Guidance Sheet 1:

Screening and Eligibility

Trial Participants

The trial population is made up of two groups:

1. Preterm stratum - Infants born less than 28 weeks of gestation (can be randomised up to 3 months post EDD)

2. HIE stratum - Infants born at 35 weeks of gestation or more who receive therapeutic hypothermia for hypoxic ischaemic encephalopathy (HIE) (irrespective of neuroimaging findings) (can be randomised up to EDD plus 28 days)

Preterm infants can be consented up to discharge home either:

- in-person at a recruiting site OR
- remotely after transfer to another hospital

Preterm infants cannot be consented after discharge home.

HIE infants can be consented:

- in-person at the recruiting site OR
- remotely after transfer to another hospital OR
- **from home after discharge from hospital**.

See **Guidance Sheet 2 - In-Person and Remote Informed Consent.**

Screening for infants

- Sites are asked to regularly screen for potential participants. This should include reviewing admission and discharge lists.
- Screening and eligibility checks can be undertaken by clinicians, research nurses and health care professionals who have undergone sufficient local training and have sufficient knowledge to undertake screening, but final eligibility can only be confirmed by a delegated individual, as recorded on the **DOLFIN Site Delegation Log**.
- All infants who are born preterm, less than 28 weeks of gestation, should be screened for eligibility. Infants who have been transferred to another hospital should also be screened for eligibility.
- Infants born at 35 weeks gestation or more who receive therapeutic hypothermia for hypoxic ischaemic encephalopathy (HIE) should be screened for eligibility. Infants who have been transferred to another hospital or discharged home should also be screened for eligibility.
- Parents with legal parental responsibility for infants identified as being potentially eligible should be approached to join the study.
- The approach may take place in-person or remotely using a telephone or video call. If infants are transferred or discharged prior to parents making a decision on participation, sites should follow up with the parents where possible. For remote consent of preterm or HIE infants, the transfer hospital does not need to be an approved Continuing Care Site (CCS).

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- HIE infants who are transferred or discharged home prior to being approached or prior to parents making a decision can be provided with the **DOLFIN Recruitment cover letter to parents (HIE)** at home (sent via email or post).
- Consent may be taken at the time of the initial consent discussion, or an initial approach may be made with a follow-up approach agreed with parents.
- Sites should make parents aware of the recruitment window in which consent can be given (3 months post EDD for preterm infants and EDD plus 28 days for HIE infants)
- Sites are asked to approach all eligible infants even if they are likely to be transferred or have already been transferred. If approvals are not in place at a CCS supplement can be restarted when approvals are in place or after discharge home. This is outlined clearly in the PIL for parents to consider.
- To ensure that potentially eligible infants are not missed, all NNU staff should be familiar with the **DOLFIN Study Protocol** and sites should engage support from wider teams where possible.
- To maximise awareness of the study, study information should be made widely available throughout the NNU in the form of DOLFIN-specific resources including posters, postcards, banners and information leaflets which will be provided to sites.
- If parents are willing to participate and consent to the trial, follow instructions provided in **Guidance Sheet 2 - In-Person and Remote Informed Consent.**

Inclusion criteria

- Preterm stratum: Infants born less than 28 weeks of gestation, up to discharge home from hospital (can be randomised up to 3 months post EDD)
- HIE stratum: Infants born at 35 weeks of gestation or more, who have received therapeutic hypothermia for HIE (can be randomised up to EDD plus 28 days)
- Individual with parental responsibility able to give consent.
  In the event that the mother is unable to give consent, or does not have parental responsibility, consent can be given by another person who has parental responsibility. Maternal consent for the purposes of maternal data collection will be sought as soon as practical
- Parents able to comply with the protocol
- Infants likely to tolerate full enteral feeds
- Infant has realistic prospect of survival beyond discharge

Exclusion criteria

The infant is not eligible if ANY of the following apply:

- Infants with middle cerebral artery infarcts
- Infants with major congenital brain malformation, or genetic condition with abnormal brain development
- Infants with galactosaemia
- Infants receiving all feeds via jejunal tube, who do not receive any gastric or oral feeds

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Co-enrolment

Co-recruitment to other trials is permitted where agreed by the DOLFIN Chief Investigators (CIs). Please contact the DOLFIN study team to confirm if co-enrolment can take place. Interventional trials which have a neurodevelopmental primary outcome must be reviewed and co-enrolment agreed between trial Chief Investigators.

If co-enrolment is not permitted we ask that parents are offered any studies their infant may be eligible for (at the same time) so that parents can choose which, if any, they wish to participate in.

Eligibility/Screening Log

- A record of all infants screened should be maintained at site on the **DOLFIN Eligibility/ Screening Log**. Please include all infants screened, even if the parent(s) decline participation.
- A paper version of the **DOLFIN Eligibility/Screening Log** is available in the DOLFIN document box. A blank electronic copy is included in the eISF. Paper logs are not expected to be submitted back to the DOLFIN study team, these can be filed locally in the site folder included in the Document Box.
- The **DOLFIN Eligibility/ Screening Log** should include the date the infant was assessed for eligibility, corrected gestational age (in weeks), and whether the infant was eligible for and then recruited to DOLFIN. Please include reason why the infant was not randomised to DOLFIN, where this is known. **Personal identifiers should not be included on screening logs.**
- There should be one entry per infant with an entry edited until an outcome is known (enrolled or declined). If parents have been approached but a decision has not yet been made you can mark this on the screening log using the “Still under consideration” option. Please remember to follow up initial approaches, including if infants have been transferred to another hospital or discharged, as remote consent may be possible.
- If an infant under consideration goes on to be randomised, please update their screening log entry to record that they were randomised and include their study ID. When an infant is randomised, they are automatically added to the electronic screening log, so there will be two entries for the infant. NPEU will take duplicate entries into account when reviewing the screening log.
- Internal identifiers may be used by sites on the screening log – you do not need to include these if not applicable. Once a month, please enter summary data for infants screened on to the DOLFIN randomisation website by visiting https://rct.npeu.ox.ac.uk/dolfin, entering the site login details and selecting the screening log menu option. We will send a monthly reminder for screening logs – these are automated so you will receive this reminder even if you have completed the screening log.

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