LACunar Intervention (LACI) Trial-3: Assessment of efficacy and safety of cilostazol and isosorbide mononitrate to prevent adverse outcomes in patients with cerebral small vessel disease (lacunar) ischaemic stroke

Trial Information

Co-Sponsors	The University of Edinburgh & Lothian Health Board (ACCORD)
Funder	National Institute for Health and Care Research NIHR Health Technology Assessment (NIHR HTA)
Sponsor Reference	AC24127
IRAS number	1008629
ISRCTN number	44436843
REC number	24/SS/0095
Chief Investigator	Professor Joanna M Wardlaw

Contact information

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Contents

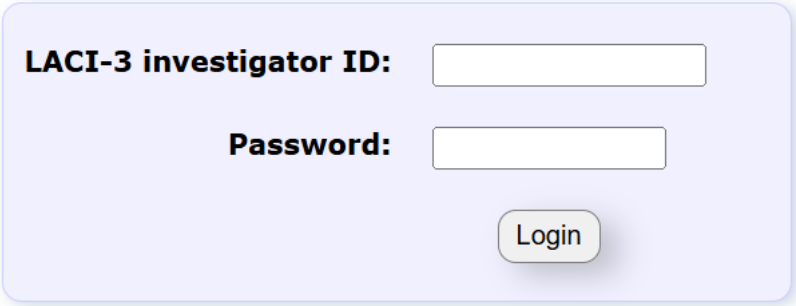
1. Introduction

This document provides guidance to assist users in completing the electronic case report forms (eCRFs) on the LACI-3 trial website. Users can access the database at the following address:

https://stroke.nottingham.ac.uk/sif/live/sif_login.php?sid=LACI-3

2. User account access

New users must be on the signed delegation log, a copy of which must be sent to the trial office along with a current email address.
The trial office will register users who will then receive login details via email. Users will be required to change their password at the first login. Users should never share their username and password with anyone.



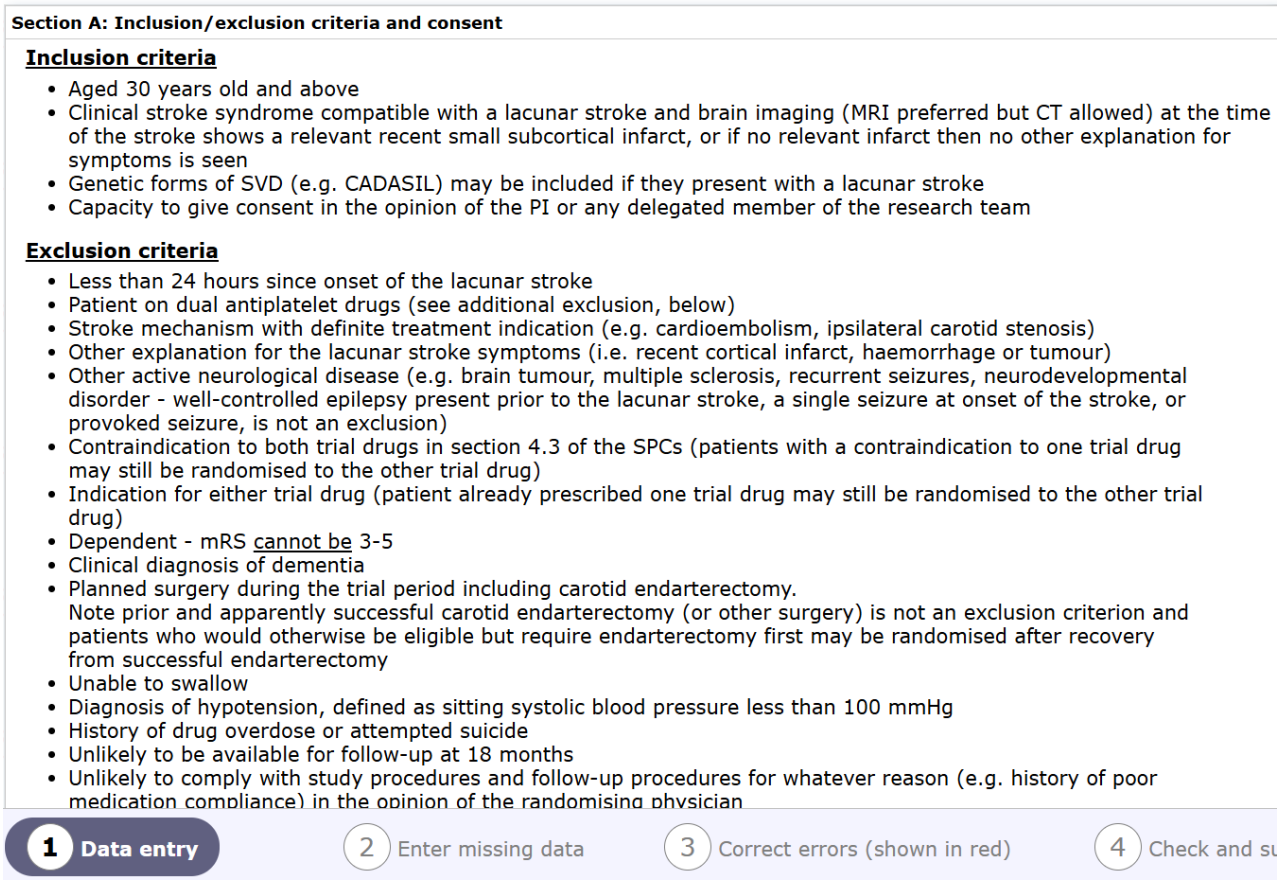
3. Main menu and Visit details

Once logged, proceed to the 'participant list' page where you will see a participant ID list with visit details. Trial documents including PDFs of all CRFs can be accessed via the link to 'trial documents for downloading' at the top right.

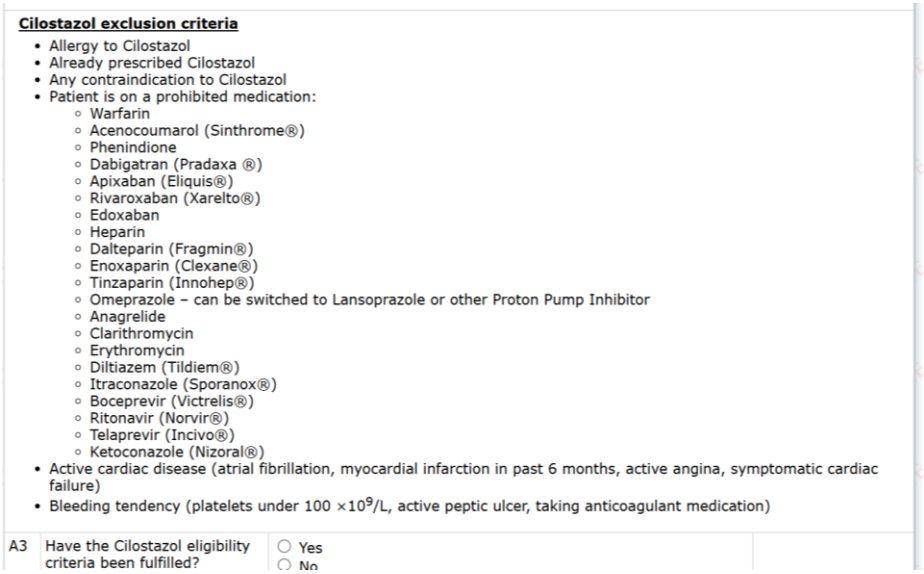
4. Randomising a new participant

To randomise a new participant, click the link at the top left:

This will open a data entry form with a reminder of the inclusion and exclusion criteria.



Exclusion criteria for both drugs are listed. Review these and complete the check box for both drugs.



Cilostazol exclusion criteria

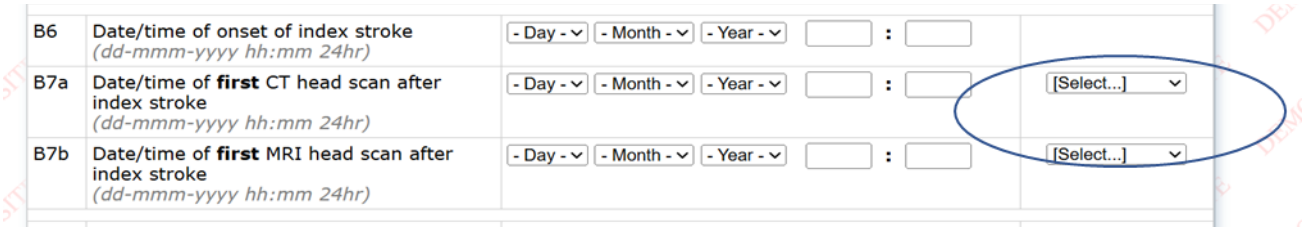
- Allergy to Cilostazol
- Already prescribed Cilostazol
- Any contraindication to Cilostazol
- Patient is on a prohibited medication:
  - Warfarin
  - Acenocoumarol (Sinthrome®)
  - Phenindione
  - Dabigatran (Pradaxa ®)
  - Apixaban (Eliquis®)
  - Rivaroxaban (Xarelto®)
  - Edoxaban
  - Heparin
  - Dalteparin (Fragmin®)
  - Enoxaparin (Clexane®)
  - Tinzaparin (Innohep®)
  - Omeprazole – can be switched to Lansoprazole or other Proton Pump Inhibitor
  - Anagrelide
  - Clarithromycin
  - Erythromycin
  - Diltiazem (Tildiem®)
  - Itraconazole (Sporanox®)
  - Boceprevir (Victrelis®)
  - Ritonavir (Norvir®)
  - Telaprevir (Incivo®)
  - Ketoconazole (Nizoral®)
- Active cardiac disease (atrial fibrillation, myocardial infarction in past 6 months, active angina, symptomatic cardiac failure)
- Bleeding tendency (platelets under 100 $\times 10^9$/L, active peptic ulcer, taking anticoagulant medication)

A3	Have the Cilostazol eligibility criteria been fulfilled?	○ Yes ○ No

If criteria are not met, the CRF cannot be completed.

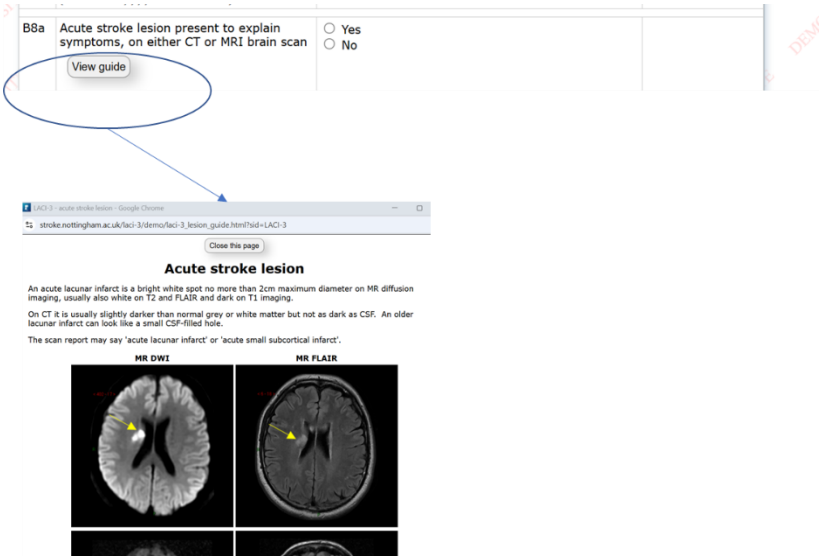
Participant details, SVD score, blood pressure, medications, mRS, NIHSS and MoCA are collected.

Some questions offer a not applicable option on the right hand column. Ensure this is completed where appropriate.



B6	Date/time of onset of index stroke *(dd-mmm-yyyy hh:mm 24hr)*	- Day - - Month - - Year - :	
B7a	Date/time of **first** CT head scan after index stroke *(dd-mmm-yyyy hh:mm 24hr)*	- Day - - Month - - Year - :	[Select...]
B7b	Date/time of **first** MRI head scan after index stroke *(dd-mmm-yyyy hh:mm 24hr)*	- Day - - Month - - Year - :	[Select...]

Some questions have a pop up guide with more information to assist completion.



B8a	Acute stroke lesion present to explain symptoms, on either CT or MRI brain scan	○ Yes ○ No

View guide

Close this page

Acute stroke lesion

An acute lacunar infarct is a bright white spot no more than 2cm maximum diameter on MR diffusion imaging, usually also white on T2 and FLAIR and dark on T1 imaging.

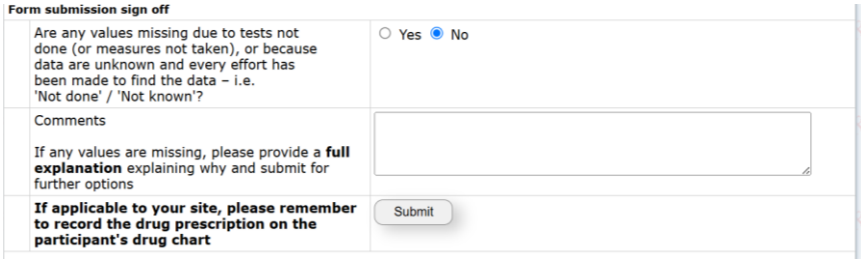
On CT it is usually slightly darker than normal grey or white matter but not as dark as CSF. An older lacunar infarct can look like a small CSF-filled hole.

The scan report may say 'acute lacunar infarct' or 'acute small subcortical infarct'.

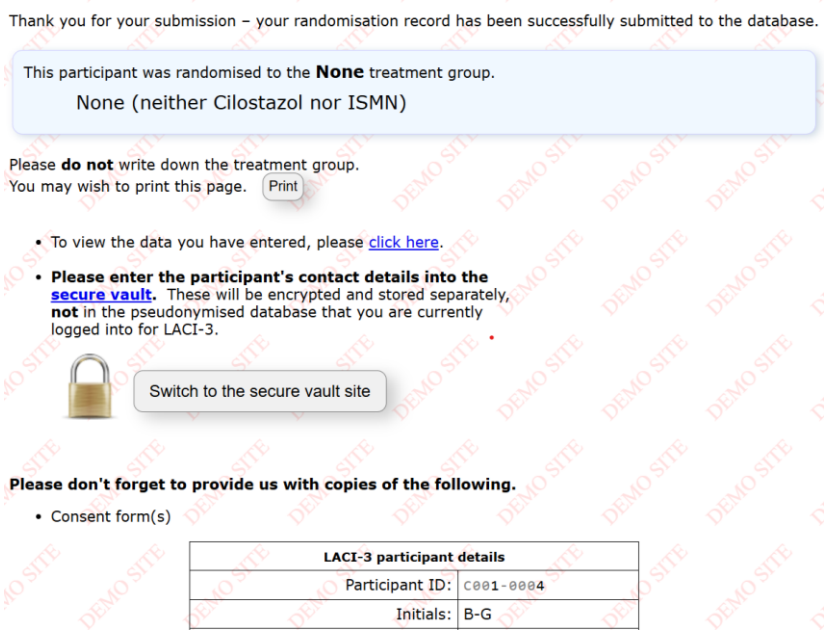
MR DWI MR FLAIR

5. Submitting the randomisation form

When you submit, you will be prompted to check all answers are correct prior to submitting

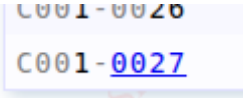


You will then be given the randomisation result and prompted to enter the participant contact details [image from the demo database, this is not a real participant]:



Please print the randomisation result for your records. This needs to be filed in the ISF and provided to pharmacy if applicable. The randomisation allocation does not appear on the automatically generated notification email due to blinding in place for the LACI-3 central team.

Should you need to view the randomisation result again, you can go to the participant list and click on the linked trial number. This is only available for the first 2 weeks after randomisation.



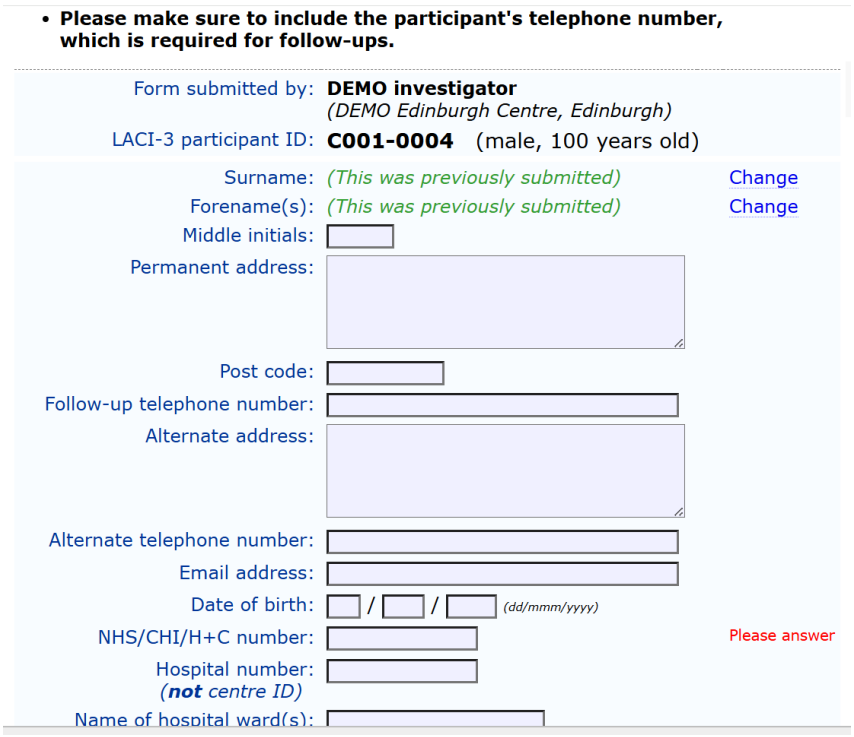
All CRF questions must be completed prior to submission

Drafts can be saved and the form completed at a later date

Forms are accessed by entering the participant DOB and initials

6. Contact database

Following completion of the randomisation form you will need to complete the contact details in the secure database. Please double check all details are valid and up to date.



- **Please make sure to include the participant's telephone number, which is required for follow-ups.**

Form submitted by: **DEMO investigator**
(DEMO Edinburgh Centre, Edinburgh)
LACI-3 participant ID: **C001-0004** (male, 100 years old)

Surname: *(This was previously submitted)* Change
Forename(s): *(This was previously submitted)* Change
Middle initials:
Permanent address:
Post code:
Follow-up telephone number:
Alternate address:
Alternate telephone number:
Email address:
Date of birth: / / *(dd/mmm/yyyy)*
NHS/CHI/H+C number: Please answer
Hospital number: *(**not** centre ID)*
Name of hospital ward(s):

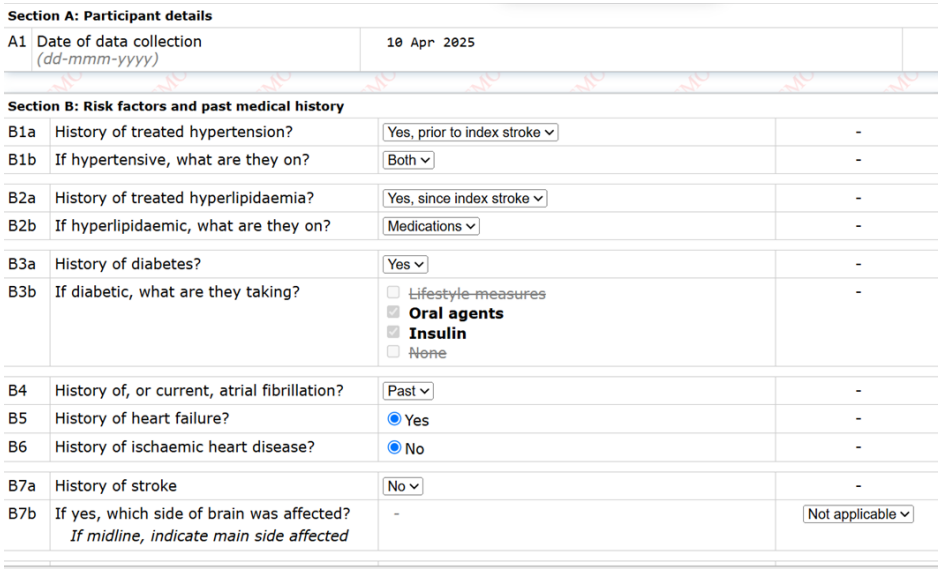
7. Baseline and Follow-up CRFs

Once randomisation is complete, you will be able to access the baseline CRF

Participant ID/age at randomisation		Event date	Randomised (day 0)	Contacts/ documents	Baseline	Week 1-2 follow-up	Week 3-4 follow-up	Prescription issue	No set visit	SAEs	Centre transfers
C001-0001	81	3 Mar 2025	10 Apr 2025	Y Y	10 Apr 2025	10 Apr 2025	10 Apr 2025	Select ×1	Select ×1	Select ×1	Select
C001-0002	79	1 Jan 2024	11 Apr 2025	Y N	11 Apr 2025	22 Apr 2025	6 May 2025	Select	Select	Select	Select
C001-0003	76	7 Jan 2023	18 Apr 2025	Enter	18 Apr 2025	29 Apr 2025	13 May 2025	Select	Select	Select ×1	Select
C001-0004	100	3 Feb 2023	2 May 2025	Y N	2 May 2025	13 May 2025	27 May 2025	Select	Select	Select	Select

Switch to mobile site

Information is collected on medical history, risk factors, index stroke, carotid status, investigations, employment and some assessments (MMSE, Trails, ED-5D-5L).



Section A: Participant details			
A1	Date of data collection *(dd-mmm-yyyy)*	10 Apr 2025	
Section B: Risk factors and past medical history			
B1a	History of treated hypertension?	Yes, prior to index stroke	-
B1b	If hypertensive, what are they on?	Both	-
B2a	History of treated hyperlipidaemia?	Yes, since index stroke	-
B2b	If hyperlipidaemic, what are they on?	Medications	-
B3a	History of diabetes?	Yes	-
B3b	If diabetic, what are they taking?	~~Lifestyle measures~~ **Oral agents** **Insulin** ~~None~~	-
B4	History of, or current, atrial fibrillation?	Past	-
B5	History of heart failure?	Yes	-
B6	History of ischaemic heart disease?	No	-
B7a	History of stroke	No	-
B7b	If yes, which side of brain was affected? *If midline, indicate main side affected*	-	Not applicable

The ideal date of the follow up appointments will appear in the participant table once the baseline is completed. Aim to complete the visit as close to this date as possible

The 1-2 and 3-4 week follow up CRFs includes details of participant status at follow up

Section A: Participant details			
A1	Date of data collection *(dd-mmm-yyyy)*	10 Apr 2025	
A2	Status of the participant	Available - postal questionnaires returned	
A3	If died, date of death *(dd-mmm-yyyy)*	-	Not applicable
A4	Explanation if follow-up cannot be completed. *If deceased, please supply as much information as possible (cause, where, etc.)*	-	Not applicable
If died since last visit, please complete an outcome CRF.			

Section B: Symptoms			
B1a	Headache	No	-
B1b	If present did it stop normal activities?	-	Not applicable
B1c	Frequency	-	Not applicable
B2a	Palpitations	No	-

Symptoms, medication, BP and outcomes are also collected.

8. Entry of missing data

Some questions may provide "Not applicable", "Not done" and/or "Not known" options.

- Not applicable - should be used if a measure was not required for that participant
- Not done - should be used if data are unavailable, either because a measure was not taken or a test was not performed
- Not known - should be used if the data are unknown, and every effort has been made to find the data

For each question on a CRF, you should either enter a value in the central column(s) or use the drop-down lists in the right-hand column to indicate why the value is missing - but not both. A response must be given in this way for every numbered question on the CRF.

The "Not done" and "Not known" options relate to missing data. Some of these options may be hidden when a LACI-3 online CRF is first accessed, i.e. before any data have been submitted. This is because the options provided reflect the data we need to collect for proper analysis of the trial.

However, some required data may still be missing for legitimate reasons. For example, it may not be possible to measure a participant's weight in the emergency department. In such cases, to access the hidden "Not done" and "Not known" options, please go to the bottom of the page and set the missing data control to "Yes". Enter a full explanation and submit the form.

After this, you can complete the CRF as usual and submit. Check through your answers and re-submit to store the data that you have entered.

Note that once the hidden options have been revealed, they will continue to be displayed even if you have no missing data (i.e. when none of the questions have "Not done" / "Not known" selected). If no data are missing, please set the control at the bottom of the page to "No" and re-submit. In this case no explanation is required so may be left blank, however relevant comments may always be entered

9. Data queries and corrections

The coordinating centre may raise data queries if there is missing data or if something is not quite right. You will see an alert for any outstanding data queries when you click on participant list, click on this and it will show open queries for actioning

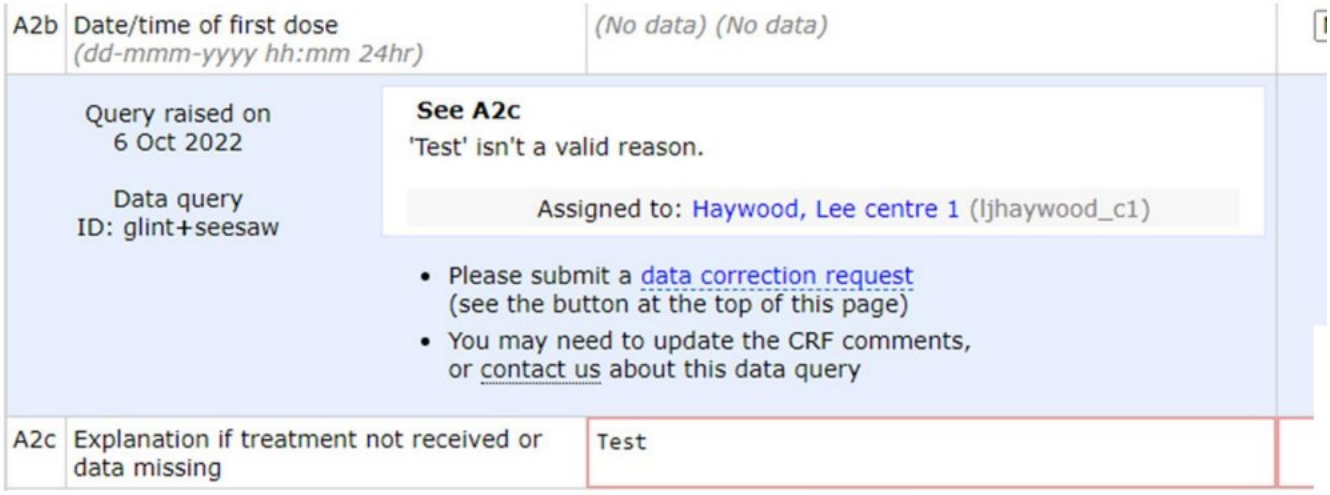
Please click on the CRF where the data query is located i.e. in this example Day 7. You can also they can also click on the issue ID (glint+seesaw) to go directly to the specific query/questions.

Open queries for C001
NOTTINGHAM, Nottingham DEMO Hospital, UK

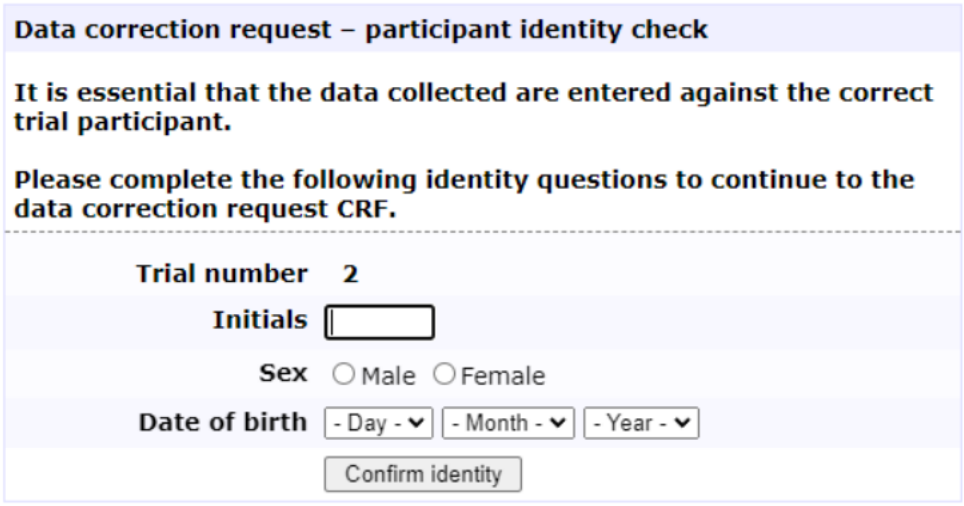
Participant ID	CRF	Question IDs/query details	Date/time/ data query ID	Assigned to
C001-0002-ONK	Day 7 ☐	A2c 'Test' isn't a valid reason.	6 Oct 2022 12:50 glint+seesaw	Haywood, Lee centre 1

Found one matching data query

The data query will show above the question where the data is to entered/amended. Please click on the link for 'data correction request'



You will then complete a participant identity check.



The data correction request form **does not** support draft records.
The form **must** be submitted completely, otherwise the data will be lost.

You will need to complete a table detailing the change made and the reason:

A5: Question ID and label is the number and title of question and the data originally entered

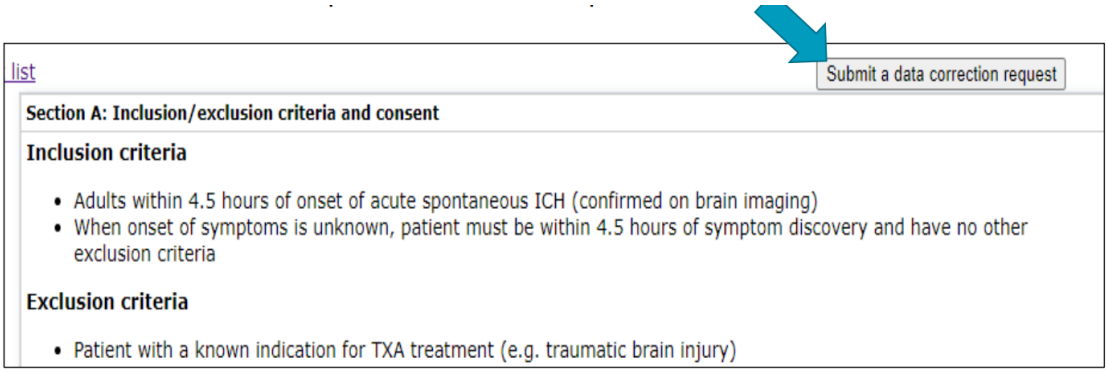
A6: Enter question ID of where the new data is to be entered, and the values that should appear once the CRF record has been amended

A7: Please enter the reason for the change

A5	Existing data Please list each: *Question ID* *Question label* *Data shown on report*	A2c: Explanation if treatment not received or data missing - "Test". Explanation for missing data: "Transferred before day 7".
A6	New data Please list each: *Question ID* *New value(s)*	A2c: "Participant transferred for surgery before full dose given." Explanation for missing data: "Transferred on first day for surgery".
A7	Reason for change	Required full explanation had not been given.

You can submit a data correction request without a data query being raised by the coordinating centre e.g. if you put a comment that the EQ-5D-5L was not done at the time and would update the data later. When the data is available click on the 'submit a data correction request' button at the top of the eCRF.

As before, you will need to complete the participant identity check to access the data correction request form. If applicable, please also give existing/new text for the full explanation for missing data (state 'n/a' for 'New data' if text to be removed).



Common issues:

• Update data for all affected questions in a single request, when possible - especially related questions

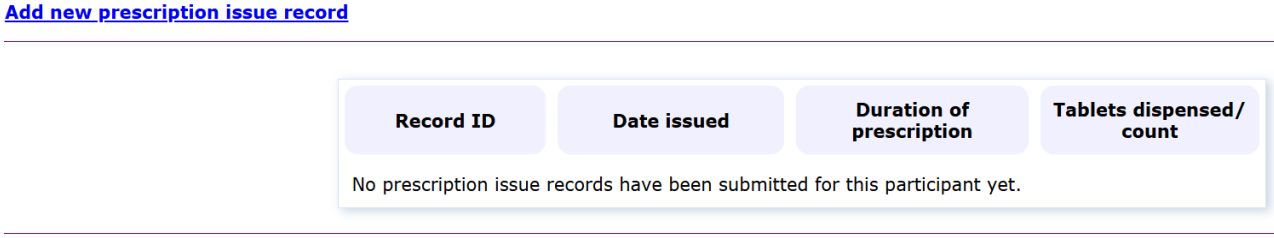
• Use one line per question

• Make sure that existing data are always given, stating "Not done" and "Not known" where previously missing

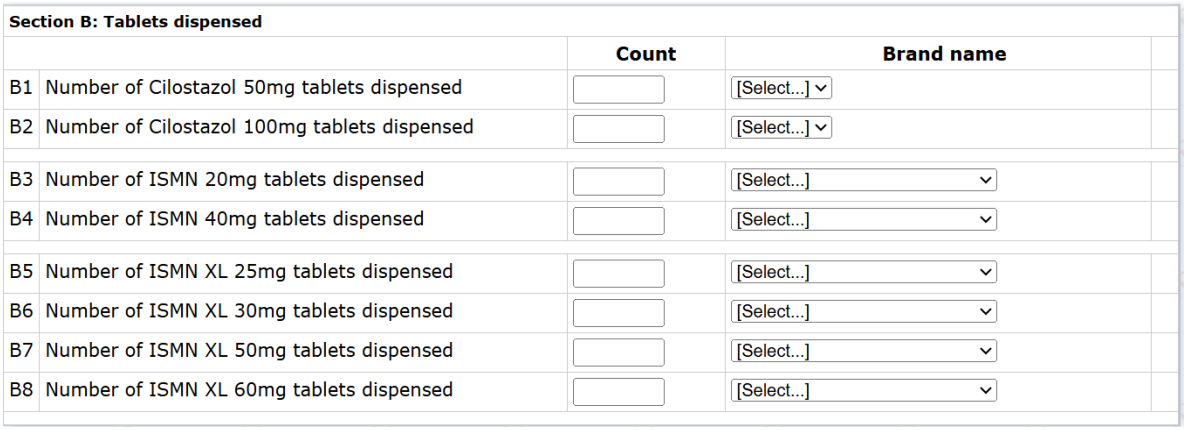
• Do not list questions whose values have not changed

10.Prescription issue form

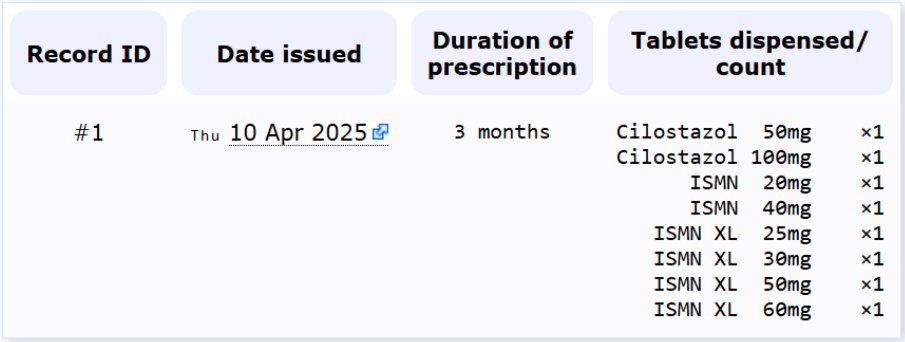
Prescription details need to be entered into the CRF using the Prescription issue form link next to the participant visit details.
Follow the link to 'add new prescription issue record' at the top left. You will be prompted to confirm the participant DOB and initials.



All prescription details should be entered into this form.



Once entered the record will be displayed under the prescription issue form link. Each new prescription should be added here.



11. No set visit form

If an unscheduled assessment is performed, then it should be captured in the database using the no set visit form. These include details about stopping or changing medications, safety and outcome events and withdrawals.

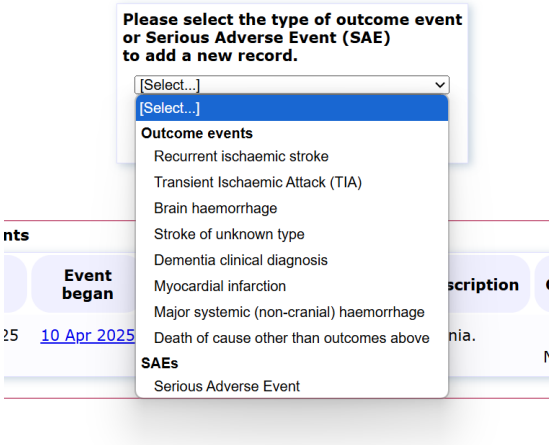
Section A: No set visit details

A1	Date of data collection *(dd-mmm-yyyy)*	02 May 2025
A2	Type of no set visit	○ Medication stopped ○ Medication changed ○ Query about medication ○ Outcome event ○ Potential AE/patient side effects (report SAEs to sponsor) ○ Potential deviation (report to sponsor) ○ Participant withdrawn ○ Death ○ Other (please specify)
A3	Details of visit/contact	
A4	Has there been a change in the status of the participant?	○ No change ○ Permanently stopped treatment (continue follow-ups) ○ Withdrawn from study IMP, continues in follow-up ○ Withdraw from study IMP and follow-up, continue collection of clinical and safety data from medical notes ○ Withdrawn consent to be contacted about other research

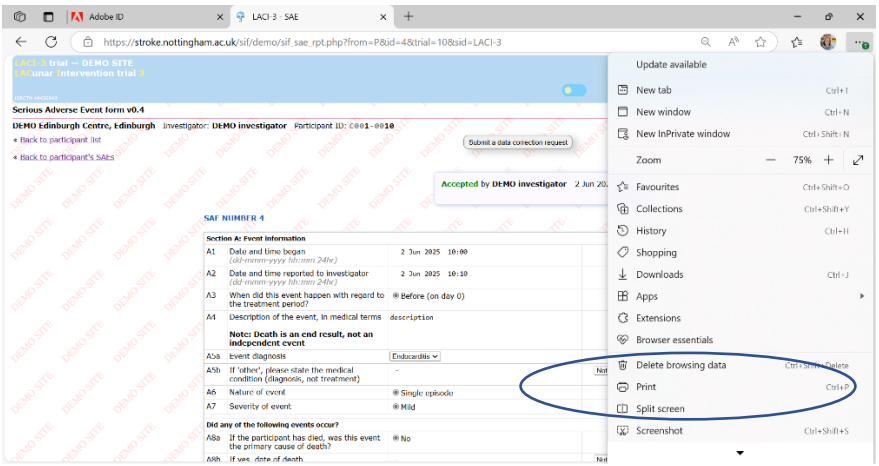
12. SAE and Outcome reporting

Please refer to the protocol and safety adjudication SOP for details of SAE reporting.

Should an SAE or outcome need to be reported, please complete the form listed next to the participant visits.
The type of event is selected from a drop-down list.

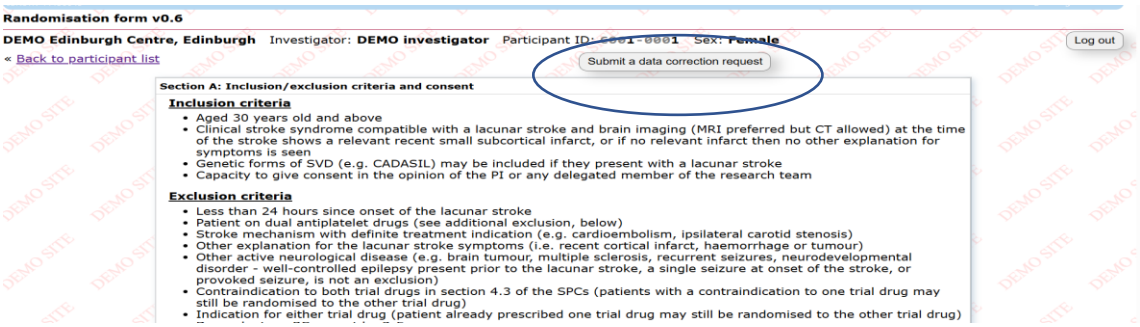


For SAEs, print a pdf of the completed form and email to safety@accord.scot within 24 hours of becoming aware.



13. Data correction requests

Data must be consistent with the patient's source documentation. Where errors occur or details need to be updated, a data correction request must be completed by following the link at the top of the page of the relevant CRF. These are then actioned by the LACI-3 programmer.



14. Technical support

First point of contact for any queries relating to the eCRF is the trial office laci-3@ed.ac.uk
Should a response not be received in a timely manner please contact Lee.Haywood@nottingham.ac.uk

15. Revision History

Date	Version number	Changes applied
25th June 2025	1.0	N/A
17th September 2025	2.0	Re-accessing randomisation result added, guidance for missing data and data queries and corrections added