SOP: enrolment and randomisation

Version	Author(s)	Date	Changes	Approved by
1.0	Mathias Lühr Hansen	16.01.19	Initial version	Gorm Greisen
1.1	Mathias Lühr Hansen	16.04.19	Textual changes in 2.0 and 3.0	Gorm Greisen
1.2	Mathias Lühr Hansen	03.05.19	1.2 Removal of text regarding data points, addition of reference to 'SOP: randomisation and data entry in OpenClinica'.	Gorm Greisen
1.3	Mathias Lühr Hansen	10.05.19	1.1 Addition on how to enroll multiple birth infants	Gorm Greisen
1.4	Mathias Lühr Hansen	24.05.19	1.2 Changing link	Gorm greisen
1.5	Mathias Lühr Hansen	12.06.19	4.0 Editing of emergency randomisation procedure	Gorm Greisen
1.6	Mathias Lühr Hansen	19.06.19	1.2 Edit of what username and password that should be used to log-in to the eCRF	Gorm Greisen
1.7	Mathias Lühr Hansen	19.05.20	1.2 and 4.0 Edit of emergency number	Gorm Greisen

Content

1.0 How do I enroll infant(s)?

1.1 Identifying infant, consent and study-ID

1. Identify possible participant (<28 weeks postmenstrual age, decision to provide full life-support, possibility to start NIRS monitoring within six hours after birth)
2. Check that an oximeter is available, multiple oximeters in the case of multiple births. If there is less oximeters available than the number of babies, the sibling(s) enrolled will be the one(s) born last.
3. Approach the parent(s), inform them of the study and hand-out *parental information** and *consent form*. It can be found in the TMF (describe where it is placed).
4. When the parent(s) have signed the consent form, put it in the Trial Master File (TMF)
5. Find the "patient inclusion list" in the TMF and note the date and hour of birth, the Personal Identification Number of the child in the first available row (beware of multiple birth infants, label them A, B, C etc.) – the children are given a participant ID at randomisation. When randomised, write the participant ID next to the Personal Identification Number (see below).

*If parents are approached after having giving birth, please use the *parental information postnatal* version. if parents are approached before giving birth (in risk of preterm labor), use the *parental information prenatal* version.

1.2 Randomisation

- Open a web-browser and go to the following page: https://safeboosc.ctu.dk/OpenClinica
- Log-in to the eCRF using your personal username (e-mail) and password. You should know your personal username (e-mail address), since it has previously been sent to mathias.safeboosc@gmail.com by the principal investigator of your site. For more information on the log-in procedure, see SOP: manual for OpenClinica: https://www.rigshospitalet.dk/english/departments/juliane-marie-centre/department-of-neonatology/research/SafeboosC-III/Documents/sops/sop-manual-for-openclinica.pdf
- Click the 'Go to Patient Randomisation' button, fill-in data, and press 'Perform randomisation'. For more detailed information, please see 'SOP: manual for OpenClinica'.

After you have pressed the Randomisation button, you are presented with a summary, including the randomisation outcome and a participant ID. Carefully note the participant ID in the patient inclusion list, as described under '5.' in '1.1', and the randomisation outcome **before** logging out!

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 Mathias Lühr Hansen at mathias.luhr.hansen@regionh.dk

In case you experience problems with the randomisation that requires urgent help, please contact Mathias Lühr Hansen (+45 27142144) or Gorm Greisen (+45 40460747) directly. NB! The phone numbers are not toll-free.

1.3 Write in participants clinical file/day-to-day records/notes

- Participates in the clinical trial Safeboosc III in the control group 'treatment at usual'
  Or
- Participates in the clinical trial SafeboosC III in the experimental group. Monitoring of cerebral oxygenation is to be done until 72 hours of age. In case of cerebral hypoxia refer to the treatment guideline. Monitoring was started at (note data and hour)

2.0 What to do when using deferred informed consent?

When using deferred informed consent, do as described in "1.0 how do I enroll a participant(s)?", but skip step 3 and step 4 under "1.1 identifying participant, consent and study-ID". Parents will be approached, informed, and asked for consent later, when the emergency situation has settled. Write in the participant's file as described in 1.3.

2.1 Deferred informed consent

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

1. Approach the parent(s), inform them of the study, what group the participant has been randomised to, and hand-out *parent information control group* or *parent information intervention group* as suitable, and *consent form*. They can be found in TMF.
2. After the parent(s) have signed the consent form, put it in the Trial Master File (TMF)
3. If the parent(s) do not sign the consent form, you remove the cerebral oximeter if in the experimental arm, record the parent's decision in the clinical records and inform CTU (see contact information above) with the study number (you can find it in the patient inclusion list in the Trial Master File). The infant must be excluded from the study.

3.0 What to do when using 'opt-out' as consent?

When using 'opt-out' as consent method, the parents will be approached immediately as in 1.1. However, when using 'opt-out' parents will not be asked to participate (opt-in), since their baby already will be enrolled as default, see method below:

3.1 Identifying participant, inform on 'opt-out' and study-ID

1. Identify participant (<28 weeks postmenstrual age, decision to provide full life-support, possibility to start NIRS monitoring within six hours after birth)
2. Approach the parent(s), inform them of the study including that they have been enrolled as default, and hand-out *parent information for prior assent/'opt-out' consent method*. It can be found in TMF.
3. If the parents do not decide to 'opt-out' write in the participants clinical file, that parents have been informed of the study and that they did not choose to 'opt-out', Then go to step 5.
4. If the parents decide to 'opt-out', you remove the cerebral oximeter if in the experimental arm, record the parent's decision in the clinical records and inform CTU with the study number (you can find it in the patient inclusion list in the Trial Master File). The infant must be excluded from the study.
5. Find the "patient inclusion list" in the TMF and note the date and hour of birth, the Personal Identification Number of the child in the first available row (beware of twins, label them A and B) – the children are given a study-ID at randomisation. When randomised, write it next to the Personal Identification Number.

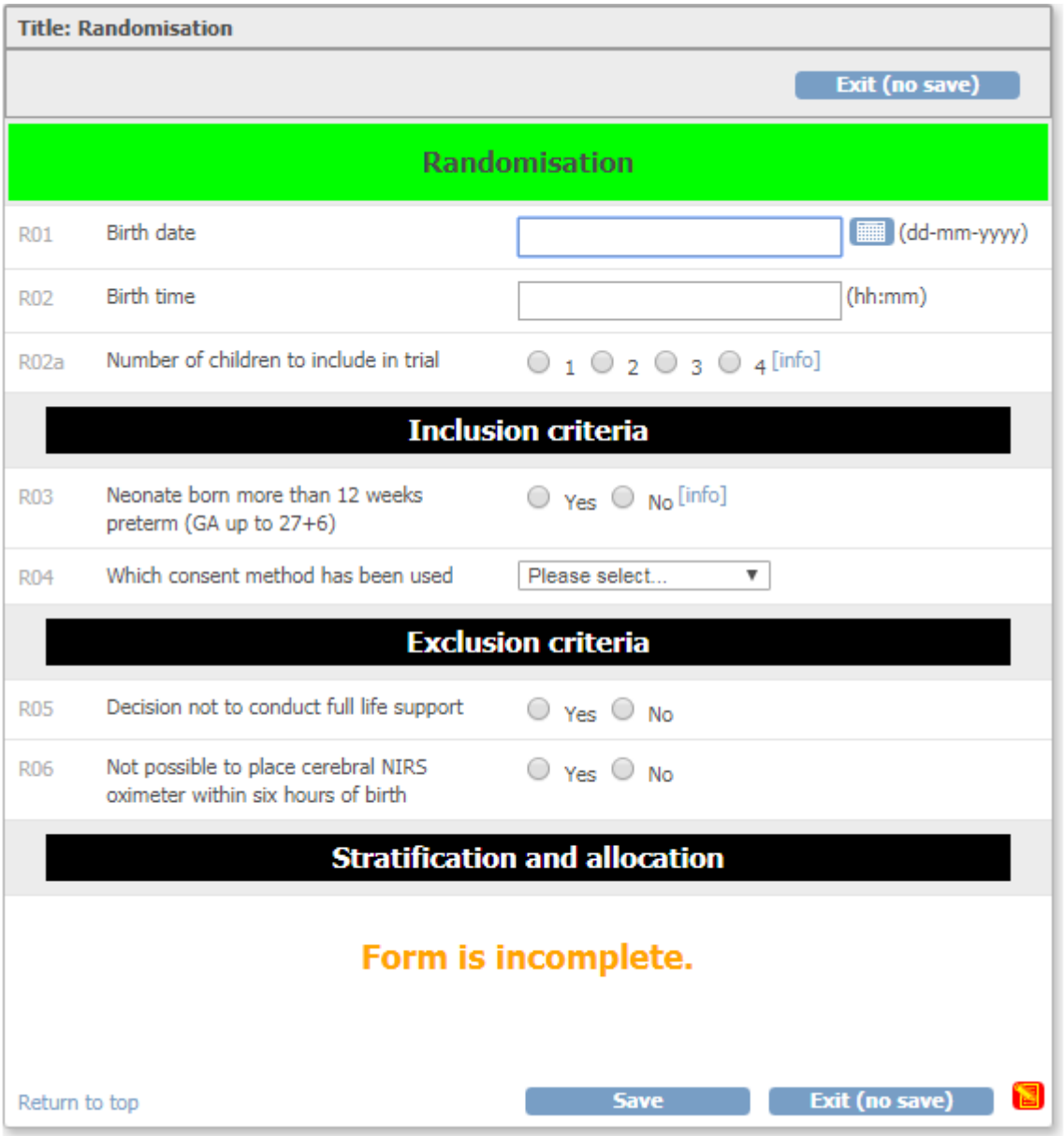
Randomisation and **notation in participants clinical file** is the same as used under "1.0 How do I enroll infant(s)?".

4.0 Emergency randomsation

In case OpenClinica is not working

Please call Mathias Lühr Hansen (+45 27142144) or Gorm Greisen (+45 40460747)

They will need to know all information normally needed in order to randomise a baby, according to the Randomisation module in OpenClinica:



They will perform the randomisation for you and tell you which group the baby/babies is/are randomised to.