SafeBoosC-IIIv Steering Committee meeting

28 August 2024

Attendees: Caroline Kamp (CTU), Johanne Juul Petersen (CTU), Janus Christian Jakobsen (CTU), Mathias Lühr Hansen (CTU), Gorm Greisen (Denmark), Siv Fredly (Norway), Gerhard Pichler (Austria), Jakub Tkaczyk (Czech Republic), Tomasz Szcapa (Poland), Livia Ognean (Romania), Adelina Pellicer (Spain), Gabriel Dimitriou (Greece), Gabriel Musante (Argentina), Eugene Dempsey (Ireland), Laishuan Wang (China), Monica Fumagalli (Italy), Hans Fuchs (Germany).

Moderator: Caroline Kamp
Minute taker: Johanne Juul Petersen

1) **Approval of the agenda**
   Agenda approved.

2) **New members of the Steering Committee**
   No new members have joined the Steering Committee since the last meeting. The list of participating countries was discussed. Canada is currently not involved, but both Gene and Gerhard will reach out to contacts in Canada. Colombia is currently not involved, although Caroline has been in contact with them previously without luck. Adelina will try to reach out again.

   Caroline briefly presented the organization's structure. The Executive Steering Committee will undertake the trial's day-to-day running, but the Steering Committee will make all decisions.

3) **Central updates**
   - **Ethics approval**
     Caroline gave an update on the ethics approval in Denmark. The protocol version 2.0 was submitted in June 2024 to the Danish Research Ethics Committee. Due to a new EU regulation, the trial was rejected. It should instead be submitted as a medical device trial of a device that has already obtained CE marking. This has changed since the last ethics approval. The protocol version 2.0 has now (August 2024) been resubmitted as a medical device trial. A response is expected within 60 days.

     Gene raised concerns about the complexity of ethics approval, if the trial is considered a medical device trial, whether it would need to be submitted to a central EU regulatory authority, and if any approvals in one country would affect other participating EU countries. Mathias went through the information received from the Danish authorities. Mathias was informed that all countries would still seek national ethics approval instead of a central EU regulatory approval. Since the device is already CE marked, the process should be simple. In Denmark, they already had a brief look at the protocol and no changes were made. Caroline will reach out to the

Danish Research Ethics Committee to confirm that all countries should seek individual ethics approval.

4) **National Coordinator update**
   - **Gabriel Musante, Argentina:** Currently working on funding for sensors and GCP monitoring. Masimo recently declined, but Gabriel is in contact with MedTronic. Caroline will also forward the contact information on OxyPrem. Perhaps Argentina will begin with four/five centers in Buenos Aires to make the GCP monitoring feasible. Gabriel has also reached out to Adelina and Jorge to translate the documents.
   - **Gerhard Pichler, Austria:** Two centers are joining. Working on ethics approval. Funding will not be a problem.
   - **Jakub Tkaczyk, Czech Republic:** One center is joining. Additional centers are interested, but they primarily have extremely preterm babies, and thus might not reach the criteria for authorship. Authorship is ultimately a decision made by the Steering Committee.
   - **Jorge Fabres, Chile:** Update on email. 14 centers are interested in participating. Jorge will schedule a meeting to coordinate their involvement.
   - **Laishuan Wang (represented by Ling Zhao), China:** Currently recruiting centers and working on ethics approval. Support from Enginmed has been obtained.
   - **Hans Fuchs, Germany:** Two centers are joining, but it is difficult to recruit the centers without funding. The contracts might take time to be ready.
   - **Gabriel Dimitriou, Greece:** Five centers are interested in joining. The consent forms will be edited to align the information on insurance coverage with Greek regulations. Gabriel has been in contact with OxyPrem and Masimo to seek support.
   - **Saudamini Nesargi, India:** Update on email. St. Johns has submitted for ethics approval, worked on Health Ministry Screening Committee (HMSC) clearance, and registered the trial on the Indian trial registry (CTRI). CTRI and HMSC will cover all Indian centers. Goa has also submitted for ethics approval. Orissa will submit for ethics approval this week. Ethics approvals are expected by October. Waiting for OxyPrem to share their agreement. Working on a protocol for a secondary study, which should be ready to share soon.
   - **Eugene Dempsey, Ireland:** Two centers are joining, and two additional centers are interested. Ethics should not be a problem. The contracts might take time to be ready.
   - **Monica Fumagalli, Italy:** Currently recruiting centers.
   - **Siv Fredly, Norway:** One center is joining. Difficulties in recruiting centers, as they are not interested in NIRS. Funding will not be a problem.
   - **Tomasz Szcapa, Poland:** 12 centers are interested, but they might not be able to include enough participants. Funding will be sought from governmental funds and OxyPrem.
   - **Livia Ognean, Romania:** Four centers are interested. Monitors will be received in the end of the year. Livia is working on translating the documents.
   - **Adelina Pellicer, Spain:** More than 10 centers will join, and all documents have been submitted to the ethics committee. Funding will not be a problem.
   - **Cornelia Hagmann, Switzerland:** Update on email. Aim to submit for ethics approval for three centers in November.

All collaboration agreements were sent out from CTU in June. If any centers did not receive it, please reach out so we can send it again.

5) **Protocol**

Caroline goes through the inclusion criteria, exclusion criteria and stop criteria, as this has come up during several meetings with principal investigators:

Inclusion criteria:

- Newborns with gestational age more than or equal to 28+0 weeks
- Postnatal age less than 28 days
- Expected to receive invasive mechanical ventilation for at least 24 hours, as judged by the physician intending to randomise (i.e., not including CPAP or BiPAP)

There was a discussion about the third inclusion criteria and the examples in the brackets, as it currently does not cover all examples of non-invasive ventilation. It was decided to replace the examples in the brackets with "intubation" after invasive: *Expected to receive invasive mechanical ventilation (intubation) for at least 24 hours, as judged by the physician intending to randomise*. This will be included in protocol version 2.1.

Exclusion criteria:

- Suspicion of or confirmed brain injury or disorder (e.g. perinatal asphyxia, cerebral haemorrhage, cerebral malformation, genetic or metabolic disease)
- Suspicion or diagnosis of congenital heart malformations likely to require surgery

In protocol version 2.1 the wording will be revised to include major brain haemorrhage (grade 3 or 4) and severe hypoxic-ischemic encephalopathy in the brackets as examples of exclusion criteria to guide the physician. This was decided at the last Steering Committee meeting.

Stop criteria:
Cerebral oximetry will be continued until:

- The cardio-pulmonary function has been stabilised as indicated by the need for respiratory and circulatory support and evaluated by the responsible physician
- Extubation
- 28 days after birth
- Death

6) **Any other business**

Next Steering Committee meeting will be 30th of October 2024, 20:30 CEST.