DOLFIN

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NHS The Newcastle upon Tyne Hospitals NHS Foundation Trust

NPEU Clinical Trials Unit

OXFORD POPULATION HEALTH NPEU

# DOLFIN Training Refresher: 4

## End of pilot changes – Nov 2023

# End of pilot changes

- Amendments based on feedback from sites; DOLFIN families; and parent/public groups during 9 month pilot.
- Minimal changes to trial processes – very little change to how the study runs at sites.
- Amends to existing parent documents, new documents
- Minor changes to some site CRFs
- Study app updated to reflect changes
- Guidance Sheets updated

# Changes to trial processes

- **Recruitment** – both preterm and HIE infants can be remotely consented (previously only HIE infants)
  - Preterm infants can be consented in-person or remotely in hospital prior to discharge home (at recruiting site or after transfer to Continuing Care Site (CCS).
  - HIE infants can be remotely consented either in hospital (at recruiting site or after transfer to CCS) or after discharge home

CCS does not need to be an approved CCS for remote consent.

# Screening and Consent

- **Eligibility -** no change to eligibility criteria, wording changed to make clearer period of time infants can be consented up to:
  - Preterm infants - up to 3 months post EDD
  - HIE infants - up to EDD plus 28 days
- **Screening** – Screening Log will have ‘under consideration’ option.
- **Recruitment letter to parents (HIE)** (new document) –letter which can be sent to HIE parents not approached or consented prior to transfer/discharge home.

# Supplementation

- No changes to supplementation, additional information/guidance.
- Treatment and control (not active and placebo).
- Difference between treatment and control supplements more clearly outlined (more detailed constituent parts not possible).
- Additional information e.g. making up with sterile water; continuous feeds.
- Clearer wording in protocol that parents can administer supplement in at CCS's and supplement can be started at CCS.
- Guidance for sites to allocate packs to parents at home.
- Sites can allocate a pack to go parent's home for both preterm and HIE infants (as both now can be remotely consented).

# Supplement Info for Parents

- Clearer guidance on methods of supplement administration – supplement ‘shot’ and bottle/tube feed.
- Supplement Leaflet and Dosing Charts colour coded for methods of feeding.
- More information for adding to weaning foods.
- Breastfeeding Leaflet optional in discharge pack.
- PIL includes information about transfers and potential pauses if approvals are not in place.

# Parent Information Leaflet (PIL)

- Reordering of sections, clearer and more concise.
- **Supplement** – make clearer differences between treatment and control supplement; rational and potential benefits.
- **What taking part involves** - bulleted list (adherence reporting, app).
- **Transfers and Continuing Care Sites** – details process for transfers and supplement may be paused at another hospital.
- **Summary PIL** (new document) – one sheet with QR code to introductory video, can be used initial approach.
- **Easy Read PIL** (new document) – simplified visual version of PIL available to give to families.

# PIL changes

DOLFIN

Developmental Outcome of Long-term Feed Supplementation in Neonates

## Introduction to the DOLFIN Study

The DOLFIN study aims to find out if adding a daily nutrient supplement to a baby's usual milk and weaning food can help improve their neurological child development.

Babies born very early or who have difficulties around birth have a higher risk of problems with neurological child development (e.g. how they think, communicate, play, and interact with others) than babies born close to their due date.

A small UK study using the same supplement showed it was safe, and that it may improve neurological child development, but we need to find out more. We'd like to invite you and your baby to take part in a new study using the supplement to help us find out more.

### Your baby's involvement

Babies taking part will receive either a nutrient treatment supplement or a control supplement. You cannot choose which supplement your baby will receive. So we can properly measure whether there is any difference between the effects of the treatment and control supplements, you and your health professionals won't know which supplement your baby is receiving.

### What is the supplement?

The supplement is a powder which is mixed with your baby's usual milk or weaning foods, and is given every day for around one year. It can be given alongside any medication, fortifiers or vitamins your baby is receiving.

The treatment supplement contains nutrients needed for healthy brain development, within Recommended Daily Amounts. The control supplement contains most of the same nutrients as the treatment supplement but in much smaller amounts.

### Taking part

While your baby is in hospital, the staff caring for your baby will give the supplement and then help you to do this. You will need to continue the supplement at home.

We will ask you to tell us how much supplement you have given your baby each week using the DOLFIN study app, or by text or email.

There are short questionnaires to fill out when your baby joins the study, at hospital discharge, and at 3, 6, 12, 18 and 24 months of age.

### Further information

For more information about the study, please see the DOLFIN Parent Information Leaflet. If you have any questions please ask the staff caring for your baby. You can also contact the DOLFIN study team at *dolfin@npeu.ox.ac.uk*

We have a video about the study on our website.

To watch follow the link (*www.npeu.ox.ac.uk/dolfin*) or use this QR code.



## WHAT IS THE DOLFIN STUDY ABOUT?

DOLFIN

The DOLFIN study is aiming to find out if a nutritional (food) supplement can help child development.

The research team carried out a small study using the supplement. This showed the supplement is safe, and may help child development. Now we need to do a bigger study to find out more.

We will look at whether the supplement helps with things like how a child thinks, communicates, and plays.

If the study shows that the supplement helps child development, it might be given to other babies in the future.

This leaflet will tell you more about the study.

If you would like to watch a video about the study, follow the link (www.npeu.ox.ac.uk/dolfin), or scan the QR code.

# Adherence Reporting (parents)

- **Adherence data** *(if infant receiving supplement) is* important:
  - to identify infants not receiving supplement (potential barriers)
  - for data analysis, to show that any difference is due to supplement vs. supplement not being given.
- Added question about giving supplement to parent questionnaires as extra source *(but adherence data priority).*
- Information from parents/sites via email/phone cannot be used as adherence data – must be via agreed method.
- Balance between minimising parent/site burden, and data required for trial validity.

# Adherence Reporting (parents)

- **Support parents with using app** – download prior to discharge (checklist), app user guide, outlined in PIL.
- **Offer alternatives to study app**:
  - Link via text/email (same as parent questionnaires)
  - Site completes via link directly onto OpenClinica *(notify NPEU as requires set-up)*
  - **Paper adherence diary (new document)**
- **Contact letter to parents** – template letter to send to parents via post if non-contactable *(last option after previous attempts made, discuss with NPEU)*

# Adherence Reporting (parents)

**Change:** Report adherence daily for first month (previously 3 months), report weekly after 1 month

  – reduces burden for parents, 1 month gives parents and sites time to feel confident with dosing.

- Parent cannot choose whether they report daily or weekly.
- Parents can choose whether they receive daily or weekly reminders (via app settings – see app user guide).
- **Supplement should be given daily, only reporting / reminders changes.**

# Adherence Reporting (parents)

- **Paper adherence diary (new document)** - alternative to using study app or link via email/text *(study app preferred where possible).*
  - Parents complete daily diary for 1 month, and then move to weekly diary *(same as study app)*.
  - Returned via FREEPOST envelope to NPEU who enter onto OpenClinica.
  - If parent returns to site photocopy and enter onto OpenClinica.

# Parent Questionnaires

- **Maternal data collection** – added text that some questionnaires ask about maternal quality of life, so prefer all are completed by person who gave birth if possible.
  - Baseline relates to maternal data so should be completed by mother, other questionnaires mother preferred.
- **Questions about breastfeeding** moved from start to later (based on feedback about emotions around breastfeeding).
- **3, 6, 12-month questionnaires:** added a new question asking how often parent has been giving supplement, to source adherence data in case parents are unable or unwilling to report on a daily/weekly basis. We still want adherence data where possible.
- **Paper CRFs** given as option more readily *(electronic completion preferred).* Returned via FREEPOST envelope to NPEU to enter onto OpenClinica. If parent returns to site photocopy and enter onto OpenClinica.

# Site CRFs

- **Randomisation/Trial entry form** – amended questions to take into account remote consent; asks if infant is at a recruiting site, a continuing care site, or home.
- **HIE NE questionnaire** - added wording about assigning total score if daily assessments not carried out.
- **Transfer/Discharge form** - added option for “no imaging performed” for worst scan; worst scan can be post-discharge.
- **Change of consent** - added in wording clarifying which question goes with which optional clause on consent form.
- ***Supplement starter form*** *– to be completed for all infants, will ask if started at home or in hospital (TBC)*

# Promotional

- **Eligibility cards** (new document) – for site staff to carry or placed in staff areas for reference:
  - Inclusion/exclusion criteria
  - QR code links to introductory video (can be used with parents)
- **QR cards** (new document) – for site staff to use in parent approaches or placed in clinic spaces for parents to take.
  - QR code links to introductory video about study.
- **Parent poster** – updated to emphasise two stratum and that HIE infants can be recruited post-discharge.
- **Postcard** – can be given to parents (in–person or via post) or left in clinic spaces for parents to take.

# DOLFIN

**This study is for infants born less than 28 weeks and infants born at 35 weeks or more who have received cooling therapy for Hypoxic Ischaemic Encephalopathy (HIE)**

**www.npeu.ox.ac.uk/dolfin**

## Inclusion Criteria

- ✓ Preterm stratum: Infants born less than 28 weeks of gestation, up to discharge home (can be consented 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 consented up to EDD plus 28 days)
- ✓ Individual with parental responsibility able to give consent
- ✓ 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

DOLFIN Eligibility Card V1.0, 02-10-2023 IRAS: 303421


## Dear Parents,

**If your baby was**

Born less than 28 weeks old

OR

Born at 35 weeks or more and has received cooling therapy for Hypoxic Ischaemic Encephalopathy (HIE)

**They may be eligible to take part in the DOLFIN Trial**

**The DOLFIN trial is looking at whether giving a specially developed nutritional supplement via breast or formula milk helps with brain development.**

If your baby is eligible you may be approached about joining this study, or if you want to find out if you may be eligible please ask your local hospital team.

**For more information please contact:**

DOLFIN Trial Manager dolfin@npeu.ox.ac.uk 01865 617919

**www.npeu.ox.ac.uk/dolfin**

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The Newcastle upon Tyne Hospitals NHS Foundation Trust

NPEU Clinical Trials Unit

Oxford Population Health NPEU

DOLFIN Postcard v1.0, 27-09-2023 REC Ref: 20/EM/0003 IRAS ID: 303421

# Diversity and Inclusivity

- **Easy Read PIL and Supplement Leaflets**
  - Parents must consent using main PIL
  - These are supplementary documents which can be offered to families to support participation
    - e.g. introduction to study; partner/wider family; language barriers; people who find simplified or visual document easier to understand.
- Due to post-discharge requirements (e.g. questionnaires, supplement dosing, adherence reporting), parents need to have a level understanding of English, or support from home, to consent to the study (site decision).

# Diversity and Inclusivity

- We are working with groups who specialise in diversity to discuss next steps.
- Identifying and resolving barriers to recruiting families from minority groups:
  - Short introductory videos in different languages
  - Translations or post-discharge language support
  - Networking with cultural and religious community groups and PPI stakeholders

# Other changes

- **Localisation** – only PILs and Supplement Leaflets (main and Easy Reads) will have local contact details *(we can provide local contact detail labels).*
- Reference to EDEN co-enrolment and data sharing removed *(as no longer taking place).*
- **Change of consent:** clarification to wording, change of consent only if parent changes consent to something (e.g. questionnaires); discontinuation of supplement only is not change of consent.
- **Safety Reporting:** additional foreseeable SAE's. Guidance Sheet – clearer guidance on which SAE's are reportable/non-reportable.

# When will amendment be implemented?

- Received ethical approval for amendments (Sub Amend 4 and 5) – sent to sites, 35 days to raise objection.
- Hardcopy documents will be sent to sites (please confirm any changes to contact details asap) *(in process)*
- To ensure sites are using the same documents across the trial and to ensure systems updated (study app, OpenClinica) we are planning for a global implementation date of 28th November (we will confirm).
- Continuing Care Sites will be sent relevant updated documents.

# What do sites need to do?

- Confirm any changes to local contact details as soon as possible
- File any electronic documents in eISF
- Confirm receipt of hardcopy documents *(when received)*
- Complete and sign notice of new documentation *(when received)*
- Review documents to familiarise yourself with changes, read all updated guidance sheets carefully *(summary of document changes provided).*
- Completing Training Log not required but sites may find it useful.
- Await R&D confirmation of continued C+C. If R&D do not raise an objection within 35 days the amendment can be implemented.
- Await email from DOLFIN study team confirming amendment can be implemented.