BLINDING OF FOLLOW-UP AND DATA ENTRY ON SAFEBOOSC III

The principal investigator, (MA) will verify the follow-up dates of each infant included in Safeboosc III. MA is not involved in the infants follow-up.

In our hospital, extremely preterm infants are followed up according to the current protocol at least when they reach 40 weeks, 2, 4, 8, 12 and 24 months of postmenstrual age (PMA). At 24 months of PMA, the Bayley III scale is applied and recorded in the clinical history.

MA will contact the families not attending the 24 months PMA visit by phone and/or mail to explain and provide the PARCA-R questionnaire.

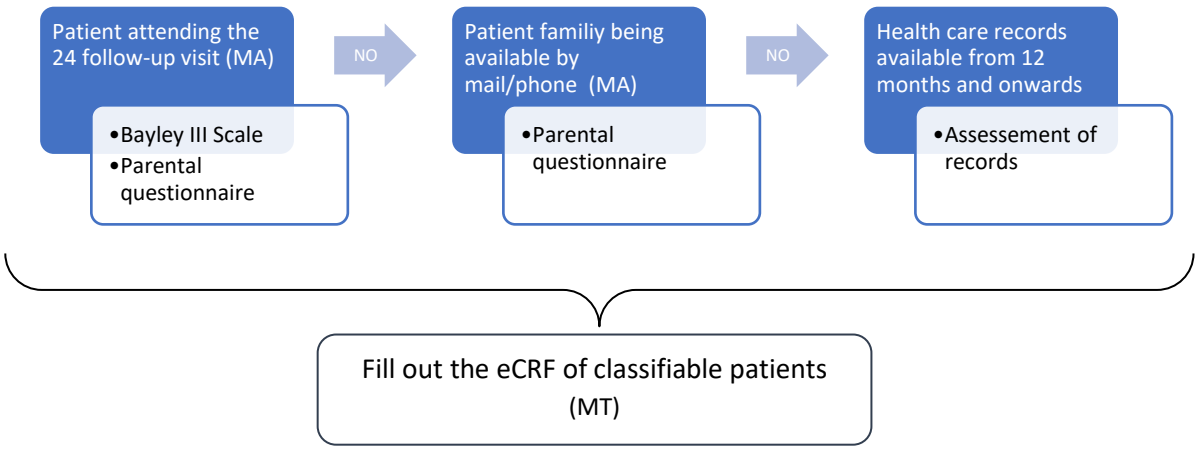
Families attending the visit will be also invited to fill out the PARCA-R questionnaire during the visit to assist them in case of questions. In case they don't attend the visit, or cannot complete the questionnaire within this time, they will be given a mail address to answer the questions.

MT is the blinded co-investigator; she will only be developing research tasks during the Safeboosc-fu period in Hospital Clinic and neither she nor the neonatologists who carry out the follow-up will not be aware of the infants allocation group.

In case there are no relevant health care records from corrected age 18-30 months the records will be accessed by MT and all health care records from corrected age 12 months and onwards will be informally assessed to conclude whether or not the child has moderate-or-severe neurodevelopmental disability.

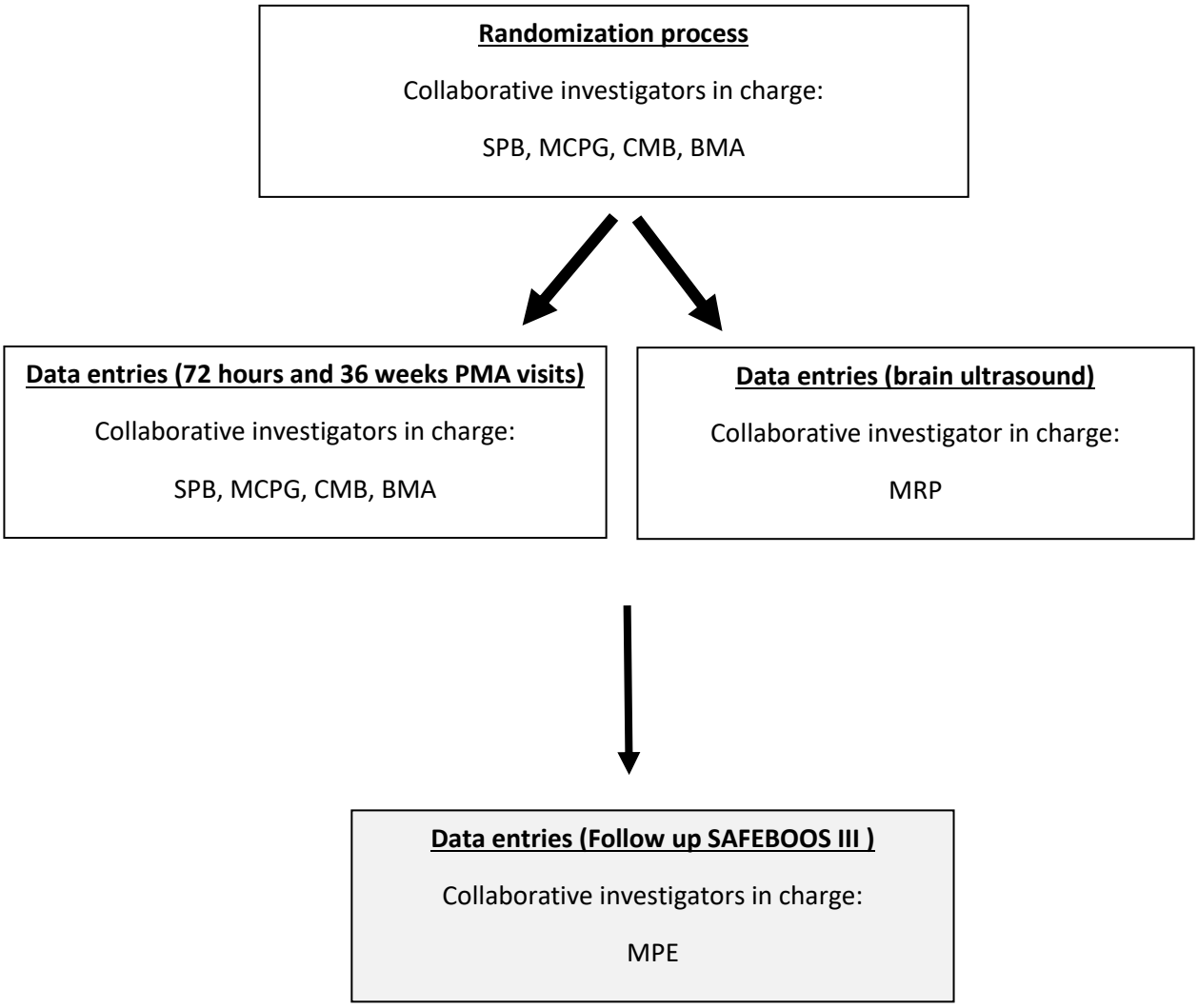
MT will record the requested items on the eCRF obtained from the Bayley III scale assessment, the parental questionnaire, or the informal assessment

The availability of classifiable data will be recorded in a column in the participant-inclusion-list (PIL). The custodian of the list will be the PI (MA).



Examples of blinding procedures in the SafeBoosC-III follow up study

Blinding procedure:



- **SPB (PI), MCPG (CI), CMB (CI), BMA (CI**) are neonotologists who knows the allocation group of every patient.
- **MRP (CI)** is a pediatric radiologist blinded for the allocation group.
- **MPE (CI)** is a neonatologist who will not know the allocation group of the patient in the moment of the follow up data entries. She has not access to the general database. She will check the clinical file of the patient to fill in the eCRF the follow up data. There is a research note in the clinical file of the patient, but it only include information about the parental agreement to voluntary participate in the study. This research note does not reveal the allocation group. MPE will receive a list of the patients with the clinical record and the ID corresponding to study participation. Group allocation will not be revealed neither in the list of patient. It will be the same list of patient that is sent to MRP.

Abbreviation: PI, principal investigator; CI, collaborative investigator.

Examples of blinding procedures in the SafeBoosC-III follow up study

SafeBoosC-III follow up blinding procedure

All the infants enrolled in the study are included in the routine clinical follow-up provided by our unit.

The follow-up visits at 12 and 24 months corrected age include:

- pediatric visit (anthropometric measures, collection of recent clinical history, medical examination) – available on electronic charts
- Neurodevelopmental test (Griffith-III or Bayley-III)
- Neurodevelopmental assessment (clinical evaluation of motor development, neurodevelopmental issues) – available on electronic charts

All the staff involved in the follow-up clinic doesn't work in the NICU therefore they are blind to child enrollment and allocation in clinical trials at birth. Of course, they have access to the electronic chart of the NICU and theoretically they could read each daily diary and therefore see child enrollment and allocation. However, during the first follow-up visit (usually 10 days- 1 months after discharge) a new clinical follow-up chart is completed on the basis of the discharge summary that doesn't report previous enrollment in clinical trials. During all the following follow-up visits the information are retrieved from the follow-up clinical chart.

A neurodevelopmental therapist (CF) and a neonatologist (SP) blinded to child allocation and not previously involved in the first part of the SafeBoosC-III study, will collect data from follow-up clinical records after each visit and complete the e-CRF.

The two co-investigators have a wide experience with preterm infants both in the NICU and at follow-up.

In our follow-up we have an online agenda and appointments are scheduled on a 6 months -1 year basis.

The co-investigators completing the e-CRF and collecting all follow-up data for the SafeBoosC-III fup study can access the online agenda and look at all the scheduled appointments. Therefore, there is no need for an anticipated notice or contact with the follow-up staff.

If a child misses the follow-up appointment the staff of the follow-up clinic reschedule the appointment within 1-3 months and indicate the new appointment on the online agenda.

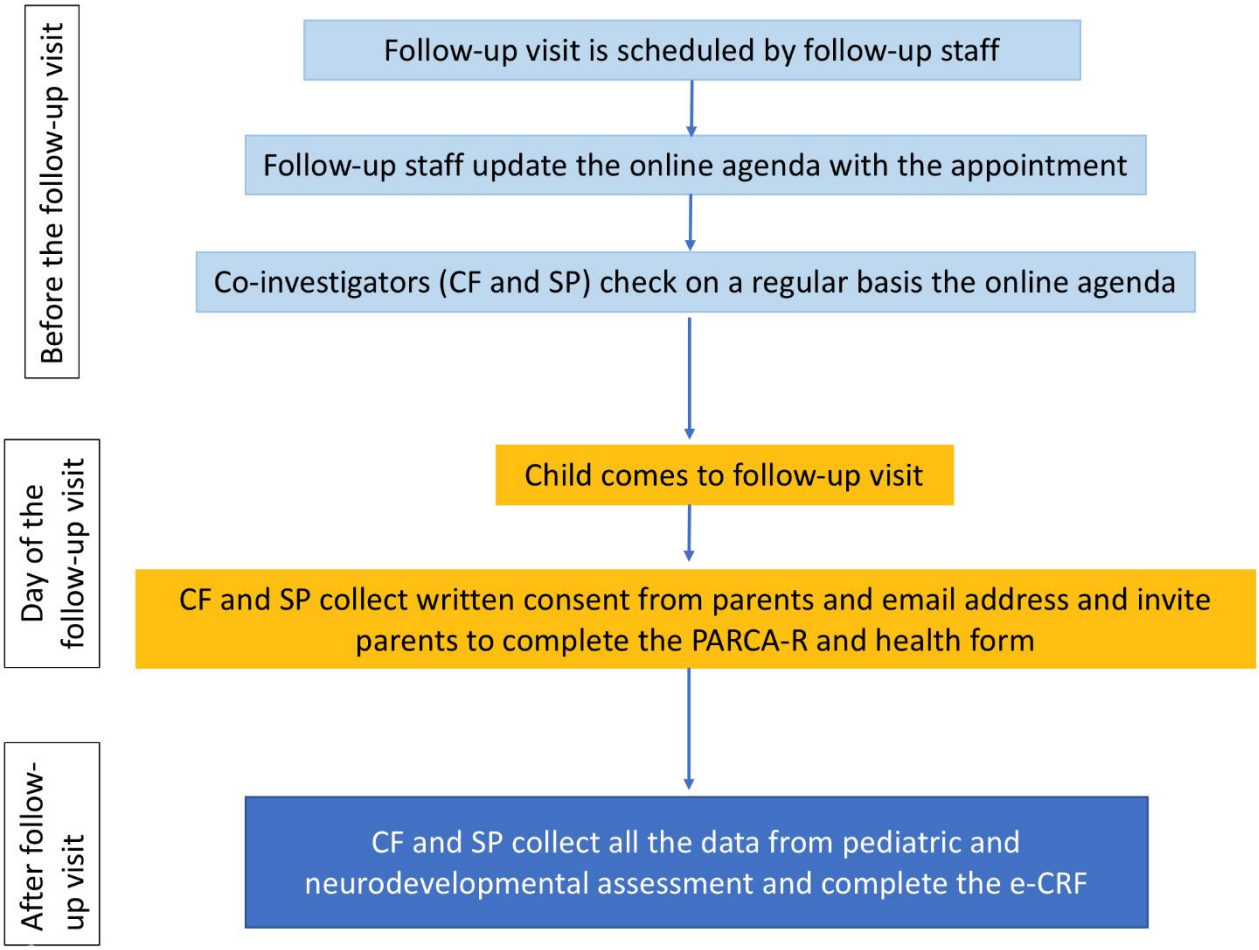
On the day of the follow-up, after the visit, co-investigators will collect the written consent from parents and, if not already present in the SafeBoosC-III records or in the clinical records, they will also collect email addresses and invite parents to complete the PARCA-R and health form available online.

The parental questionnaires (PARCA-R and heal and developmental questionnaire) that are not included in the standard clinical follow-up will be administered to parents online after the child follow-up visit.

Co-investigators will prospectively collect follow-up data at 12 and 24 months including parental questionnaires. For those infants that have already performed the 12 months follow-up visit we will only collect data from pediatric and neurodevelopmental visits.

Examples of blinding procedures in the SafeBoosC-III follow up study

Flowchart



Examples of blinding procedures in the SafeBoosC-III follow up study

Blinding procedure

1- There will be an appointed physician that will do the FU assessment who is completely blind as she is only assigned to the FU outpatient Clinique (CD).

2- We have already edited a list on the patients, the dates for FU and the alarm date (6 months ahead, to be sure that they will be attending the 2-years FU) (attached). To avoid any follow up delay, EV (responsible of the SafeBoosC-III main outcome assessment) is also involved to follow the patients' track.

3- Regarding on how to get the infants' information, we have routine serial FU appointments every 3 months during the first year, and every 6 months during the second year (structured neurological exams, hearing and visual assessments, growth patterns,...). All this information is recorded on the hospital clinical records (electronic). In this visits, relevant information about health issues and other specialists visits are gathered. Since a few months, PARCA is also offered to parents. And BS-III will be done at 24months (corrected age). CD will enter the information into the SafeBoosC-III FU eCRF.

There are only clinical records regarding SafeBoosC group allocation at the beginning of the infants's stay. The day the infant is enrolled (<6h) and during intervention, if in the experimental group (first 72h). Beyond that, the NIRS device is removed and no additional comments-notes are recorded either during the doctors clinical rounds (and nurses notes) which are tons (long hospital stays usually). When the infant is discharged a document is edited (summary of clinical course) with no mention to the trial.

At the FU visits, the doctors open a new visit every time the child attends a visit, so they do not enter into the first admission records (this should be an intended action). So, no risk to unblind.