neoGASTRIC

Guidance Sheets
1,2,3,4,5,6,7,8,9,11

V2.0, July 2025

This study is funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (Reference Number [NIHR134216]).
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1. neoGASTRIC Trial Summary

GUIDANCE SHEET 1

The neoGASTRIC Trial

Avoiding routine gastric residual volume measurement in neonatal critical care. A multi-centre, pragmatic, unblinded, 2-arm, parallel group, opt-out, randomised controlled trial, with an internal pilot (and embedded process evaluation), and an integrated health economic analysis.

WHY?

To determine whether avoiding the routine measurement of gastric residual volumes in preterm infants less than 34 weeks' gestation reduces the time taken for an infant to reach full enteral feeds without increasing harm.

WHO?

7040 infants will be recruited across hospitals in the UK and Australia, who fulfil the following eligibility criteria:

Inclusion criteria:

- Gestational age at birth less than 34^{+0} gestational weeks^{+days}
- Nasogastric or orogastric tube in place

Exclusion criteria:

- Infant has received more than 15 ml/kg/day of milk for more than 24 hours
- Gastrointestinal surgical condition prior to randomisation
- Major congenital abnormalities
- No realistic prospect of survival
- A parent has opted out of infant's participation in neoGASTRIC

WHAT?

Two standard care pathways will be compared:

1. No routine measurement of gastric residual volumes, and
2. Routine, up to 6 hourly, measurement of gastric residual volumes

The allocated care pathway will be followed:

- for as long as routine gastric residual volume measurement is standard local practice or,
- gastric feeding tubes are no longer required or,
- the infant is discharged home or,
- the infant reaches 44^{+0} gestational weeks^{+days}

WHEN?

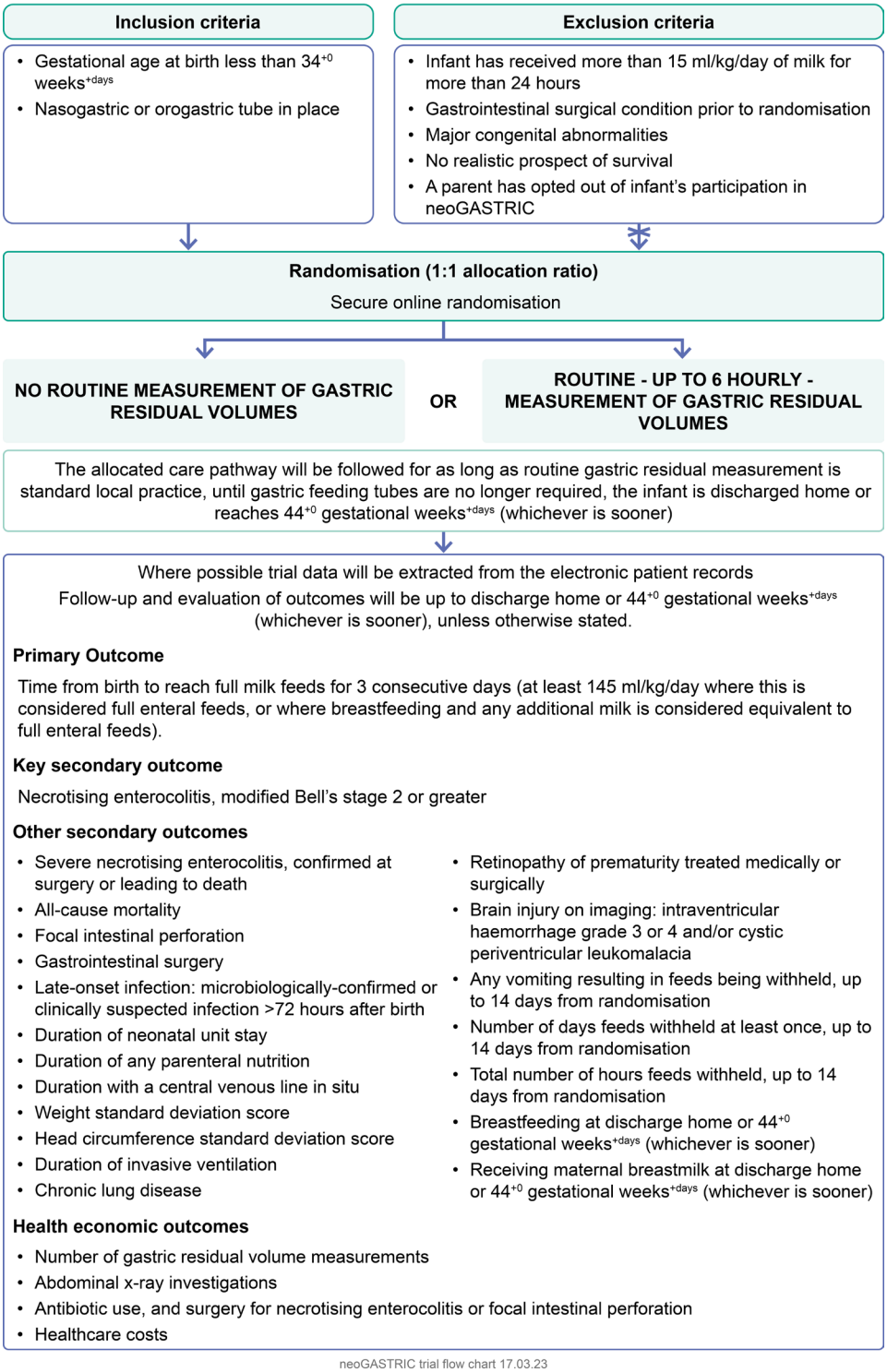
Recruitment started in 2023 and the plan is to end in early 2026.

HOW?

The neoGASTRIC trial is funded by the NIHR and the NHMRC and is NIHR portfolio adopted. The trial will be coordinated separately for UK and AU sites with dedicated trial management teams:

- National Perinatal Epidemiology Unit Clinical Trial Unit (NPEU CTU), University of Oxford, Oxford, England.
- Monash Newborn, Monash Children's Hospital, Monash Health, Clayton, Australia.

The neoGASTRIC Trial: Avoiding routine gastric residual volume measurement in neonatal critical care



neoGASTRIC trial flow chart 17.03.23

CONTACT

For all queries please contact the Trial Coordinating Centre, National Perinatal Epidemiology Unit Clinical Trials Unit (NPEU CTU) via email: neogastric@npeu.ox.ac.uk or telephone: 01865 617927.

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2. Screening, Eligibility, Enrolment & the Screening Log

GUIDANCE SHEET 2

Screening infants to check eligibility

Appropriately trained and delegated clinicians, research nurses and healthcare professionals can carry out screening and eligibility checks. *Please note that these members of staff must be trained and listed on the delegation log.*

The inclusion and exclusion criteria for the study are:

Inclusion criteria

- Gestational age at birth less than 34^{+0} gestational weeks^{+days} (up to and including 33^{+6} gestational weeks^{+days})
- Nasogastric or orogastric tube in place

Exclusion criteria

- Infant has received more than 15 ml/kg/day of milk for more than 24 hours
- Gastrointestinal surgical condition (including suspected necrotising enterocolitis (NEC) and focal intestinal perforation) prior to randomisation
- Major congenital abnormalities
- No realistic prospect of survival
- A parent has opted out of infant's participation in neoGASTRIC

Notes on eligibility criteria:

- If the infant has suspected NEC, do not include the infant.

- An infant can be enrolled if they have a congenital anomaly that would not affect the way that the infant can be fed, compared to another infant without the congenital anomaly but of a similar gestational age. *Please note that the exclusion criteria lists major congenital anomaly, which is left open for a local clinician's discretion.*

- If you think a parent/carer is not able to make an informed decision about the study and what is involved, please do not enrol the infant and make a note in the infant's patient notes.

Maximising study awareness:

Posters and a banner are provided. Please put these up in prominent places around your unit e.g., breastfeeding rooms, parent kitchen/break-out rooms, parental boards and corridors, and reception areas. Additionally, please use promotional and stationery items, which could act as visible reminders for screening and recruitment.

What to provide to parents

The printed neoGASTRIC parent information sheet (PIS) can be shared with parents/legal guardians:

- At antenatal or neonatal clinics and/or once the infant is admitted to the ward (NICU/LNU/SCBU).
- The PIS is available in additional languages. *Please see Section 1 of the document box.*
- We also suggest adding the PIS to your admission pack.
- If you were selected to receive a tablet in your document box, please use this to show the parents/legal guardians the neoGASTRIC video presentation.

Enrolment

Infants that meet the eligibility criteria (and parents have not opted them out) should be randomised and included in the trial.

Co-enrolment to other studies:

neoGASTRIC is supportive of co-enrolment in other interventional studies and other studies will be crosschecked to ensure compatibility. Please refer to the FAQs on the website for the most up to date details - FAQs | neoGASTRIC | NPEU. **If you have any queries regarding co-enrolment, please contact the neoGASTRIC Coordinating Centre.**

Screening Log

Please complete the Screening log for all infants on your unit who were born preterm at less than 34^{+0} gestational weeks^{+days}. **Please note that all infants that have been randomised will automatically be added to the Screening Log.**

- The neoGASTRIC screening log should be completed online via the randomisation website. This can be reached from the *screening log* link on the randomisation home page.
- The Local ID should not be the infant's NHS number.
- The screening log can be updated periodically i.e. monthly

PLEASE DO NOT ADD ANY PATIENT IDENTIFIABLE INFORMATION ON THE SCREENING LOG

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3. Opt-out Consent

- **Opt-out consent makes it easier for parents and infants to take part in research**
- **The parent information sheet makes it clear that opt-out consent is being requested**
- **The Parent Information Sheet (PIS) must be given to parents before the infant is randomised**

Why opt-out consent?

1. **Both interventions in the trial are standard procedures already performed in hospitals across the UK.**

2. **There are no parent questionnaires and no follow-up required after discharge.**

3. **The trial does not involve administering any medications.**

This trial addresses a practice that varies among hospitals, where, outside the neoGASTRIC trial, care allocation depends on the hospital or staff. The neoGASTRIC trial uses formal randomisation of different care pathways to determine the optimal approach.

How does opt-out consent work in practice?

Even though neoGASTRIC uses an opt-out consent model, it is still important that parents/carers/ legal guardians are provided with information about the trial so they have an opportunity to opt their infant out of the trial if they so wish.

The guidance below aims to help ensure that we are consistent in how parents are informed about neoGASTRIC and their ability to opt out of the trial for their infant.

- **Parent Information Sheet must first be given to parents/carers**

For example, when giving out leaflet/pack you might say: 'We are a research active unit and one research study we are taking part in is called neoGASTRIC. There is more information about neoGASTRIC in this pack. Your baby will be included in the neoGASTRIC study unless you tell us you don't want your baby to take part – you can do this at any time'.

- **No need to discuss trial with parents**
  - But be available to discuss if parents/carers have questions

- **Only record in infant's notes if parents opt-out**
  - They will have around 24 to 48 hours to do this in almost all cases, and in many cases a lot longer (given how long it takes for an infant to be established on feeds >15ml/kg/day for more than 24 hours in many neonatal units).
  - It is optional to record that parent information sheet has been given to parents, but we suggest this is good practice to do for your records.

GUIDANCE SHEET 3

Key Notes and Responsibilities:

1) **Displaying Information**
    a) Please display **neoGASTRIC posters and banners** prominently in areas parents frequently use in your unit e.g., breastfeeding rooms, parent kitchen/break-out rooms, parental boards and corridors and reception areas.
2) **Informing Parents/Carers**
    a) Ensure parents, carers, or legal guardians receive the Parent Information Sheet upon their infant's admission to the neonatal unit, ideally as part of an admission pack, prior to randomisation.
    b) Even if parents have seen neoGASTRIC materials antenatally, give them the leaflet again upon admission so they can **make an informed decision**.
    c) Provide information at a suitable time, particularly delaying for very sick infants if necessary.
3) **Follow Guidance Sheet 4 when randomising an infant**
    a) Infant's, who are meeting the eligibility criteria and whose parents have **not opted out**, will be randomised and included in the trial. An infant is eligible to be randomised up until the point where they have been receiving more than 15ml/kg/day of milk for more than 24 hours.
4) **Ensuring capacity**
    a) It is important for site staff to determine whether it is feasible for parent/carer to fully understand the opt-out consent process (language barrier, mental capacity etc.).
        - PIS is available in the 10 most common UK languages to support this.
            - Local translation support can also be used if relevant.
        - If the parent/carer cannot understand the process, record this in the infant's notes and do not recruit.
5) **Ensuring consistency in communication**
    a) Ensure that all site staff are thoroughly acquainted with the trial details to answer any parent questions and provide consistent information.
    b) **Ongoing Parental Awareness:** If an infant has been enrolled in neoGASTRIC, parents should be aware that their infant is part of the trial and that they could have opted out at the beginning or can at any time during the trial.

There **will not be a signed consent form** for the trial.

Parents should know that their infant is in the trial, and they should know that they can ask for their infant not to be in neoGASTRIC.

Parents can opt out both before and after randomisation. For detailed instructions on what to do in those cases, please refer to Guidance Sheet 7.

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4. Randomisation

Before Randomisation

Please ensure the following steps are completed before randomising infants into the neoGASTRIC trial:

- **Eligibility Confirmation:**
  A delegated individual listed in the neoGASTRIC Site Delegation Log must confirm eligibility.
- **Opt-out Status:**
  Verify that the parent has not opted out of the study
- **Parent has received the Parent Information Sheet**.

Randomising infants to neoGASTRIC

The randomisation process is conducted through a secure, web-based randomisation tool hosted by the NPEU CTU Oxford. Telephone backup is available at all times for assistance.

- **Training:**
  Training on how to use the randomisation tool will be provided through a short instructional video. This video will guide you through the process step by step.

- **Access:**
  Your site will receive a username and password to access the web-based randomisation tool in the document box on a sticker.

- **Technical Support:**
  If you experience any technical difficulties, please refer to the technical support section at the end of this guidance sheet.

Quick guide to completing Randomisation

To randomise an infant, please follow the following steps:

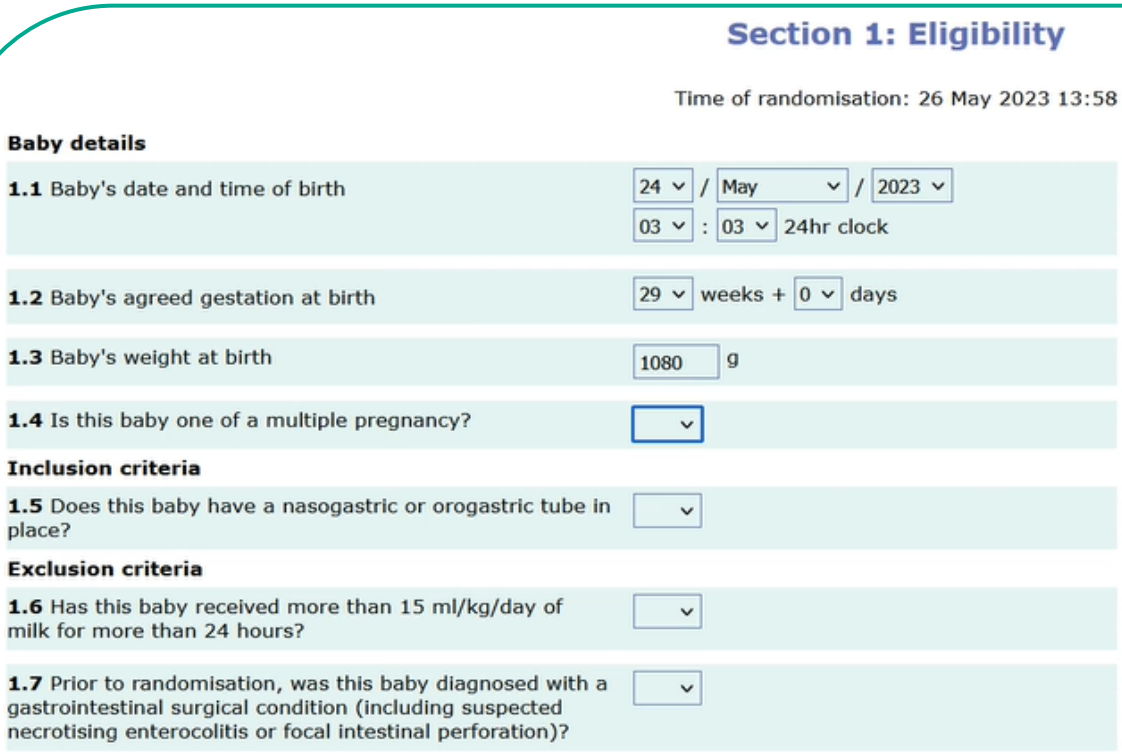
1) Access the online randomisation website at: https://rct.npeu.ox.ac.uk/neogastric/
   a) Select your centre from the drop-down list
   b) Enter your site username and password (located in your neoGASTRIC Document Box)

2) Once logged in, click "Enter baby"
   a) Complete the questions related to eligibility of the infant. The person completing the form must be on the Delegation Log for randomisation.
   b) Once the form has been completed, click "Continue"

   Note: If any data indicates the infant is ineligible, the system will flag it, and you will be unable to proceed *any further.*

GUIDANCE SHEET 4

Checking Eligibility



Section 1: Eligibility

Time of randomisation: 26 May 2023 13:58

Baby details

1.1 Baby's date and time of birth	24 / May / 2023 03 : 03 24hr clock
1.2 Baby's agreed gestation at birth	29 weeks + 0 days
1.3 Baby's weight at birth	1080 g
1.4 Is this baby one of a multiple pregnancy?	
Inclusion criteria	
1.5 Does this baby have a nasogastric or orogastric tube in place?	
Exclusion criteria	
1.6 Has this baby received more than 15 ml/kg/day of milk for more than 24 hours?	
1.7 Prior to randomisation, was this baby diagnosed with a gastrointestinal surgical condition (including suspected necrotising enterocolitis or focal intestinal perforation)?	

If unsure about the infant's eligibility please discuss with the local PI before progressing with the randomisation.

3) Please add **your name and email address (not the baby's name)**

4) Check that the data are correct. If any information is incorrect, click "Amend" and enter the corrected information before clicking "Complete"

5) On the randomisation screen, each infant will be assigned a neoGASTRIC Study Number and allocated to one of the following:
   - **No Routine Measurement of Gastric Residual Volumes**
   - **Routine, Up to 6-Hourly, Measurement of Gastric Residual Volumes**

Note: Multiples should be randomised to the same arm

Each time an infant is randomised a notification email will be sent to site staff that have been requested to receive this. If you want to add or remove anyone from this list, please email the neoGASTRIC team.

Contact Details

After randomisation, click the "Enter contact details" button. This will open up a new window to enter the additional details as required.

Technical Support

If you experience technical difficulties with internet access or the Randomisation website, or require technical support, please contact the neoGASTRIC study team using the contact details below:

- During office hours (Mon – Fri, 9am – 5pm), contact the neoGASTRIC study team on: 01865 617927 / neogastric@npeu.ox.ac.uk
- In the case of urgent out-of-hours queries, please see the **Emergency Queries Guidance Sheet**.

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5. Daily Feed Log & Late-onset Infections and Gut Signs Forms

GUIDANCE SHEET 5

DAILY FEED LOG

When to start and stop completing the Daily Feed Log

All infants must have a Daily Feed Log (Days 0 – 14) completed, covering 14 days after randomisation. After that, continue completing a Daily Feed Log (Day 15 onwards) until:

- the infant has reached full feeds for the last three consecutive days **OR**
- the infant no longer requires a gastric feeding tube **OR**
- the infant is aged 44^{+0} gestational weeks^{+days}
- the infant has been discharged

Please note that: if an infant reaches full feeds during the first 14 days post randomisation, the whole feed log must still be completed for the 14 days, but the feed log then stops here.

On the day of randomisation (Day 0)

The day of randomisation (Day 0) will nearly always be a partial day. Therefore, complete the daily feed log for the whole 24-hour period, irrespective of the time of day the infant was randomised. The feeding log should then be completed for each calendar day (24 hours from 00:00) onwards.

Enteral feeds

The known total milk feed volume per day should include all types of milk received. If the infant is mixed feeding, both expressed breast milk and supplement milk should be included in the daily total. If the infant is breastfed at all, please tick the 'baby sucking at the breast' option.

Withheld feeds

If an infant has had their feed withheld due to clinical reasons or vomiting, the clinical reasons **do not need to be captured**. Just enter the total time, in hours, for how long feeds were withheld that day. There is a section on the form to record whether the infant was nil by mouth (with the intention that this was for 4 or more hours). If this occurs for five consecutive days, **consider a Late-onset Infection and Gut Signs Form.**

Reaching full feeds

Full feeds are when an infant has reached about >=145ml/kg/day for three consecutive days. If an infant is being breastfed, in addition to having a gastric tube, it will be up to the clinical staff to decide when an infant has reached full feeds.

If an infant has not reached full feeds after 14 days, please continue recording on the Daily Feed Log (day 15 onwards) until:

- the infant has reached full feeds for the last three consecutive days **OR**
- the infant no longer requires a gastric feeding tube **OR**
- the infant is aged 44^{+0} gestational weeks^{+days} **OR**
- the infant has been discharged.

LATE-ONSET INFECTIONS & GUT SIGNS FORM

When to complete the Late-onset Infections & Gut Signs form

You will need to complete the Late-onset Infections and Gut Signs form if any of the following are applicable:

- If an infant has an episode of microbiologically-confirmed or clinically-suspected late-onset (blood or CSF) infection (72 hours or more after birth)
- If an infant has received at least 5 days of intravenous antibiotic or antifungal treatment for suspected or proven late-onset infection (not prophylaxis)
- If they are transferred to another unit with presumed late-onset infection
- If they have died from suspected or proven late-onset infection
- If they have received at least 5 days of treatment for gut signs
- If they are transferred to another unit with gut signs
- If they have surgery for gut signs
- If they have died with gut signs

Please continue to complete the Infection & Gut Signs forms until the infant has been discharged home, withdrawn or reached 44^{+0} weeks gestational age.

Antibiotic / antifungal treatment

The Daily Feed Log also includes a section to record whether the infant was given antibiotics or antifungals intravenously for treatment of suspected or proven infection. When this occurs for five consecutive days, **complete a Late-onset Infection and Gut Signs form.**

Do not answer "Yes" on the feed log to the question about antibiotics/antifungals if these were given for prophylaxis.

If antibiotic treatment occurs 72 hours or more after birth

This counts as a late-onset infection. Please complete the Late-onset Infection and Gut Signs form for this infant.

Please remember to refer to the neoGASTRIC website for a comprehensive list of all FAQs related to data collection and all other aspects of the study.

Enquiries

For all queries please contact the Trial Coordinating Centre, National Perinatal Epidemiology Unit Clinical Trials Unit (NPEU CTU) via email: neogastric@npeu.ox.ac.uk or telephone: 01865 617927. For any urgent queries outside of office hours (9am – 5pm) please see: **Guidance Sheet 9: Emergency Queries**

GUIDANCE SHEET 5

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6. Transfer of infants

IMPORTANT: PLEASE NOTIFY TRANSFER SITE OF ANY PLANNED OR COMPLETED INFANT TRANSFERS AS SOON AS POSSIBLE

Note: Do not share participant identifiable data when contacting the transfer site or neoGASTRIC team

Completing the Transfer to an approved or unapproved Continuing Care Site (CCS)

Infants should be transferred according to usual local processes regardless of a site's involvement in the neoGASTRIC study.

When an infant is being transferred to another site (recruiting, approved or unapproved Continuing Care Site), sites should:

1.	Contact the receiving site to inform them that the infant is in the neoGASTRIC study. Key contact details for neoGASTRIC sites can be found on the website - Sites | neoGASTRIC | NPEU. If unsure of a site's participation in the neoGASTRIC study, please get in touch with the neoGASTRIC Coordinating Centre
2.	Provide a photocopy of the Daily Feed Log or print out of the last 5 days and include this in the neoGASTRIC Transfer Pack (if feed log is still being completed)
3.	Send the appropriate neoGASTRIC Transfer Pack for the study arm the infant was allocated to with the infant for transfer
4.	Complete the Transfer/Discharge form in OpenClinica
5.	Enter all data into OpenClinica as it is returned by the receiving/transfer site.

To note:

- When a transfer is to a site that is not participating in the neoGASTRIC study, please still try to collect as much known data as possible from the electronic patient record. If the discharge date is known, please do complete a Transfer/Discharge form with as much known information.
- When a transfer occurs overnight or over the weekend, please continue to let the transfer site know that the infant is participating in the neoGASTRIC trial, even if this information reaches the new site a day or so after the transfer has occurred.
- If you are having any issues with contacting the Continuing Care Site, please get in touch with the neoGASTRIC Coordinating Team.
- **If an infant transfers to another recruiting site, you can just send an empty transfer envelope with the front cover completed.**

GUIDANCE SHEET 6

Study Number: ☐☐☐☐☐

neoGASTRIC Infant Transfer Pack

neoGASTRIC

Complete this cover page if a neoGASTRIC baby is being transferred to another hospital:

Trial ARM

DO NOT Measure GRV

Baby Name: _____

Date of Birth: D D / M M / Y Y **Date of Randomisation:** D D / M M / Y Y

Name of Transferring Hospital: _____

Name of Receiving Hospital: _____

Has the infant reached full milk feeds? **Please note: Full milk feeds refers to 3 consecutive days of the infant being fed more than 145ml/kg/day from NGT/OG tube*

Yes ☐ **No** ☐

Has the infant completed 14 days after randomisation?

Yes ☐ **No** ☐

Please state the date and day the infant has reached on the feed log.

D D / M M / Y Y Day *(e.g. Day 15)*

If the infant has completed day 14 after randomisation and has reached full milk feeds, remove the feed log from this pack.

RECRUITING SITE TO ADD WHERE RELEVANT BEFORE SENDING:

- ☐ Photocopy of current Daily Feed Log
  OR print out of the Daily Feed Log just from the last 5 days
- ☐ One Thank you Card for parents if this has not been provided to them yet
- ☐ Ongoing SAE forms
- ☐ neoGASTRIC pen/post its
- ☐ Recruiting site address to the return envelope
- ☐ Recruiting site contact email address

Transfer documentation prepared by: _____ Date: D D / M M / Y Y

GUIDANCE SHEET 6

Key points to remember

- When a Continuing Care Site returns a completed paper version of the **Daily Feed Log**, it will be the responsibility of an individual at the original recruiting site to enter this data into OpenClinica.
- The Continuing Care Site (receiving site) should notify the initial recruiting site as soon as an infant has been discharged, transferred, or died.
- In the event of twins or higher order multiples, a separate **neoGASTRIC Transfer Pack** should be sent for each individual infant.

Continuing Care Sites must continue to report safety events (e.g. SAEs) until the infant has reached 44^{+0} gestational $weeks^{+days}$ or been discharged home.

! A reminder that it is the recruiting site's responsibility to follow up with the receiving/transfer sites with reminders to both complete the paper data collection forms and to return these forms promptly to your recruiting site.

Enquiries

For all queries please contact the Trial Coordinating Centre, National Perinatal Epidemiology Unit Clinical Trials Unit (NPEU CTU) via email: neogastric@npeu.ox.ac.uk or telephone: 01865 617927.

For any urgent queries outside of office hours (9am – 5pm) please see: **Guidance Sheet 9: Emergency Queries**

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7. Withdrawal and Discontinuation of trial pathway

GUIDANCE SHEET 7

Once an infant has been randomised into the trial, a parent/carer can request that their infant's level of involvement of the trial be changed, reduced, or end entirely, at any point and for any reason.

This may include the parent/carer requesting that their infant's allocated trial pathway be permanently discontinued.

As well or instead of this, the infant's clinical care team may decide that the infant's allocated trial pathway needs to be permanently discontinued.

If a parent/carer requests that some or all data collection for their infant halts, this is a **withdrawal.**

The following events **do not** constitute a **withdrawal or a permanent discontinuation**:

- **Clinical need for gastric residual measurement:**
  If an infant allocated to the *No routine measurement of gastric residual volumes* care pathway develops a condition for which conducting a gastric residual measurement(s) is clinically indicated.

  Document this event on the Daily Feed Log. Once measurements are no longer needed, the infant should return to their original randomised care pathway, if clinically appropriate.

- **Error in randomisation:**
  If an infant is randomised in error (e.g., they are found ineligible), contact the neoGASTRIC Coordinating Centre (NPEU CTU) for guidance **before completing any forms or discussing with parents or carers.**

A. Withdrawal

If a parent wishes to withdraw their infant from some or all data collection for the trial, please follow these steps:

1. **Discuss Concerns:**
   If deemed appropriate, the clinical team should discuss any potential concerns or misconceptions related to withdrawal with the parent or carer.

2. **Clarify what the parent(s) would like to change:**
   - May the study team continue to use the infant's medical records for data collection?
   - Does the parent still give permission for indirect long-term follow-up using routine national databases?
   - Does the parent also want the infant's allocated trial pathway to halt?

Important: Agreement to ongoing data collection does not constitute a withdrawal but a discontinuation of the allocated trial pathway. Refer to section B of this guidance sheet.

3. **Reassure:**
    - Assure the parent or carer that withdrawal will not impact their infant's ongoing clinical care or hospital stay.
    - Inform them that data collected up to the point of withdrawal will be used in the study.

4. **Record the Withdrawal:**
    - Document the decision on the Withdrawal eCRF in OpenClinica.
    - Record the decision in the infant's medical notes.

5. **Detail the Reason:**
    - Include the reason for the withdrawal in the "Further Information" section of the eCRF if provided.
      Note: Parents are not obligated to provide a reason for withdrawal.

If the parent(s) would also like to permanently discontinue their infant's allocated trial pathway, complete the steps outlined in Section B.

B. Discontinuation of allocated trial pathway

If a parent wishes to permanently discontinue their infant's allocated trial pathway, please follow these steps:

1. **Discuss Concerns:**
   If deemed appropriate, the clinical team should discuss any potential concerns or misconceptions related to discontinuation with the parent or carer.

2. **Confirm Permission for Data Collection:**
    - Remind the parent or caregiver about the following aspects of the trial:
        - The use of the infant's medical records for data collection after reverting to standard care.
        - For UK infants: the use on neoGASTRIC of routinely recorded clinical data from the National Neonatal Research Database
        - Indirect long-term follow-up using routine national databases

If the parent wishes for any of these to halt, this is a withdrawal and needs to be documented on the Withdrawal form. Please refer to the steps in Section A of this guidance sheet.

If the parent is willing for all data collection to continue, no withdrawal form needs to be completed.

(Note: the neoGASTRIC withdrawal form does not relate to any request for an infant's data not to be stored in the National Neonatal Research Database.)

3. **Reassure:**
    - Assure the parent or carer that the discontinuation of the trial pathway will not impact their infant's ongoing clinical care or hospital stay.
    - Inform them that data collected up to the point of discontinuation will be used in the study.

4. **Record the discontinuation:**
    - Document the decision on the Discontinuation eCRF in OpenClinica.
    - Record the decision in the infant's medical notes.

5. **Detail the Reason:**
    - Include the reason for the discontinuation in the "Further Information" section of the eCRF if provided.
      Note: Parents are not obligated to provide a reason for requesting discontinuation of trial pathway.

If a clinician wishes to withdraw or discontinue the allocated pathway of an infant in the best interest of the infants' health, the procedure detailed in Section B4-5 should be followed.

If you are unsure whether a Withdrawal or a Discontinuation form needs to be completed, contact the trial Coordinating Centre in the first instance to discuss.

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8. SAE & Incident Reporting

Procedures for Recording Adverse Events (AEs) and Reporting Serious Adverse Events (SAEs)

This guidance sheet outlines the different types of events that need reporting; in what timeframe these must be reported; and how to report them. For more information on safety reporting, please refer to the **neoGASTRIC Study Protocol – Adverse Events**

Key notes and definitions

Due to the nature of the patient population, a high incidence of adverse events is foreseeable during their routine care and treatment. Consequently, **only those adverse events identified as serious will be recorded for the trial.**

The **safety reporting window** for this trial will be from the time the infant is randomised until the end of trial follow-up (discharge home or 44^{+0} gestational weeks^{+days}, whichever is sooner).

Any staff member can report a safety event.

Definitions

ADVERSE EVENT (AE) is any untoward medical occurrence in a participant, which does not necessarily have a causal relationship with the trial intervention.

SERIOUS ADVERSE EVENT (SAE) is any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- is a congenital anomaly or birth defect (not relevant in this trial)

Other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

GUIDANCE SHEET 8

Events exempt from immediate reporting

Foreseeable SAEs that do not require expedited reporting via an SAE Form:

Outcomes

The following events are expected in the population, and information will be collected by recruiting sites during the intervention period as outcomes, therefore do not require reporting as SAEs. Data pertaining to these events will be reviewed by the Data Monitoring Committee (DMC) at a frequency to be determined by the DMC (at least annually).

- Death (unless cause not anticipated in this population)
- Necrotising enterocolitis or gastrointestinal perforation
- Bronchopulmonary dysplasia or chronic lung disease
- Late-onset infection
- Intraventricular haemorrhage (grade 3 or 4)

Known complication(s) of prematurity

Any event that is deemed by the investigator to be a known complication of prematurity at that gestational age should not be reported as an SAE but should be recorded in the infant's medical notes, as per usual practice. They do not require reporting as SAEs unless considered that they may be causally related to the allocated pathway of care, in which case they must be reported as detailed in *Section 8 of the Protocol*. All other serious adverse events are classed as unforeseeable SAEs and must be reported.

1. Causality assessment

Do not delay SAE reporting whilst awaiting a causality assessment.

A medically qualified individual, listed on the delegation log, must determine the relationship of each adverse event to the allocated pathway of care according to the following definitions:

Not related – where an event is not considered to be related to the trial allocation pathway.

Possibly – although a relationship to the trial allocation pathway cannot be completely ruled out, the nature of the event, the underlying condition, concomitant medication or temporal relationship make other explanations possible.

Probably – the temporal relationship and absence of a more likely explanation suggest event could be related to the trial allocation pathway.

Definitely – the trial allocation pathway is the most likely cause.

GUIDANCE SHEET 8

All SAEs labelled possibly, probably or definitely **will be** considered as related to the allocated pathway of care.

If an appropriate delegated individual is not available to make the causality assessment, send in the SAE Reporting Form without this information. Then resend the form as soon as this assessment has been made.

A Physician who is not a member of the study team may offer an opinion as to whether the event was related to the investigational intervention(s) and this opinion should be documented in the infant's medical records.

2. Reporting Serious Adverse Events

All unforeseeable SAEs, and foreseeable SAEs deemed causally related to the allocated pathway of care must be reported on the **SAE Report Form** to the relevant coordinating centre (UK or Australia) as soon as possible after the site becomes aware of the event being defined as serious. **If you have any issues accessing the online forms, please get in touch with your UK/Australian Coordinating Centre.**

Use one of the following SAE reporting methods:

1. Staff with access to the study electronic database on OpenClinica **should complete the SAE form online**. For sign off, please add signature directly onto OpenClinica. An automatic email notification to the coordinating centre staff will be triggered for SAEs reported electronically.

2. The eISF contains **editable PDF** versions of the forms. Once the PDF has been completed and saved, it must be printed and signed (a signature cannot be added through the PDF). A scan of the signed copy should be sent **via the TADA document upload tool or via email to the relevant coordinating centre**.

3. **Paper forms**, with instructions, are provided in the neoGASTRIC Document Box. The completed SAE form **must be scanned and emailed to the relevant coordinating centre** (for UK SAEs - neoGASTRIC Coordinating Centre neogastric@npeu.ox.ac.uk and for Australian SAEs - Newborn Research, Monash University School of Clinical Sciences (SCS) amy.hutchison@monashhealth.org)

4. Where the above routes are not possible, then the SAE may be reported **by telephone** to the local coordinating centre and the SAE form will be completed by the relevant Coordinating Centre. Please see the Emergency Queries guidance sheet.

To note: If printing from OpenClinica, click on the SAE form, then click through every SAE page before printing)

Ensure **ALL** details of the SAE are documented in the infant's medical records (if applicable), including the assessment of causality, which must be documented in the medical records. Please file the completed SAE Reporting Form in your eISF.

Follow-up SAE information should be reported by filling out a new SAE form and stating that it is a follow-up report in the relevant question.

Procedure for Recording and Reporting Incidents

Incident Reporting

Any deviations from the neoGASTRIC Study Protocol, study specific procedures, Good Clinical Practice (GCP) or regulatory requirements must be reported as soon as possible to the neoGASTRIC study team, using the **neoGASTRIC Incident and Deviation Reporting Form**. Any member of the team included on the neoGASTRIC Site Delegation Log can report incidents.

> Examples of incidents in this context might be a study activity performed by an individual not listed on the delegation log or who is listed on the delegation log but not delegated for that specific activity; forms not amended in accordance with GCP; consent forms not signed and dated correctly; or use of a superseded form.

Sites can complete the form either as an editable electronic (PDF) form (provided as part of the neoGASTRIC electronic Investigator Site File (e-ISF) or paper forms (provided in the neoGASTRIC Document Box) can be completed and scanned copies sent to neogastric@npeu.ox.ac.uk

If using the paper form, please complete all documentation clearly and legibly. If an error is made whilst completing the form, cross through the error with a single line with the initials of the person completing the form and date next to it.

PLEASE DO NOT SEND PATIENT IDENTIFIABLE INFORMATION

If you are unable to complete the 'resolution' section of the form in the first instance, send the partially completed form to the neoGASTRIC Coordinating Centre and then resend the form with 'resolutions' at a later date.

Copies of all completed **neoGASTRIC Incident & Deviation Reporting Forms (Incident Form)** relevant to the site should be filed in the e-ISF.

Serious Breaches

Incidents and protocol deviations will be defined as a serious breach if there is a breach of GCP or study protocol which is likely to affect to a significant degree either:

- The safety, physical or mental integrity of the subjects of the trial
- The scientific value of the trial

The neoGASTRIC study team will assess all reported incidents to determine if they should be classified as a serious breach.

GUIDANCE SHEET 8

This study is funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (Reference Number [NIHR134216]).
The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

9. Emergency Queries

Contacting the neoGASTRIC Trial Team

If you need to reach the trial team, please use the appropriate contact information below:

During Office Hours (9 AM – 5 PM, Monday to Friday)

- **Main Office Number:** 01865 617927
- **Alternative Numbers:** 01865 289714 or 01865 289747

Out-of-Hours (For Urgent Queries)

For urgent queries outside of office hours, please call **0800 138 5451.** This is a freephone number that connects you to a 24-hour emergency support call centre. Be prepared to provide the following information so an appropriate person can return your call:

- Your name
- The hospital you are calling from
- Your full phone number
- The name of the trial: neoGASTRIC

Non-Urgent Queries

If your query is not urgent, please use one of the following options:

- **Email:** neogastric@npeu.ox.ac.uk
- **Study Answerphone:** Leave a message on 01865 617927

GUIDANCE SHEET 9

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11. For Continuing Care Sites

GUIDANCE SHEET 11

General Information

The infant being transferred to your hospital is enrolled on the neoGASTRIC study.

neoGASTRIC is a multi-centre, unblinded, 2-arm, opt-out, randomised controlled trial. The aim of the neoGASTRIC trial is to determine whether avoiding the routine measurement of gastric residual volumes in preterm infants less than 34 weeks gestation reduces the time taken for an infant to reach full enteral feeds without increasing harm, up until discharge home or 44^{+0} gestational $weeks^{+days}$.

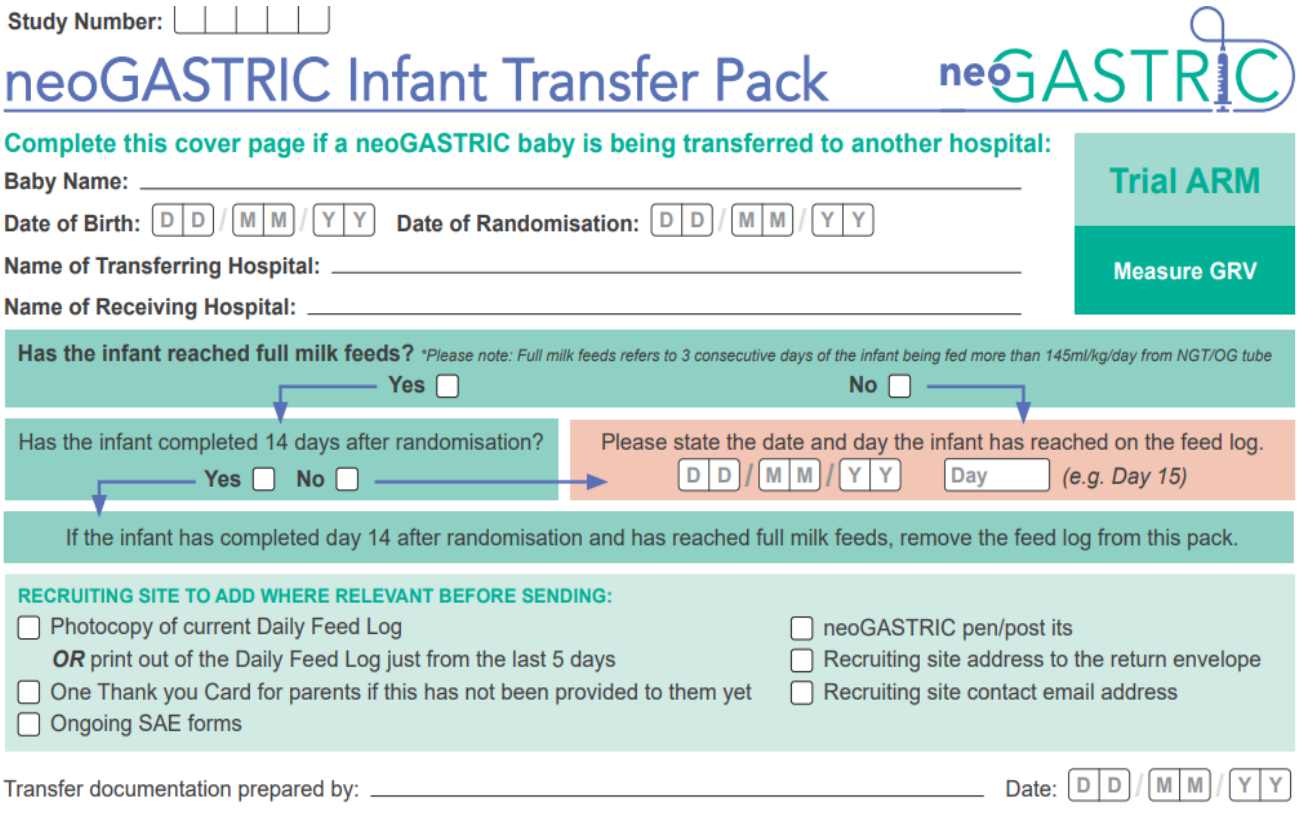
For further information about the study visit the study website https://www.npeu.ox.ac.uk/neogastric

Infants will have been randomised to one of the allocated care pathways:

No routine measurement of gastric residual volumes	OR	Routine – up to 6 hourly – measurement of gastric residual volumes

This Guidance Sheet provides guidance on the forms and supportive merchandise contained within the Transfer Pack which should have accompanied the infant. The Transfer Pack will also highlight which one of the allocated care pathways the infant is following.

An example of the 'Measure GRV' Infant Transfer Pack envelope:



Study Number: | | | | |

neoGASTRIC Infant Transfer Pack

Complete this cover page if a neoGASTRIC baby is being transferred to another hospital:

Trial ARM

Measure GRV

Baby Name: _____

Date of Birth: D D / M M / Y Y Date of Randomisation: D D / M M / Y Y

Name of Transferring Hospital: _____

Name of Receiving Hospital: _____

Has the infant reached full milk feeds? *Please note: Full milk feeds refers to 3 consecutive days of the infant being fed more than 145ml/kg/day from NGT/OG tube

Yes ☐ No ☐

Has the infant completed 14 days after randomisation?

Yes ☐ No ☐

Please state the date and day the infant has reached on the feed log.

D D / M M / Y Y Day (e.g. Day 15)

If the infant has completed day 14 after randomisation and has reached full milk feeds, remove the feed log from this pack.

RECRUITING SITE TO ADD WHERE RELEVANT BEFORE SENDING:

- ☐ Photocopy of current Daily Feed Log
  OR print out of the Daily Feed Log just from the last 5 days
- ☐ One Thank you Card for parents if this has not been provided to them yet
- ☐ Ongoing SAE forms
- ☐ neoGASTRIC pen/post its
- ☐ Recruiting site address to the return envelope
- ☐ Recruiting site contact email address

Transfer documentation prepared by: _____ Date: D D / M M / Y Y

Role of the Continuing Care Site

Instructions to the continuing care site

1. Continue with the allocated care pathway (where possible) until an infant is discharged home or reaches 44^{+0} gestational $weeks^{+days}$
2. Look at the red section on the front of the envelope and follow the instruction on either 3a or 3b

3a) If this section is blank, you do not need to complete any feed logs. Please go to number 4.

3b) If there is a date in the red section then please complete the feed log.

NOTE: All infants must have a Daily Feed Log (Days 0 – 14) completed, covering 14 days after randomisation. After that, continue completing a Daily Feed Log (Day 15 onwards) until:

- The infant has reached full feeds for the last three consecutive days ***OR***
- The infant no longer requires a gastric feeding tube ***OR***
- The infant is aged 44^{+0} gestational $weeks^{+days}$.

4. If required, complete the relevant reporting form(s) – enclosed in this envelope.
5. Inform the recruiting site when infant is discharged home or transferred.
6. Securely return all completed data collection forms to the recruiting site via secure email.

All data collection forms are on paper and copies are in the Transfer Pack. Once completed, please return to the recruiting site via secure email or post.

If you require additional forms, please get in touch with the neoGASTRIC Coordinating Centre.

See the next pages for guidance on the data collection requirements for neoGASTRIC

GUIDANCE SHEET 11

DATA COLLECTION

Completing the Daily Feed Log

The Daily Feed Log is the primary data that needs to be captured during the neoGASTRIC study. **Infants will transfer with either a complete or incomplete feed log. If the feed log is complete you do not need to continue collecting this data**.

For guidance related to the Daily Feed Log please refer to Guidance Sheet 5: Daily Feed Log & Late-onset Infections and Gut Signs Forms FAQs.

Completing all other reporting forms

Late-onset Infections & Gut Signs

You will need to complete the Late-onset Infections and Gut Signs form if any of the following are applicable:

- If an infant has an episode of microbiologically-confirmed or clinically-suspected late-onset (blood or CSF) infection (72 hours or more after birth)
- If an infant has received at least 5 days of intravenous antibiotic or antifungal treatment for suspected or proven late-onset infection (not prophylaxis)
- If they are transferred to another unit with presumed late-onset infection
- If they have died from suspected or proven late-onset infection
- If they have received at least 5 days of treatment for gut signs
- If they are transferred to another unit with gut signs
- If they have surgery for gut signs
- If they have died with gut signs

Please continue to complete the Late-onset Infection & Gut Signs forms until the infant has been discharged home, withdrawn or reached 44^{+0} weeks gestational age. **Please also remember to complete this form when the feed log prompts you**.

Transfer/Discharge

The Transfer/Discharge form is completed for infants when they either transfer to another hospital or are discharged home. This form is not applicable for any internal transfer that may occur, for example, transfer from NNU to a surgical ward.

If an infant is due to be transferred or discharged, you should:

1. Immediately notify the original recruiting site (see contact details on the back of the Parent Information Sheet or those that were provided with the transfer pack).
2. Complete the paper Transfer/Discharge Form. The PI at your site can sign off this form. If not available, the form can be returned to the recruiting site for their sign off.
3. Return the completed Transfer/Discharge form to the original recruiting site. The recruiting site will then input the transfer/discharge data into OpenClinica, which is the online data collection platform.

Incident Reporting

Deviations from the Protocol, trial specific procedures or Good Clinical Practice (GCP) must be reported to the neoGASTRIC Trial Coordinating centre using the Incident form. For guidance on how to report incidents please refer to Guidance Sheet 8. SAE and Incident Reporting.

GUIDANCE SHEET 11

Serious Adverse Event (SAE) Report

All Serious Adverse Event's (SAEs) that are deemed reportable (according to the protocol) must be reported as soon as possible after your site has become aware of the event. For the neoGASTRIC study, only adverse events identified as serious will be recorded.

! Please see Guidance Sheet 8. SAE and Incident Reporting for guidance on how to report an SAE and/or incident.

! To note: This guidance sheet states that individuals must be delegated to complete causality as documented on the neoGASTRIC Site Delegation Log however, for continuing care sites, this can be completed by any medically qualified investigator.

! To remember: Do not delay reporting an SAE whilst waiting for a causality assessment. The SAE can be sent to the neoGASTRIC trial coordinating centre initially without the causality assessment completed. An updated SAE form must then be sent to the recruiting site when the causality assessment is complete.

Withdrawals and Discontinuation

Parent(s) have a right to withdraw their infant from the study at any time and do not need to specify reasons for withdrawal. If the infant is being permanently withdrawn from their trial-allocated pathway of care or if the parent(s) express a wish to opt out of neoGASTRIC**, please contact the recruiting site to complete the appropriate paperwork**.

! To note: If an infant allocated to the non-measurement arm has developed a condition for which regular gastric residual measurement is clinically indicated, this does not mean a withdrawal or discontinuation. When regular gastric residual measurement is no longer clinically indicated the infant should be allocated back to their original trial arm if this is considered clinically appropriate.

Queries

Queries should first be directed to the recruiting site. Please see the Transfer Pack for the Recruiting Site Contact Details. You can also contact the neoGASTRIC Coordinating Centre with any queries. See contact details below.

Contacting the recruiting site

If you are having trouble contacting the recruiting site or if contact details were not provided with the Transfer Pack, please get in contact with the neoGASTRIC Coordinating Centre who will be able to link you with the recruiting site and share their contact details.

neoGASTRIC Coordinating Centre Contact Details

If you need to contact the neoGASTRIC Coordinating Centre, you can contact the team via email neoGASTRIC@npeu.ox.ac.uk or telephone during office hours (i.e., 09.00 – 17.00 Monday to Friday) on 01865 617927.

Out of hours

If you require any assistance outside of regular hours or have an emergency query, please see the Emergency Queries Guidance Sheet 9.

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