

Overview

Case Report Form (CRF)	Format:	When to complete:
		Completed by recruiting site staff
		Completed by parent(s) / carer(s)
Consent form	Self-carbonating paper copy	As soon as parent(s) decide to take part (having had appropriate time to consider and ask questions) and before any data is collected
Randomisation Contact details form	TOAST Randomisation website	As soon as possible after the consent form is completed
Entry form	OpenClinica: Sections 1 and 2 are autocompleted from TOAST Randomisation website, Section 3 completed on OpenClinica	
Baseline questionnaire	Via email/SMS link to the mother of the infant, onto OpenClinica (paper available if requested)	As soon as possible after the consent form is completed
Daily Dosing log	Paper copy, then transcribed to OpenClinica	After randomisation, daily as TOAST medication is given
Discontinuation of medication	<i>If infant is in hospital: as paper copy (within Dosing Log) then transcribed onto OpenClinica</i> <i>If infant has been discharged home: OpenClinica</i>	Only if the infant has the TOAST medication permanently discontinued
Transfer/discharge form	OpenClinica	Whenever infant is transferred to another hospital, when they are discharged home, or if they die
Parent daily adherence data	Via the TOAST app	Daily for 28 days following randomisation and parent set-up on the TOAST app
Parent weekly adherence data	For parents who cannot use the app: email/SMS link to OpenClinica or paper diary	Once a week after the first 28 days of using the app until the infant is 12 months old
Outcomes forms	OpenClinica	At 3, 6, 9, 12, 18 and 24 month follow-up visits
Parent follow-up questionnaires	Via email/SMS link, onto OpenClinica (paper available if requested)	When the infant is 3, 6, 9, 12, 18 and 24 months old
Change of consent form	OpenClinica	Only if the parent no longer wishes to provide data or wish to change the consent they originally provided
NPEU Serious Adverse Event (SAE) form	OpenClinica	As soon as possible after site becomes aware of event being defined as serious. Only if any reportable SAEs occur from when infant starts medication up until infant is 12 months

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Instructions for Case Report forms

Data entry can only be completed on OpenClinica by trained individuals listed on the TOAST delegation log. Individual log-ins and password will be required.

Randomisation and Contact Details

Please refer to **TOAST Guidance Sheet 5: Randomisation**

Complete the **Contact Details Form** as soon as possible after randomisation so that the TOAST Study team can send the link for the baseline questionnaire to the mother. Only the parent(s) who have signed the consent form should have their details entered onto the contact details form.

Please ask parents to provide an email address that they do not expect will change, as this email will then be linked to the app. If a parent wishes to update their email address, **contact the TOAST Study team**. For all other changes to contact details, please update these via the Contact Details Form.

The contact details form asks whether the mother has consented to Question 10 (“I agree to complete the questionnaires specified for the mother”) on the consent form. If the mother is currently unavailable to consent to this, please answer “Not yet (is currently unavailable)”. If the mother does not wish to consent to this or otherwise will never be able to provide this consent, please answer “No”. If you answer “Not yet...” and the mother later provides consent, please return to the Contact Details Form and update the answer to “Yes”.

Please also indicate on the Contact Details form whether the parents will use the TOAST app to report adherence, or another method. See also the section on Daily and Weekly Adherence Data, below.

All required fields on the contact details form will be flagged if left blank. It is possible to save despite missing data if absolutely necessary; please try to provide this missing data as soon as possible.

Entry Form

The participant’s record on OpenClinica will be created automatically on randomisation, and Sections 1 and 2 of the Entry form on OpenClinica are completed automatically from the information entered during randomisation. **Never create a participant record manually on OpenClinica.**

Review information in Section 1 of the Entry Form, then complete Section 3. Section 2 can never be edited. If any information was incorrectly entered at randomisation, the correct data should be entered in Section 1. You cannot edit data through the TOAST randomisation website.

Baseline Questionnaire

All parent questionnaires will be sent as a unique link to the recipient via text message and/or email. (the parent will receive both a text message and an email.) The Baseline Questionnaire will only be sent electronically once you have confirmed on the Contact Details form that the mother has consented to complete questionnaires, and provided both a contact mobile number and email address.

Please encourage the mother to complete the parent baseline questionnaire as soon as possible after her infant has been randomised.

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If the mother is unavailable to complete the baseline questionnaire, please wait until she is available. Do not ask the father or another family member to complete it on her behalf. If the mother will never be available to complete the baseline questionnaire, please let the TOAST Study team know that the questionnaire will never be received. Other participant questionnaires can be completed by the non-maternal consenting parent.

Parents should be supported to complete questionnaires electronically wherever possible. Please contact the TOAST Study team if electronic completion is not possible.

Daily Dosing Log

Complete a separate Dosing Log for each pack of TOAST medication. Please ensure that Dosing Logs are entered onto OpenClinica as soon as possible (at the latest, once a pack is finished, or the paper Dosing Log is full). Please be aware that the 'Notes' field at the bottom of each page does not need to be entered and will not be used for the study. Legible scanned copies of the Dosing Logs should be stored in the eISF. Original paper copies may be retained in the infant's medical notes according to local site policy. If an infant is transferred, a scanned copy of the Dosing Log should be retained at the recruiting site, and the paper Dosing Log included in the Transfer Pack.

If an infant receives a dose from another infant's pack, this must be reported as an incident.

Discontinuation of Medication

Please note that TOAST medication can be paused where necessary without this constituting a permanent discontinuation. Missed doses do not constitute discontinuation; they should be recorded on the Dosing Log (by site staff) or the app or equivalent (by the parent/carer).

If the infant permanently discontinues medication, complete the Discontinuation of Medication Form:

- If the infant is in hospital: enter the information from the Discontinuation of Medication section in the paper Dosing Log onto the OpenClinica Discontinuation of Medication Form.
- If the infant is at home: enter the information directly onto the Discontinuation of Medication Form on OpenClinica following a conversation with the parent/carer.

Please refer to the **TOAST Guidance Sheet 13: Discontinuation of Medication and Change of Consent**.

Transfer/Discharge Form

Complete the Transfer/Discharge Form whenever an infant is transferred to another hospital, is discharged home, or dies whilst in hospital. Some infants will have multiple Transfer/Discharge Forms completed. If an infant is discharged home from, transfers from, or dies at a continuing care site, **the recruiting site is responsible for completing the Transfer/Discharge Form(s)**.

If an infant dies before they are twelve months old, this **must also be reported as a Serious Adverse Event**. Please refer to **TOAST Guidance Sheet 10: Safety and Incident Reporting**.

Please let the TOAST Study team know about an infant's discharge home as soon as possible.

If you do not have time to complete a Transfer/Discharge form immediately, please contact the TOAST Study team to confirm the date an infant has been discharged home. Parents are not able to start reporting data in the app until there is a discharge date recorded on NPEU's systems.

Parent Daily and Weekly Adherence Data

Please encourage parents to download the TOAST app as soon as possible. Parents will use the app to record whether they have given the TOAST medication to their infant – this will be daily for the first month, and then weekly until the medication stops at 1 year of age.

Should a parent(s) inform site staff of any issues with the app, please pass this information onto the TOAST Study team to resolve. If a parent is unable or unwilling to download the app, they can report adherence via an OpenClinica form, which can be accessed via any Internet browser. Paper diaries are also available if a parent cannot report data electronically. Please ensure you have indicated any of these scenarios on the Contact Details Form.

If parents are regularly not reporting adherence, the TOAST Study team may ask site staff to follow up with them by phone to see if they are having any issues.

Outcomes Forms

Outcomes forms should be completed as close to the stated time point as possible but within 2 weeks either side of the 3, 6, 9 and 12 month follow-up visits, and within 4 weeks either side of the 18 and 24 month follow-up visits. If a follow-up visit within this timeframe is not possible, please consider obtaining information from the infant's medical notes and by telephone with the parent.

Parent Follow-up Questionnaires

The TOAST Study team will oversee distribution of Parent Questionnaires in the form of unique links via email / text message. The same parent/carer should complete these questionnaires each time. This should ideally be the mother, as the questionnaires contain a section relating to maternal quality of life.

Should you become aware of a change of address, email or mobile number please update the Contact Details Form on the TOAST Randomisation website and inform the TOAST Study team that you have done this. Do not send any updated contact details via email.

Change of Consent Form

Please refer to **TOAST Guidance Sheet 13: Discontinuation of Medication and Change of Consent**.

Serious Adverse Event (SAE) Form

Please refer to **TOAST Guidance Sheet 10: Safety and Incident Reporting**. SAEs must be reported to the TOAST Study team as soon as possible, even if you do not have all the information available yet.

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