TOAST Study Summary and Preparation, Administration and Disposal of Allocated IMP

Purpose of this Training

This training sheet provides essential Good Clinical Practice (GCP) guidance for bedside staff who will be preparing, administering and disposing of the TOAST medication once it has been allocated and prescribed to a randomised TOAST participant. It outlines your responsibilities to ensure participant safety, trial integrity, and compliance with regulatory and protocol requirements.

Please ensure that **all bedside staff** complete the following before commencing TOAST Study IMP activity:

- Read this document and keep a copy for their reference. The **final page should be signed** as confirmation of training and **stored in your TOAST Site File**.
- Signed-off for the responsibility *'Preparation, administration and disposal of allocated IMP (on the Neonatal Unit)'* by the site PI (or Delegate) on the **TOAST Delegation log.**
- Any training required by the local hospital.

Key GCP Principles

Participant Safety

- The **rights, safety, and well-being** of TOAST participants take precedence over all other considerations.
- Discuss any safety concerns with the site TOAST PI, a member of the local research team, or the TOAST Study team at NPEU as soon as possible.
- Prior to discharge home, ensure that any death or Serious Adverse Reaction (SAR – a Serious Adverse Event that could be related to the TOAST medication) of a TOAST participant is **reported to the TOAST Study team at NPEU immediately (at least within 24-hours).**

Follow the Approved Protocol

- The TOAST medication should be prepared and administered **exactly as specified** on this training sheet according to the TOAST Study protocol.
- TOAST medication doses should be given according to the prescription. The route of administration can be determined by the infant's surgical team, based on their capability for enteral feeding post-surgery.
- Any **deviations** from the TOAST protocol or GCP requirements should be **reported as an incident to the TOAST Study team**. Complete an Incident Form (paper copies found in the TOAST Document Box) or report via email or phone.

Accurate Documentation

- Use a paper copy (see TOAST Document Box) of the **TOAST Daily Dosing Log** to **document each dose of TOAST medication administered** to a TOAST participant. Supplementary pages (see TOAST Document Box) are available if required. Alternatively, administered doses can be recorded using your sites electronic drug chart.

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- Each daily dose of TOAST medication should be confirmed by providing the name and signature of the bedside staff member administering the medication. The pack ID, route, infant's working weight and medication volume should also be recorded.
- If a dose of TOAST medication is missed, you should still complete an entry in the Daily Dosing Log, and give a reason for this missed dose.
- The Daily Dosing Log should also be used to **document disposal of unused vials or partially used bottles** of TOAST medication on the Neonatal Unit. This is important to ensure accountability of the TOAST medication whilst at site. If your site uses electronic drug charts, this disposal information must still be completed on the paper Daily Dosing Log.
- Once the Daily Dosing Log is complete (e.g. the TOAST participant has been discharged home, or has been allocated another pack of TOAST medication and started a new Daily Dosing Log), the Daily Dosing Log should be given to a member of the local research team.

Pack IDs	IV: ☐☐☐☐☐ Enteral: ☐☐☐☐☐						
Date (DD/MM/YY)	TOAST medication given?	Reason for not giving medication (see key*) if not given:	ID of pack used: (If not one of those at top of form, complete incident form, then continue completing this log)	Medication administered: Route: Intravenous or enteral medication given? (IV and Enteral have different pack IDs)	Infant's working weight (in kg):	Volume (mls):	Name & Signature
*Reason for not giving medication: 1 = Clinician decision, 2 = Pack availability, 3 = Other. If Other, give details							
D D / M M / Y Y	Yes ☐ No ☐		Pack ID ☐☐☐☐☐	IV ☐ Enteral ☐			
D D / M M / Y Y	Yes ☐ No ☐		Pack ID ☐☐☐☐☐	IV ☐ Enteral ☐			

*Example from **TOAST Daily Dosing Log v4.0 (07/01/2026)** - table to log administration of TOAST medication*

IV medication pack ID: ☐☐☐☐☐

Each vial to be administered intravenously as soon as possible after reconstitution and within 2 hours and the remainder to be disposed of. Complete this table for any vials not administered.

All vials must remain in the cardboard blinding shroud during disposal.

Vial number		Date disposed of:	Disposed of by:
	☐ Full vial disposed of (not needed) ☐ Damaged	D D / M M / Y Y	Name: Signature:

Enteral Medication Pack ID: ☐☐☐☐☐

Reconstituted bottles must be disposed of after 28 days or when the infant is transferred/discharged
Please complete below for each bottle from this pack

Number of bottles in pack (6 or fewer): ☐

Bottle number	If NOT reconstituted		If reconstituted:			
	☐ Transferred with infant to other hospital ☐ Sent home with discharged infant ☐ Not needed* ☐ Batch expired	*If "Not needed" / "Batch expired":* Date disposed of: D D / M M / Y Y Disposed of by: Signature:	Stored in fridge at 2 – 8ºC ☐	REC**: D D / M M / Y Y DIS***: D D / M M / Y Y	☐ Empty (used up) ☐ No longer needed* ☐ Passed discard date ☐ Damaged ☐ Batch expired	*For non-empty bottles:* Date disposed of: D D / M M / Y Y Disposed of by: Signature:

*Examples from **TOAST Daily Dosing Log v4.0 (07/01/2026)**– tables to log disposal of allocated intravenous/enteral TOAST medication vials/bottles on the Neonatal Unit*

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Pre-Administration Responsibilities

- Retrieve the TOAST medication from the pharmacy or Neonatal Unit storage location.
- Perform TOAST medication pack checks before administering the dose:
  - → Check the Study ID number of the participant matches the Study ID on the TOAST medication pack and vial/bottle.
  - → Check the TOAST medication expiry date is within range.
  - → For intravenous TOAST medication, check that the tamper-proof seals on the cardboard blinding shroud are intact. The TOAST intravenous medication vial should remain blinded (cardboard shroud to remain intact) throughout the preparation, administration and disposal process.
  - → For enteral TOAST medication, check the reconstitution date written on the IMP bottle label by site staff is within 28 days of today's date. Once the TOAST enteral medication has been reconstituted, it should be stored in a fridge at 2-8°C and has a shelf-life of 28 days. After 28 days, the bottle should be discarded and a new bottle reconstituted.

IMP Preparation and Administration

TOAST Study is a blinded clinical trial, and blinding should be maintained for all site staff and the participant's family throughout. Do not attempt to identify blinded products. Report any accidental unblinding to the TOAST Study team immediately.

At randomisation, each TOAST participant will be allocated one intravenous (7-day supply), and one enteral (approximately 6-months supply) TOAST medication pack.

Intravenous TOAST Medication

- Daily administration of 0.5 mg/kg dose until the infant is able to feed enterally.
- Each pack contains 7 vials, each providing up to one dose of medication.
- Follow these instructions exactly to ensure adequate reconstitution of a blinded vial of TOAST intravenous medication:

1. Remove the grey cap from the top of the vial and clean the stopper as per usual practices. ***Do not remove the cardboard blinding shroud***
2. Reconstitute the medication vial with 5 ml of 0.9% sodium chloride (with marketing authorisation) to obtain a solution containing 8 mg in 1 ml (or placebo).
3. Invert the vial 5 times to dissolve the powder.
4. Allow the vial to stand for at least 5 minutes to allow the powder to dissolve.
   Use the TOAST digital timer
   Follow steps 3 and 4 exactly, as you will not be able to visually check that the powder has dissolved due to study blinding
   You now have 5 ml medication in the vial at a concentration of 8 mg/ml.
5. Withdraw 1 ml of the medication solution from the vial into a syringe and add a further 15 ml of 0.9% sodium chloride. The resultant solution has a total volume of 16 ml and contains 0.5 mg in 1 ml (or placebo).
6. Move the syringe gently to disperse the solution evenly.
7. Withdraw the required volume of medication according to the prescription from the syringe prepared in Step 5 into a new syringe. Discard any remaining solution.
8. Administer as a bolus infusion over 10 to 30 minutes, **as soon as possible and within 2 hours of reconstitution.**

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Enteral TOAST Medication

- Daily administration of 1 mg/kg dose while the infant is able to feed enterally, until 1 year of age.
- Each pack contains 6 bottles individually sealed in foil pouches, each providing up to 28-days of medication doses.
- Follow these instructions exactly to ensure adequate reconstitution of a blinded bottle of TOAST enteral medication:

1. Remove a bottle from the foil pouch.
2. Check that the tamper-evident seal on the bottle is still intact. If the seal looks damaged, do not use the medication and contact the TOAST Study team.
3. The bottle is a two-compartment system and contains powder in both the red cap and the bottle. Shake the bottle for 10 seconds to loosen the powders.
4. Twist the red cap anti-clockwise until the seal is broken. The powder and a red mixing disc will drop from the red cap into the bottle. The red mixing disc should remain in the bottle, and should not be removed after reconstitution.
5. Twist the red cap back to the original position, making sure it is securely fastened onto the bottle.
6. Shake the bottle vigorously for 10 seconds to mix the powders.
7. Tap the base of the bottles 3 times to make sure all powder is in the bottle and not in the cap.
8. Reconstitute the powder with 64 ml sterile water using a suitable measuring device.
9. Securely fasten the red cap onto the bottle and shake vigorously for 30 seconds.
10. Finally, attach the bottle adaptor. To do this, remove the cap and red ring and throw these away. Insert the colourless, transparent bottle adaptor into the neck of the bottle, and replace the red cap with the grey plastic screw cap.
11. Leave the medication at room temperature for 15 minutes before use, to reach its final consistency. The medication concentration is now 2 mg/ml.
12. The dosage for the enteral medication is 1 mg/kg, and the concentration is 2 mg/ml. The volume to be given is 0.5ml/kg which can be given according the prescription. Administer the required volume using the oral syringe provided in the medication pack.
13. Store the reconstituted enteral TOAST medication bottle in the fridge at 2-8°C for 28-days.

IMP Disposal

Once allocated to a TOAST participant at randomisation, TOAST medication vials or bottles should be disposed of via normal waste routes on the Neonatal Unit. This applies vials/bottles that are empty, broken, partially used or beyond their shelf-life. Blinding should be maintained throughout the disposal process. Full, unopened packs of TOAST medication should be returned to Pharmacy for destruction if they have expired or are not required e.g. participant was not nil-by-mouth so did not require the intravenous TOAST medication.

Contact Details

Any queries, please contact your local research team, or:

TOAST Study team (NPEU CTU)
Email - toast@npeu.ox.ac.uk
Phone (office hours) – 01865 289278
Phone (urgent out-of-hours) – 0800 138 5451

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Pages 1-4 can be retained by the Neonatal Bedside Staff member for their reference.

This page should be signed by the Neonatal Bedside Staff member and stored in the TOAST site file as confirmation of training.

Confirmation of Training

I confirm that I have read the 'TOAST for Neonatal Bedside Staff: Study Summary and Preparation, Administration and Disposal of Allocated IMP' training document (**v2.0 30/03/2026**).

I will ensure that I am signed-off on the TOAST Delegation Log by the Site PI (or delegate) for the responsibility '*Preparation, administration and disposal of allocated IMP (on the Neonatal Unit)'* before commencing this study activity.

Name: _____

Hospital: _____

Role: _____

Date: _____

Signature: _____

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