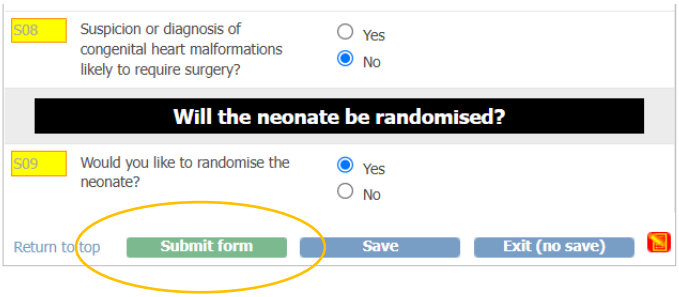
*If parents are approached after having given birth, please use the *postnatal information sheet*. If parents are approached before giving birth, use the *prenatal information sheet,* available in the ISF.

5. Go to https://safebooscciiiv.ctu.dk/OpenClinica/
6. Log in by using your username (e-mail address) and password which you have previously received from the principal investigator.

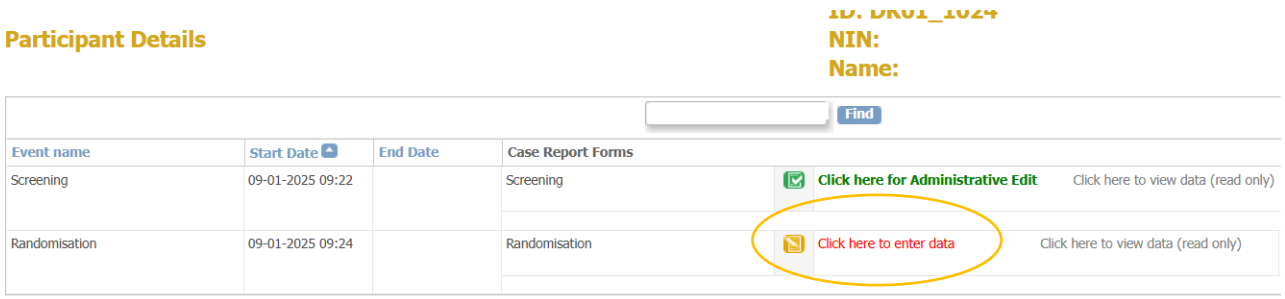
7. Click “Go to Patient Screening”:



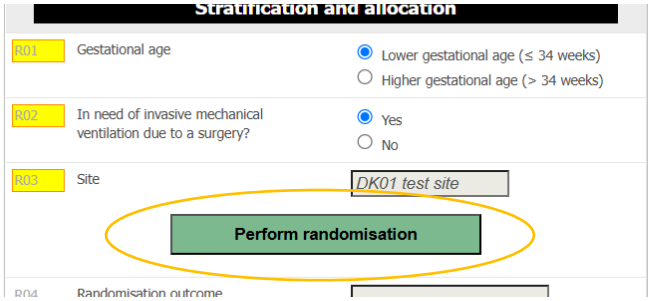
8. Fill in the data and click ‘Submit form’:



9. Once the form is submitted, the screening is registered, and you will be redirected to the ‘Participant Details’ page. You will now be able to randomise the infant by clicking ‘Click here to enter data’ within the ‘Randomisation’ row:



10. In the randomisation form, fill in data and click ‘Perform randomisation’



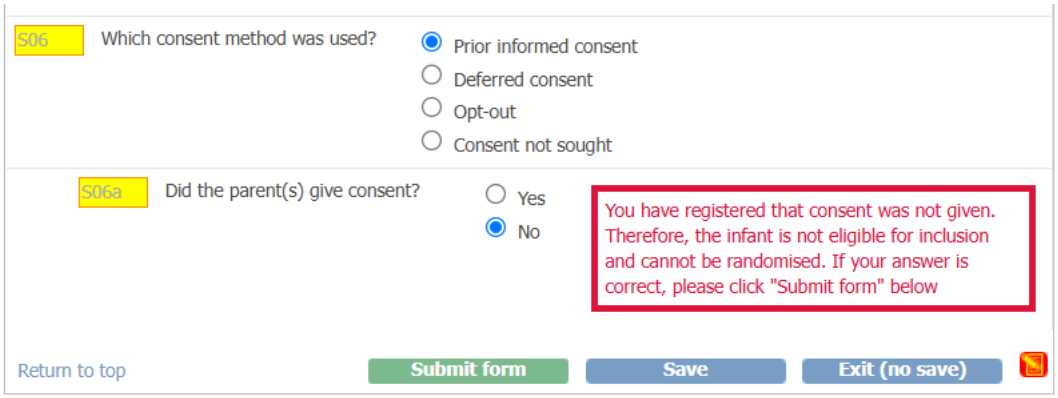
11. Afterwards, you will be presented with the randomisation outcome and participant ID. Find the participant inclusion list in the ISF and note the participant ID, the infant's national identification number, and the date of birth.
12. After randomisation, you must write a note in the infant's clinical records. The content is dependent on the randomisation outcome.
    a. For infants randomised to the usual care group: *'The patient participates in the SafeBoosC-IIIv trial and is randomised to the usual care group.*
    b. For infants randomised to the cerebral oximetry group: *'The patient participates in the SafeBoosC-IIIv trial and is randomised to the cerebral oximetry group. Cerebral oximetry monitoring should be continued until 1) the cardio-pulmonary function has been stabilised as indicated by the need for respiratory and circulatory support, and evaluated by the responsible neonatologist, 2) extubation, 3) 28 days after birth, or 4) death. In case of cerebral hypoxia, please refer to the SafeBoosC treatment guideline. Cerebral oximetry monitoring was started at (date and hour).*

Screening <u>not</u> followed by randomisation

In some cases, you will have identified an infant fulfilling the eligibility criteria, but the infant will not be randomised. Reasons for this could be many, including:

- Cerebral oximetry monitoring could not be initiated within six hours from initiation of mechanical ventilation (this could happen if the parental consent process took longer than expected, if there are no available cerebral oximeter, or if staff was busy with other tasks).
- Parents did not consent for their infant to participate (or decided to opt-out before randomisation).

If the infant fulfils the eligibility criteria but will not be randomised, you still need to register the screening. Log in as described above, click 'Go to Patient Screening' and complete the screening form. Once you register the reason why the infant will not be randomised, you will be able to submit the screening form without randomisation. Below you can see an example of the screening form, in a case where the parents did not give consent:



Screening and randomisation when using deferred consent

When using deferred consent, skip step 3 and step 4 under 'Screening followed by randomisation'. Parents will be approached, informed, and asked for consent later, when the emergency situation has settled.

Obtaining deferred consent

When you believe the time is suitable, and parents are ready to be approached regarding continuing participation in the study:

1. Approach the parents, inform them of the study, what group the participant has been randomised to, and hand out *'Control group information'* or *'Intervention group information'* as suitable, and *'Consent form'*. They can be found in the ISF.
2. Once the parents have signed the consent form, place it in the ISF.
3. If the parents do not sign the consent form, remove the cerebral oximeter if in the cerebral oximetry group, record the parents' decision in the clinical records, and inform the trial manager (caroline.kamp@ctu.dk). Caroline will need to know the infant's participant ID and will then exclude the infant from the study. For details on how to handle data entries, please see 'SOP: Deletion of data due to withdrawal of consent or declined participation' (available at www.safeboosc.eu under 'SOPs and templates').

Screening and randomisation when using opt-out

When using opt-out, parents will be approached before randomisation as described under 'Screening followed by randomisation'. However, parents will not be asked if they want to participate (opt-in), since their infant by default will be enrolled and randomised.

Therefore, when using opt-out, replace step 3 and step 4 under 'Screening followed by randomisation' with the steps below:

1. Approach the parents, inform them of the study and that their infant has been enrolled in the trial by default, and hand out the parental information *for prior assent/opt-out consent method*. It can be found in the ISF.
2. If the parents do not decide to opt-out, you must write in the infant's clinical records that the parents have been informed of the study and that they did not choose to opt-out. Proceed to step 5 under 'Screening followed by randomisation'.
    a. If the parents decide to opt-out before randomisation, complete the screening form as described under 'Screening not followed by randomisation'.
    b. If the parents decide to opt-out after randomisation, remove the cerebral oximeter if in the cerebral oximetry group, record the parents' decision in the clinical records and inform the trial manager (caroline.kamp@ctu.dk). She will need to know the infant's participant ID and will then exclude the infant from the study. For details on how to handle data entries, please see 'SOP: Deletion of data due to withdrawal of consent or declined participation' (available at www.safeboosc.eu under 'SOPs and templates').

Issues with randomisation

Incorrect stratification parameters

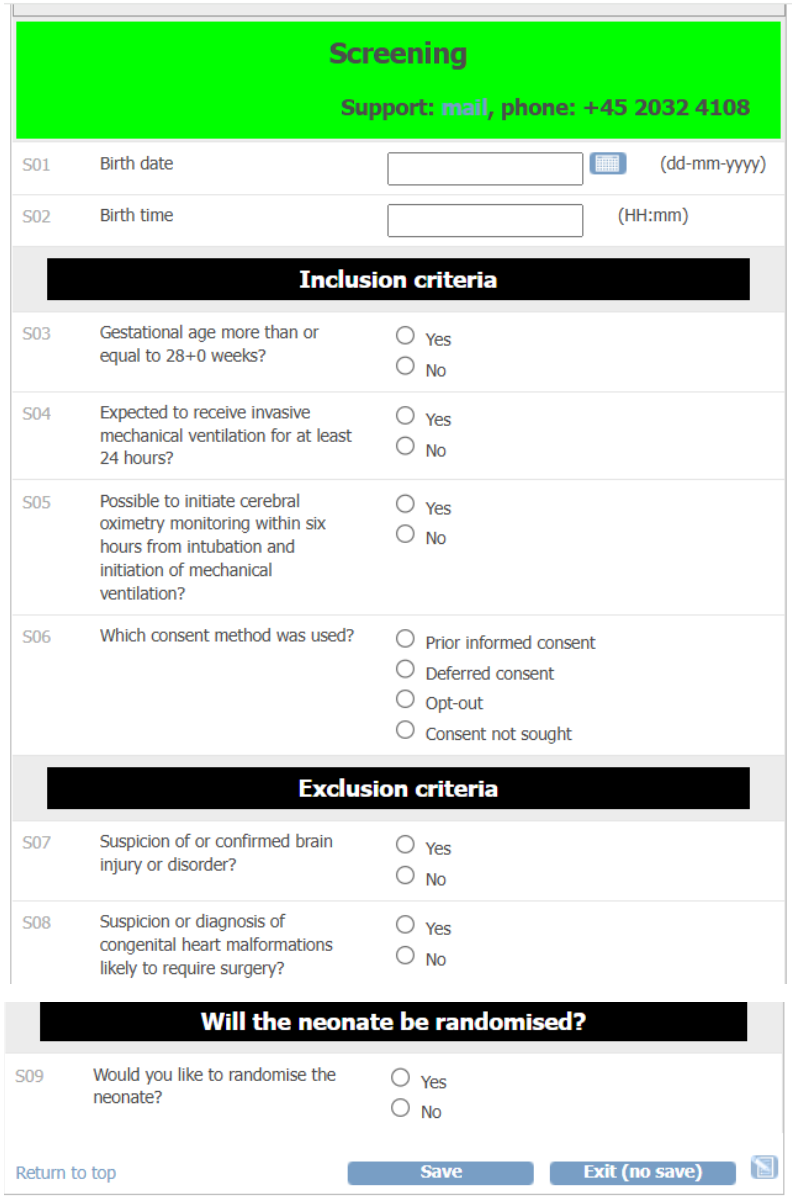
If you have performed a randomisation with incorrect stratification parameters, you should NOT perform the randomisation again but use the randomisation allocation already given. Next, contact Caroline Kamp at caroline.kamp@ctu.dk.

Emergency randomisation

In case you experience problems with randomisation that requires urgent help.

Please call Caroline Kamp (+45 20324108). NB! The phone number is not toll-free.

If Caroline cannot solve the problem, she will conduct an emergency randomisation. She will need to know all the information normally needed to screen and randomise an infant in OpenClinica (see below):



Screening

Support: mail, phone: +45 2032 4108

S01	Birth date		(dd-mm-yyyy)
S02	Birth time		(HH:mm)

Inclusion criteria

S03	Gestational age more than or equal to 28+0 weeks?	○ Yes ○ No
S04	Expected to receive invasive mechanical ventilation for at least 24 hours?	○ Yes ○ No
S05	Possible to initiate cerebral oximetry monitoring within six hours from intubation and initiation of mechanical ventilation?	○ Yes ○ No
S06	Which consent method was used?	○ Prior informed consent ○ Deferred consent ○ Opt-out ○ Consent not sought

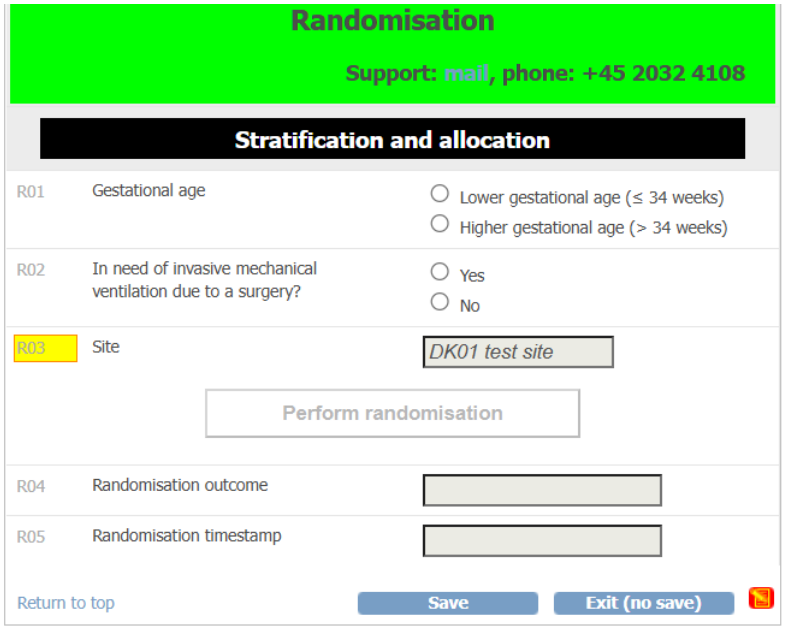
Exclusion criteria

S07	Suspicion of or confirmed brain injury or disorder?	○ Yes ○ No
S08	Suspicion or diagnosis of congenital heart malformations likely to require surgery?	○ Yes ○ No

Will the neonate be randomised?

S09	Would you like to randomise the neonate?	○ Yes ○ No

Return to top Save Exit (no save)



Once the clinical information has been provided, the randomisation will be conducted as described below:

1. Coin toss by Caroline Kamp in front of a witness. Heads = cerebral oximetry group, tail = usual care group.
2. The result will be given to the investigator by phone.
3. Caroline will ensure that the necessary clinical information including the result of the coin toss will be sent to the data manager, who will then create the randomisation in OpenClinica. Once this is done, Caroline will inform the principal investigator by e-mail, including the participant ID.