SepTiC

Sepsis Trials in Critical Care

Randomisation Guide

V3.0 01-OCT-2024

Sponsor: Imperial College London

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Study Coordination Centre:
Imperial Clinical Trials Unit
IRAS ID: 1005848
REC ref: 23/LO/0339

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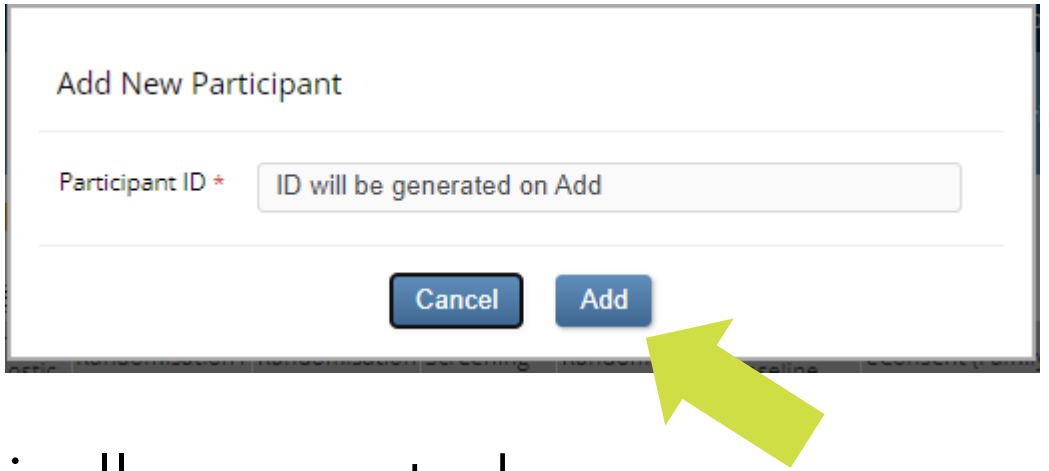
FUNDED BY
NIHR | National Institute for Health Research

Randomisation

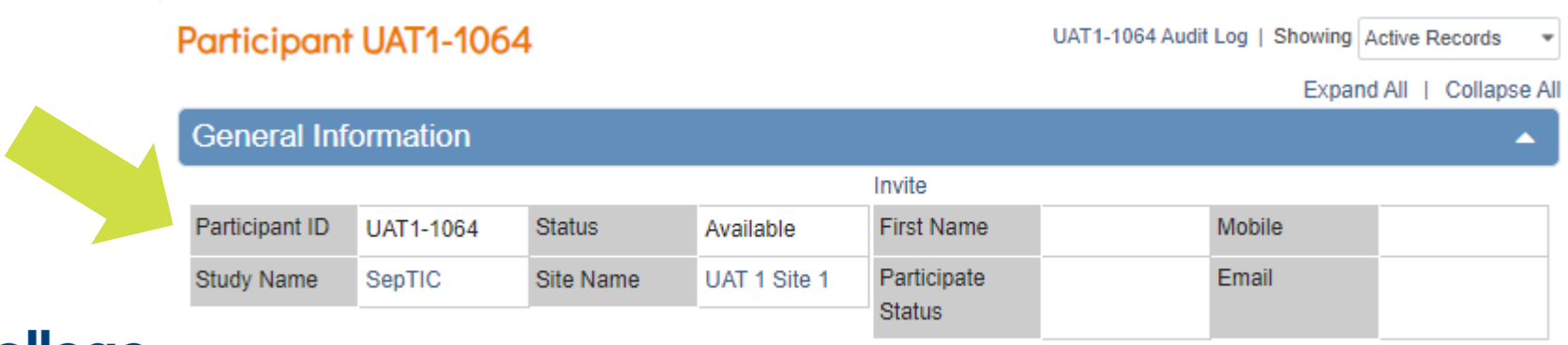
- Randomisation should be performed soon after confirming eligibility and prior to anticipated start of randomised treatment
- Randomisation performed using a web-based system in OpenClinica
- OpenClinica is a browser-based electronic data capture system (EDC) accessed via the link https://imperial.openclinica.io/OpenClinica with email address and password to log-in
- We advise site teams to use Google Chrome as a browser where possible
- Record each randomisation on screening/randomisation log and print randomisation form from the OpenClinica system
- Ensure the participant's trial ID is recorded in their medical records

Adding a new participant

+ Navigate to the participant matrix
+ Click 'Add New Participant'



+ The participant ID will be automatically generated



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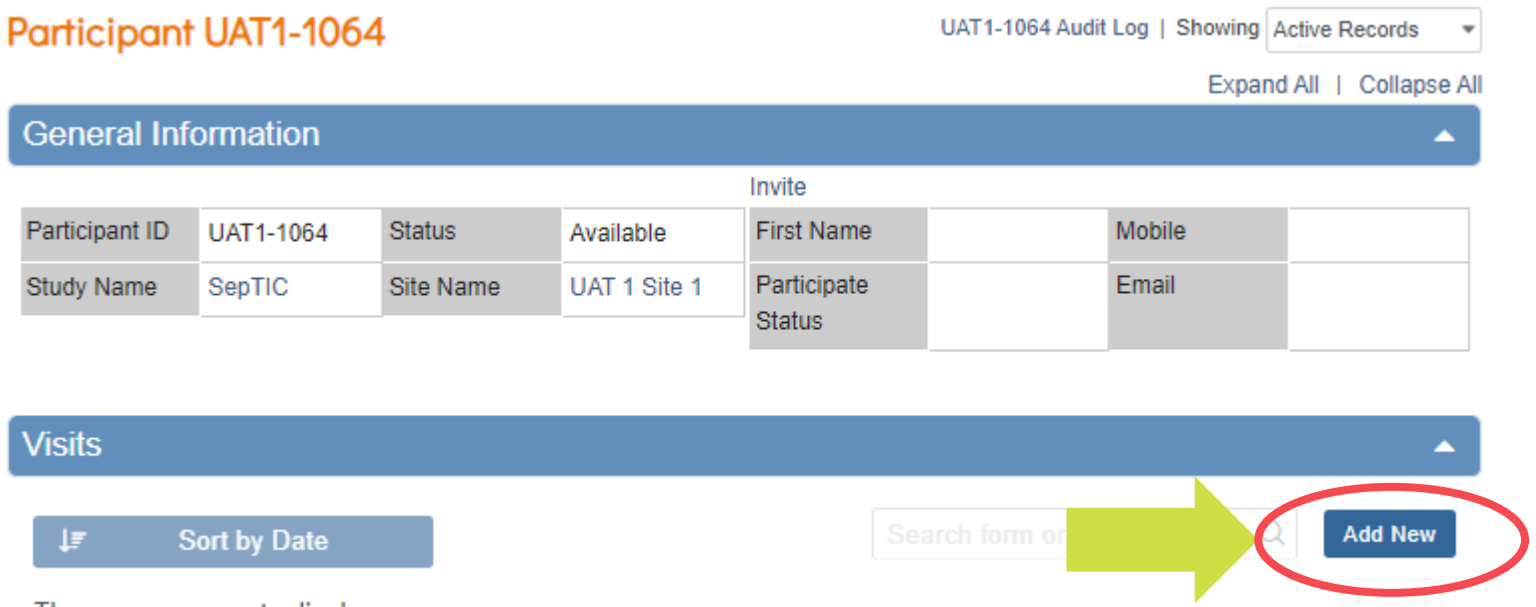
Adding a visit

- The forms on the database are organised into ‘visits’ which reflect the different timepoints of the study
- To add a visit click ‘Add New’



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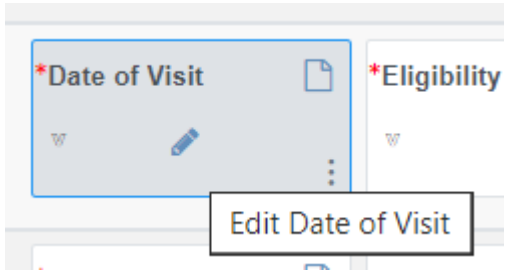
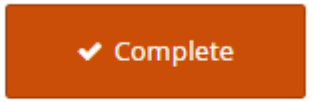
Completing a form

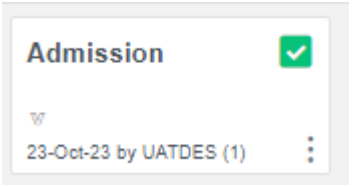
+ After adding a visit, you will need to click on the pencil icon to edit a form



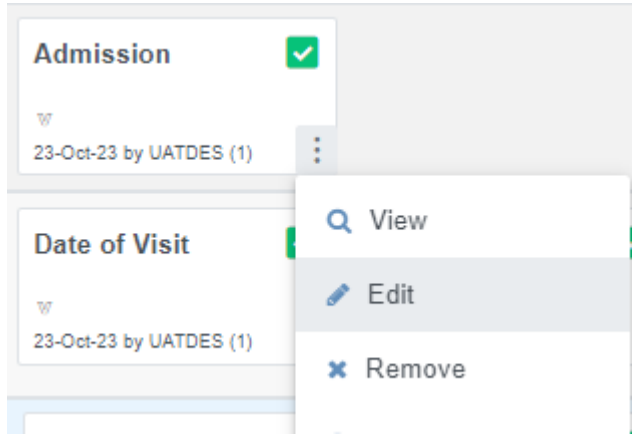
+ Clicking on the edit icon will open the form
+ Data entry is automatically saved, so even if you close a form the data will save
+ Once you have completed data entry on a form, click the orange 'Complete' button



+ Forms that are complete will have a green tick



+ If you need to edit data on a form that is complete, click the three dots, and then click 'Edit'



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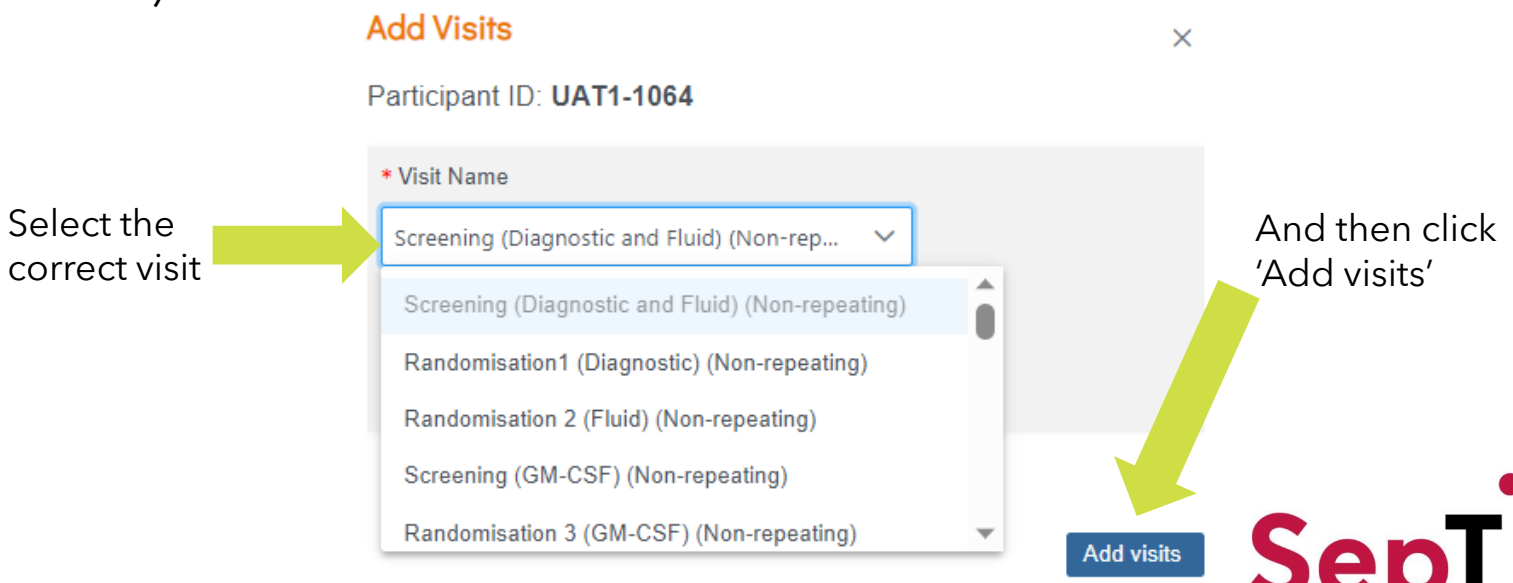
Randomising patients onto Trials 1 and 2: Diagnostic and Fluid

- The screening visit **must be** completed prior to randomisation
- This is to confirm eligibility of the patient
- The system will not allow you to randomise before completing screening
- A drop-down list should appear with all the visits
- Select 'Screening (Diagnostic and Fluid)'



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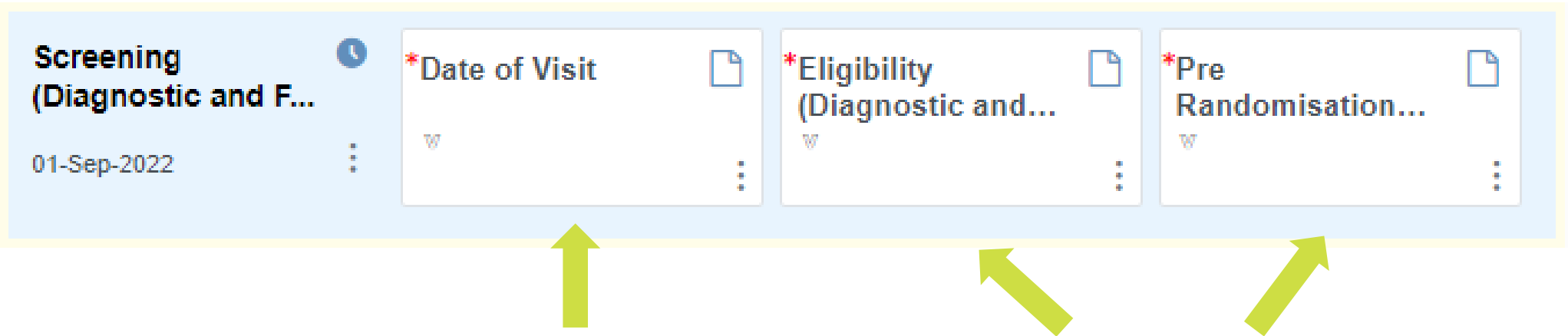
Completing the screening visit

+ Once you have added the screening visit, there should be 3 forms to complete



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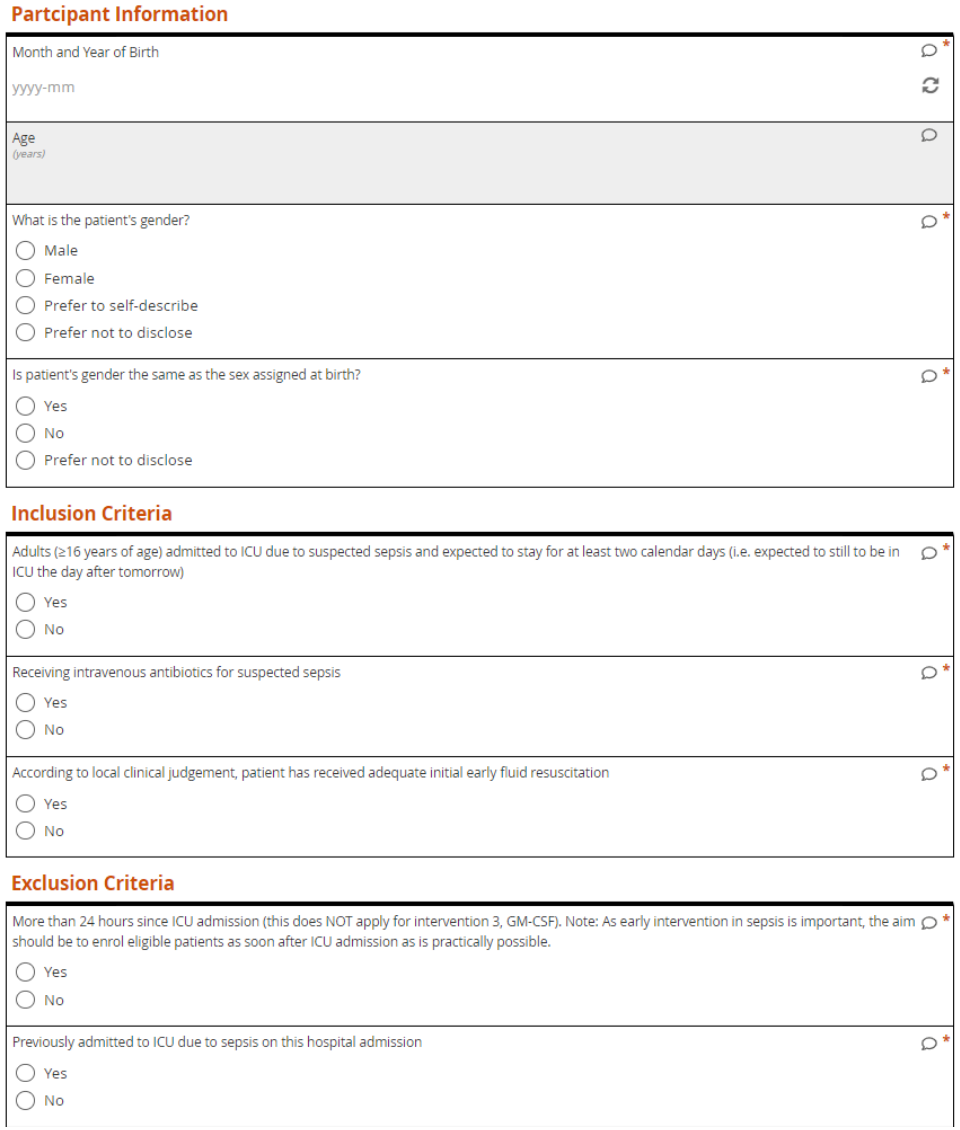
Complete the Eligibility form



Partcipant Information

Month and Year of Birth *

yyyy-mm

Age
(years)

What is the patient's gender? *

- Male
- Female
- Prefer to self-describe
- Prefer not to disclose

Is patient's gender the same as the sex assigned at birth? *

- Yes
- No
- Prefer not to disclose

Inclusion Criteria

Adults (≥16 years of age) admitted to ICU due to suspected sepsis and expected to stay for at least two calendar days (i.e. expected to still to be in ICU the day after tomorrow) *

- Yes
- No

Receiving intravenous antibiotics for suspected sepsis *

- Yes
- No

According to local clinical judgement, patient has received adequate initial early fluid resuscitation *

- Yes
- No

Exclusion Criteria

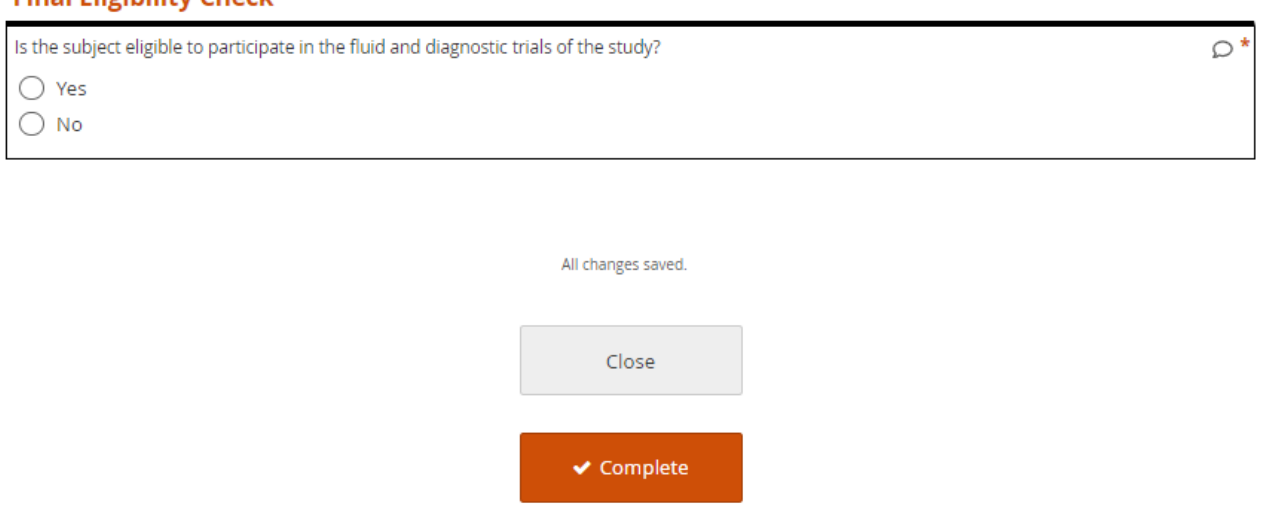
More than 24 hours since ICU admission (this does NOT apply for intervention 3, GM-CSF). Note: As early intervention in sepsis is important, the aim should be to enrol eligible patients as soon after ICU admission as is practically possible. *

- Yes
- No

Previously admitted to ICU due to sepsis on this hospital admission *

- Yes
- No

Confirm the participant is eligible for the study by selecting 'Yes' and click 'Complete'



Final Eligibility Check

Is the subject eligible to participate in the fluid and diagnostic trials of the study? *

- Yes
- No

All changes saved.

Close

✔ Complete

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Complete the Pre-randomisation Data form

Has the patient been in hospital >48h or is known to have been readmitted within 30 days *

- Yes
- No

Is the patient receiving vasopressors? *

- Yes
- No

Is the patient receiving respiratory support? *

- Yes
- No

Close

✔ Complete

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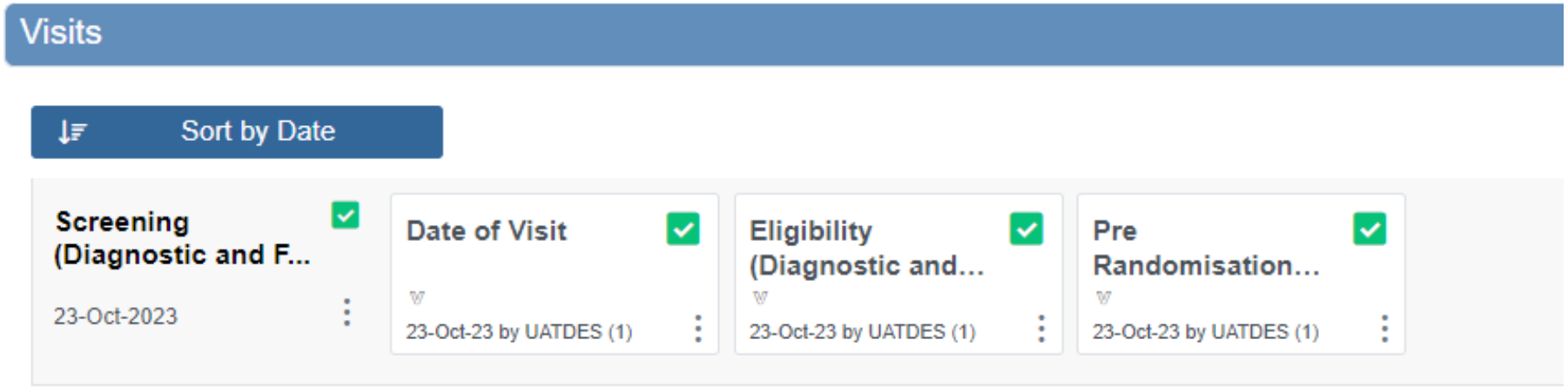
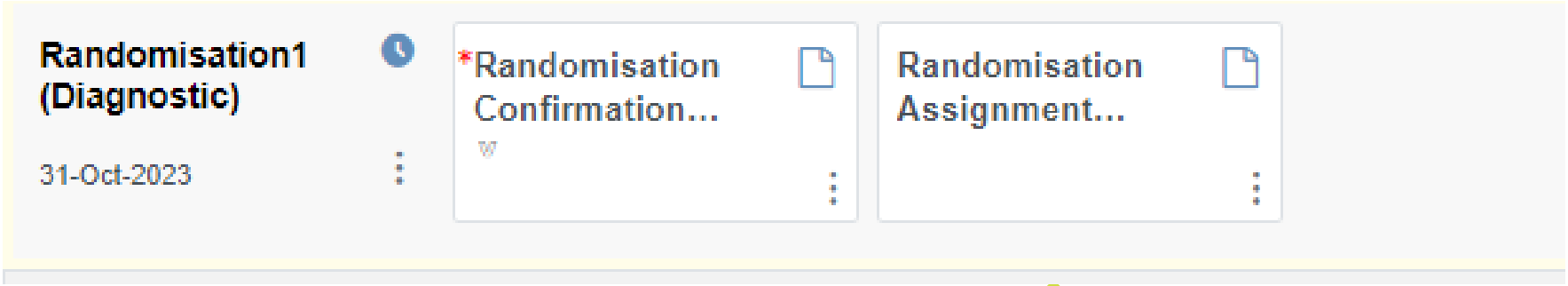
+ You are now ready to randomise the patient once the screening visit is complete



Add the randomisation visit for Trial 1: Diagnostic

+ To randomise patients onto Trial 1: Diagnostic, you will need to add the randomisation visit and complete the forms in the order below



Complete the randomisation confirmation

The assignment will be on this form

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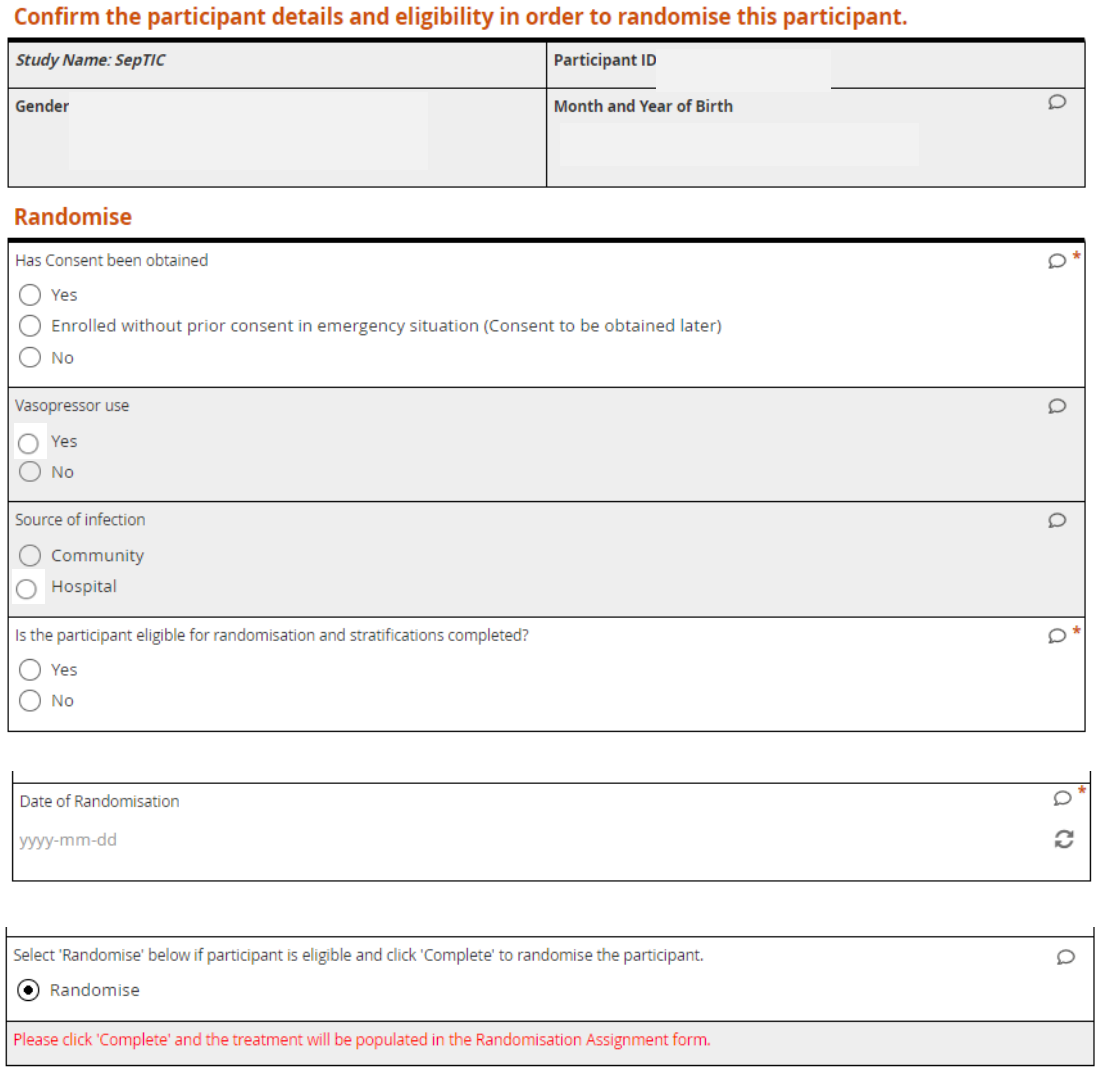
Complete the diagnostic randomisation confirmation to confirmation eligibility

These questions will be automatically completed with answers from the screening visit



These questions will appear once the previous question is answered

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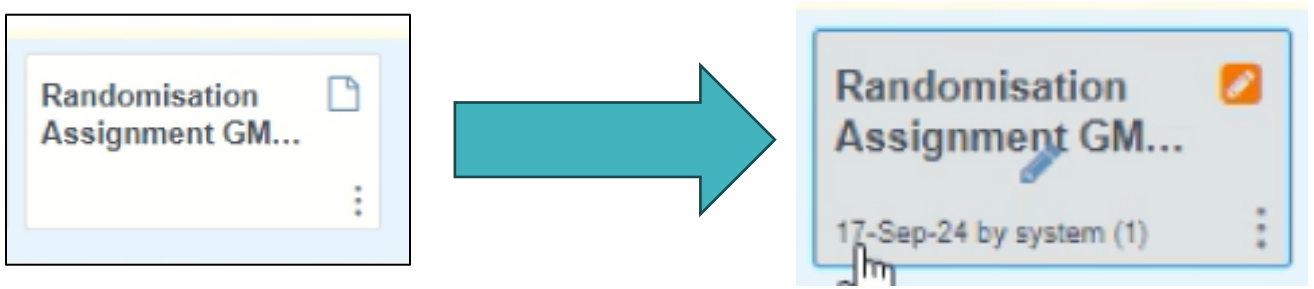
The randomisation allocation will not appear immediately on the assignment form

- This is because there is a small lag between the assignment being generated and then appearing on the form
- Once you close any randomisation confirmation page, **WAIT** for the assignment form to change to **orange** and show that the system has updated the form



- If the assignment page does not update, **refresh** the browser
- Only open the assignment form once it shows that it has updated

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View the randomisation assignment form to see the diagnostic treatment allocation

- This form is **read-only**, no data will be entered on the form
- The participants details will appear from the eligibility form
- The allocation will be under 'Treatment'

Example:

Participant details:

Study Name: SepTIC	**Participant ID** UAT1-1085
Gender Male	**Month and Year of Birth** 1961-06

Allocation:

Date of Randomisation 2023-10-31
Treatment PCR-based pathogen testing and PCT

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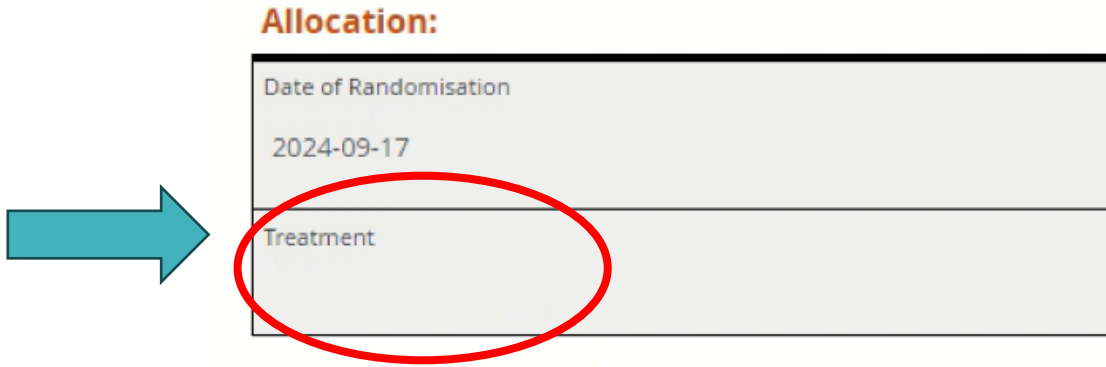
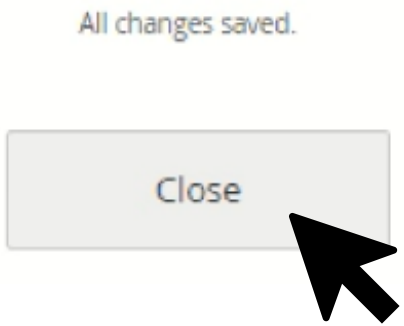
If you do not wait for the system to sync, the allocation will not appear

+ If you open the form before waiting for it to update, the treatment allocation will be blank





+ If this happens, do not panic. There are steps to take to allow the data to sync.
+ First click '**CLOSE**' to exit the form

Do not click 'Complete' as this will lock the form.

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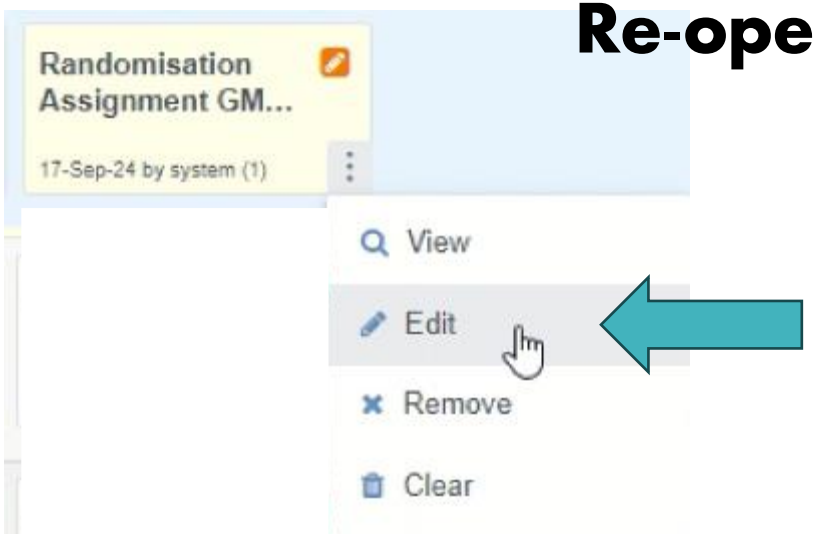
Re-open the form in ‘Edit’ mode



- On the participant home page, click on the 3 dots next to the randomisation assignment form
- Click ‘Edit’
- This will re-open the form in edit mode

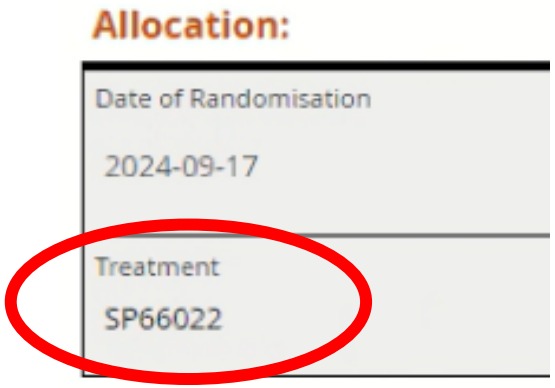
- The treatment allocation has now populated under the ‘Treatment’ header

Treatment allocations per intervention:

Diagnostic: Standard Care **or** PCR-based pathogen testing and PCT

Fluid: Standard Care **or** Conservative fluid therapy with de-resuscitation

GM:CSF: Kit number (as shown in image)



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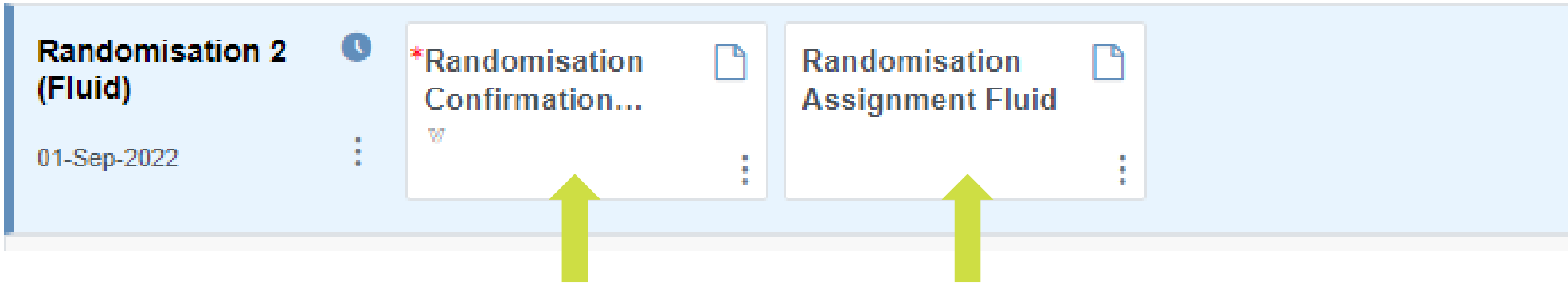
Repeat for Trial 2: Fluid

+ To randomise patients onto the Fluid Trial, there should be 2 forms to complete



Complete the randomisation confirmation

The assignment will then appear on this form

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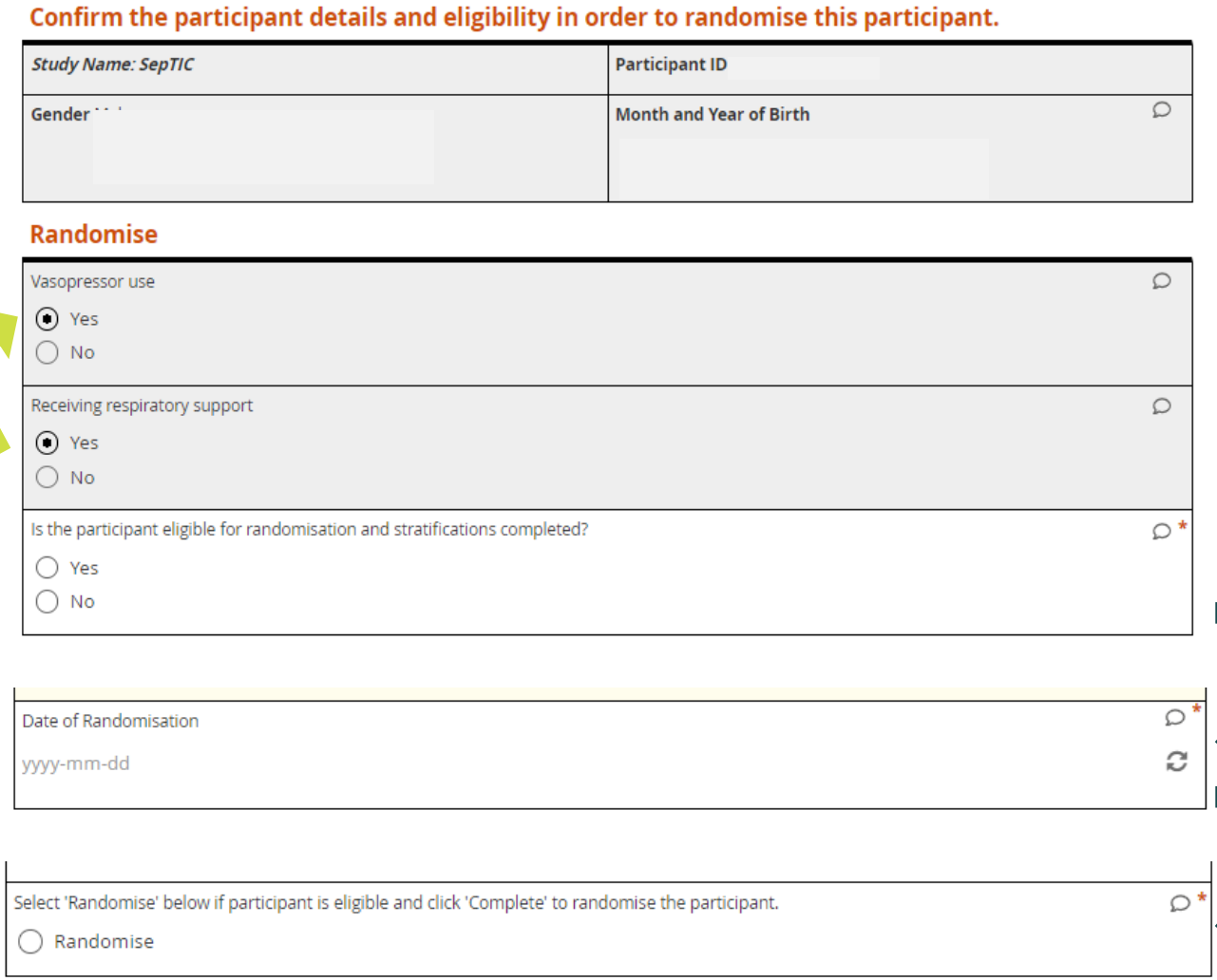
Complete the Fluid Randomisation Confirmation Form

These questions will be automatically completed with answers from the screening visit



These questions will appear once the previous question is answered

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View the randomisation assignment form to see the fluid treatment allocation

- This form is **read-only**, no data will be entered on the form
- The participants details will appear from the eligibility form
- The allocation will be under 'Treatment'

Example:

Participant details:

Study Name: SepTIC	**Participant ID** UAT1-1085
Gender Male	**Month and Year of Birth** 1961-06

Allocation:

Date of Randomisation 2023-10-31
Treatment Conservative fluid therapy with de-resuscitation

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Randomising patients onto Trial 3 GM-CSF

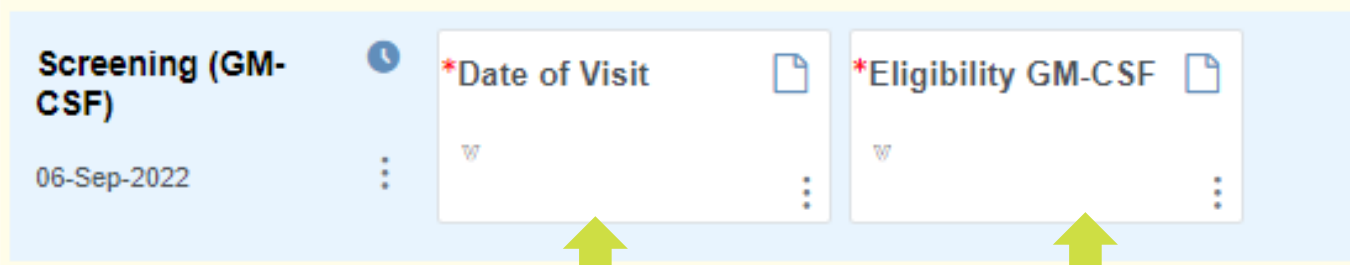
+ Ensure the patient meets the additional inclusion criteria and none of the additional exclusion criteria for GM-CSF
+ To randomise patients to the GM-CSF trial, the following events/forms must be complete:

Screening (Diagnostic and Fluid)

this visit must be completed regardless of whether the patient was randomised to the Diagnostic and Fluid trials

Complete screening visit for Trial 3: GM-CSF

- The screening visit must be completed **before** randomising
- Add the 'Screening (GM-CSF)' visit and complete the forms in the order shown below



This should be todays date (date of randomisation)

Then complete eligibility form

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Inclusion Criteria GM-CSF

Intubated and mechanically ventilated and expected to continue for another 24 hours or requiring two organ support (i.e. vasopressors or renal replacement therapy) *

- ○ Yes
- ○ No

An absolute lymphocyte count < 1.2 x10^9/L on two consecutive calendar days at least 12 hours apart, with no values >1.2 x10^9/L in between. *

- ○ Yes
- ○ No

Exclusion Criteria for GM-CSF

More than 120 hours (5 days) since ICU admission *

- ○ Yes
- ○ No

Already receiving G-CSF or GM-CSF *

- ○ Yes
- ○ No

A total white blood cell count >50 x10^9/L *

- ○ Yes
- ○ No

Known to be pregnant or breastfeeding *

- ○ Yes
- ○ No

Known recent (required treatment within the last 5 years) haematological malignancy *

- ○ Yes
- ○ No

Solid organ or bone marrow transplantation *

- ○ Yes
- ○ No

Patient weight >125kg *

+ Complete the GM-CSF eligibility form
+ Confirm patient eligibility on the final eligibility check before continuing

Final Eligibility Check

Eligibility results from first eligibility check, is patient eligible:-	Is the subject eligible to participate in the GM-CSF trial of the study?
	◉ Yes ○ No

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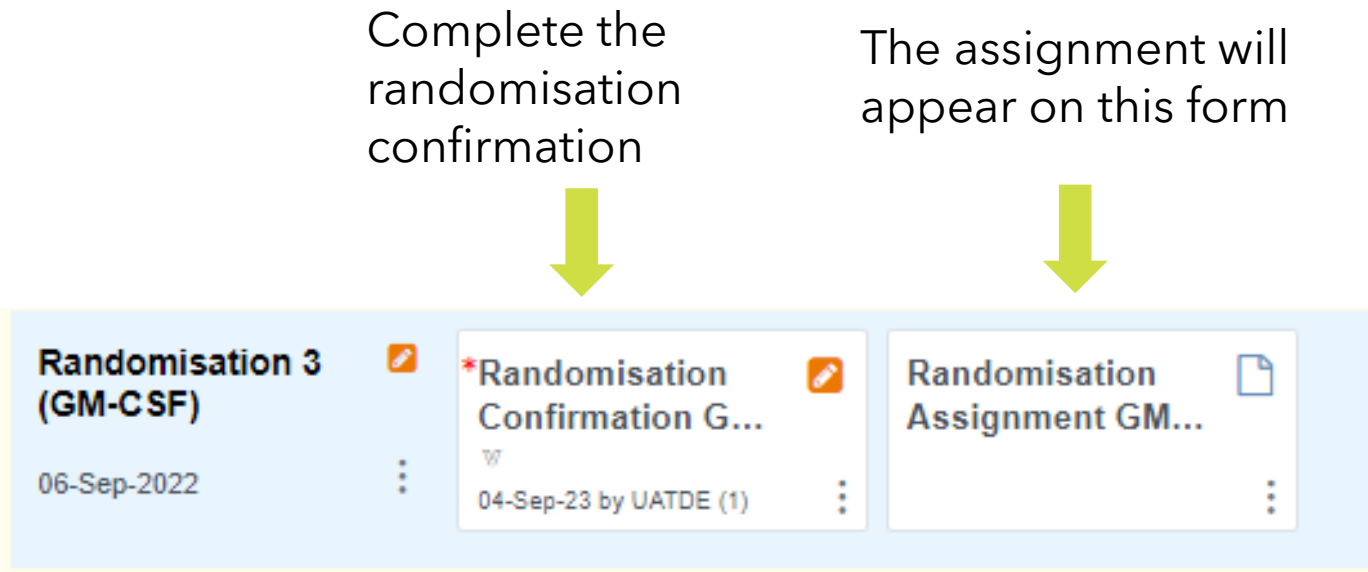
Add the Randomisation 3 GM-CSF visit

+ Then complete the forms as shown below

Complete the randomisation confirmation

The assignment will appear on this form



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Complete the GM-CSF randomisation confirmation page

Confirm the participant details and eligibility in order to randomise this participant.

Study Name: SepTIC	**Participant ID** UAT1-1085
Gender Male	**Month and Year of Birth** 1961-06

Randomise

Treatment Allocation from Randomisation 1

- ○ Standard care or Not Randomised
- ◉ PCR/procalcitonin based diagnostics

Treatment Allocation from Randomisation 2

- ○ Standard care or Not Randomised
- ◉ Conservative fluid strategy

Source of infection

- ○ Community
- ◉ Hospital

Is the participant eligible for randomisation and stratifications completed?

- ◉ Yes
- ○ No

Date of Randomisation

2023-10-31

Select 'Randomise' below if participant is eligible and click 'Complete' to randomise the participant.

- ◉ Randomise

Please click 'Complete' and the treatment will be populated in the Randomisation Assignment form.

These questions will be automatically completed from previous forms

These questions will appear once the previous question is answered

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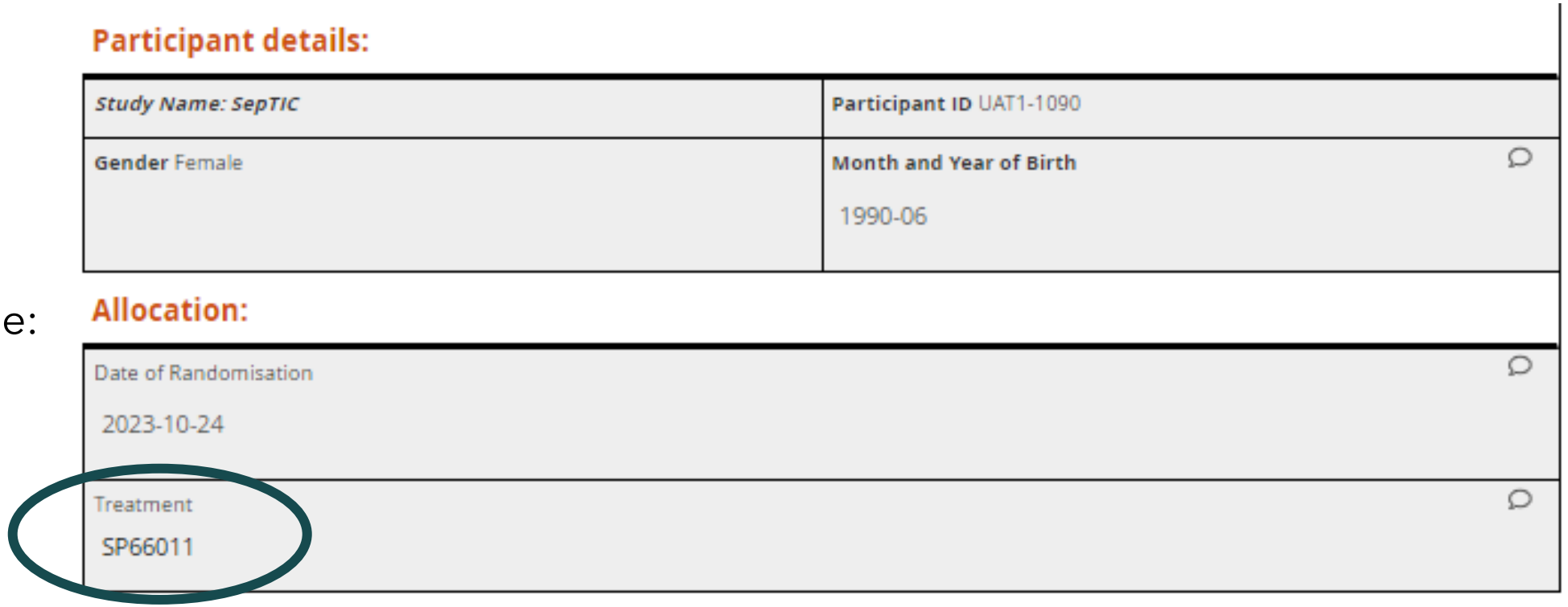
The GM-CSF randomisation assignment form will have the fluid treatment allocation

Example:



Participant details:

Study Name: SepTIC	**Participant ID** UAT1-1090
Gender Female	**Month and Year of Birth** 1990-06

Allocation:

Date of Randomisation 2023-10-24
Treatment SP66011

The treatment will be the kit number that the patient has been assigned to. Make a note of the kit number.
Click 'Complete to close the form'

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Randomising Guidance

- If you cannot see the treatment allocation, only try re-opening the form in edit mode **ONCE**
- OpenClinica have informed us if this does not work, do not try again
- Contact the SepTiC trial team to guide you through clearing the forms and randomising again

septic@imperial.ac.uk

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