Guidance Sheet 8:

Continuing Care Sites

This guidance sheet is for use by Continuing Care Sites (CCSs) when an infant being transferred to the hospital is enrolled on the DOLFIN study, or when an infant is remotely consented by a recruiting site after they have been transferred. The **DOLFIN Transfer Pack** includes additional Guidance Sheets for Continuing Care Sites (CCSs).

Sites can check whether a hospital is a participating site in the DOLFIN trial by going to the DOLFIN study website (http://www.npeu.ox.ac.uk/dolfin/) and selecting the 'Sites' link, or contact the DOLFIN study team.

If the transfer hospital is an approved CCS study activity can take place. Please read the guidance sheets carefully and contact the DOLFIN study team if you have any questions or require any support.

If the transfer hospital is not an approved CCS study please contact the DOLFIN study team as approvals may be in process or it may be possible to obtain approvals. Parents are advised that supplementation may be paused at transfer, hospitals can contact the DOLFIN study team on the next working day that is practical.

DOLFIN study team contact details (between the hours of 9am – 5pm Monday to Friday):

Tel. No.: 01865 617919 / 01865 617924

Email: dolfin@npeu.ox.ac.uk

Study Intervention

DOLFIN is a multicentre, blinded, stratified, randomised placebo-controlled trial investigating whether nutritional supplementation with a nutrient blend of long-chain polyunsaturated fatty acids (LCPUFAs), choline, uridine-5'-Monophosphate (UMP), and cytidine-5'- monophosphate (CMP) plus usual care from birth to 12 months post EDD improves cognitive development at 24 months post EDD, compared to infants receiving a matched control supplement plus usual care. The matched control contains fractions of the active components contained in the treatment supplement and no UMP and CMP. Powder supplement is added daily to an infant's usual milk feed (breast or formula) when infants reach full milk feeds (approx. 120–150ml/kg/day). Supplementation is administered by parents at home until 12 months post EDD.

There are two strata in the DOLFIN trial:

(1) Infants born < 28 weeks of gestation (preterm group) (who can be randomised up to 3 months post EDD)

(2) Infants born ≥ 35 weeks of gestation receiving therapeutic hypothermia for HIE (HIE group) (who can be randomised up to EDD plus 28 days).

- Preterm infants can be consented in-person at the 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 after discharge home.

GUIDANCE SHEET 8

Further information and resources for sites and parents can be accessed via the DOLFIN study website: https://www.npeu.ox.ac.uk/dolfin

See **Guidance Sheets 4a and 4b – Study Intervention** for further information on the supplement and supplementation.

Approved Continuing Care Sites (CCSs)

The recruiting site continues to have responsibility for the infants within the trial and continue to support the family for the duration of the study. Any trial related queries should be directed to the recruiting site or the DOLFIN study team.

Supplementation

If local approvals are in place, supplementation can commence or continue whilst the infant is at that hospital. Supplement can be given by the clinical team at the CCS or by parents (according to local policy and parent preference). Please liaise with the site or DOLFIN study team to confirm when the infant has started the supplement or to confirm that supplementation has continued.

Recruiting sites are asked to notify the DOLFIN study team if an infant is transferred. The recruiting site or the DOLFIN study team may contact the CCS to ensure the transfer process goes smoothly. Any relevant personal identifiable or medical information should be shared directly between local clinical teams at the recruiting site and Continuing Care Site, personal identifiable information must not be included in any emails to the DOLFIN study email address.

Sufficient supply of supplement for use at the CCS should be sent with the infant. If supplement is not sent at time of transfer, please contact the DOLFIN study team.

For guidance on preparing and administering the supplement, please see **Guidance Sheets 4a and 4b**. The **DOLFIN NNU Daily Dosing Log,** included in the **DOLFIN Parent Discharge Pack**, should be completed daily with each feed.

Further supplement will be delivered directly to the family home on final discharge using the distribution service that is managed by the DOLFIN study.

If an infant is transferred, discharged home or dies, please immediately inform the DOLFIN study team on dolfin@npeu.ox.ac.uk or 01865 617919 and/or the recruiting site (contact details can be found on the back of the Parent Information Leaflet (PIL).

For paediatric readmissions or short stays away from home during the intervention period (up to 12 months post EDD), where locally permitted, parents can continue to give their infant supplement in line with local policies, and considered clinically appropriate by the treating clinician.

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If a parent indicates that they wish to discontinue the supplement or change their consent to participate in the study please notify the recruiting site or the DOLFIN study team.

A **DOLFIN Transfer Pack** will be sent with the infant. The contents of the **DOLFIN Transfer Pack** are:

- DOLFIN NNU Daily Dosing Log
- DOLFIN Parent Information Leaflet (Preterm or HIE)
- DOLFIN Serious Adverse Event (SAE) Report Form
- DOLFIN Incident and Deviation Form
- DOLFIN Cot Card
- DOLFIN Guidance Sheet 8 for Continuing Care Sites (CCS's)
- DOLFIN Guidance Sheets 4a, 4b, 5, 7, 9 and 10
- FREEPOST Envelope (for returning Daily Dosing Log)
- DOLFIN Discharge Pack (for parents at discharge)

If a DOLFIN Transfer Pack is not sent at time of transfer, please contact the DOLFIN study team.

Data Collection Forms

Approved Continuing Care Sites (CCSs) are responsible for completing the following Case Report Forms (CRFs):

1. **DOLFIN NNU Daily Dosing Log** to record daily supplementation (whilst the infant is at the CCS until they are transferred to another hospital or discharged home)
2. **DOLFIN Serious Adverse Event Report Form** – to report any Serious Adverse Events (SAE's) that they are made aware of whilst the infant is at the CCS
3. **DOLFIN Incident and Deviation Form** – to report any incidents that they are made aware of whilst the infant is at the CCS

No other data collection is required by CCS and the recruiting site will have responsibility for data entry and any data queries. The recruiting site may contact the CCS with very limited queries about the infant's hospital stay at the CCS but where possible recruiting sites will use central NHS records. CCS are not required to provide this but we would appreciate your support where possible.

1. DOLFIN NNU Daily Dosing Log

- To be used to record whether supplement was given or not.
- Please ensure treatment pack ID is added to the **Dosing Log**. Doses from each new pack should be recorded on separate dosing logs: start a new dosing log when a new pack is begun.
- If an infant is mistakenly given a dose from another infant's pack, this should be reported as an incident (see **Guidance Sheet 9 – Safety Reporting**).

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- Once you use up a pack or run out of space on a paper dosing log, or the infant is discharged home, the completed log should be sent to the DOLFIN study team using the FREEPOST envelope provided or by scanning a copy to dolfin@npeu.ox.ac.uk.
- If an infant is transferred to another hospital, the log should be sent with the infant.
- **Please retain a copy of the completed Dosing Log** (scanned or photocopied) before sending to another hospital or the DOLFIN study team.

2. DOLFIN Serious Adverse Events Form

The safety reporting window for the DOLFIN study for each participant will be from the start of supplementation up to two weeks after completing the supplement (that is, 12 months + 2 weeks post Estimated Date of Delivery (EDD)).

SAEs must be reported as soon as possible of the site becoming aware of the event. Please refer to **Guidance Sheet 9: Safety and Incident Reporting** for detailed guidance on what constitutes an SAE and how to report SAEs to the DOLFIN study team.

Please note that the following events require expedited reporting:
- Serious prolonged gastrointestinal disturbance (except necrotising enterocolitis)
- Serious prolonged gastrointestinal disturbance associated with culture/growth of an unusual organism
- Sepsis associated with culture/growth of an unusual organism

Any member of staff can report SAEs.

Causality assessment is required for SAEs: **Guidance Sheet 9 - Safety & Incident Reporting** states that individuals must be delegated to complete causality as documented on the DOLFIN Site Delegation Log. However, for continuing care cites, this can be completed by any medically qualified individual.

Do not delay reporting the SAE whilst waiting for a causality assessment. The SAE can be sent to the DOLFIN study team initially without the causality assessment completed. An updated SAE form must be sent when the causality assessment is complete.

Completed SAE forms should be scanned and sent via email to the DOLFIN study team on dolfin@npeu.ox.ac.uk.

If this is not possible, then the SAE may be reported to NPEU CTU by telephone. In the case of out-of-hours reporting, please phone 0800 1385 451 (see **Guidance Sheet 10 – Emergency Queries**).

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3. DOLFIN Incident Reporting Form

Any deviations from the **DOLFIN Study Protocol**, study-specific procedures, or Good Clinical Practice (GCP) or any regulatory requirements must be reported to the DOLFIN study team, using the **DOLFIN Incident and Deviation form**.

For guidance on how to report incidents, please refer to **Guidance Sheet 9 - Safety & Incident Reporting.**

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