OpenClinica eCRF Completion Guidelines for PANTHER Study

Version: **1.0**

Date: **17-OCT-2025**

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1. OpenClinica Support

Contact Clinical Data Systems (CDS) Production Support for any OpenClinica related queries.

By e-mail: cds_support@imperial.ac.uk

By phone: +44 (0)207 5942614

Links to the OpenClinica training modules can also be found on the Website:

https://www.imperial.ac.uk/clinical-trials-unit/clinical-data-systems/cds-openclinica/training-openclinica-40/

2. Study Database Access

Upon successful completion of the OpenClinica role(s) based training, a user can request an OpenClinica account by completing the OpenClinica User Activation Form (UAF) accompanied by the relevant training certificate to your Regional Manager.
The form requires approval by the Study Manager. Once the form has been completed and sent to CDS Production Support, the requested role will be created in OpenClinica.

You will receive a time sensitive email from OpenClinica inviting you to the study, which includes details of the URL and a link to setup your password. You will have 14 days to click on the link to activate your account. If the time passes and the link becomes inactive, contact the CDS Production Support team and they will send you the invitation again. Please try to complete process in a timely manner.

URL: https://imperial.openclinica.io/OpenClinica

OpenClinica is a cloud-based system which is accessible via one URL to access all studies you are assigned to.

Once your account has been activated, enter the unique username and password to gain access to OpenClinica.

Username and password are personal and must not be shared or transferred to other persons.

2.1 Password Management

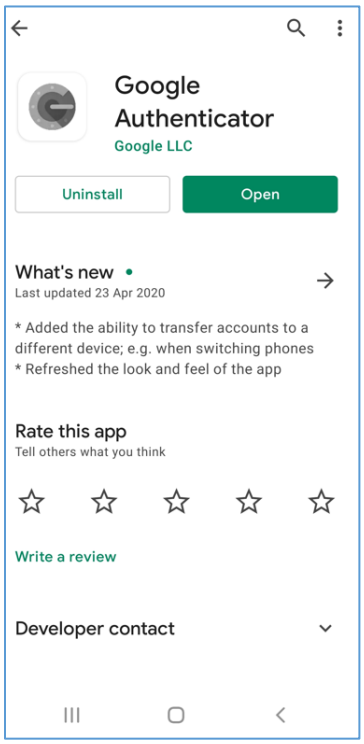
If you forget or enter an incorrect password more than twice you need to click on the "Don't remember your password?" link on the login page and answer the questions provided, the answers are based on those set up when you first logged in.

OpenClinica will send an automatic email to the registered email address (provided on the UAF) with a link to reset the password. This does not affect the QR code or the MFA login details.

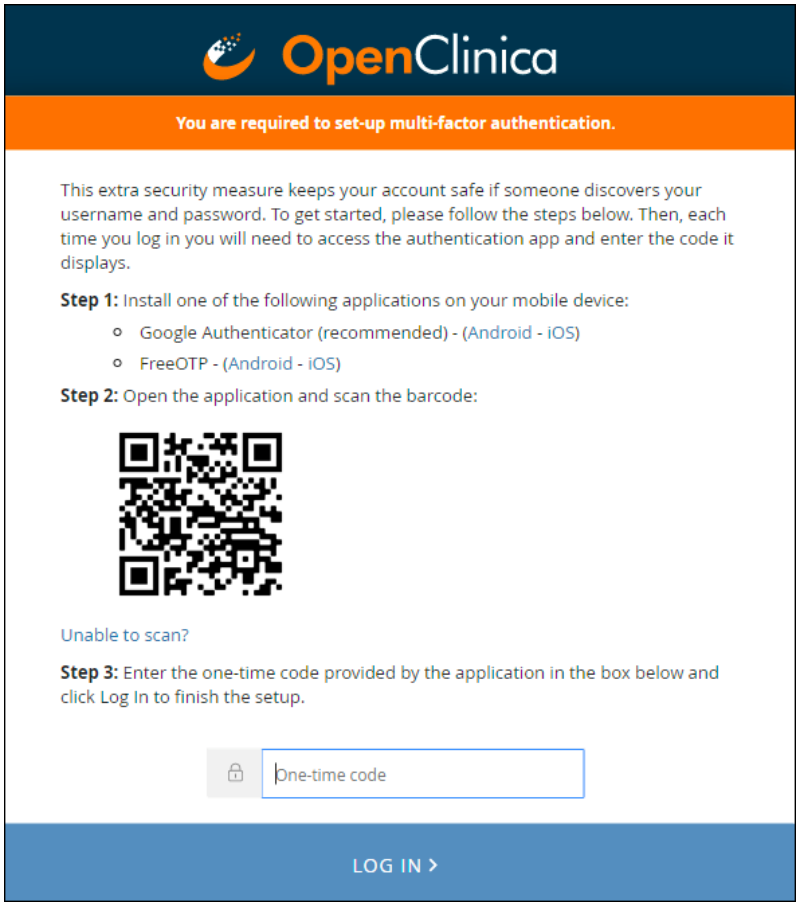
For forgotten log in details please contact the CDS Production Support who will be able to resend you the invitation.

3. Using Multi Factor Authentication (MFA) to log into OpenClinica

1. Firstly, install **Google Authenticator** on your mobile device. You will be required to use this app each time you sign in to OpenClinica.



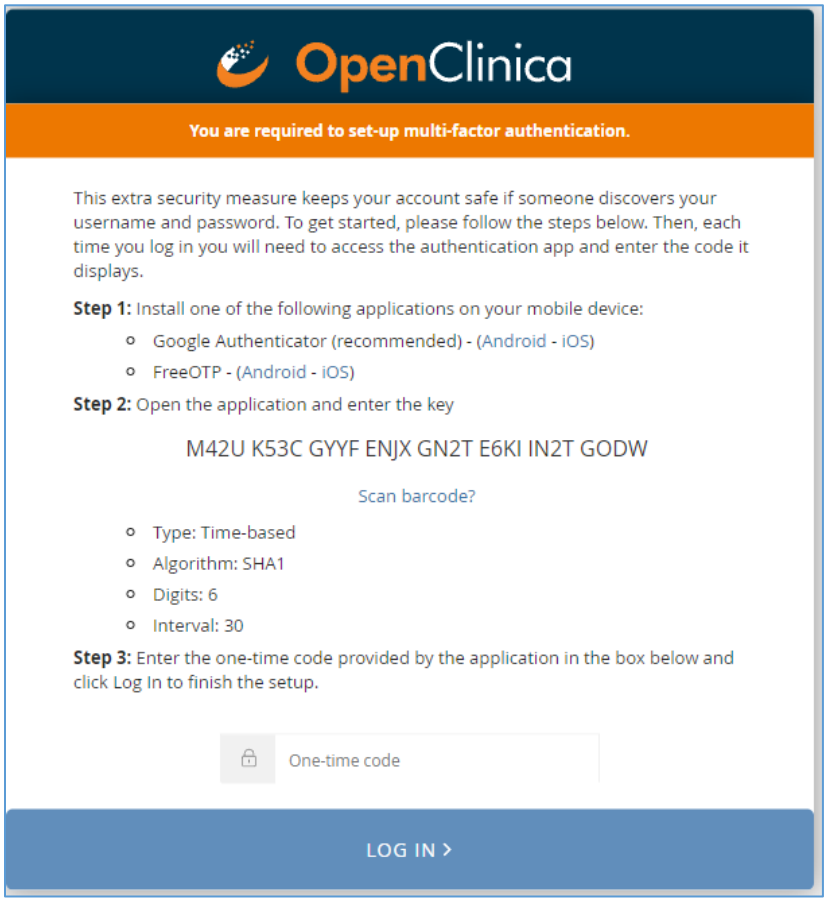
2. Open OpenClinica webpage (https://imperial.openclinica.io/OpenClinica/MainMenu) on your computer and login to your account with your existing username and password. Open the **Google Authenticator** on your mobile phone and scan the QR code displayed on the next page.



3. You will be provided with a 6-digit code on your mobile device after scanning the QR code on the computer screen.
4. Enter the 6-digit code into the field on the OpenClinica login page and click on “Log in”.

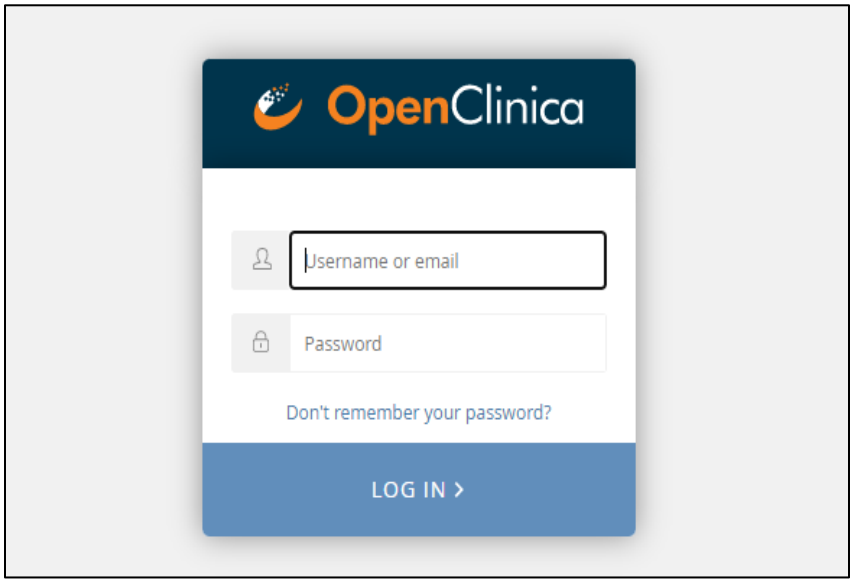
If you are unable to scan a QR Code

5. For users that are unable to scan the QR code, click on "**Unable to scan**" link on OpenClinica webpage after entering your username and password. This will provide 32-key code.

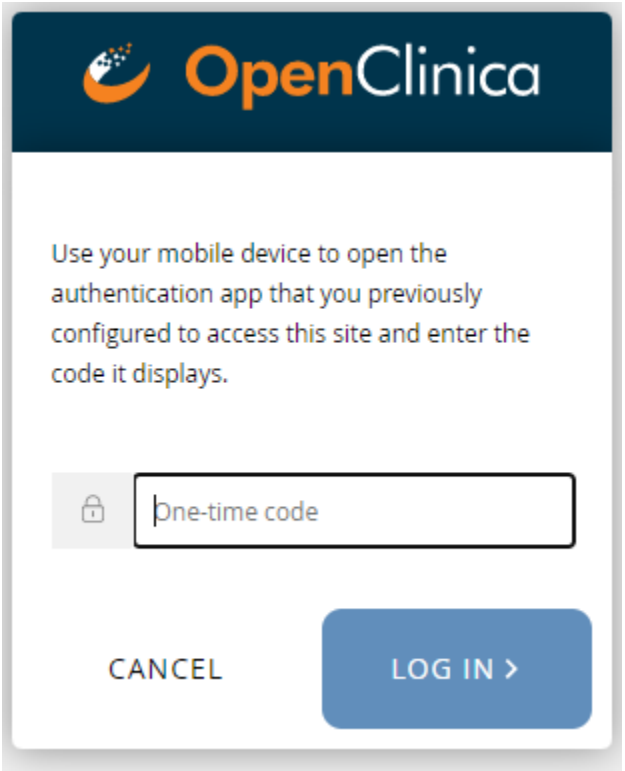


6. On the mobile app (**Google Authenticator**), select "**Enter a setup key**" and enter the 32-key code provided in the step above. This will generate a 6-digit code that will need to be entered into the field on the OpenClinica login page and click on "Log in".
7. The scanning of the QR code (or entering the 32-digit key code) is a one-time step.

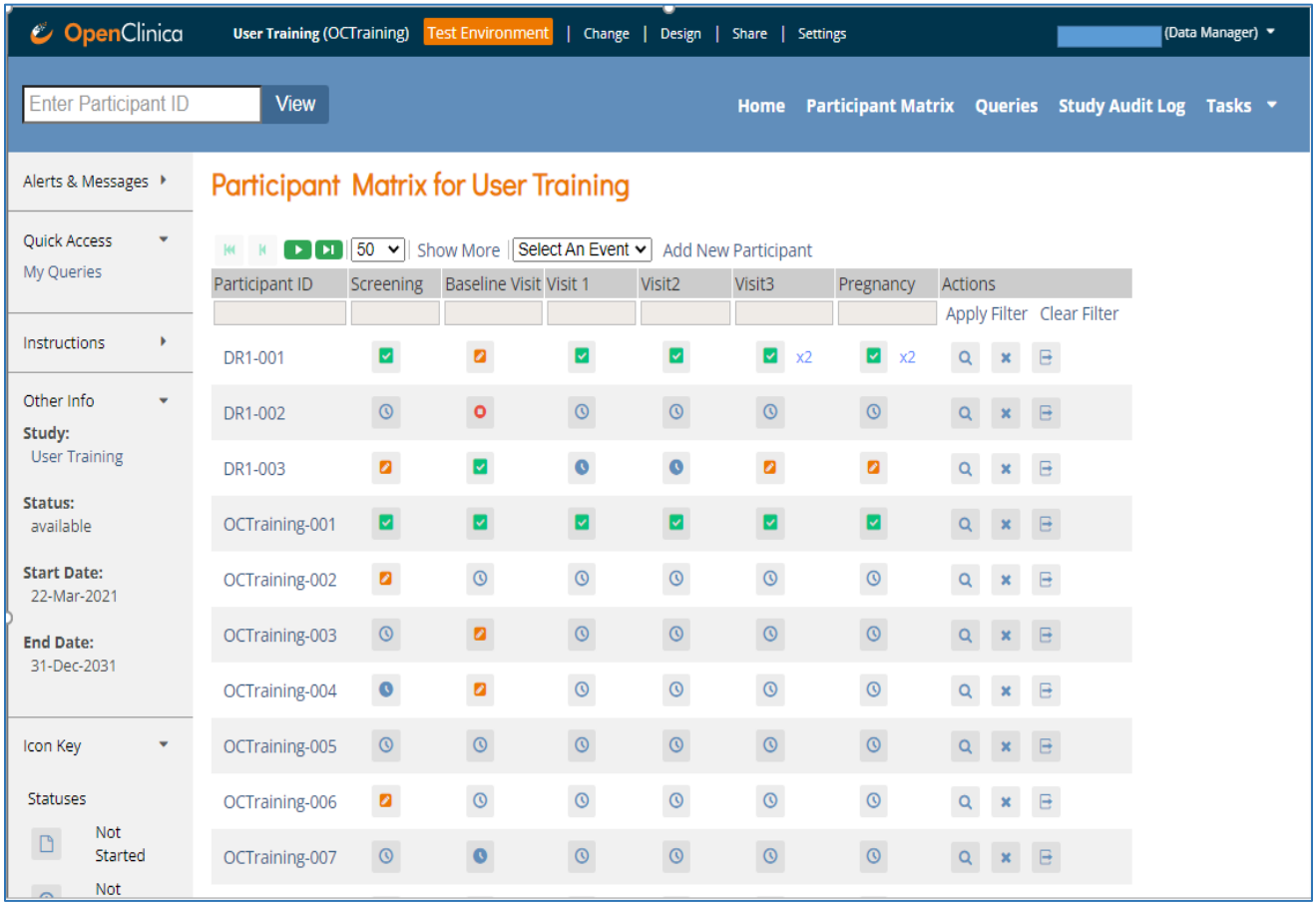
Once this is setup, the account is saved on Google Authenticator app and the 6-digit codes are generated automatically without the need for a QR Code or a key code each time you try to login.



Once these details are entered, click “LOG IN”. The system will then display another screen in which to enter your one time code, this is generated by the Google Authenticator app on your smartphone. You will be required to download the Google Authenticator app to retrieve this code before you can access your study. Enter the code that appears in the authenticator app into the and click “LOG IN”



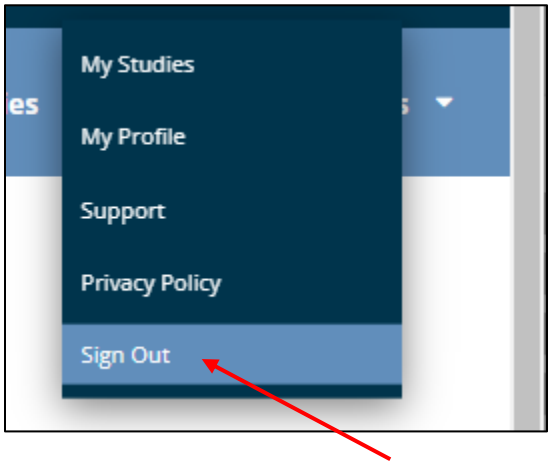
The system will then display a **HOME** screen which is dependent on your user role. Monitor role will have a different home screen to Data Entry, CI and PI roles (Participant Matrix home screen will be displayed). The HOME screen showing this study information {Title, CI, Site etc.)



It is good practice to log out once you have finished using the OpenClinica application. This is particularly important if you are not using your own computer.

After a set period of inactivity (1 hour by default) you will be automatically logged out of the system.

To log out click on the 'Sign Out' button in the navigation bar at the top right hand side of the page.



4. General Data Entry Guidelines

Data entry must be completed for ALL subjects. To adhere to **Good Clinical Practice (GCP)**:

- Data entry for a completed visit should be performed within **14** business days.
- Data queries should be answered within **14** business days
- Data entry must only be completed by authorised personnel who have received trial-specific and OpenClinica training and are competent in eCRF completion
- Avoid using abbreviations in text fields (other than NA - **Not Applicable**, ND - **Not Done**, NK - **Not Known** and UNK - **Unknown**) and acronyms, unless they are approved medical abbreviations known to be acceptable.
- Avoid using abbreviations that are ambiguous or could be interpreted differently.
- Anywhere on the eCRF that **'other (specify)'** is selected, there is usually an entry in the space provided describing what 'other' means.
- Subject identifiers **should not** be used anywhere on the eCRF, such as subject's name, initials, address, hospital number etc., in order to maintain the confidentiality of the subject.

4.1 General data entry guidelines for PANTHER in OpenClinica

1. **Browser – Google Chrome**

- When using OpenClinica, Google Chrome is the preferred browser option set by the manufacturer, if possible, please use this browser during data entry.

2. **Common formatting**

1. **Dates and Time**

Enter date by choosing from the manual calendar, the format is year/month/day i.e., yyyy-mm-dd for example 13th August 1999 is 1999-08-13.

Enter time in a 24-hour clock format i.e., HH:MM e.g., 3:25pm would be entered as 15:25

2. **Values**

For values with decimal points, you may need to round the value up or down. To do this:

Decide which is the last number to keep.

Leave it the same if the next number is less than 5 (called rounding down) OR

Increase it by 1 if the next number is 5 or more (called rounding up)

Example 1: To round a value up or down to the nearest <u>whole</u> number

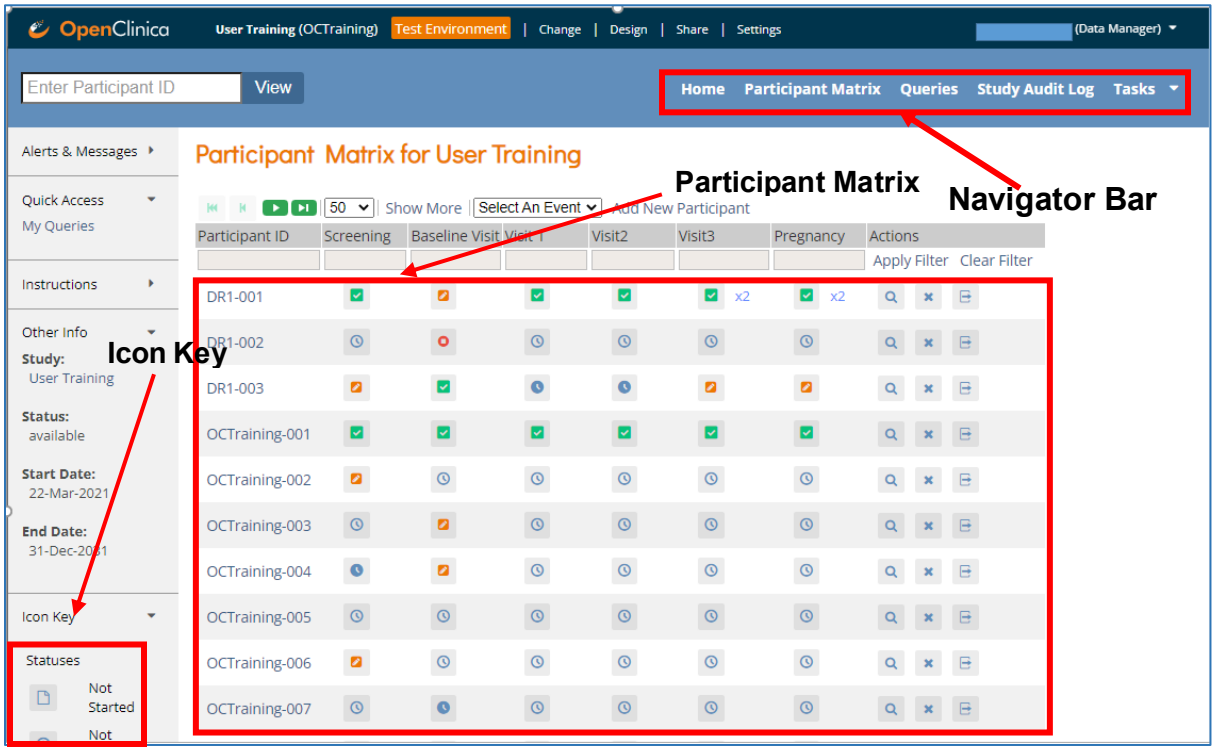
- 72.26 would be rounded down to 72 (as the next number is less than 5)
- 72.53 would be rounded up to 73 (as the next number is 5 or more)
- 72.81 would be rounded up to 73 (as the next number is 5 or more)

Example 2: To round a value up or down to 2 decimal points

- 72.2638 would be rounded down to 72.26 (as the next number is less than 5)
- 72.2684 would be rounded up to 72.27 (as the next number is 5 or more)

4.2 Study Home Page

After login and selecting the study, you will be directed to the respective eCRF. Here you find the 'Navigation Bar' and an overview about the status of the study which is the 'Participant Matrix'. The 'Icon Key' can also be found.



4.3 Navigation Toolbar

The Navigation toolbar provides access to some additional task features:

Home: Use to navigate to the Home page designed for your study. which can be the **Welcome** screen, **Participant Matrix**, or **Source Data Verification** screen (depending on role)

Participant ::.Matrix: This screen displays the Participant's general information, Events, and Forms.

: **Queries:** Displays query statuses information on your study

Study Audit Log: Displays audit trail history for each participant in the study

Tasks: Also lists associated tasks

4.4 Adding a Participant

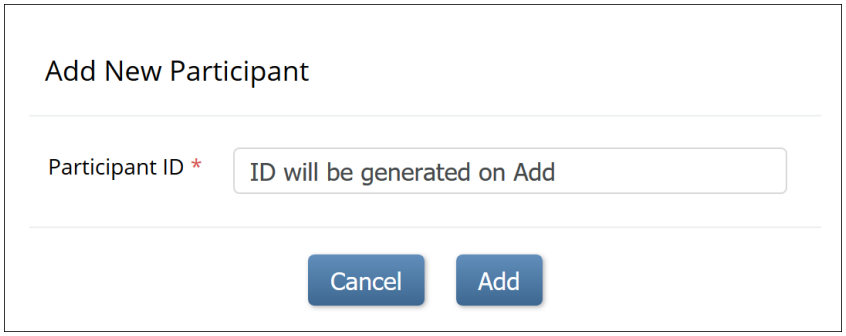
Participants can be added automatically this will be dependent on the chosen method of creation for your study.

:

1: Click on '**Tasks**' in the Navigation Bar and then select '**Add Participant**'

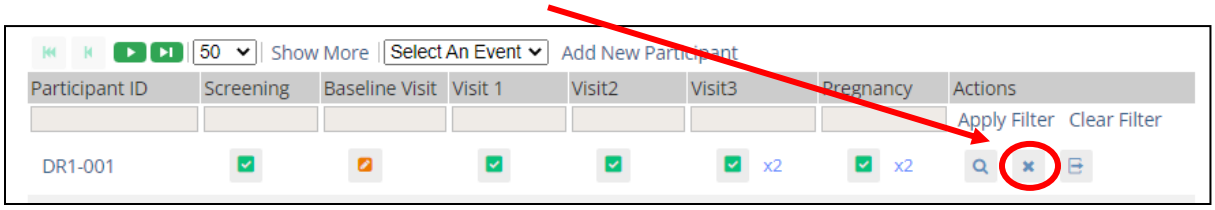
To add a participant automatically:

1. Set the **Method of Creation** field to **System-generated** (see above).
2. From the **Tasks** menu, select **Add Participant,** or on the **Participant Matrix** screen, click **Add New Participant** above the matrix.
3. Click the **Add** button in the **Add New Participant** screen to generate a Participant ID.



5. Removing/ Restoring Participant Data

Data Manager and CI or PI user roles only - If you want to REMOVE a participant from the study, open the **Participant Matrix** and remove the subject by selecting the ( ) icon in the **Actions** column.



You will be redirected to the screen '**Remove Participant from Study' → Click 'Remove Study Participant**' to confirm you want to delete the subject from the eCRF.

This action can be undone by clicking on the Restore icon ().

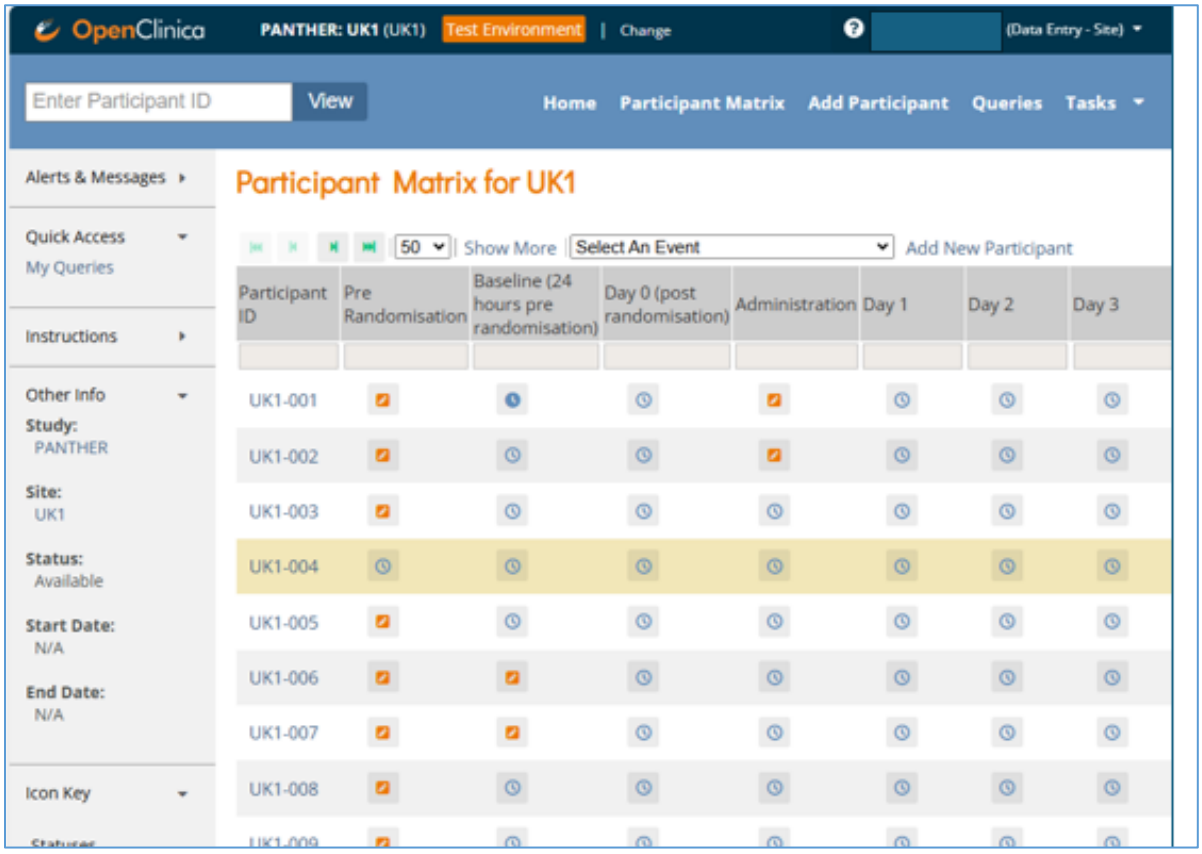
6. Participant Information

6.1 Participant Matrix

The 'Participant Matrix' displays a table for allparticipant subjects) and their data entry status in the Study (per site). One participant per row, with the Study Participant ID in the first column. The other columns are for Visit events.

You can view, enter, and change data for participants. Each cell in the matrix shows an icon that identifies the status of the CRF for the participant.
Move the cursor over an icon in the matrix to view and access participants data and to access actions you can perform for that CRF. Refer to the Icon Key in the sidebar for icon descriptions and see about the Event Status for more details.

This layout provides the visit-based events for subjects showing the overall statuses, definitions of each status is found in the icon key section , bottom left of the screen.



6.2 Icon Key

Below displays the icon definitions which show the status of an Event:

Status/Action	Icon	Description
Not Started		The Event has not been started.
Not Scheduled		The Event has not been scheduled.
Scheduled		The Event has been scheduled, but no data has been entered.
Data Entry Started		A user has started to enter data. If the Event is in 'data entry started', you can't go back to previous Status.
Stopped		The Participant has temporarily stopped participating in the study. this status can be selected from the dropdown menu on the 'Update Event' screen when the current status is data entry started.

Skipped		The user has decided not to complete the Event. Any data that has been entered can still be viewed and/or exported. You can select this setting from the dropdown menu on the Update Event screen when the current status is scheduled.
Completed		A user has completed data entry for at least one Form in the Event. If further changes are needed in that Form, you are required to provide a reason for change.
Signed		The Study Event has been signed off. This icon appears in addition to the status. When the Investigator signs the casebook for a Participant, the OpenClinica system automatically sets the status for all Study Events for that Participant to 'signed.' After an Event status is 'Signed,' any changes to the CRF automatically change the Event status back to 'Completed.'
Locked		The Study Event has been locked. No data can be added, and the Event cannot be removed. This icon appears in addition to the status. This is performed by the Data Manager role. Note: You can set the status for a Study to 'frozen' or 'locked,' and while that does not change the status of any Events in the Study, it does prevent users from changing data.
Archived		The Study Event has been archived. This icon appears in addition to the status. This is performed in Study Designer.
Removed		The Study Event has been removed for a participant.

6.3 Events

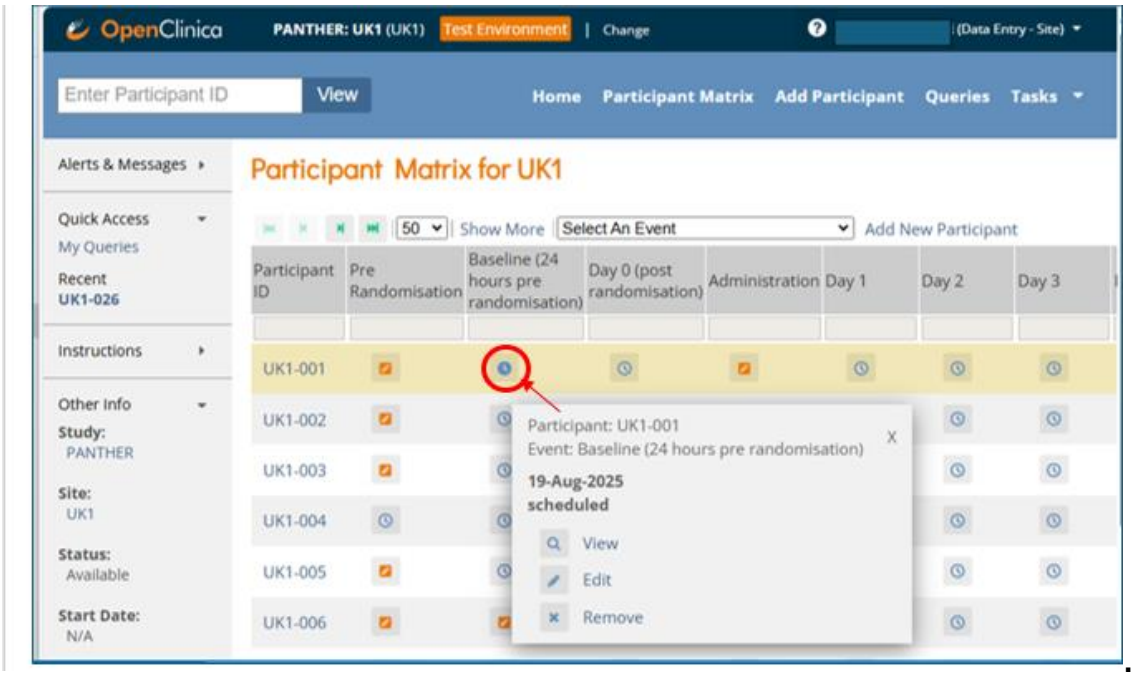
A (Study) Event (visit) is the timepoint in the study where data has to be entered in the eCRF. The following events are defined for PANTHER study:

- Pre Randomisation
- Randomisation PANTHER A; Randomisation PANTHER AB; Randomisation PANTHER B; Randomisation PANTHER C; Randomisation PANTHER CD; Randomisation PANTHER D

- Baseline (24 hours pre randomisation)
- Day 0 (post randomisation)
- Administration
- Day 1; Day 2; Day 3; Day 4; Day 5; Day 6; Day 7; Day 8; Day 9; Day 10; Day 11; Day 12; Day 13; Day 14; Day 15; Day 16; Day 17; Day 18; Day 19; Day 20; Day 21; Day 22; Day 23; Day 24; Day 25; Day 26; Day 27; Day 28
- Discharge ICU
- Discharge Hospital
- Day 90
- Day 180
- Day 365

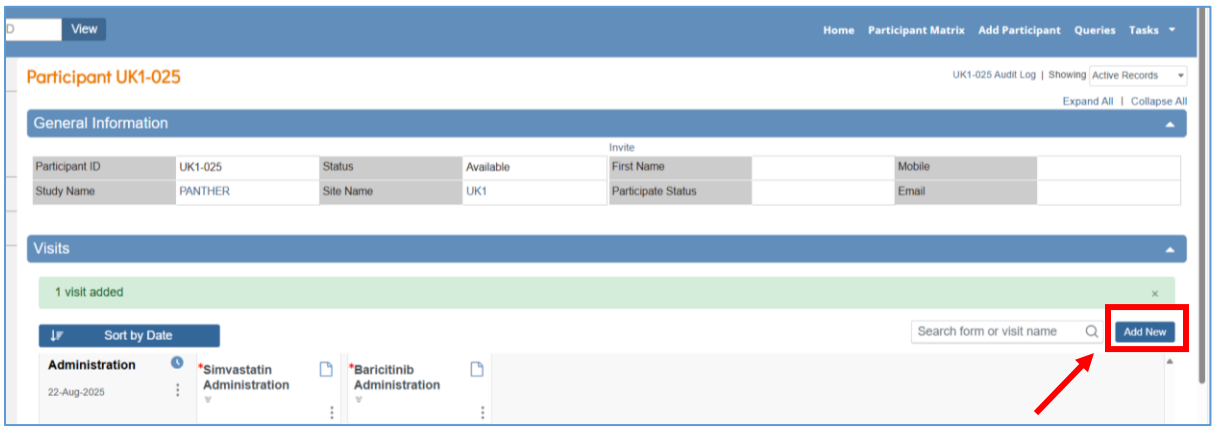
To view or Edit data for a participant

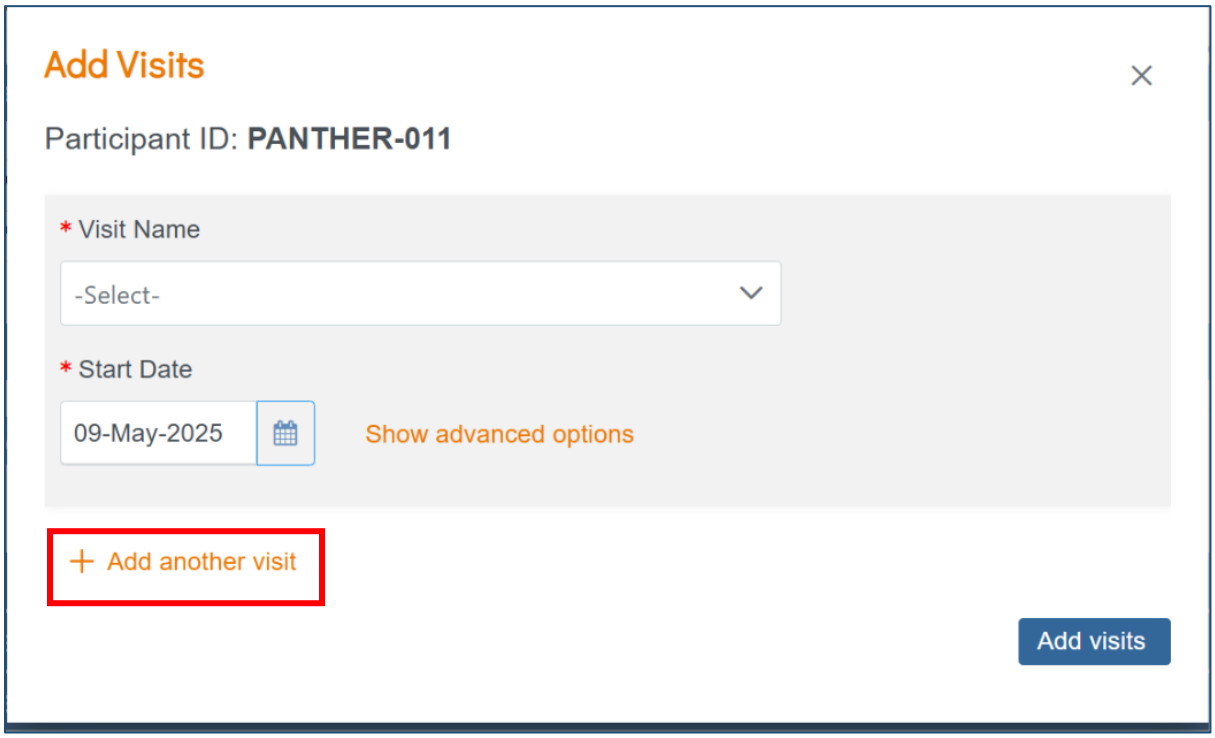
Click the icon for a **scheduled**, **data entry started**, or **completed** Event and select **View/Enter** to view the **Participant Details** screen



6.4 Adding a Study Event

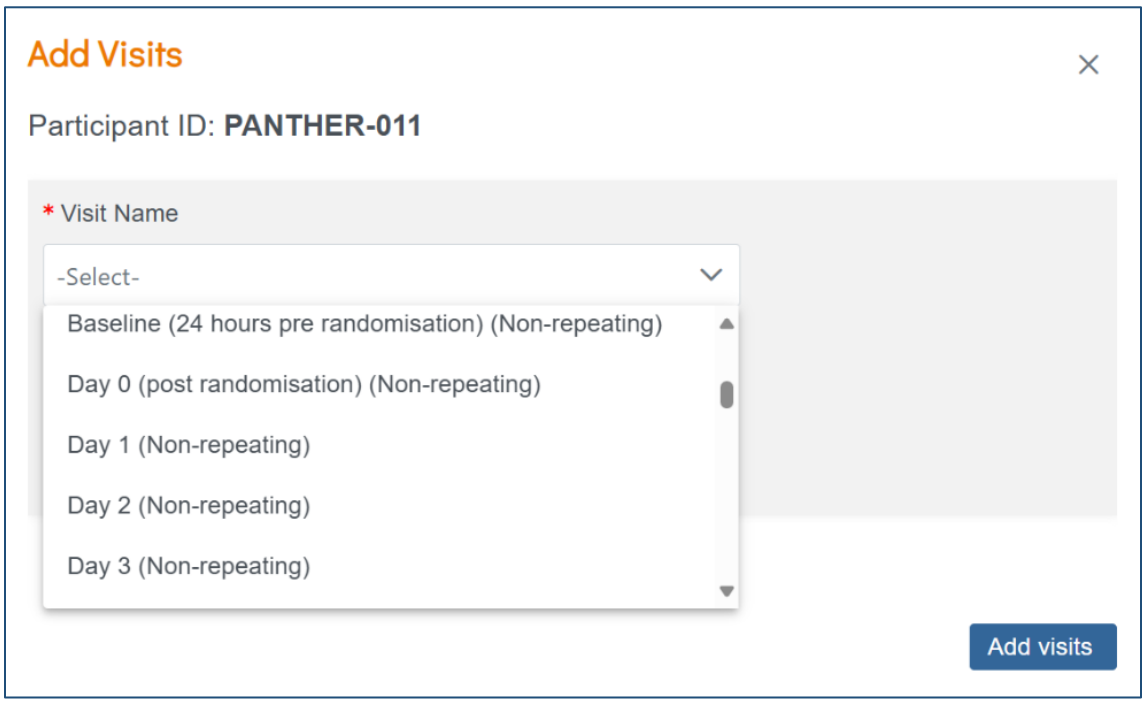
Once the patient ID has been generated, the patient visits can be added. Visits are added by clicking ‘Add New’ on the right-hand side of the Participant page. This generates the ‘Add Visits’ pop-up window.



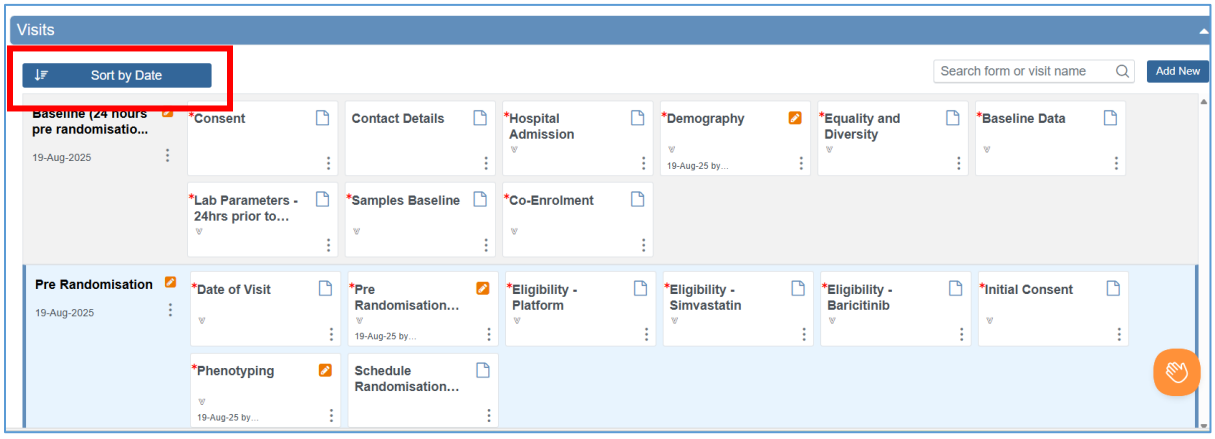


The drop-down list can be seen below, the list is chronological, and you can select which visit you want to add from this.

When the visits have been added they can be seen on the participant page, starting with the first at the bottom moving up in a chronological order. The order can be flipped with the first at the top by clicking ‘Sort by Date’ on the top left-hand side. This means that the first visit ‘Screening (Diagnostic and Fluid)’ will now be at the top of the page.



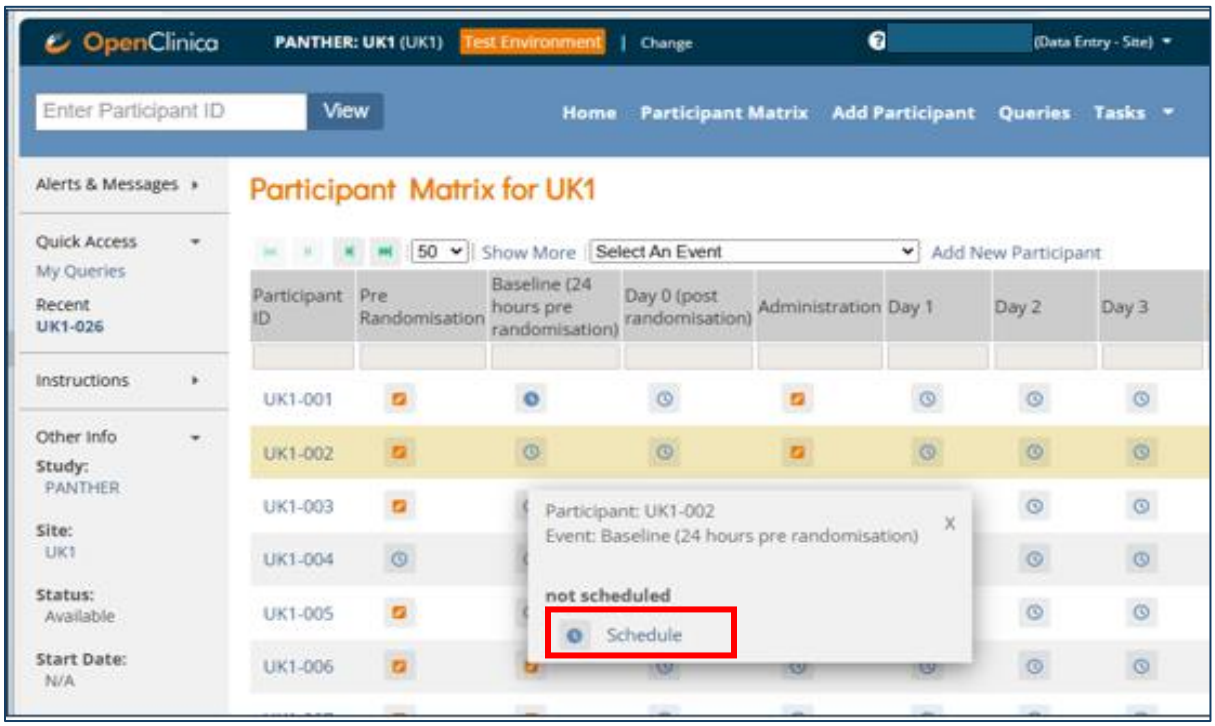
When the visits have been added they can be seen on the participant page, starting with the first at the bottom moving up in a chronological order. The order can be flipped with the first at the top by clicking 'Sort by Date' on the top left-hand side. This means that the first visit will now be at the top of the page.



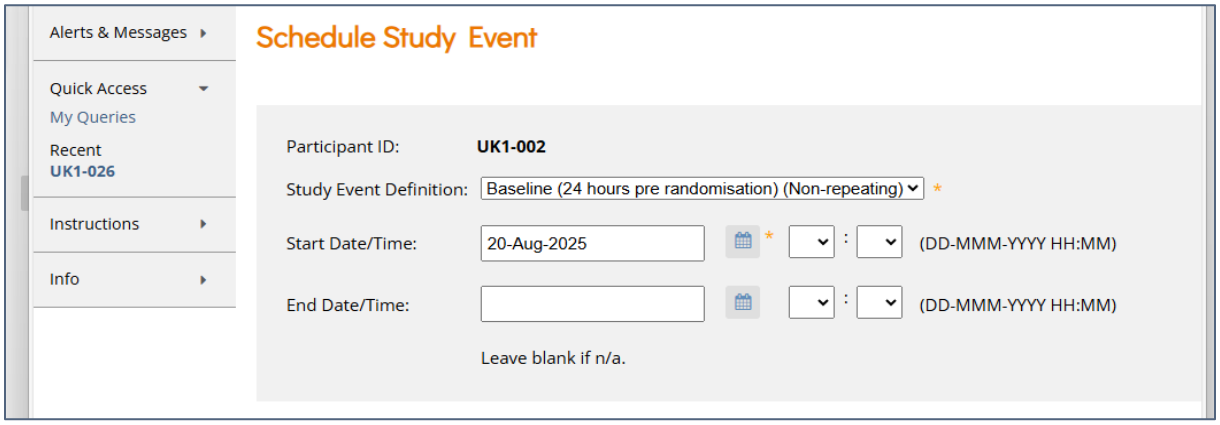
It is advised that only visits that are being completed at that moment should be added as any that are not needed can be removed however it can be problematic for the PI and CI sign off later on.

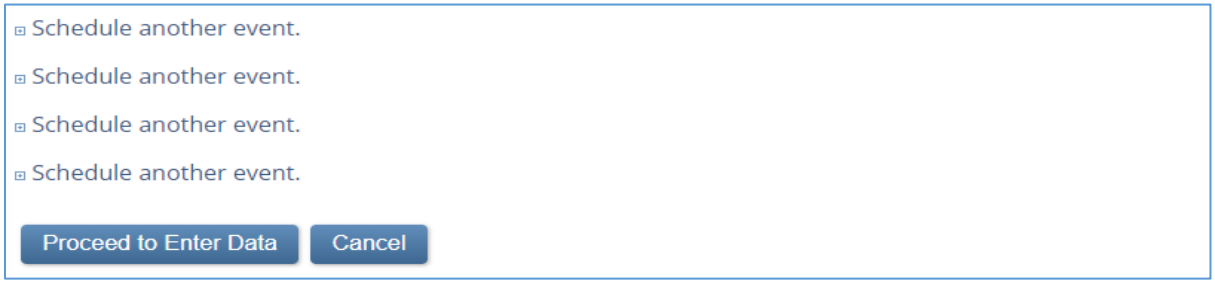
6.5 Scheduling a Study Event

If you want to enter data, you have to schedule the respective Event. This is done in the '**Participant Matrix'**. Please click on the Event you want to schedule. A window pops up and then click on '**Schedule'**.



The 'Schedule Study Event' screen appears.



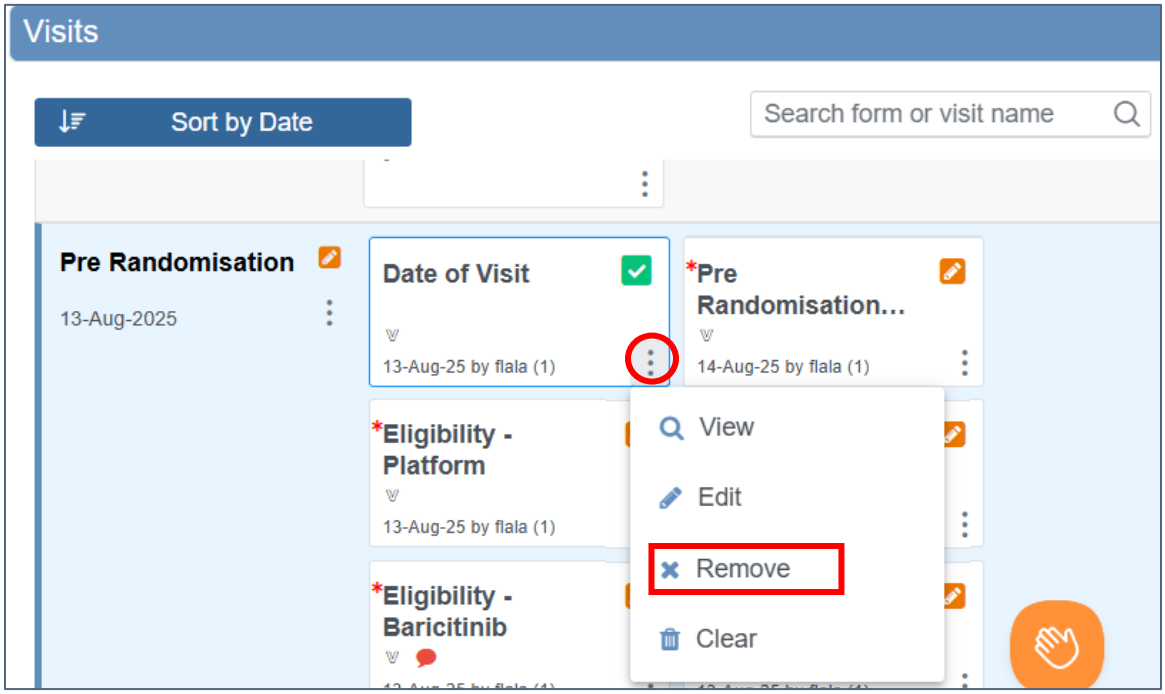


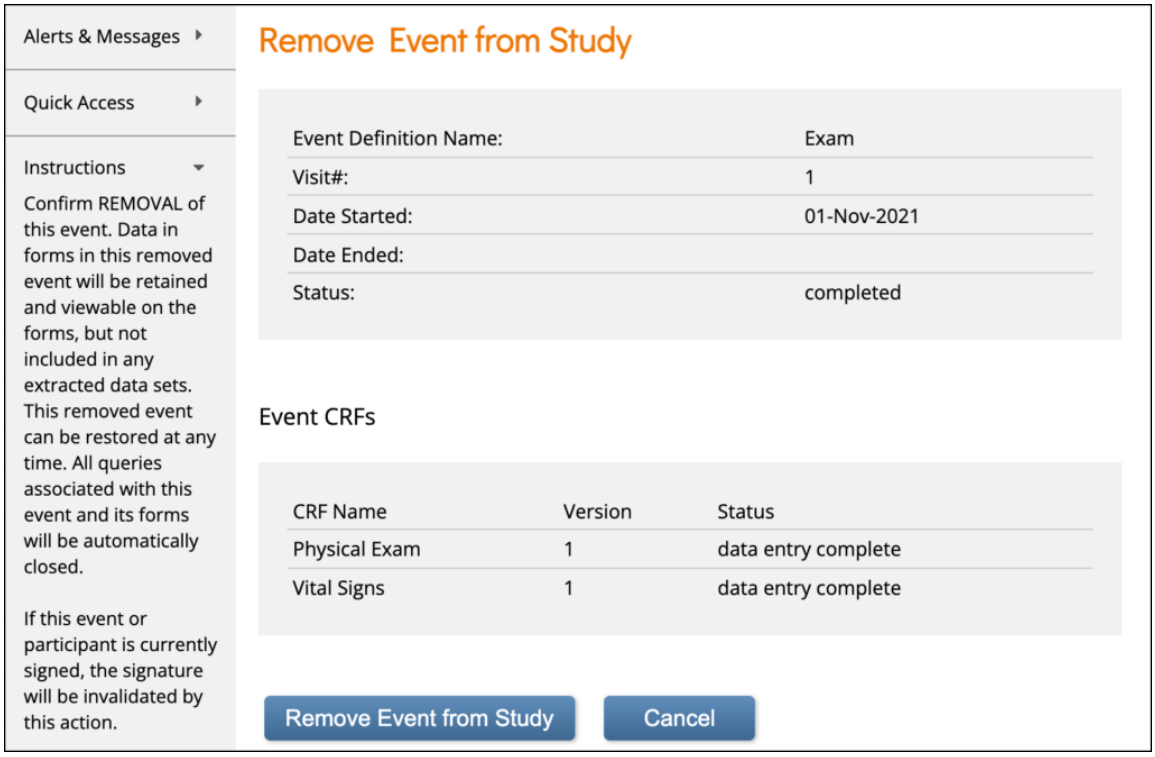
- Complete the screen details:
- **Study Event/Definition**: Select the respective event from the drop-down list.
- **Start Date/Time**: Default date is the current date when Event is scheduled in the eCRF or enter date required. This field is optional.
- **End Date/Time**: Enter date, this field is optional.
- Then click **'Proceed to Enter Data'** Now the respective event has been scheduled and you may start the data entry.

6.6 Removing an Event

If an Event has been entered in error, you can remove that event or form (examples below are shown for an Event).

To remove the event Click the **Remove** button in the **three dots** menu on the **Participant Details** screen. This is replaced with the **Restore** button.

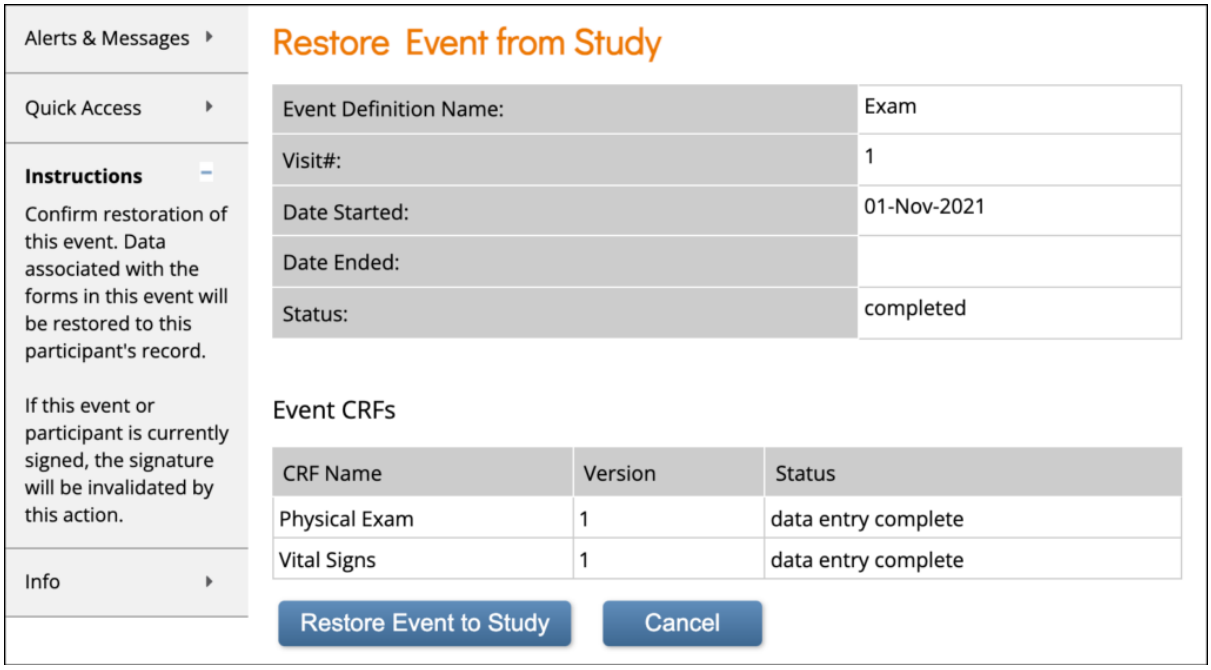




Note: If an Event is removed after being signed, the signature is invalidated, and if restored, the form must be signed again.

6.7 Restore an Event

If you have removed an Event you want to restore, click the **Restore** button in the three dot **Event Actions** menu on the **Participant Details** screen. This is replaced with the **Remove** button.

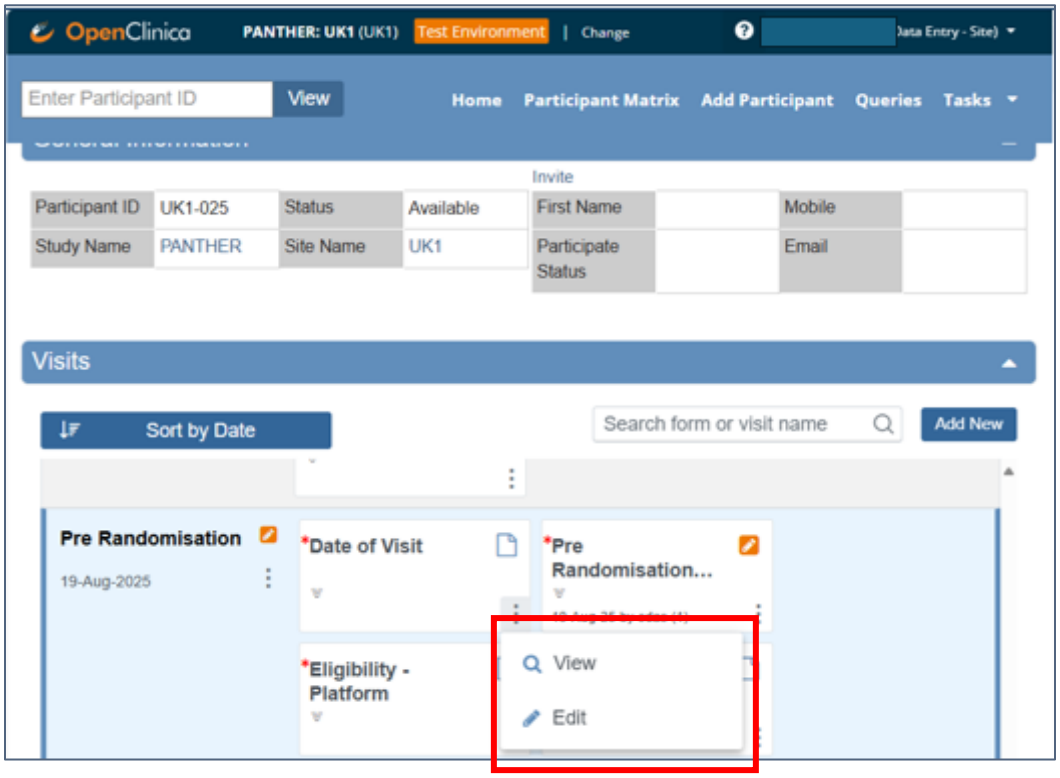


Please note: If an Event is removed after being signed, the signature is invalidated, and if restored, the Form must be signed again. When data was entered on the Form prior to the Event being removed, The event this form is in has been removed **appears at the top of the Form.**

7. Entering Data

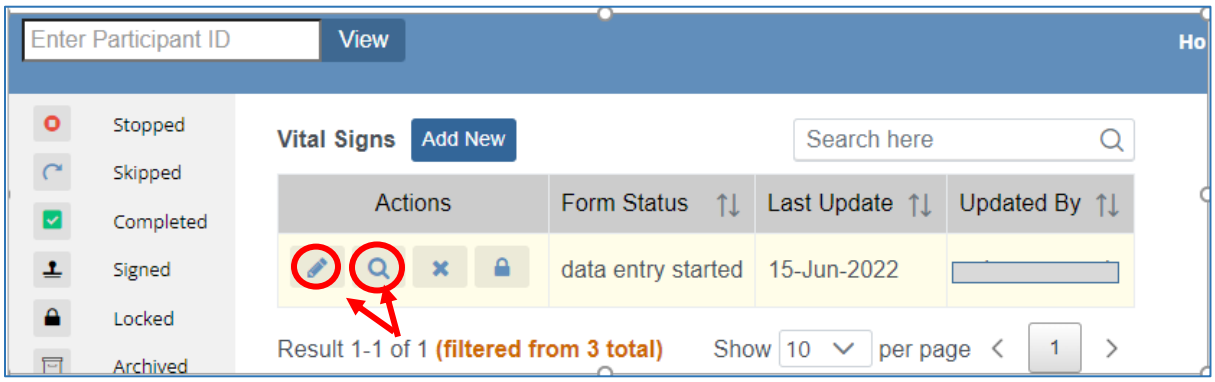
7.1 Data Entry Directly into a Form

1. Click the **Add New** button to add a form associated with the Event. This will open the form directly for you to document.
2. Click the **Edit** button in the **three dots** menu to open the form.
3. Enter information into each field.



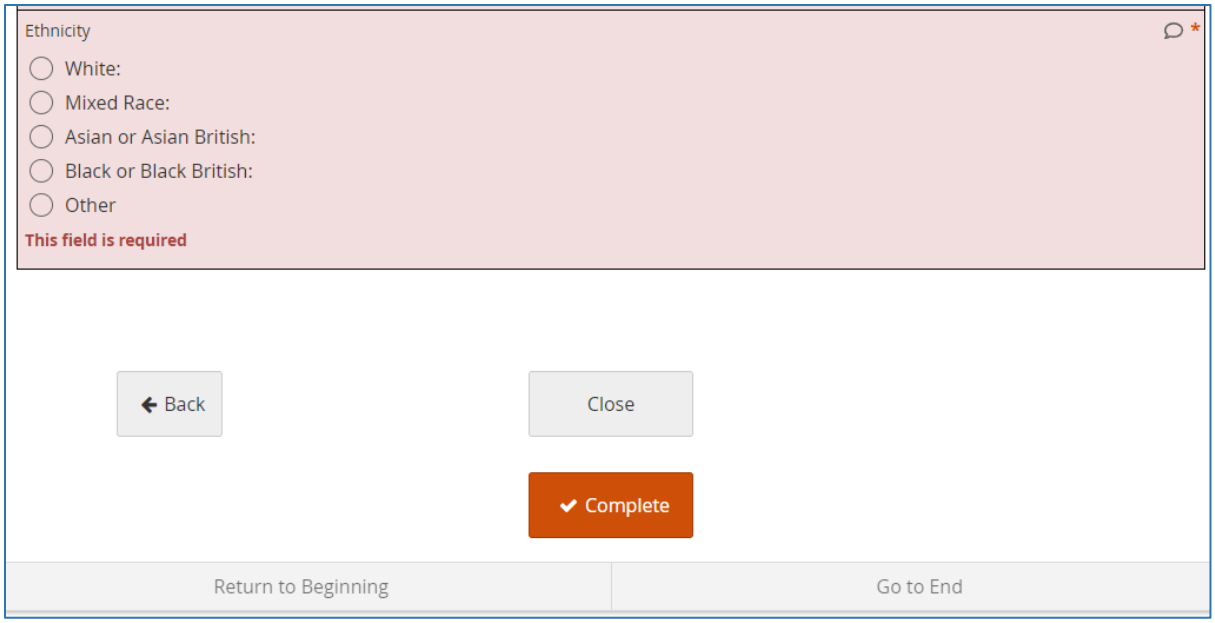
Alternatively

- Click on the pen icon to enter or edit data in the form.
- Click on the magnifier to view data in the form.



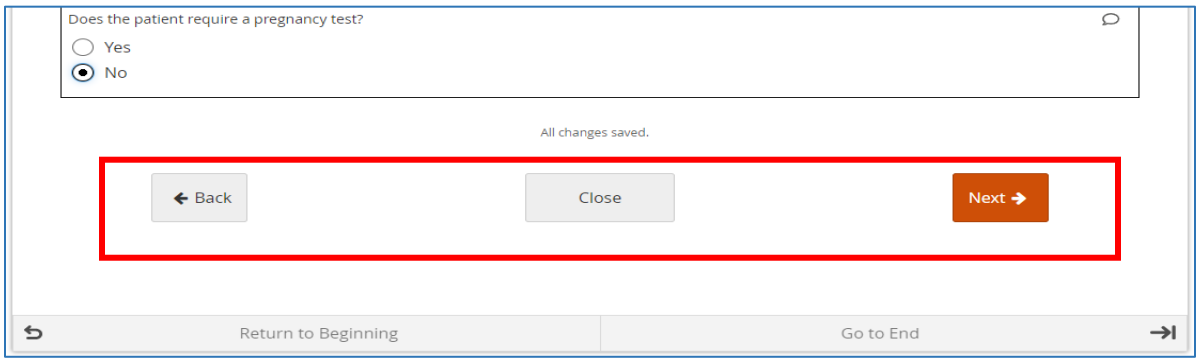
When you select the 'Pen Icon', the CRF form opens and you can start to enter data. Please fill in the entire form. When you have finished entering data, you can close the CRF Form and continue to enter data later or select **'Next'** or **'Complete'**

If you forget to enter data in at least one mandatory field, when you click 'Complete', you will receive an error message alert.



7.2 Navigating Between Forms

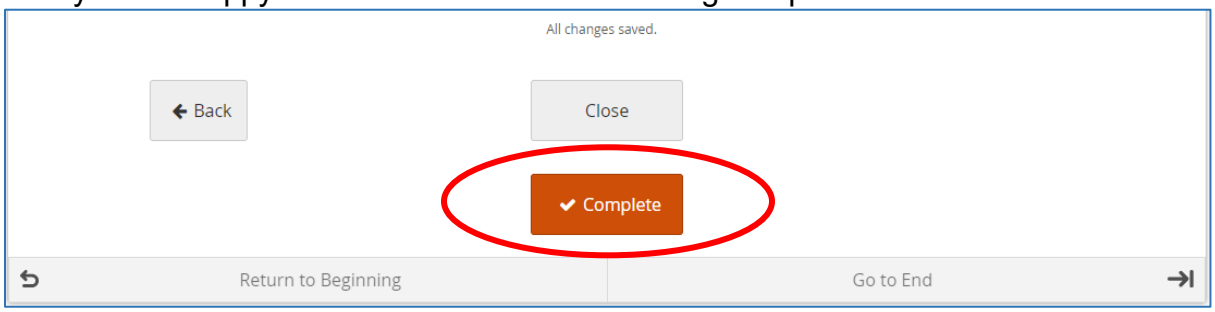
If you click **Next**, the system will automatically move you to the next page in the event form when it finishes saving the data. If you click **Back** you will go back to the previous section of the CRF. Closing the form saves all changes made.



7.3 Marking the CRF Complete

The CRF must be marked complete, after finishing data entry for the complete CRF. When all sections (of an event) are complete, select '**Complete**'.

NOTE: Please only mark the form as ‘Complete’ when all the missing data has been entered. A query will only be raised when the form is marked as complete, so make sure you are happy with all the data before clicking complete.

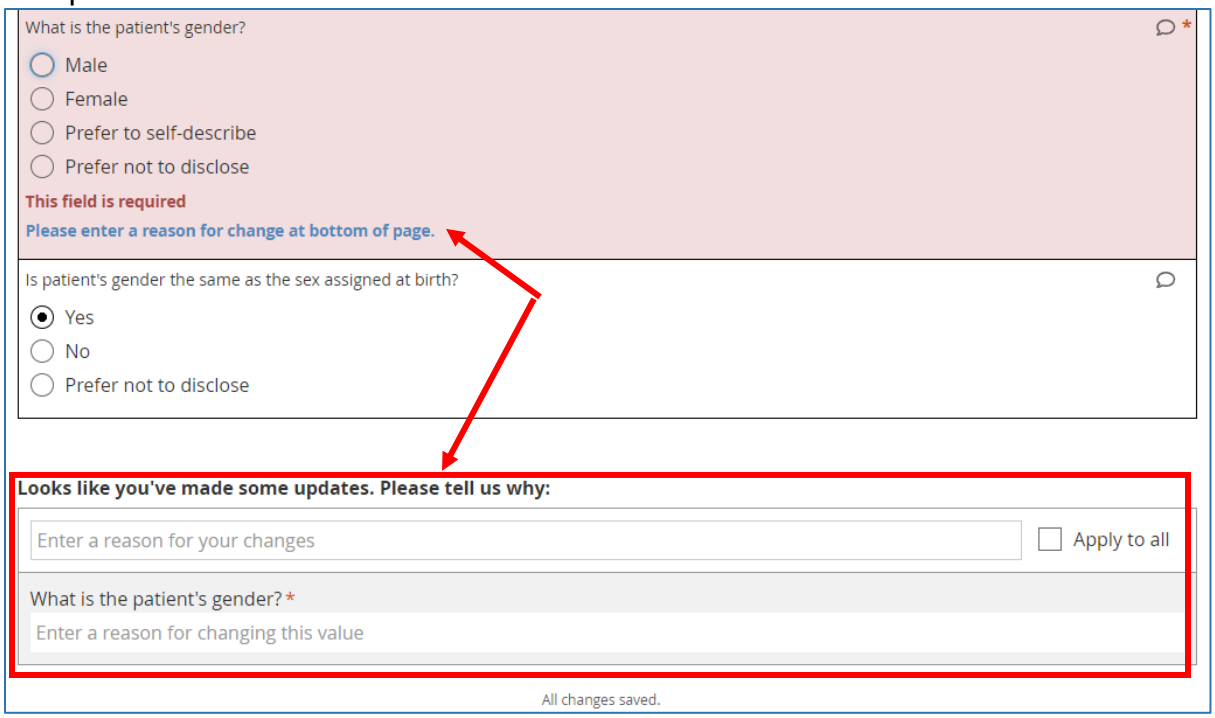


This will change the status of the CRF from ‘Data Entry Started’ to ‘Complete’ . The Status of the CRF will remain complete, even if the data is changed afterwards.

7.4 Changes made to a CRF Form after being marked Complete

If you make any changes to the data after it has been marked complete, an alert occurs and you will be required to enter a note indicating the reason for change at the bottom of the form.

Complete both fields

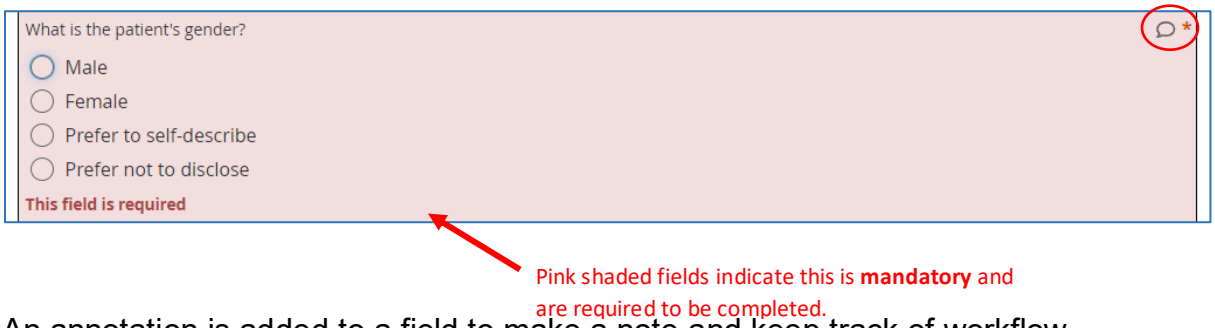


The Rights group roles that can perform data entry in OpenClinica are:

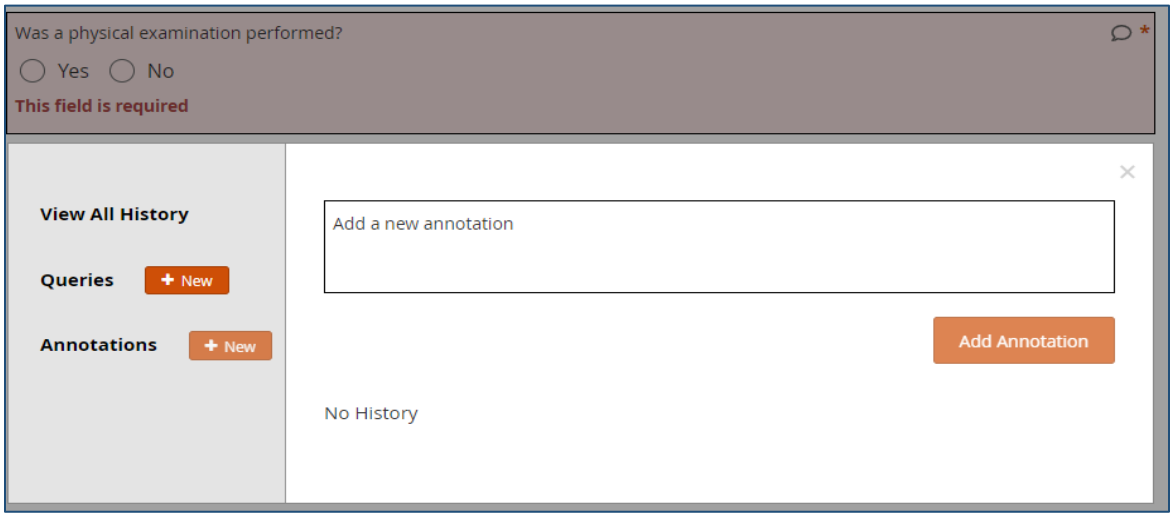
- Data Entry - Study
- CI
- PI
- Data Entry - Site

7.5 Specific Field Types: Mandatory Fields

All mandatory fields will need to be completed – these fields will remain shaded with a pink background after the form has been submitted until they are completed. If any data are permanently missing because it is not done, unknown or not applicable, the site must click on the comment bubble icon and add an **'annotation'** in order to indicate this Although this site should make every effort to complete mandatory fields wherever possible.



An annotation is added to a field to make a note and keep track of workflow.



7.6 Specific Field Types: Empty Non Mandatory fields

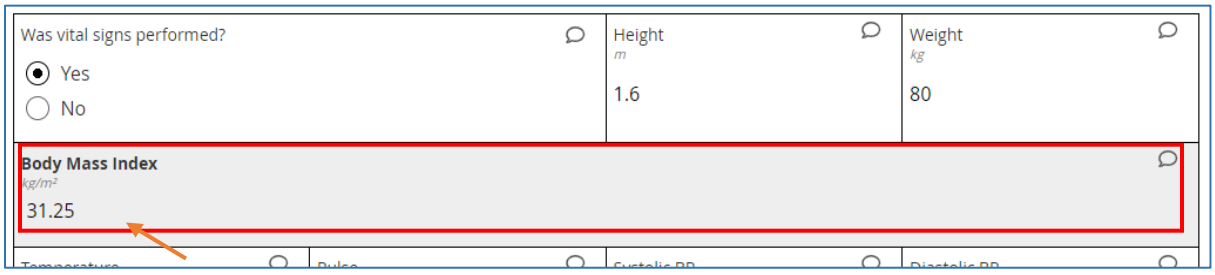
If for any reason a field is blank for any of the regular fields, within this field will be a comment bubble icon and add an annotation.

7.7 Specific Field Types: Date Fields

All date parts of the DATE field must be completed wherever possible, but there may be instances where this may not occur. Some dates are set up to allow partial dates to be entered. Where a date field is unknown this should be entered on the system. Your study requirements will have pre-defined date formats where applicable on the CRF forms.

7.8 Specific Field Types: Auto Calculate

You may see a field that does not have an area for you to enter data, but instead is a blank greyed out space. This is an auto calculated field i.e. either a mapping field from another entered field or a calculated field. When you enter the information, the system will take some of the information recorded and uses a formula to calculate a response for that field. You do not have to do anything except enter the data in the provided fields and submit.



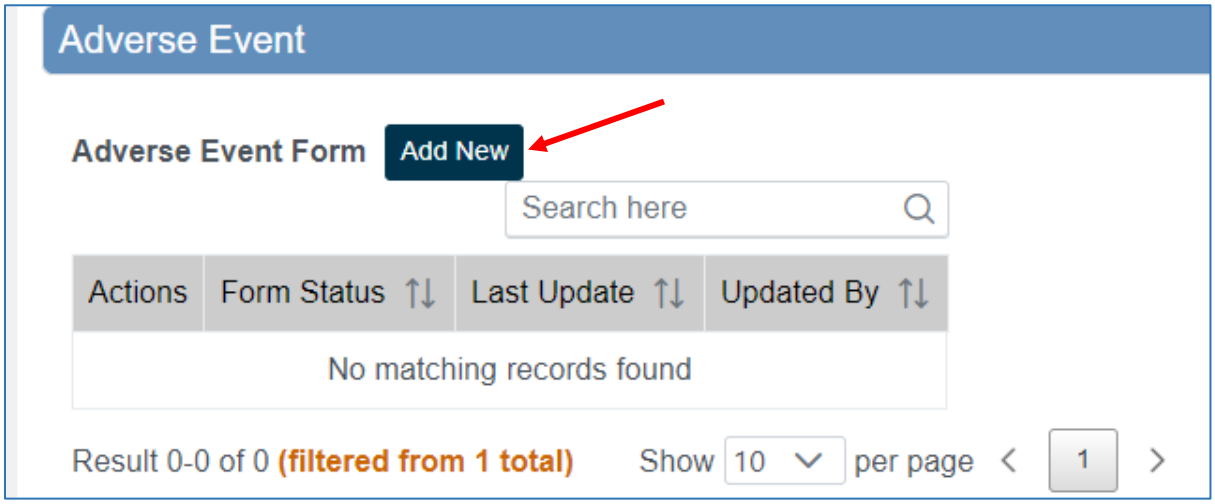
BMI automatically populated by OpenClinica system.

Data Entered and Saved - BMI has been calculated from entered height and weight.

7.9 Study Event Repeats

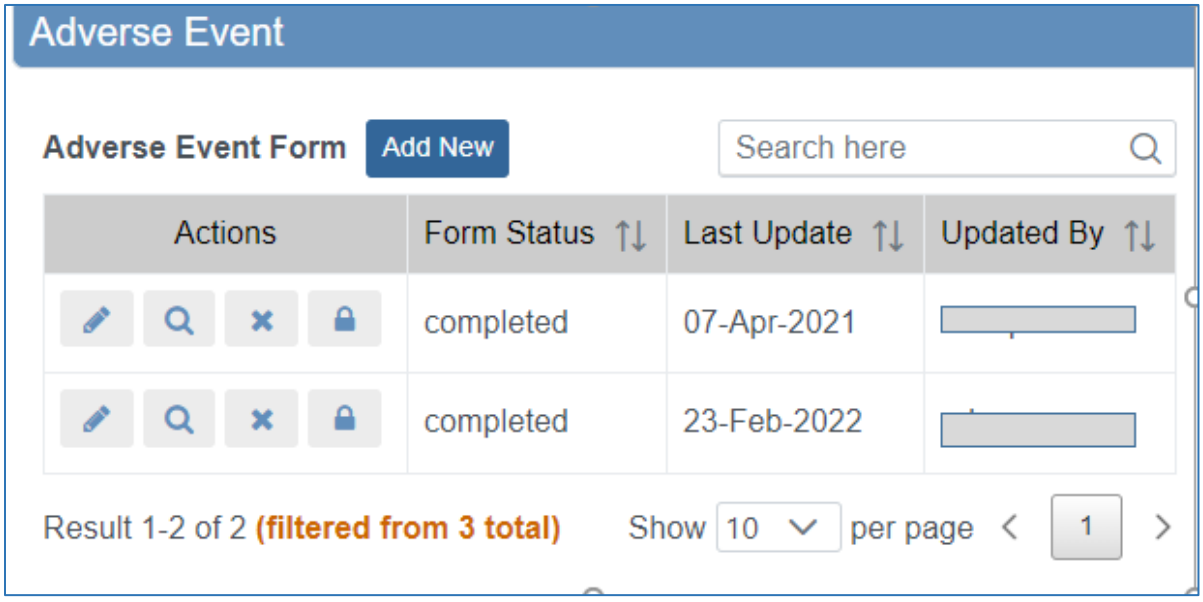
Repeating Events are used for entering multiple records of data into the same form i.e. Adverse Events.

When you first access a repeating form, you will see an empty summary. Click the **Add New** button to access the questions and create one form for entry.



Once you have completed the questions on the form, click the **Complete** button to save the data.

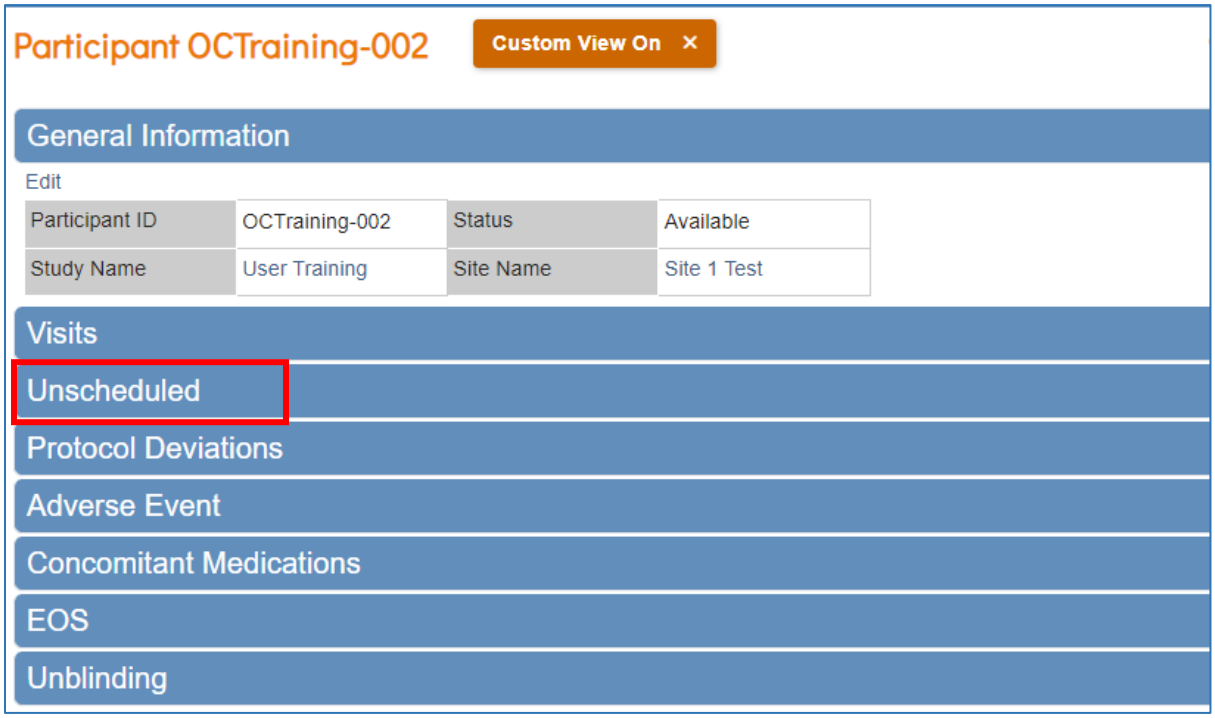
The saved record will then appear on the summary entries.



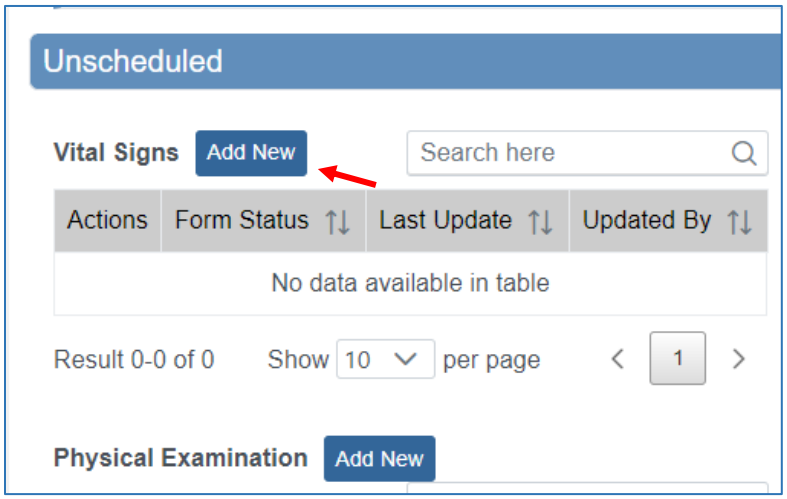
Create new, additional forms by clicking on the '**Add New'** button for additional entries as needed.

7.10 Adding Unscheduled Events

If an unscheduled event is required to be added; the '**Participants Details** include an unscheduled section.



Navigate to an unscheduled visit for the participant, if the subject does not have any unscheduled visits, in the content pane, click '**Add New'** to display a blank event at the bottom of the page.



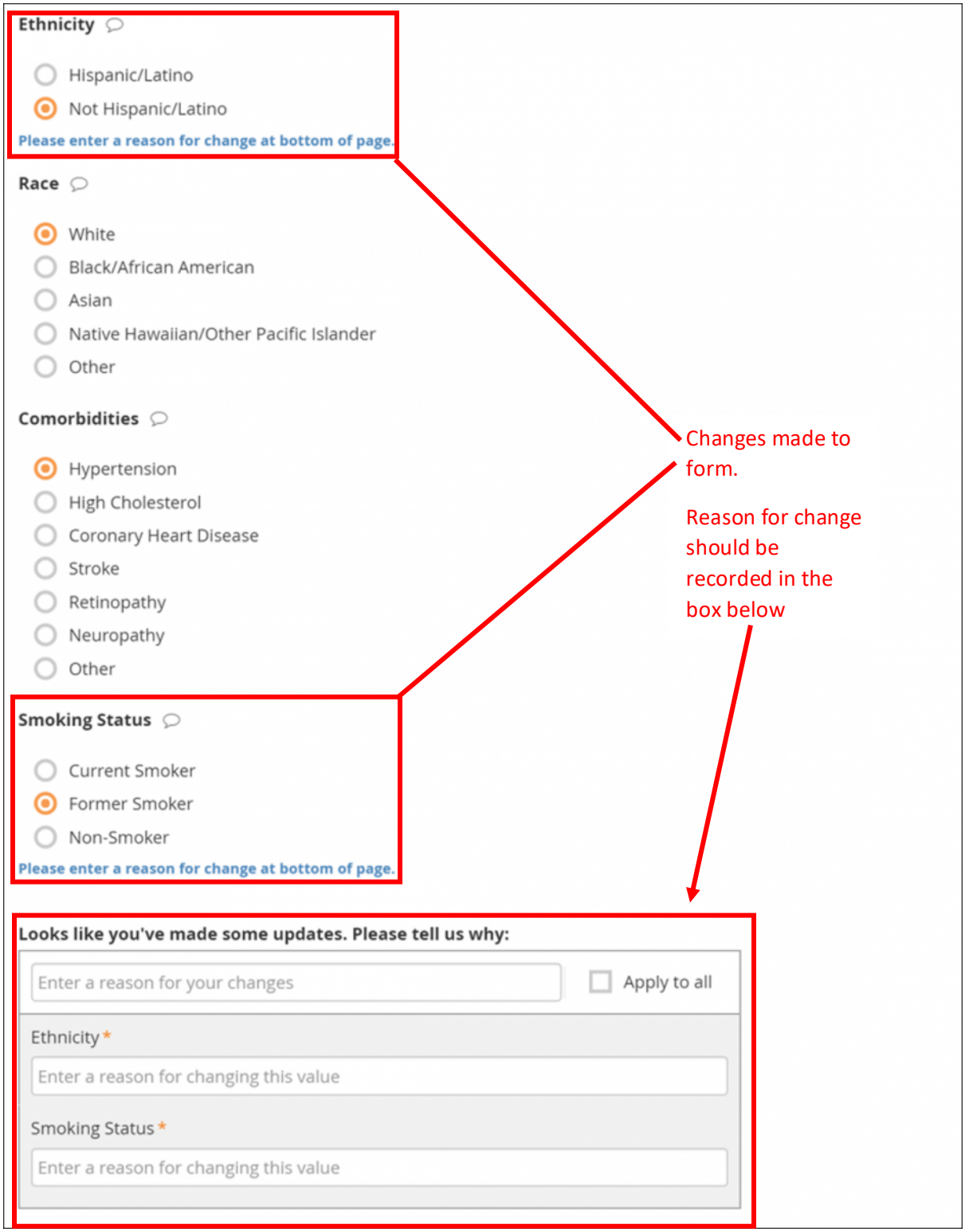
7.11 Modifying Saved Data

Once data are saved into a form, data can be modified as follows:

Click **Edit** in the **three dots** menu on the **Participant Details** screen. If you have permission to access the Form, you can start entering or editing data.

You can access the form the same way by clicking on the field that needs modifying. Correct the data as needed and provide a reason for change.

If you edit a form that has already been completed, you must enter a reason for change.



If your changes do not meet form requirements, such as constraints, you will see a message alerting you that specific values have errors and must be changed.

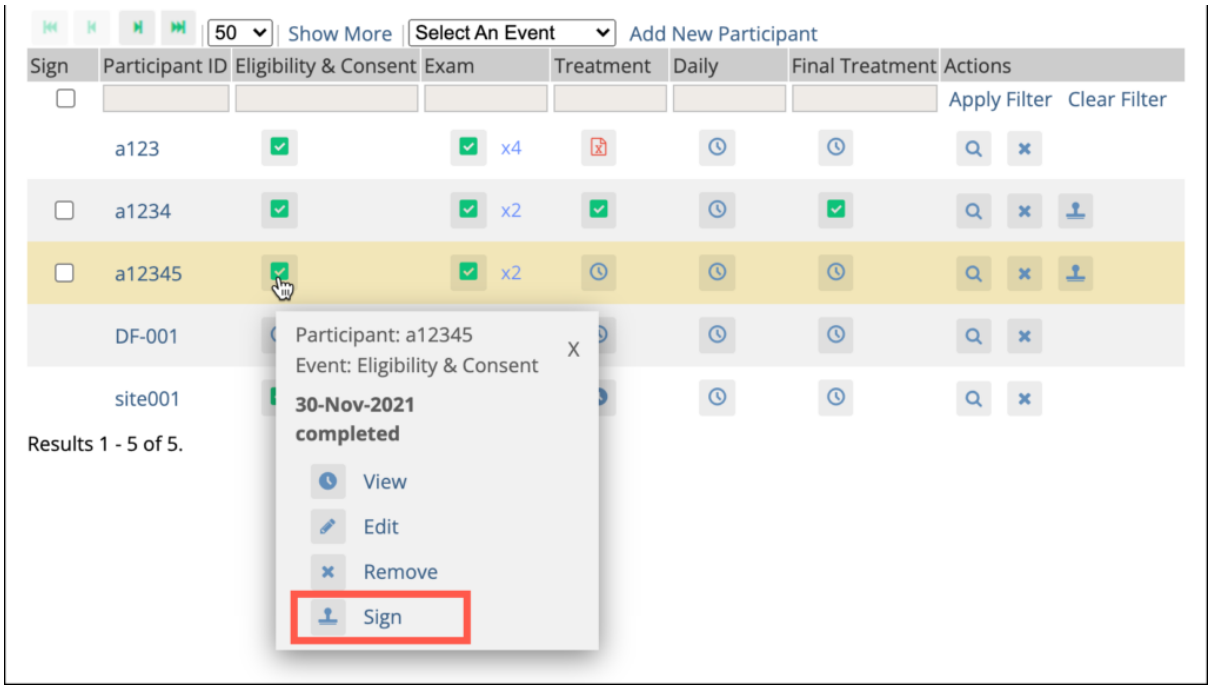
7.12 Signing an Event

After data entry of a CRF is completed, reviewed and all discrepancies are resolved, a PI (person of the site having the 'Investigator' rights in OpenClinica) must sign the CRF. When the PI signs an Event, they provide their approval of all CRF data for the CRF for the participant. CRFs are eligible for signature once the Study Events are in a "final" state i.e. (Not Scheduled, Complete, Stopped, *or* Skipped*)*

Please Note**:** If you update a signed form with a data update, OpenClinica will invalidate the previous signature and update the signature listings and each form to indicate that the form or case report book must be signed again.

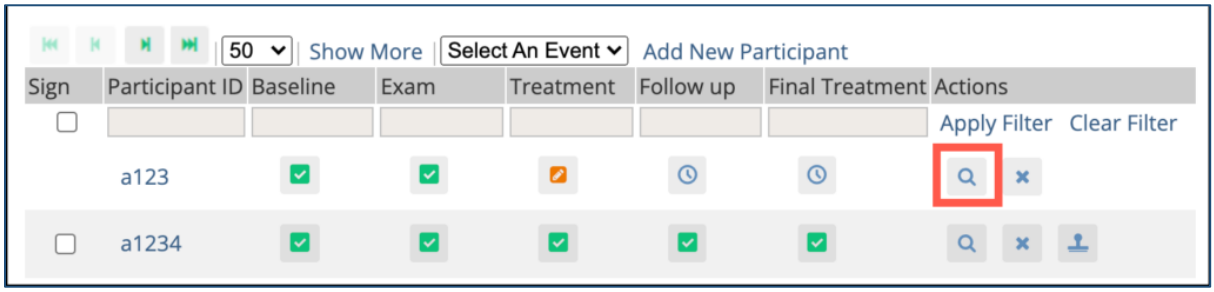
To sign a study event

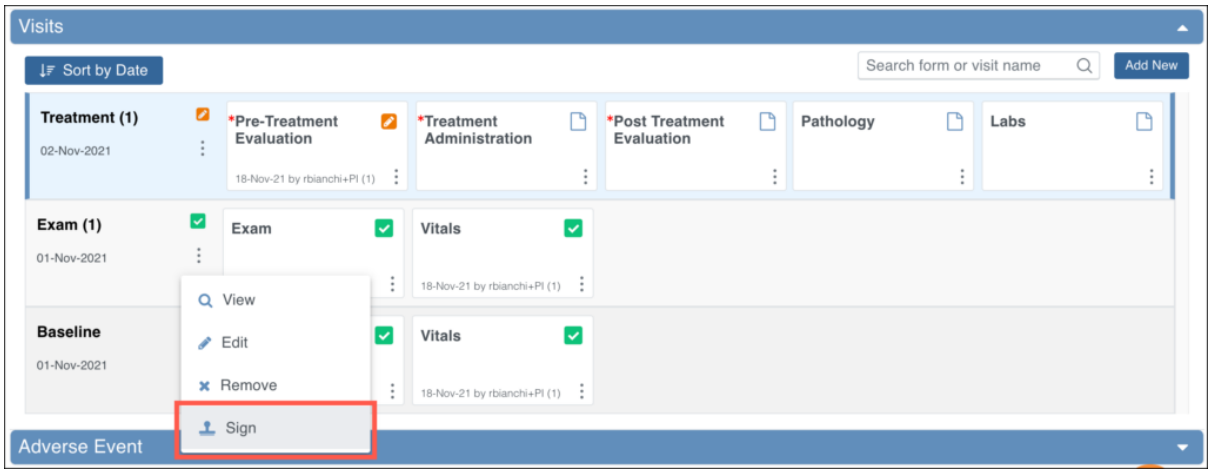
- Go to the **Participant Matrix**, then click the **Event** you want to sign.
- Select **Sign** from the drop-down list (**Sign** only appears if the event is in a final state as stated above).



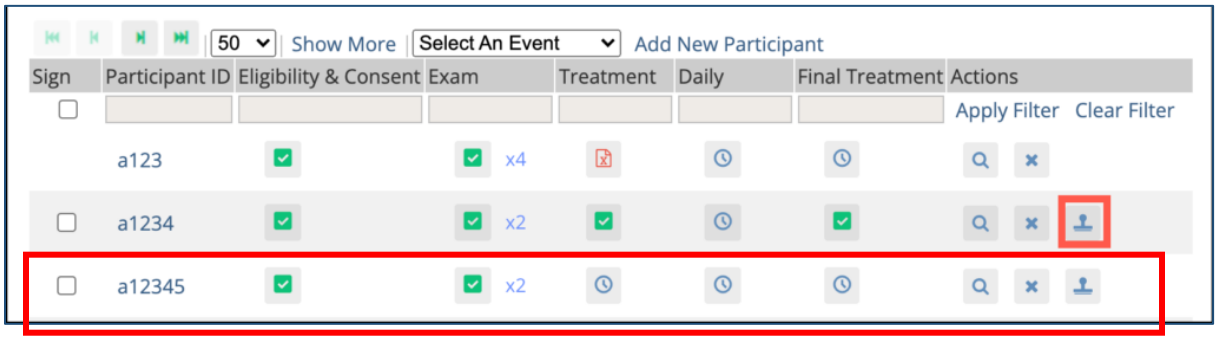
Or

- Click the **View** icon for the participant with an event you want to sign
- Find the **Event** you want to sign, and select **Sign** in the **Actions** drop-down list





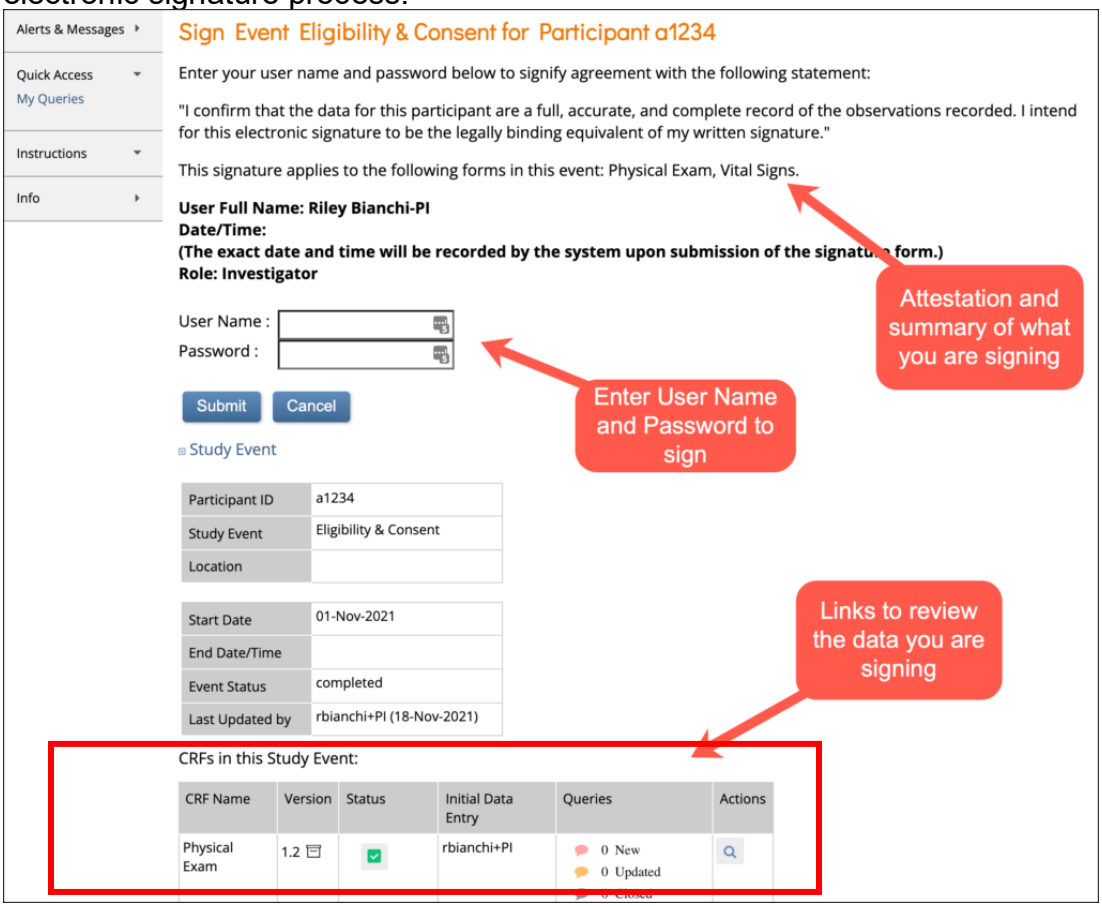
If all Events for a participant are in a final state *(*Not Scheduled, Completed, Stopped, *or* Skipped*),* then the entire participant record can be signed.



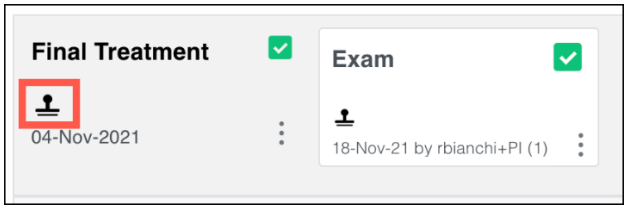
The Electronic signature screen appears.

Electronic signatures in OpenClinica are considered a legal signature and verification of the attestation provided. Signatures are applied through the use of an OpenClinica account and its associated username and password, so keep this information secure.

1. The **Electronic Signature** screen includes an attestation, your full name, a listing of the records you are signing, and a prompt to enter your username and password.
2. Scroll to the bottom of the page to see a list of forms in the Event and the status of queries for each of those Forms:
3. Enter your username and password and click **Submit** to complete the electronic signature process.



4. You will be taken back to the **Participant Details** screen to view the **Signed** icon on the event.



8. Query management

8.1 Answering System Queries

Once data entry has been performed and you click the '**Complete'** button, the system compares the data to the system queries associated with the page. The system creates queries automatically if you close a form that has unaddressed errors. You can also manually create queries as needed.

There are two options to respond to this query.

1. If the data was entered incorrectly, you can modify the data. If the updated data no longer meets the query conditions, the query will automatically close.
2. You can respond to the query with an explanation as to why the data is correct as entered.

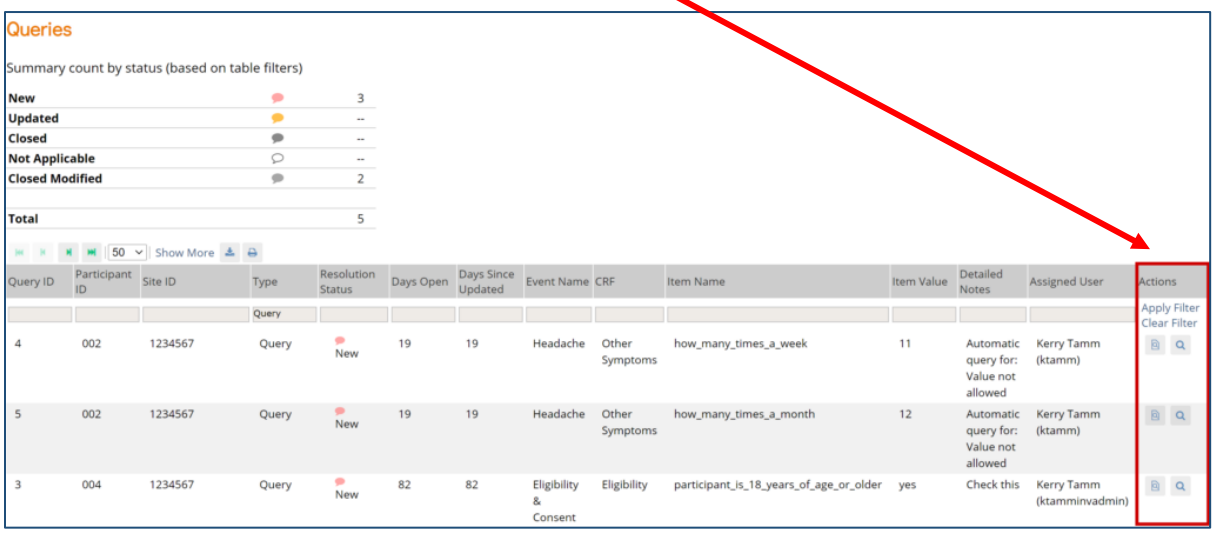
Query will then change to an "**Updated**" status.

To review data associated with a query You can either:

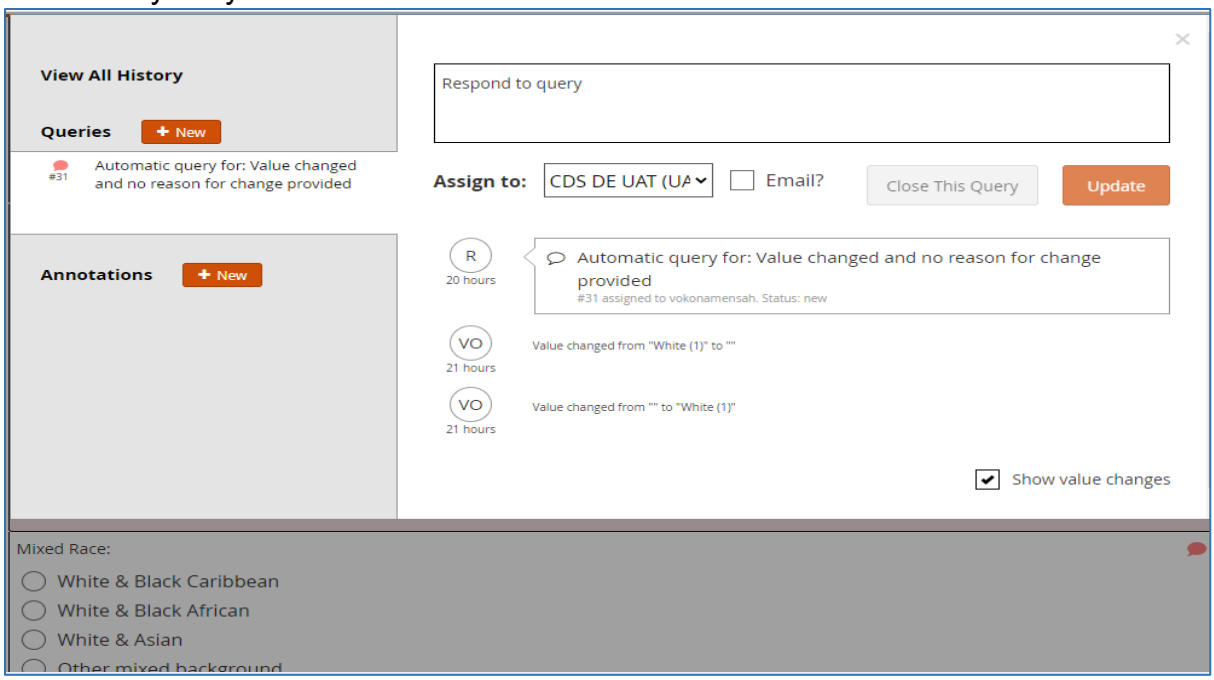
 View Query Only

 View Query within record

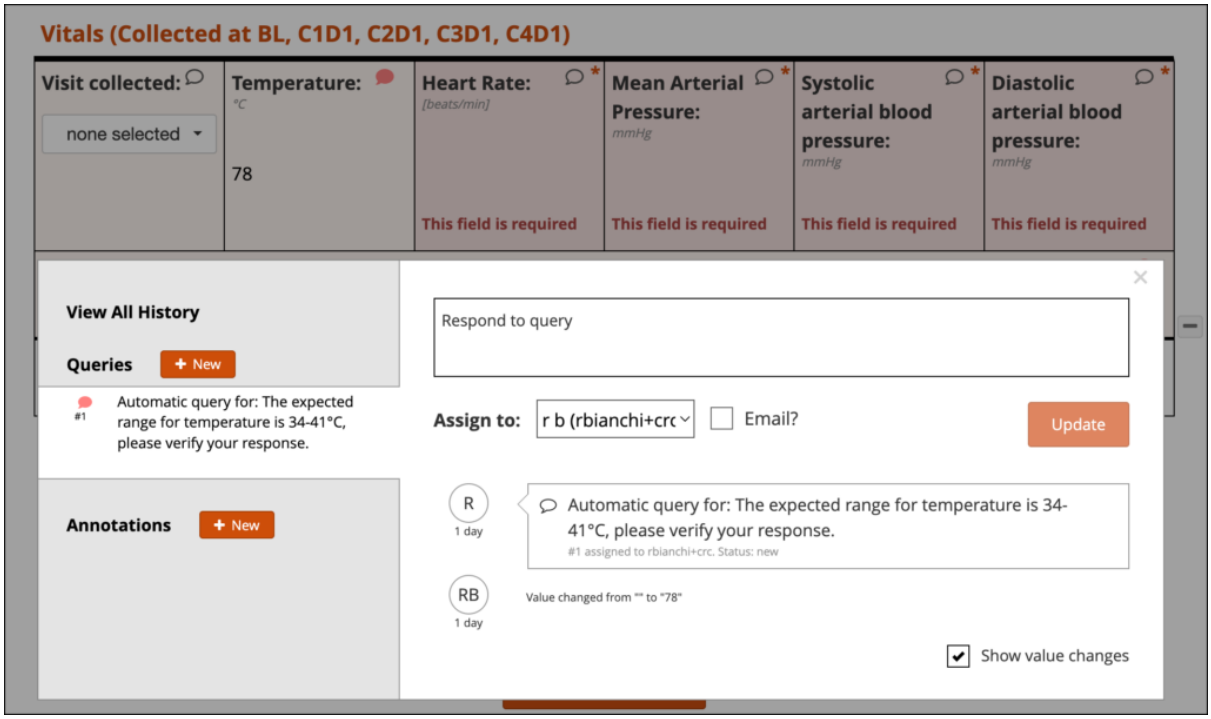
You can access these options from the **Actions** column of the **Queries** table.



View Query Only



View Query Within Record

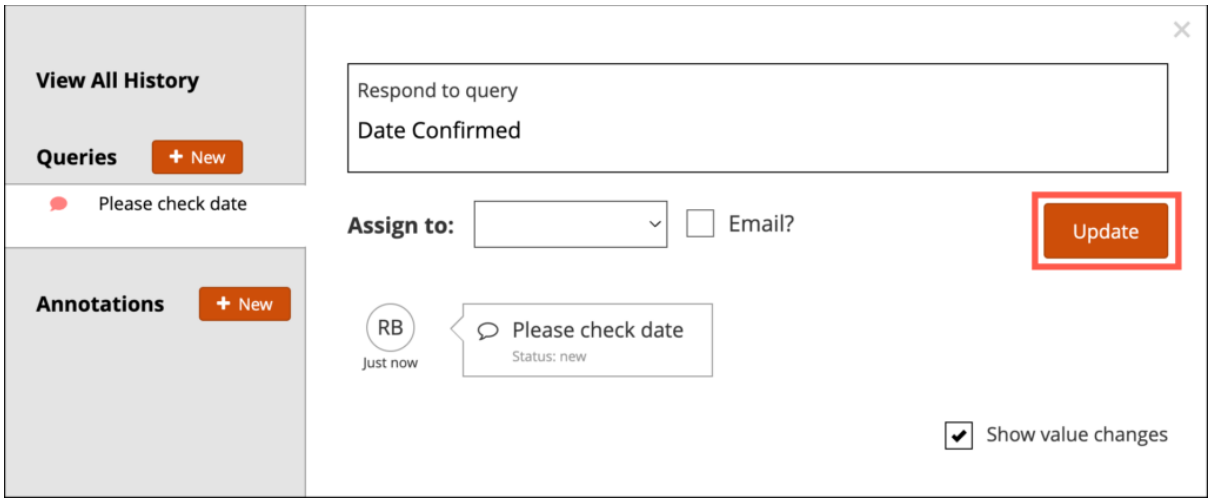


 Icon - indicates an **Open** query.

If data is changed, they will be prompted to enter a reason for change.

8.1.1 Answering System Queries: Modifying Data

- Open a Form.
- Click the **Query Bubble** in the field you want to create a query for.
- Select the query you want to respond to and/or update.
- If you need to change information in a form, close the **Query** widget, and make changes to the Form manually. You must provide a **Reason for Change** before completing the Form (Optional).
- In the **Respond to query** field, enter text explaining the query response.
- Select a user from the drop-down list next to **Assign to**. If you want to email that user to notify them about the query, check the box next to **Email**. When a query notification email is sent, it includes the Query ID for easy access (Optional)
- Click the **Update** button to add the response and leave the query open.

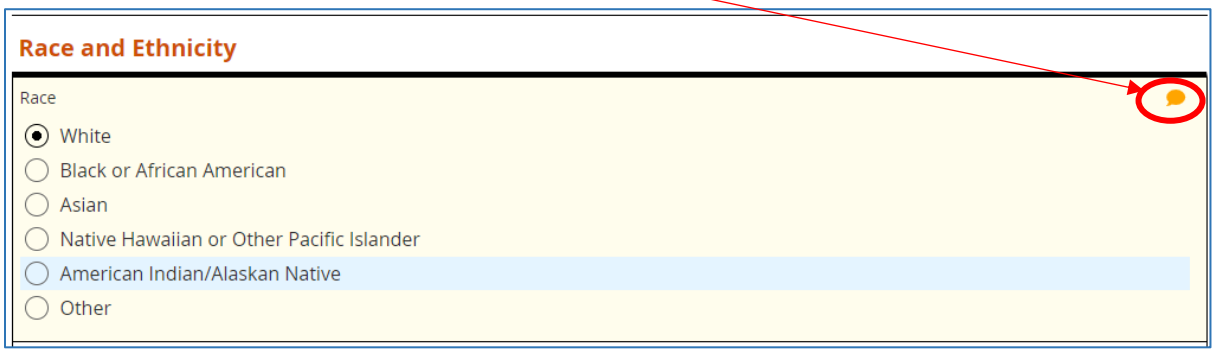


8.1.2 Answering System Queries: Providing an Explanation

If the data is correct as entered, you can respond by providing more details either by responding to the query and/or updating the field, and the query status will change. Click the '**Update'** button.

 Icon - indicates an **Updated** query.

Query status is now changed to **Updated.**



8.1.3 Answering Queries: Other Query Types

Manual Queries are entered by OpenClinica users that have permission rights, for example, a Monitor. Therefore, they do not open as an automatic query when the page is saved but may appear at any time during the conduct of the study. You have the same options to respond – to change the data or to provide an explanation. You will be required to respond to each of these queries.

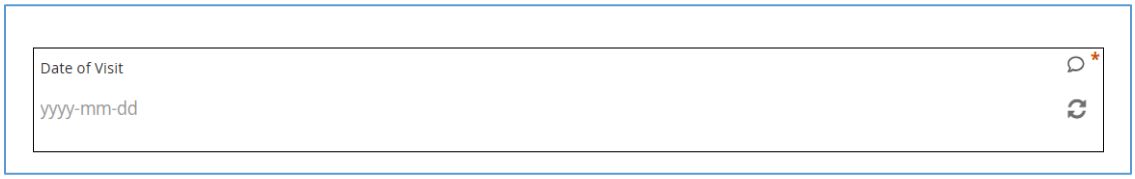
9. Study Specific Guidelines

Please refer to section 6.3 Events for the schedule of visits for the study

9.1 Schedule Pre-randomisation Event

When entering data in this visit, it is important that each form is completed in order before the patient is randomised. If they are not completed in sequential order the randomisation may not be successful.

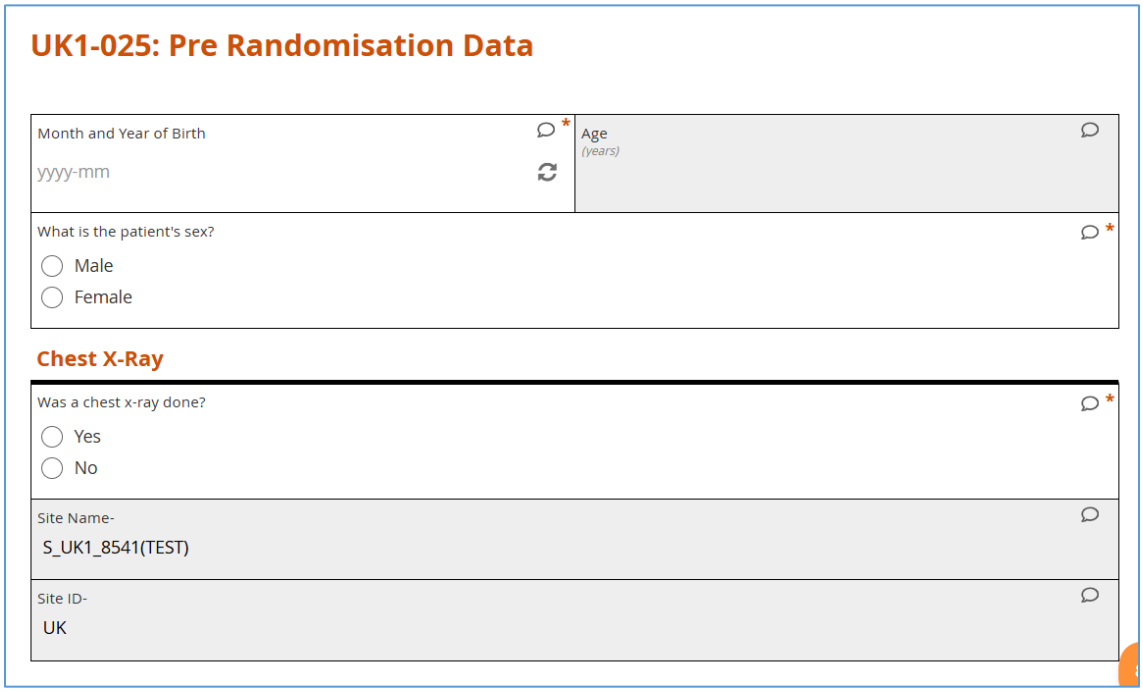
9.2 Date of Visit form



- Enter the date the screening completed.
- Screening should be completed **on the same day** as randomisation.

Click on 'Close' or 'Complete' to save the data.

9.3 Pre-Randomisation form



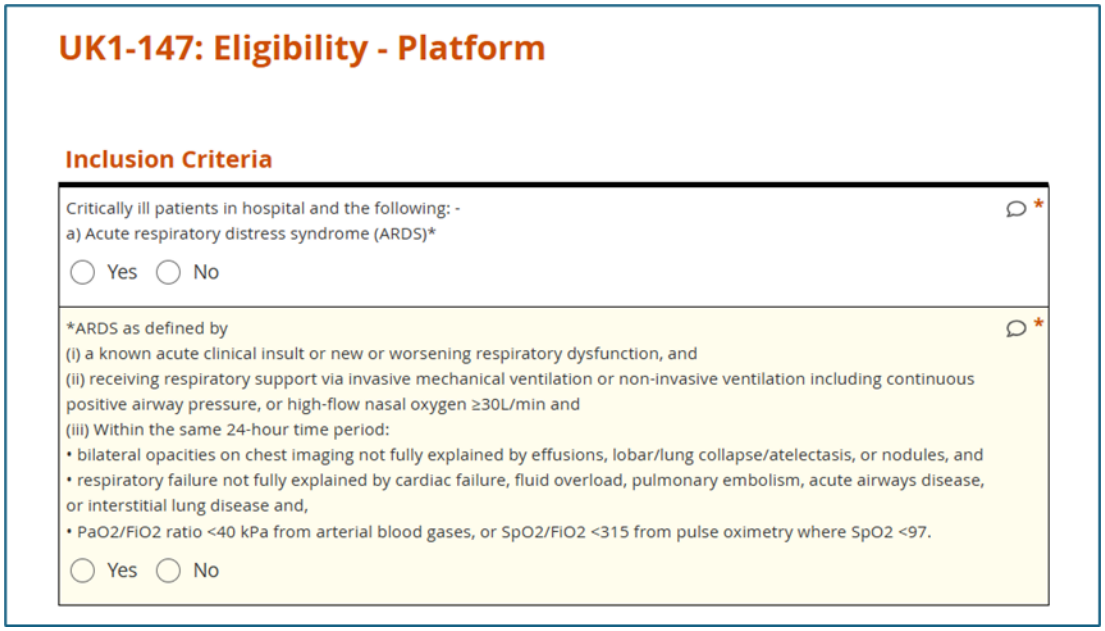
- Enter participant's Month & Year of Birth
- The Age is auto populated on the system once the Month & Year of Birth and Date of Visit has been entered.
- Enter the sex of participant.

<u>If Participant is Female –</u>

- Indicate **Yes or No** whether a pregnancy test has been completed **<u>during this hospital admission</u>**
- If No – Patient cannot be randomised and you would need to contact the study team
- If Yes - Enter Date of Pregnancy Test
- Select Result of Pregnancy Test – If Positive is selected this should be confirmed.

- Indicate **Yes or No** whether a Chest x-ray was done
- If Yes – Select the category of chest x-ray
- If No - Patient cannot be randomised and you would need to contact the study team
- If category of chest x-ray is 'Unilateral' or 'Normal' – Patient cannot be randomised, and you would need to contact the study team
- Site Name & Site ID – is Read only and mapped from site details initially entered.

9.4 Eligibility – Platform form



The patient must meet the definition of ARDS prior to randomisation. Each criterion must be met within the same 24hrs. The date and time that the criteria is met should be entered.

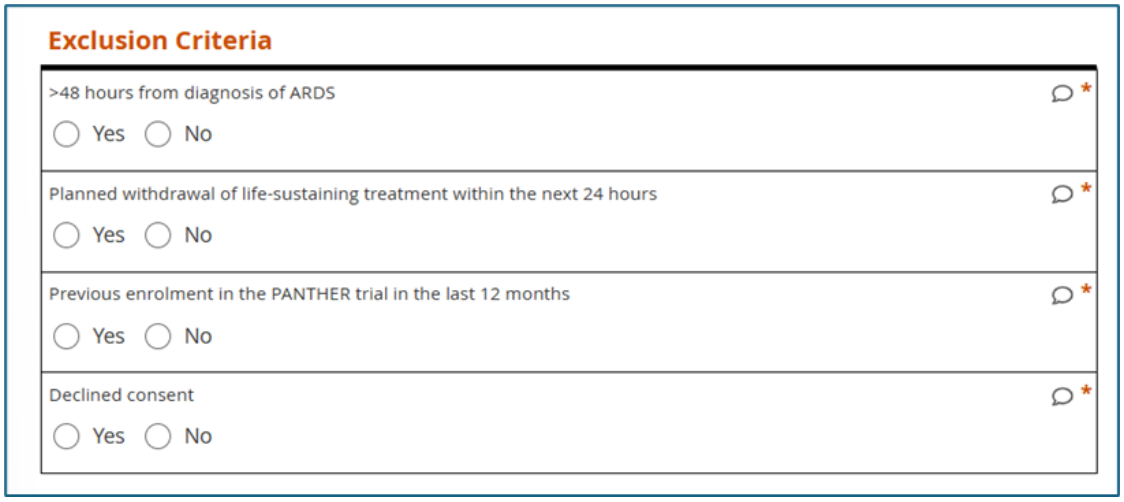
All points on the eligibility form must be completed for correct randomisation

(YES, must be selected for ALL Inclusion Criteria for patient to be eligible for randomisation)

Please make sure to fill in all of the data on the form or a query will be raised

- Indicate Yes or No for all inclusion criteria. If any is answered No,

participant should be excluded and will be added to the screening log.



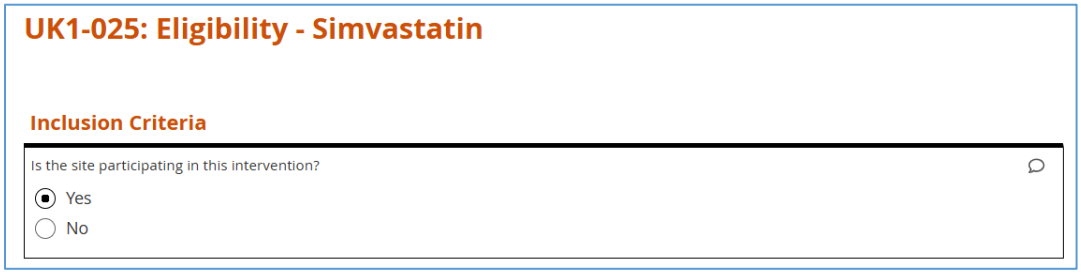
- Indicate **Yes or No** for all exclusion criteria. If any is answered Yes, the participant has failed the exclusion and should be confirmed.

At the bottom of the form there is a 'Final eligibility check'

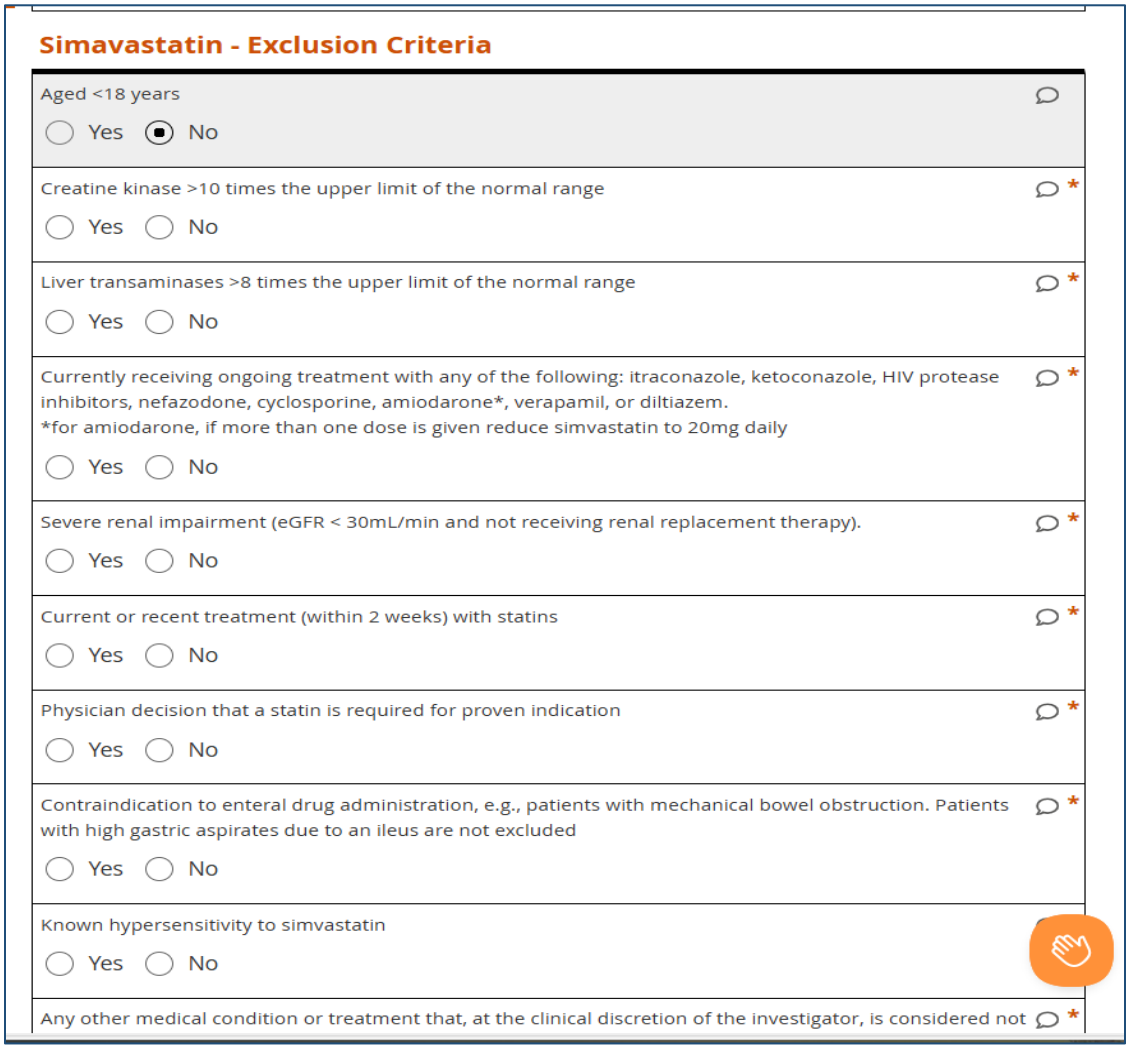
If the answer to this question is 'No', please specify which criteria was violated Participant will not be eligible to participate in the study and cannot proceed with randomisation.

Click on 'Close' or 'Complete' to save the data.

9.5 Eligibility – Simvastatin form



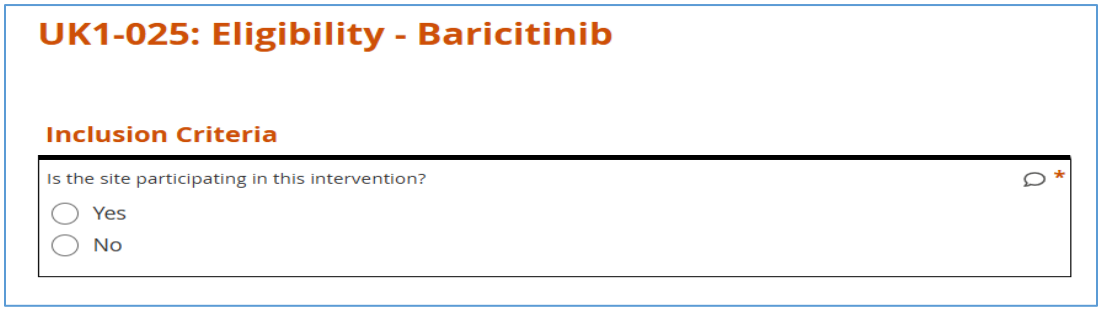
All points on the eligibility form must be completed for correct randomisation



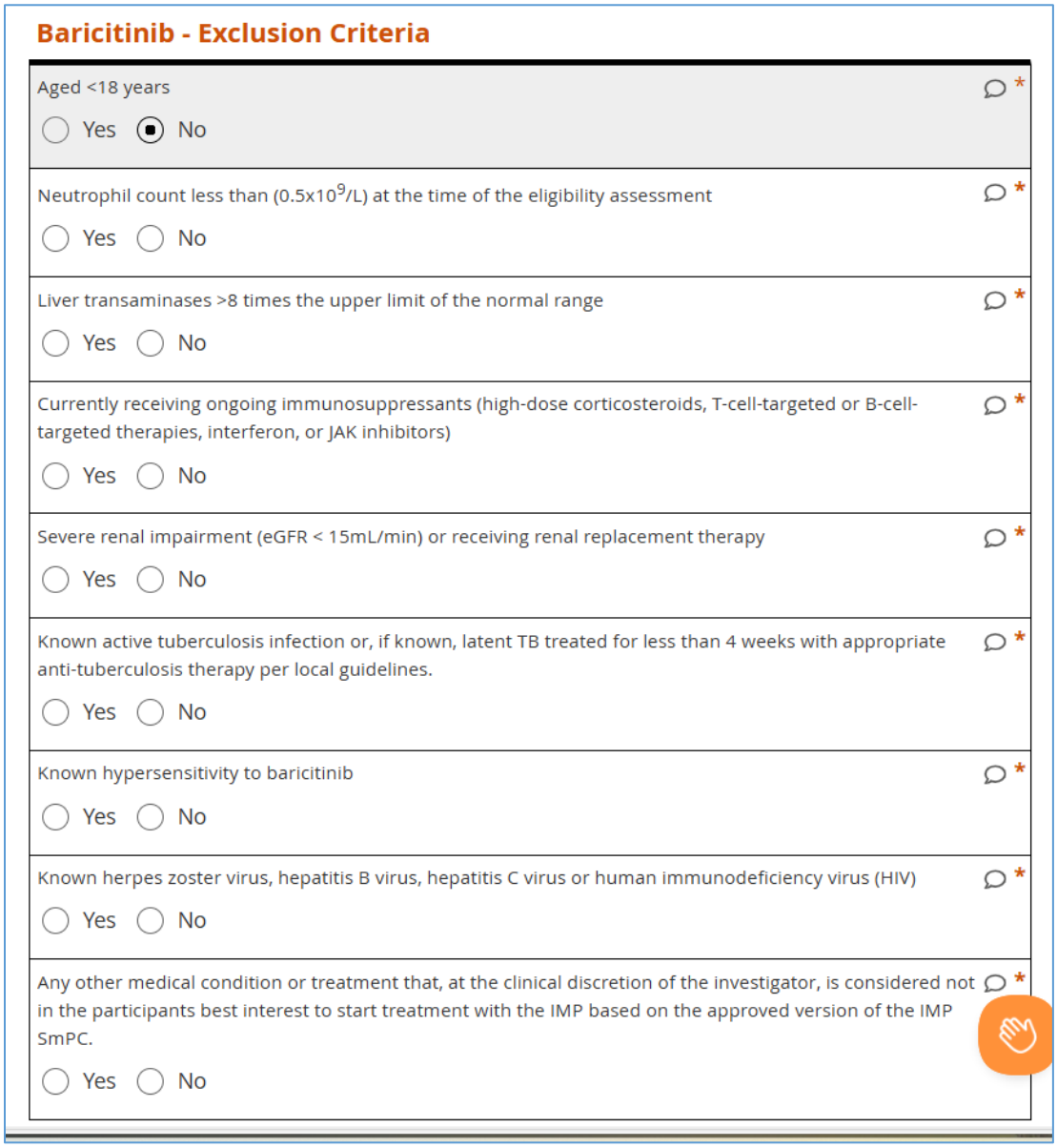
- Indicate **Yes or No** for all exclusion criteria. If any is answered Yes, participant has failed the exclusion and should be confirmed

Click on 'Close' or 'Complete' to save the data.

9.6 Eligibility – Baricitinib form



All points on the eligibility form must be completed for correct randomisation

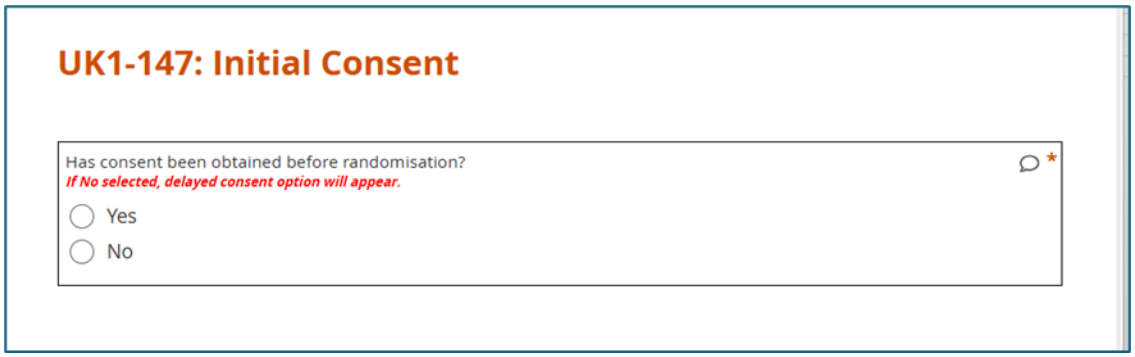


- Indicate **Yes or No** for all exclusion criteria. If any is answered Yes, participant has failed the exclusion and should be confirmed.

Click on 'Close' or 'Complete' to save the data.

9.7 Initial Consent

Refer to your Human Research Ethics Committee (HREC)/Institution Review Board (IRB) approval to determine the consent practices you should follow. In most jurisdictions to participate in the study, agreement must be obtained. Only patients who meet all inclusion criteria and none of the exclusion criteria will be randomised.



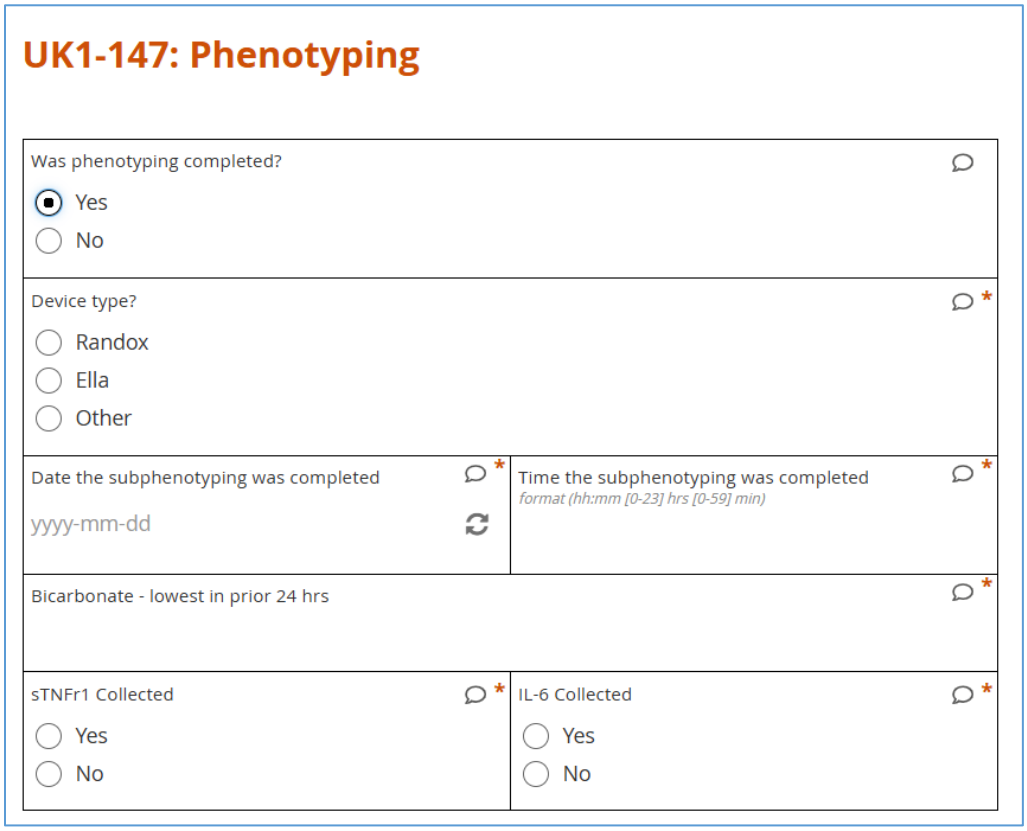
- Indicate **Yes or No** whether consent was obtained.
- If the answer 'Yes' a detailed consent will be obtained in Consent 2 at the baseline visit.

- If the answer is 'No' you should indicate whether delayed consent is allowed for your country.

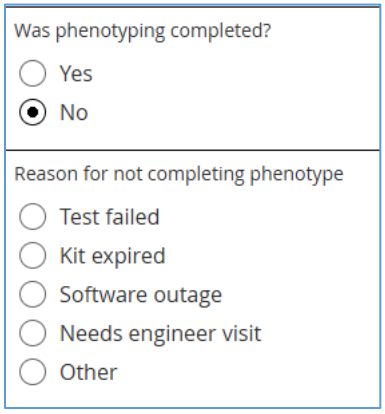
Click on 'Close' or 'Complete' to save the data.

9.8 Phenotyping form

Patients will be stratified into different subphenotype strata prior to randomisation



- Indicate **Yes or No** whether phenotyping was completed, a patient cannot be randomised without phenotyping. If phenotyping is not possible, please select 'no' and the following options will appear:-



If 'other' is selected a text box will appear to capture other reasons not listed here.

If one of these options is selected, the patient will not be randomised and considered a screen failure. These incidences will be monitored throughout the trial

- Select the device type for the device that is used: Randox, Ella, Other
- Enter the date & time subphenotyping was completed
- Enter the lowest Bicarbonate value in mmol/L
- Answer the question whether the sTNFr1 was collected then enter the sTNFr1 value in ng/ml

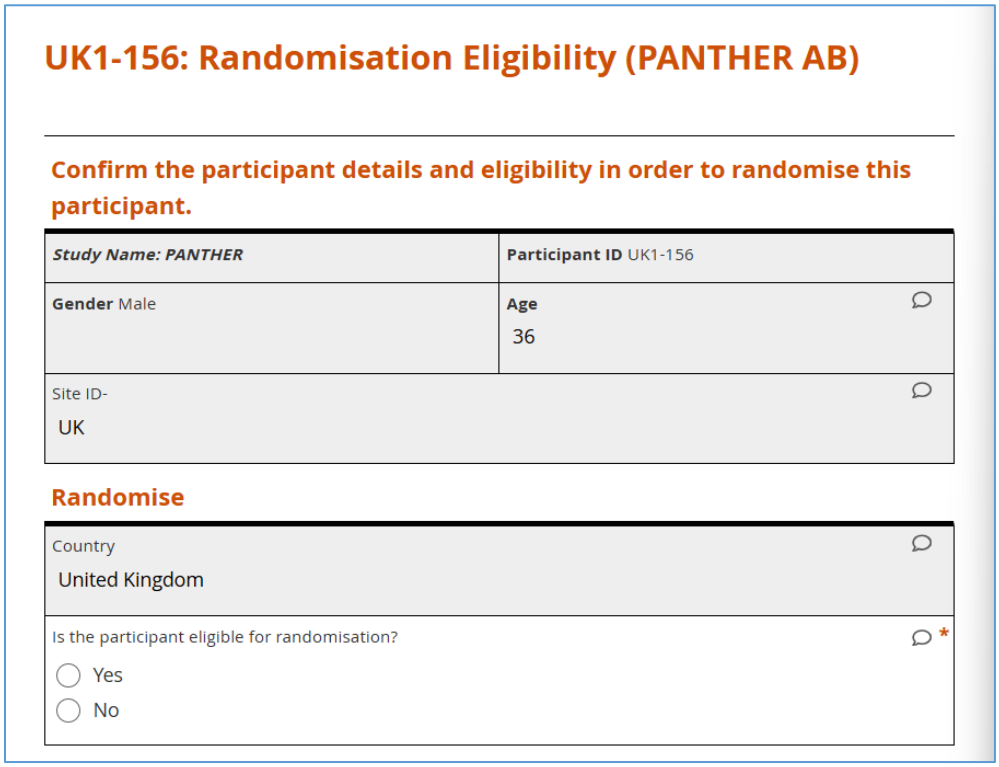
- Answer the question whether the IL-6 was collected then enter the IL-6 value in pg/ml
- Initial subphenotypes will be hyper- and hypo-inflammatory subphenotypes described in ARDS. The determination of the subphenotype of the participant will be dependent on the sTNFr1 and IL-6 values.

Note – the patient subphenotype will not be displayed on the database.

9.9 Schedule Randomisation Event form

- Ensure all the Pre-Randomisation CRF forms have been completed and in sequential order otherwise you will not be able to complete the Schedule Randomisation Event form
- Once all the Pre Randomisation forms have been completed - Indicate **Yes or No** whether the patient is ready to schedule the Randomisation Event. If Yes, the patient is ready to be randomised into one of the Randomisation Events.
- If No, the patient is not ready to be randomised and does not meet the criteria.

9.10 Randomisation Eligibility



UK1-156: Randomisation Eligibility (PANTHER AB)

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

Study Name: PANTHER	Participant ID UK1-156
Gender Male	Age 36
Site ID- UK	

Randomise

Country United Kingdom
Is the participant eligible for randomisation? * ○ Yes ○ No

- The Randomisation Eligibility form will automatically appear once the schedule randomisation event form has been completed.

- For information only one of the following forms will appear: - Randomisation PANTHER A; Randomisation PANTHER AB; Randomisation PANTHER B; Randomisation PANTHER C; Randomisation PANTHER CD; Randomisation PANTHER D.
  Note - This is part of the automated randomisation, and no further action is required with this information.

- Confirm that the patient details and eligibility to the study is correct before randomising participant. The Study Name, Participant ID, Gender, Age and Site ID are auto populated and read only fields mapped from the Pre-Randomisation form previously completed.

Randomise

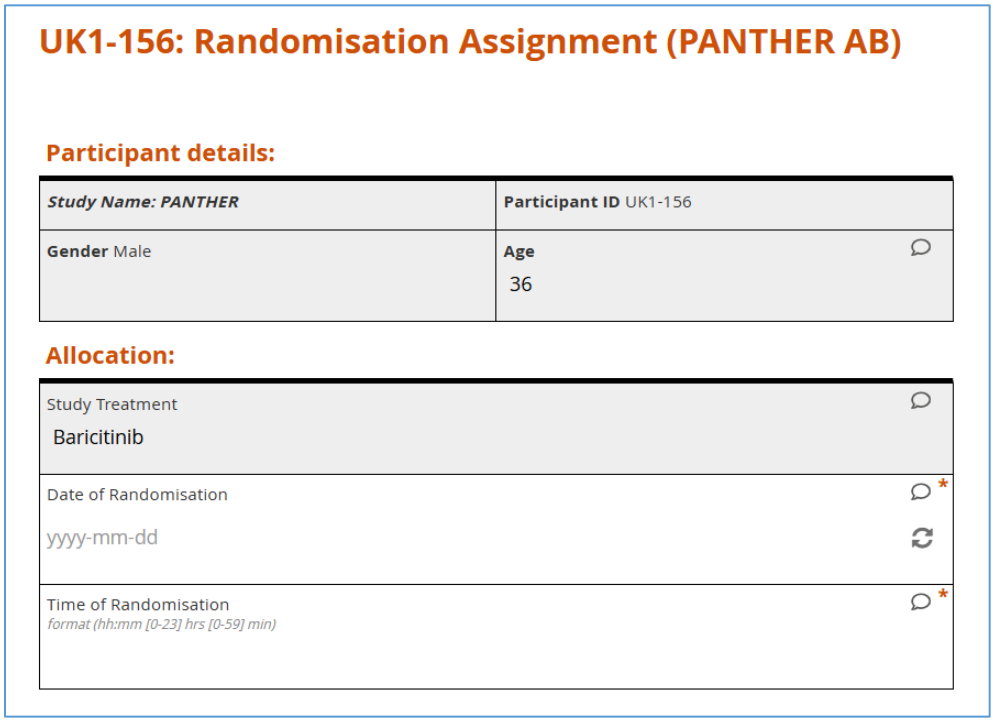
- Country - This is an auto populated and read only field which is mapped from the Pre-Randomisation form.
- Indicate **Yes or No** whether the patient is eligible for randomisation.
- If Yes – Select '**Randomise**' radio button if participant is eligible, once done, the following messages will appear: -

  Please check the allocated Study Treatment in the Randomisation Assignment form

Please note the randomisation assignment will take 5 seconds to load and appear.

- Click 'Complete' to randomise the participant. If the patient is not ready to be randomised click 'Close' to save changes only.

9.11 Randomisation Assignment



UK1-156: Randomisation Assignment (PANTHER AB)

Participant details:

Study Name: PANTHER	**Participant ID** UK1-156
Gender Male	**Age** 36

Allocation:

Study Treatment Baricitinib
Date of Randomisation * yyyy-mm-dd
Time of Randomisation * *format (hh:mm [0-23] hrs [0-59] min)*

This form details the allocated study treatment for the participant and will automatically appear.

Participant details

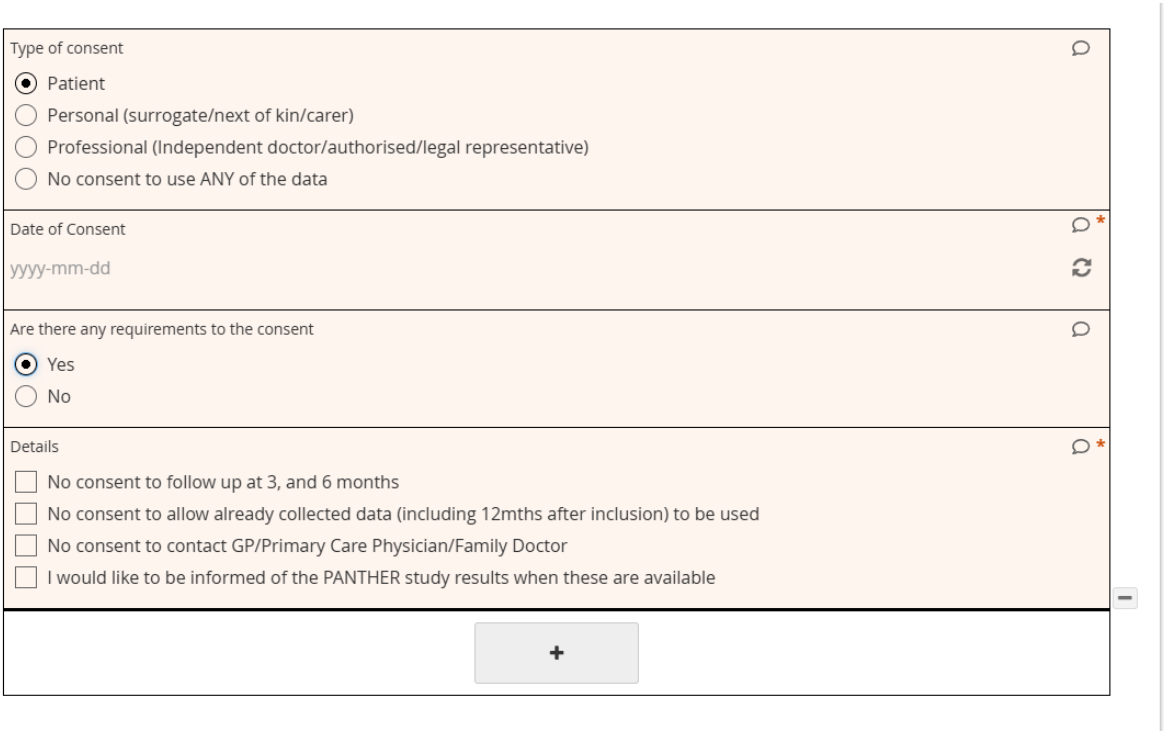
- The Study Name, Participant ID, Gender, Age and Site ID are auto-populated and read only fields mapped from the Pre-Randomisation form previously completed.

Allocation

- Study Treatment - Treatment allocation to which the patient is randomised using the Sealed Envelope automated online system.
- Enter the Date of Randomisation*
- Enter the Time of Randomisation*

*There are restrictions to these fields to ensure that the current date and time is entered. A time in the past nor a time in the future can be randomised. Please ensure that when you randomise the patient you are able to start the treatment as soon as possible

9.12 Consent



- Indicate **Yes or No** whether consent was obtained
- If Yes, Choose the type of consent from the list:
- All consents must be included, if a professional consent is obtained and a retrospective consent obtained from the patient later, ensure both consent forms are added. To add more consents use the '+' symbol at the bottom.
- Ensure 'are there any requirements to the consent' is selected as yes if requested on the consent form, such as:-
    - If on the consent form the patient/family/professional is happy to receive the trial results ensure this option is selected in the 'requirements to consent'.

Click on 'Close' or 'Complete' to save the data.

9.13 Contact Details

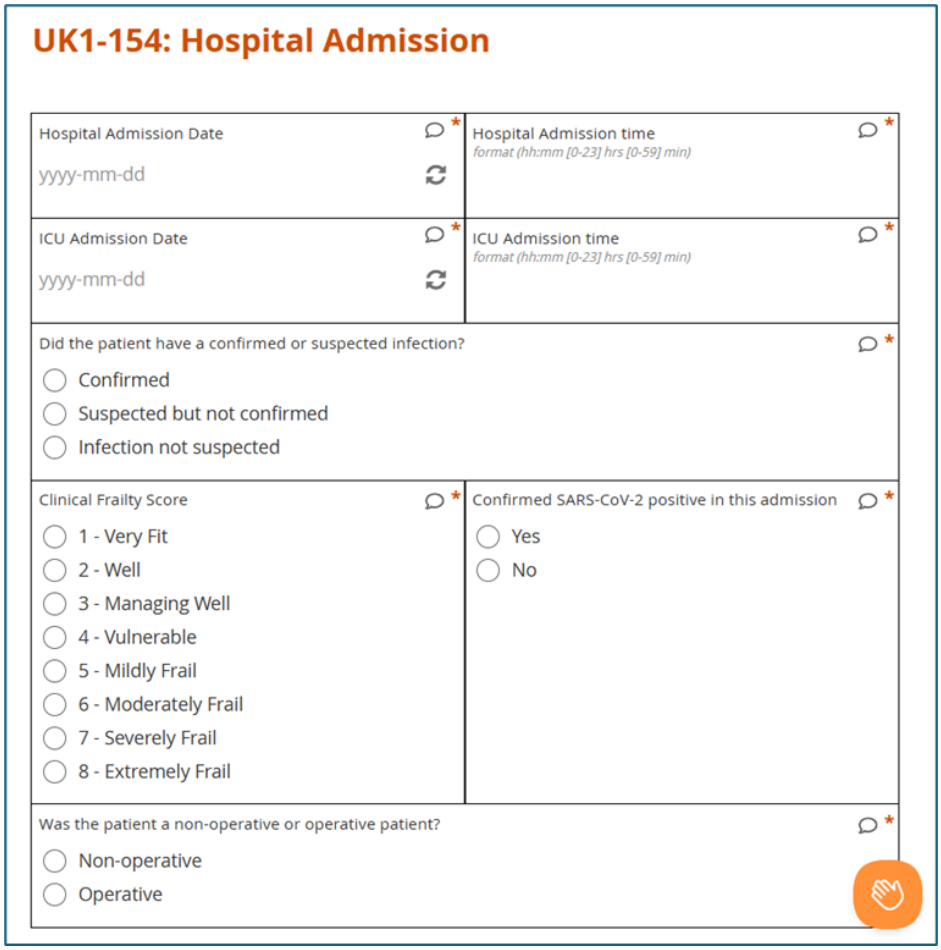
UK1-025: Contact Details

Telephone number:
Email address:
Postal address:

- If consent is received for follow up, please complete the contact details form in the database to enable the patient to be contacted.
- Enter the patient's telephone number, email address and postal address for contact purposes.

Click on 'Close' or 'Complete' to save the data.

9.14 Hospital Admission



- Enter the Date & Time Patient was admitted to hospital
- Enter the Date & Time Patient was admitted to ICU
- Indicate whether the patient has a confirmed or suspected infection

If the patient has a confirmed or suspected infection please indicate the source of infection by completing the Reason for ICU Admission section.

Reason for ICU Admission

Source of Infection

- Select from the list what was the source of the suspected or confirmed infection
- If Other please provide details
- If an infection is suspected but not confirmed please select the source of the suspected infection and for the microbiology test select ‘not confirmed’ from the list
- If an infection was confirmed, please select the positive microbiology test/s that identified the infectious pathogen - Select all that apply.

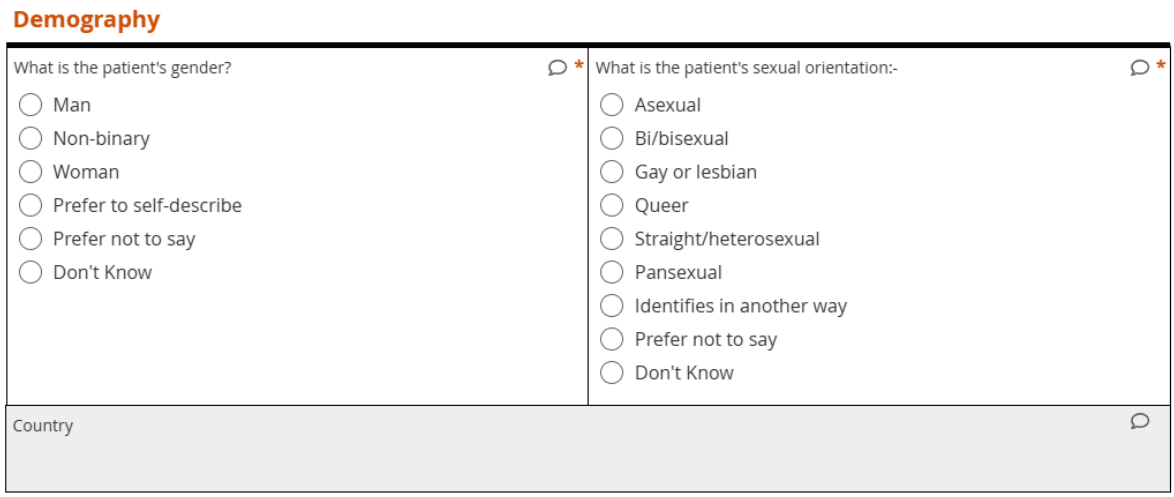
- Select the result for Clinical Frailty Score, if test was not performed select '**Not Done'**
- Indicate **Yes or No** whether the patient had a confirmed SARS-CoV-2 positive in this admission
- Select whether the patient was a non-operative or operative patient

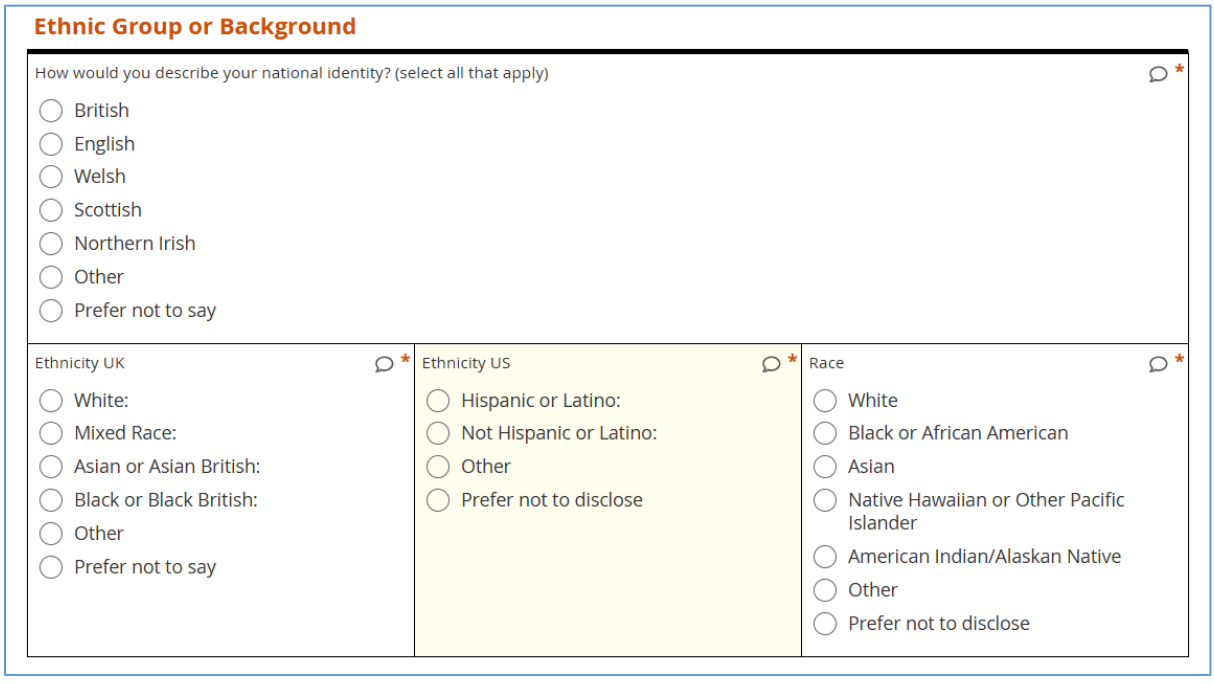
If Non-Operative – Select which diagnostic category from list	**If Operative - Select which diagnostic category from list**
Non-Operative: Cardiovascular	Post Operative: Cardiovascular
Non-Operative: Respiratory	Post-Operative: Respiratory
Non- Operative: Gastrointestinal	Post- Operative: Gastrointestinal
Non-operative: Neurologic	Post-operative: Neurologic
Non-operative Sepsis	Post-operative Sepsis
Non-operative: Trauma	Post-operative: Trauma
Non-operative: Metabolic	Post-operative: Metabolic
Non-operative: Hematologic	Post-operative: Hematologic
Non-operative: Renal and Genitourinary	Post-operative: Renal and Genitourinary
Non-operative: Musculoskeletal/ Skin disease	Post-operative: Musculoskeletal/ Skin disease
Non-operative: Other Medical Diseases	Post-operative: Other Medical Diseases
Non-operative: Undefined/ Unknown	Post-operative: Undefined/ Unknown

Click on 'Close' or 'Complete' to save the data.

9.15 Demography

UA0-028: Demography





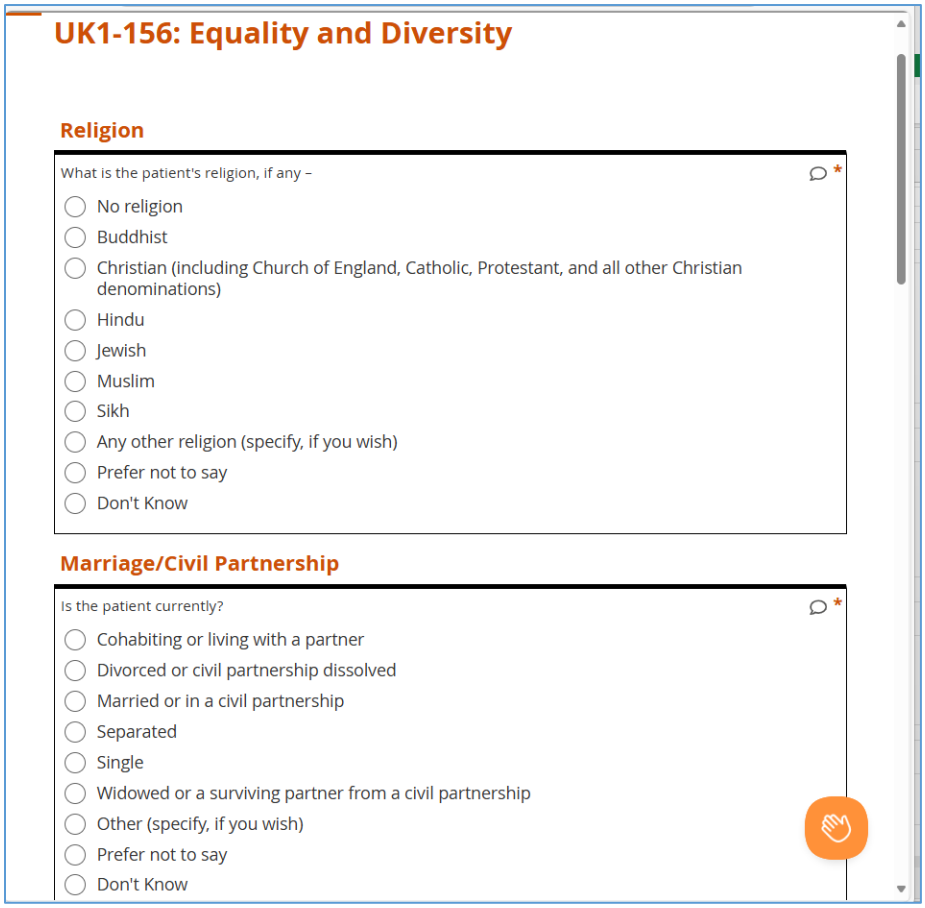
- Enter the participant's demography data. A 'don't know' option is available if the data cannot be obtained.

<u>Ethnic Group or Background</u>

- For UK sites – Select from the Ethnicity UK categories
- For US sites –Select from the Ethnicity US and Race categories
- If Other is selected for any of the questions, a 'Please specify' field will automatically appear for you to complete.

Click on ‘Close’ or ‘Complete’ to save the data.

9.16 Equality and Diversity



Enter the patient Equality & Diversity data if known, if this information is not known, please select the ‘don’t know’ option.

Religion

- State patient’s religion
- If Any Other Religion is selected this can be specified if they wish to disclose.

Marriage/Civil Partnership

- State patient’s marital status

Parental leave

- Select type of parental leave patient has taken over the past 12 months

Caring responsibilities

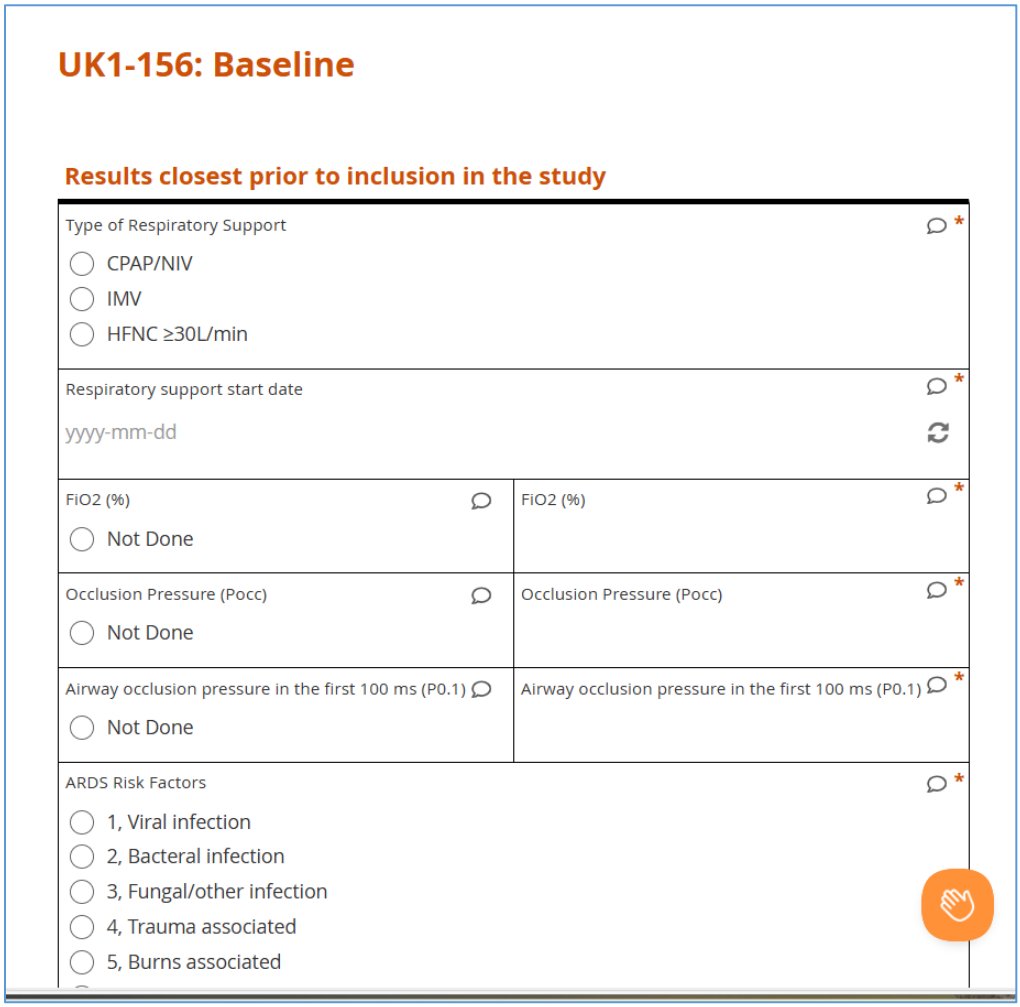
- Indicate whether the patient has any caring responsibilities

- If yes, indicate types of responsibility

Socioeconomic background

- Indicate the occupation of the patient's main household earner when patient was aged 14
- Indicate if patient has a disability
- Indicate whether the patient has any physical or mental health conditions lasting 12 months or expected to last longer than 12 months.
  Click on 'Close' or 'Complete' to save the data.

9.17 Baseline Data



Test Results: Closest result to time of inclusion. If a test was not done, please select 'Not Done'

- Indicate type of Respiratory support the patient is receiving
- Enter date Respiratory support started

If CPAP/NIV is selected:

- For Mode of Ventilation – Select the ventilation mode listed: CPAP
- CPAP: Continuous positive airway pressure (non-invasive ventilation [NIV])*

*Please note that BiPAP is listed as an IMV

If IMV is selected:

- For Mode of Ventilation – Select one of the ventilation listed:-
- A/C: Assist control (also known as V/C or AC/VC)
- SIMV (Vol): Synchronized intermittent mandatory ventilation (volume)
- SIMV (Pressure): Synchronized intermittent mandatory ventilation-pressure
- PRVC: Pressure regulated volume control
- APRV: Airway pressure release ventilation
- PCV: Pressure control ventilation (also known as P/C or AC/PC)
- PSV: Pressure support ventilation
- VSV: Volume support ventilation
- HFO: High frequency oscillation
- Jet: Jet ventilation
- BiPAP: Bilevel positive airway pressure (non-invasive ventilation [NIV])
- PAV: Proportional assist ventilation
- NAVA: Neurally adjusted ventilatory assist
- ASV: Adaptive Support Ventilation

If HFNC ≥30L/min is selected:

- For Mode of Ventilation – Select the ventilation listed: HFNC (Optiflow);

  HFNC: High-flow nasal cannula (or Optiflow)

Enter the results closest to randomisation for each test, if a test was not performed select 'Not Done' for that test. Please note that different tests will appear depending on the type of ventilation that has been selected.

Tidal volume

In many forms of mechanical ventilation, a predetermined volume of gas, or tidal volume, is delivered with each ventilator breath. Record in mL. This will appear if CPAP/NIV or IMV has been selected.

Total Respiratory Rate value

Total respiratory rate (breaths per minute), enter the highest respiratory rate. This will appear if CPAP/NIV or IMV has been selected.

Minute Volume

This value will be auto calculated from the tidal volume and Total Respiratory Rate results are entered. Please note this result will only appear when type of respiratory support has been selected as either CPAP/NIV or IMV.

Predicted Tidal Volume

This value will be auto calculated from the predicted body weight and height. Please note this result will only appear when type of respiratory support has been selected as either CPAP/NIV or IMV.

PEEP

Positive End Expiratory Pressure (measured in centimetres of H_2O, cmH_2O). PEEP provides a pressure at the end of exhalation to help improve oxygenation. This will appear if CPAP/NIV or IMV has been selected.

Plateau Pressure

Will appear only when IMV option is selected, please enter value in cmH_20

FiO2

Enter the percentage of oxygen delivered when the arterial blood gas was obtained. This value should only be obtained from the ABG, (%) value

Mean Airway Pressure

The airway pressure measured at the airway opening during the administration of positive airway pressure, averaged over an entire ventilatory cycle, please enter in cmH_20

Occlusion Pressure

Enter Occlusion Pressure (Pocc) value

This is the negative pressure generated during a single inspiratory effort (or up to 5 s) following an end-expiratory airway occlusion.

The Pocc value represents the magnitude of the swing in airway pressure. It is the magnitude of the swing that should be entered into the database. Larger negative integers representing a larger change in airway pressure between inspiration and expiration, while values closer to 0 represent smaller changes in airway pressure.

Enter the Pocc value obtained in the morning. If multiple values are available, take the Pocc and/or p0.1 value closest to 10 a.m. Ensure the respiratory support setting values entered coincide with the settings the patient was on when the Pocc/p0.1 values were obtained.

Airway Occlusion Pressure

Enter the first 100 ms (P0.1) value

This is the negative pressure generated during a single inspiratory effort (or up to 5 s) following an end-expiratory airway occlusion.
The Pocc value will always be a negative integer and represents the magnitude of the swing in airway pressure. It is the magnitude of the swing that should be entered into the database. Larger negative integers representing a larger change in airway pressure between inspiration and expiration, while values closer to 0 represent smaller changes in airway pressure.

Enter the Pocc value obtained in the morning. If multiple values are available, take the Pocc and/or p0.1 value closest to 10 a.m. Ensure the respiratory support setting values entered coincide with the settings the patient was on when the Pocc/p0.1 values were obtained.

Inspiratory Positive Airway Pressure (IPAP)
Record the set Inspiratory Positive Airway Pressure in cmH_2O.

ARDS Risk Factors
Select one the ARDS Risk Factors - if 'Other' is selected you will be required to specify in the text field provided.

Vital Signs

- Enter the patient's height in cm
- Enter the patient's weight in kg at ICU admission
- BMI will be auto-calculated and populated by the system
- Enter the patient's temperature, selecting degrees C or Fahrenheit F
- Enter the lowest Systolic blood pressure value
- Enter the Diastolic blood pressure value
- Enter the lowest Heart Rate value

Normal Ranges for some vital signs parameters on the form are listed below:

Parameter	Low range	High range
Height (cm)	130	200
Weight (kg)	40.0	250.0
Temperature (ºC)	36.0	38.0
Temperature (ºF)	80.0	100.0
Heart Rate (bpm)	0	300
BP Systolic mmHg	90	150
BP Systolic mmHg (lowest)	0	150
BP Diastolic mmHg	45	90
BP Diastolic mmHg (lowest)	0	130

$PaCO^2$
Partial pressure of carbon dioxide in arterial blood, select the correct units either kPa or mmHg and enter the value.

pH
Enter the pH (arterial) value, select either pH or H ions (nmol/L)

Mean Arterial Pressure (MAP)
Enter the value in mmHg

Vasopressors/Inotropes
Indicate **Yes or No** whether the patient received vasopressors/inotropes at the time of randomisation, if yes, select which Vasopressor/Inotrope was received.
Then indicate **Yes or No** to confirm the selection in next question, then you will be required to enter the result, note for some drugs we require the highest value. If the highest dose has not been requested, please enter the dose closest to randomisation.

RRT
Indicate **Yes or No** whether the patient received Renal Replacement Therapy at the time of randomisation.

Continuous Neuromuscular Blocking Agent
Indicate **Yes or No** whether the patient received continuous Neuromuscular Blocking Agent.

Prone position
Indicate **Yes or No** whether the patient has been in prone position in the last 24hrs, if Yes, state the amount of many hours.

ECMO
Indicate **Yes or No** whether the patient is receiving or has received ECMO in the last 24hrs.

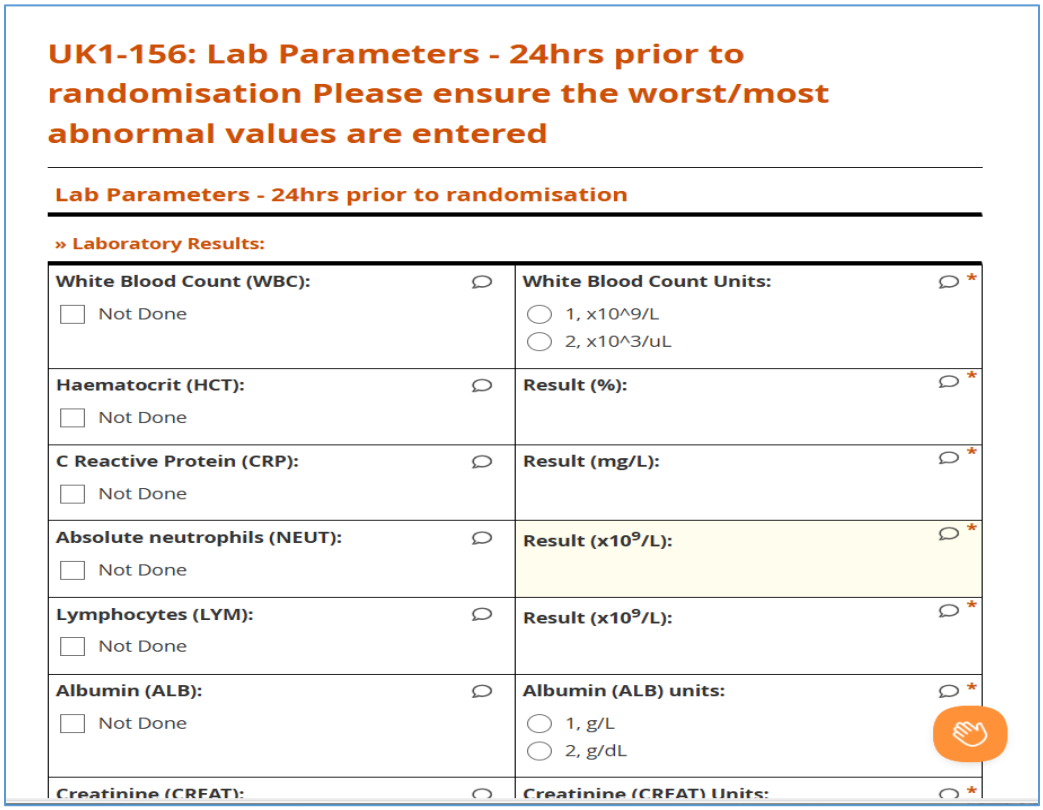
Steroid Treatment
Indicate **Yes or No** whether the patient has received any steroid in the 24hrs prior to randomisation, Enter the total daily dose and route of administration.

Comorbidities
Indicate whether the patient has any past medical history for the following conditions listed Hypertension, Obesity, Diabetes, Congestive heart failure. Alcohol Abuse and Active Smoking.

Note: There must be documented evidence that the condition existed or that the patient received therapy for the condition in the six months prior to admission to ICU.

Click on 'Close' or 'Complete' to save the data.

9.18 Lab Parameters - 24hrs prior to Randomisation



UK1-156: Lab Parameters - 24hrs prior to randomisation Please ensure the worst/most abnormal values are entered

Lab Parameters - 24hrs prior to randomisation

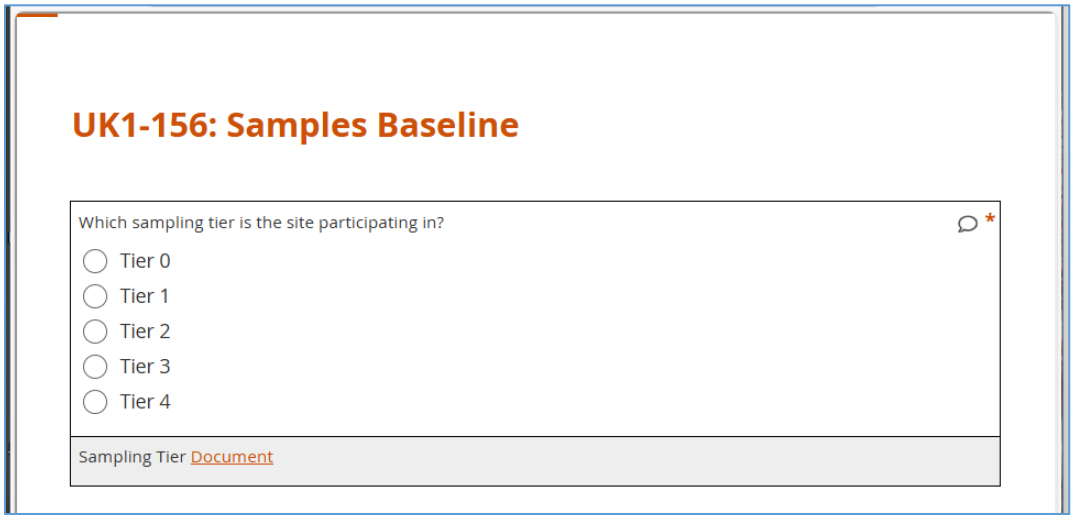
» Laboratory Results:

White Blood Count (WBC): ☐ Not Done	White Blood Count Units: * ◯ 1, x10^9/L ◯ 2, x10^3/uL
Haematocrit (HCT): ☐ Not Done	Result (%): *
C Reactive Protein (CRP): ☐ Not Done	Result (mg/L): *
Absolute neutrophils (NEUT): ☐ Not Done	Result ($x10^9$/L): *
Lymphocytes (LYM): ☐ Not Done	Result ($x10^9$/L): *
Albumin (ALB): ☐ Not Done	Albumin (ALB) units: * ◯ 1, g/L ◯ 2, g/dL
Creatinine (CREAT):	Creatinine (CREAT) Units: *

- Enter the worst/abnormal results received in the 24hrs prior to randomisation.
- For each test, please confirm whether the sample was taken
- Record each test result
- If a specific test was not performed or the result was affected, please select "**Not Done,**" which appears next to each test name

Click on 'Close' or 'Complete' to save the data.

9.19 Samples Baseline



- Select the sampling tier your site will be participating in, this can be selected per patient. Site can access the Sampling Tier Document by clicking the link on the form and selecting > manuals > sample manual.

Where aliquots are collected for a sample, ensure that the number of aliquots are selected and each aliquot ID is added by clicking the + button,

Tier 0
No samples will appear as this refers to the stratification sample only which is used and discarded.

Tier 1

- Indicate **Yes or No** whether the following samples were collected:
  Li Heparin; Serum; EDTA; PAXgene; Nasal swab; Tracheal Aspirate

  If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Tier 2

- Indicate **Yes or No** whether the following samples were collected:
  Li Heparin; Serum; EDTA; PAXgene; Nasal swab; Tracheal Aspirate
- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Tier 3

- Indicate **Yes or No** whether the following samples were collected:
  Li Heparin; Serum; EDTA; CPT Heparin; PAXgene; Nasal swab; Tracheal Aspirate.
- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Tier 4

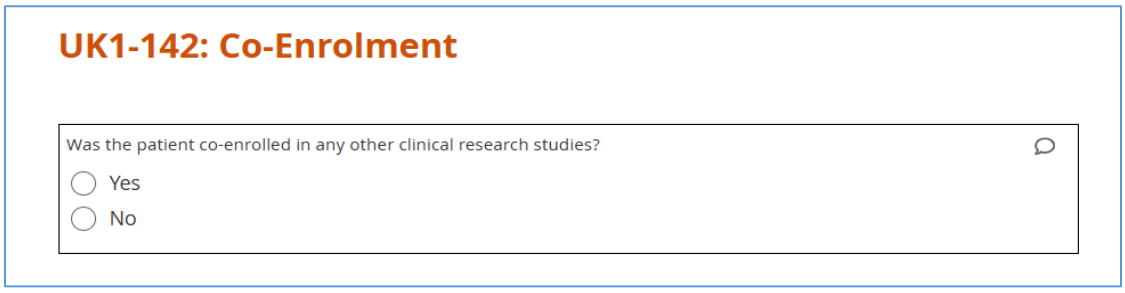
- Indicate **Yes or No** whether the following samples were collected:
  Li Heparin; Serum; EDTA; CPT Heparin; PAXgene; Nasal swab; Tracheal Aspirate; BAL
- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Next, answer the remaining questions on the form

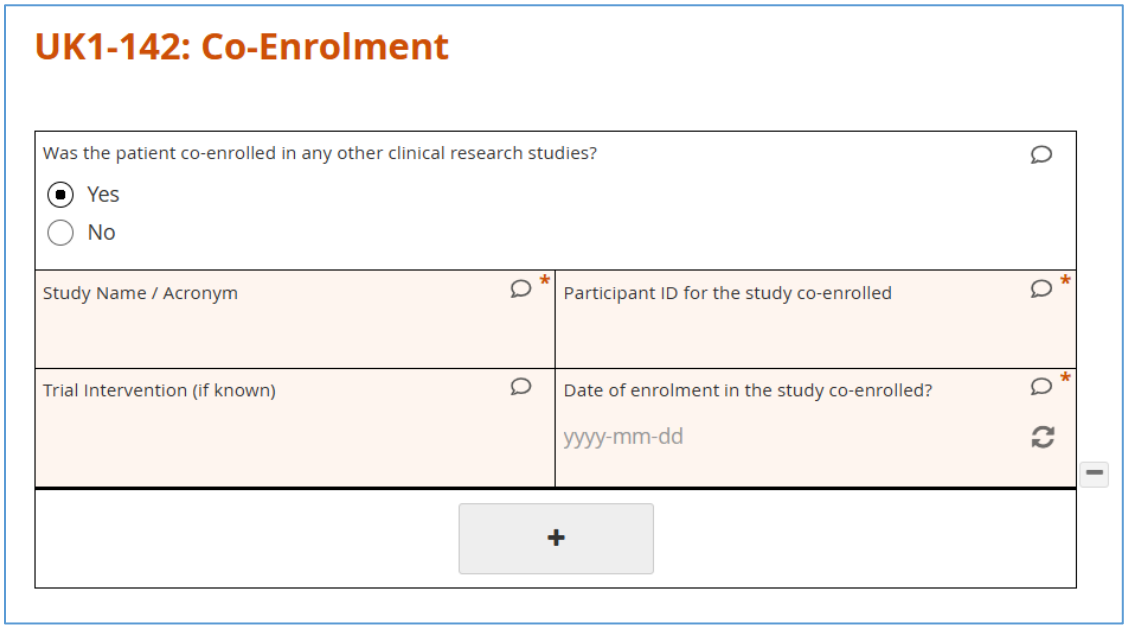
- Indicate **Yes, No or Not Applicable** whether the samples were placed directly in -80 freezer for storage. If not applicable, please select.
- Indicate **Yes, No or Not Applicable** whether the samples were placed directly in -20 freezer for storage. If not applicable, please select.
- Any further information that should be known please enter in the 'Comments' field provided.

Click on 'Close' or 'Complete' to save the data

9.20 Co-Enrolment



- Indicate **Yes or No** whether the patient is co-enrolled in any other clinical research studies

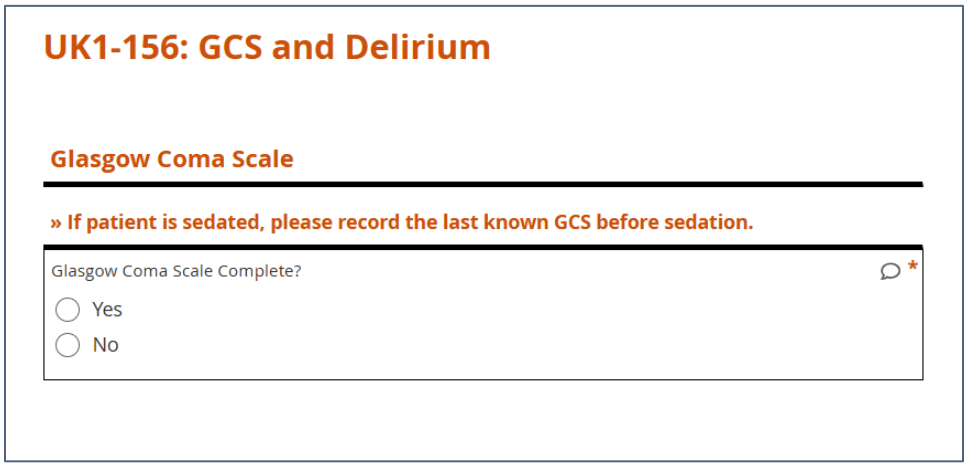


If answer is 'Yes' please complete all the remaining questions on the form

- Study Name/Acronym of study
- Participant ID for the study co-enrolled
- Trial Intervention (if known)
- Date of enrolment in the study co-enrolled
- If participant is enrolled on additional studies click '**+**' and enter details.

Click on 'Close' or 'Complete' to save the data

9.21 GCS and Delirium



- Indicate whether the Glasgow Coma Scale was Completed

If Yes,

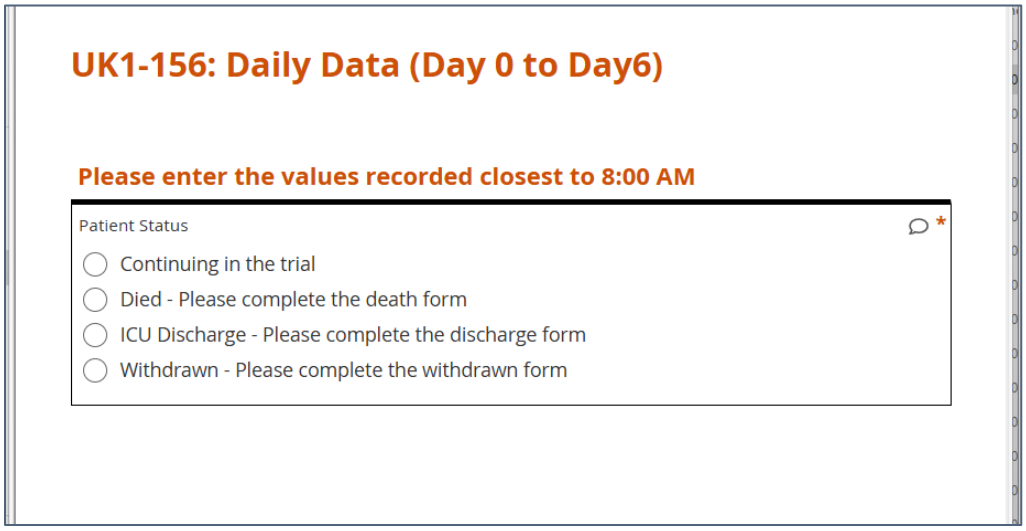
- Select the Eye opening score

- Select the Verbal response score
- Select the Motor response score
- The Total GCS Score will be auto-calculated from the scores provided from the Eye opening; Verbal response and Motor response scores.
- Please note: the Total GCS Score will not show if any of the three scores are blank.
- Enter the Delirium screening tool or if not complete select 'not known'
- If ICDSC Score is selected – Enter the Highest ICDSC for day and Highest ICDSC for night
- If CAM-ICU is selected – Enter the Highest CAM-ICU for day and Highest CAM-ICU for night

Click on 'Close' or 'Complete' to save the data

9.22 Daily data Day 0 to Day 6

This form should be used to record Daily Data from Randomisation Day 0 to Day 6
And must be completed for each day the patient is in ICU.



- This form should be used to record Daily Data from Randomisation Day 0 to Day 6.
- The values should be recorded closest to 8am on this day as possible.
- Complete the Patient Status

If patient status is **Continuing in the trial** please complete the remaining questions on the form

- Enter the date of visit day – day 0 will be the day of randomisation (short day), and day 1 will be the day after randomisation.

- Indicate **Yes or No** whether the patient is receiving respiratory support, If Yes, please select type of respiratory support

If O2 therapy is selected:
Select one of the following modes of O2 therapy:-
- o FM: Face mask
- o NP: Nasal Prongs
- o TM: Trach mask
- o T-piece

If CPAP/NIV is selected:
Select CPAP
*Please note that BiPAP is listed as an IMV

If IMV is selected:
Select from the following:-
- A/C: Assist control (also known as V/C or AC/VC)
- SIMV (Vol): Synchronized intermittent mandatory ventilation (volume)
- SIMV (Pressure): Synchronized intermittent mandatory ventilation-pressure
- PRVC: Pressure regulated volume control
- APRV: Airway pressure release ventilation
- PCV: Pressure control ventilation (also known as P/C or AC/PC)
- PSV: Pressure support ventilation
- VSV: Volume support ventilation
- HFO: High frequency oscillation
- Jet: Jet ventilation
- BiPAP: Bilevel positive airway pressure (non-invasive ventilation [NIV])
- PAV: Proportional assist ventilation
- NAVA: Neurally adjusted ventilatory assist
- ASV: Adaptive Support Ventilation

If HFNC ≥30L/min is selected:
Select HFNC (Optiflow)

Enter the results closest to 8am for each test, if a test was not performed select 'Not Done' for that test.

PaO_2
Arterial pressure of Oxygen, select the preferred units:- kPa, mmHg.

FiO2

Enter the percentage of oxygen delivered when the arterial blood gas was obtained. This value should only be obtained from the ABG, (%) value

Flow rate L/min
Enter the flow rate, the volume of gas/air delivered per minute, this option will only appear for HFNC

Mean airway pressure
The airway pressure measured at the airway opening during the administration of positive airway pressure, averaged over an entire ventilatory cycle, please enter in cmH_20

Inspiratory positive airway pressure (IPAP)
Record the set Inspiratory Positive Airway Pressure in cmH2O.

Absolute neutrophils
Enter the absolute neutrophils result in $x10^9/L$

Bicarbonate
Select the units either mmol/L or mEq/L and enter the lowest/worst result for this test

Continuous Neuromuscular Blocking Agent
Indicate **Yes or No** whether the patient received continuous Neuromuscular Blocking Agent.

ECMO
Indicate **Yes or No** whether the patient is receiving or has received ECMO in the last 24hrs.

Steroid Treatment
Indicate **Yes or No** whether the patient has received any steroid in the 24hrs prior to randomisation, Enter the total daily dose and route of administration.

SOFA Score

- **Please note, the total SOFA score may not appear at the bottom but will be calculated.**
- Enter the Mean Arterial Pressure (MAP), if test was not performed select **'Not Done'**
- Please Note: - if MAP score is greater or equal to 70 then the Cardiovascular Score will be 0 and if less than 70 then the Cardiovascular Score will be 1

Cardiovascular

- Indicate **Yes which one or No** whether the patient is receiving vasopressors or inotropes, if yes, select which Vasopressors/Inotropes was received.
- You will be required to choose which one from the following:
    - Highest Dopamine (mcg/kg/min) value.
    - Highest Dobutamine (mcg/kg/min) value
    - Highest Adrenaline (mcg/kg/min) value - *Please Note: This value is not accounted for in the calculation, e.g. If MAP Score and this value are added it will take the score of MAP into account.*
    - Highest Noradrenaline (mcg/kg/min) value
    - Highest dose Epinephrine (mcg/kg/min) value - *Please Note: This value is not accounted for in the calculation, e.g. If MAP Score and this value are added it will take the score of MAP into account.*
- Indicate **Yes or No** whether the patient received Vasopressin, Levosimendan; Milrinone.

Respiration

- P/F Ratio (PaO_2/FiO_2) – This is auto-calculated and read only so will be calculated when the PaO2 & FiO2 are entered.

Coagulation

- Enter the Lowest Platelets (x10^9/L) value, if test was not performed select **'Not Done'**
- Lowest Platelets (x10^9/L) Score – This is auto-calculated and read only so will be calculated when the Lowest Platelets (x10^9/L) is entered

Liver

- Enter the Highest Bilirubin (umol/L) Value, if test was not performed select **'Not Done'**
- Highest Bilirubin (umol/L) Score – This is auto-calculated and read only so will be calculated when the Highest Bilirubin (umol/L) value is entered.

Renal

- Indicate **Yes or No** whether the patient is receiving Renal Replacement Therapy.
- If Yes
- Renal Score – This is auto-calculated and read only so will be calculated when Yes is selected.

- If No, Enter Highest Creatinine Result and Total Urine Output (ml/d):
- Renal Score – This is auto-calculated and read only so will be calculated when Highest Creatinine Result and Total Urine Output is entered.

Glasgow Coma Scale

- GCS Score – This is read only and mapped from the GCS and Delirium form
- Total GCS Score – This is a read only field.

Total SOFA Score

- Total SOFA Score – This is auto-calculated and read only so will be calculated from the Respiration, Coagulation, Liver & Cardiovascular scores are entered. Please note this may not be displayed on the form but will be calculated.

For the remaining Patient Status questions

If patient died, ensure a Death form has been completed.
If patient has been discharged from ICU – Please complete the discharge form.
If patient withdrew - Please complete the study withdrawal form.

Click on 'Close' or 'Complete' to save the data

9.23 Simvastatin – Administration

Please note: This visit should be added only if the patient is assigned to this treatment

- Indicate **Yes or No** whether Simvastatin has been administered on first day of treatment (Day 0). Please complete for each day (up to Day 28)

If Yes

- Enter the Date of Administration
- Enter the Time of Administration
- Enter the **Creatinine kinase (CK)** result (U/L), if test was not performed select **'Not Done'**
- Enter the **Alanine aminotransferase (ALT)** result (U/L), if test was not performed select **'Not Done'**
- Enter the **Aspartate aminotransferase (AST)** result (U/L), if test was not performed select **'Not Done'**

If No

- Select the Reason Simvastatin was not administered for each day (up to Day 28)
- If Patient died - ensure a Death form has been completed.
- If patient has been discharged from ICU – ensure the discharge form has been completed.
- If patient withdrew - ensure the study withdrawal form has been completed.

***Please note: You can enter data for each day of treatment and can click 'Close' on the form for that day if not all data has been entered.**

Click on 'Close' to come back to the form later and 'Complete' once the data is complete and ready to be saved.

9.24 Baricitinib – Administration

Please note: This visit should be added only if the patient is assigned to this treatment

- Indicate **Yes or No** whether Baricitinib has been administered on first day of treatment (Day 0). Please complete for each day (up to Day 10)

If Yes

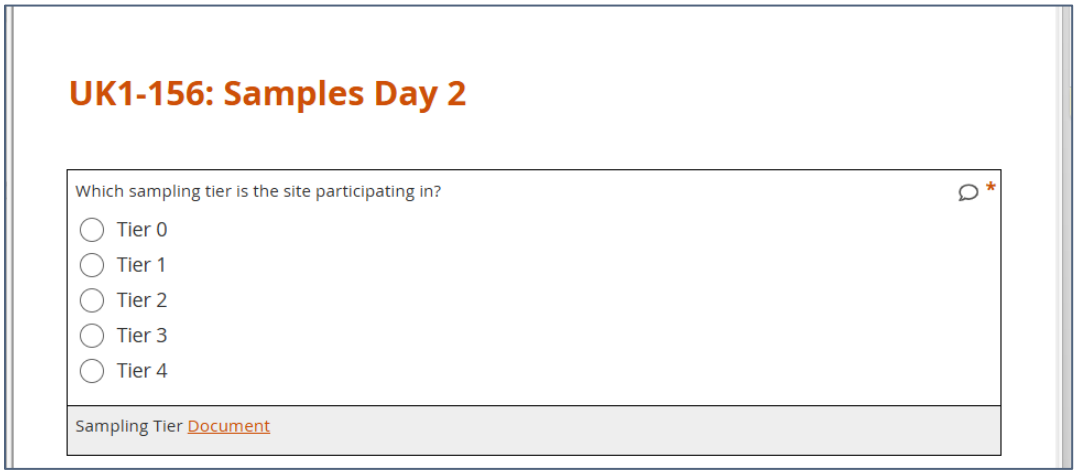
- Enter the Date of Administration
- Enter the Time of Administration

If No

- Select the Reason Baricitinib was not administered for each day (up to Day 10)
- If Patient died - ensure a Death from has been completed.
- If patient has been discharged from ICU – ensure the discharge form has been completed
- If patient withdrew - ensure the study withdrawal form has been completed.

Click on 'Close' to come back to the form later and 'Complete' once the data is complete and ready to be saved

9.25 Samples D2



- This form should be completed at **Day 2** visit
- Select the sampling tier your site will be participating in. Site can access the Sampling Tier Document by clicking the link on the form also.

- Tier 0 - No samples will appear on the form.

- Tier 1 - No samples will appear on the form.

Tier 2

- Indicate **Yes or No** whether the following samples were collected:
  Li Heparin; Serum; EDTA; PAXgene; Tracheal Aspirate.
- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Tier 3

- Indicate **Yes or No** whether the following samples were collected:

Li Heparin; Serum; EDTA; PAXgene; CPT Heparin; Tracheal Aspirate.

- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Tier 4

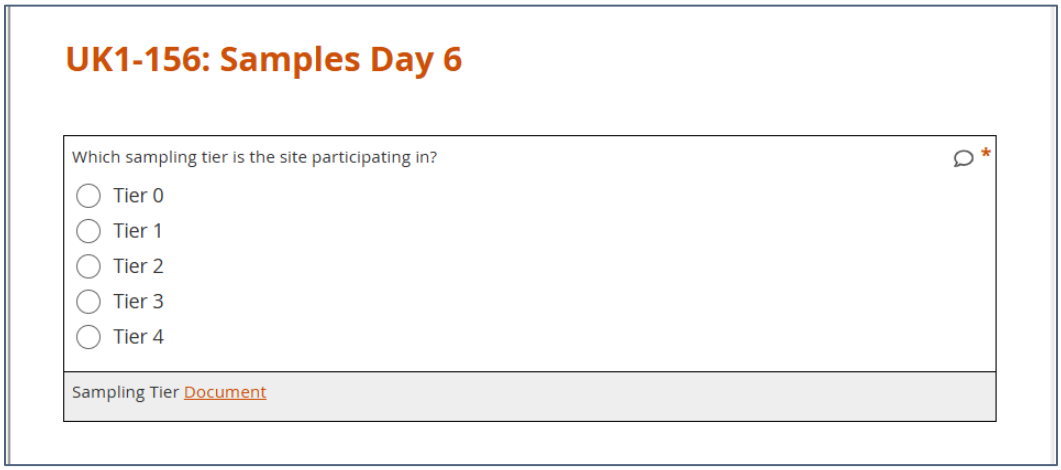
- Indicate Yes or No whether the following samples were collected:
  Li Heparin; Serum; EDTA; CPT Heparin; PAXgene; Tracheal Aspirate; BAL
- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Next answer the remaining questions on the form:

- Indicate whether the samples were placed directly in -80 freezer for storage. If not applicable, please select.
- Indicate whether the samples were placed directly in -20 freezer for storage. If not applicable, please select.
- Any further information that should be known please enter in the comments field.

Click on 'Close' or 'Complete' to save the data.

9.26 Samples D6



- This form should be completed at **Day 6** visit
- Select the sampling tier your site will be participating in. Site personnel can access the Sampling Tier Document by clicking the link on the form also.

- Tier 0 - No samples will appear on the form

- Tier 1 - No samples will appear on the form

Tier 2

- Indicate **Yes or No** whether the following samples were collected:
  Li Heparin; Serum; EDTA; PAXgene; Tracheal Aspirate
- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Tier 3

- Indicate **Yes or No** whether the following samples were collected:
  Li Heparin; Serum; EDTA; PAXgene; Tracheal Aspirate
- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

Tier 4

- Indicate Yes or No whether the following samples were collected:
  Li Heparin; Serum; EDTA; PAXgene; Tracheal Aspirate; CPT Heparin
- If Answer is 'Yes' for any of the samples enter the Sample ID; Number of aliquots collected; the aliquot ID and the Date & Time sample was collected.

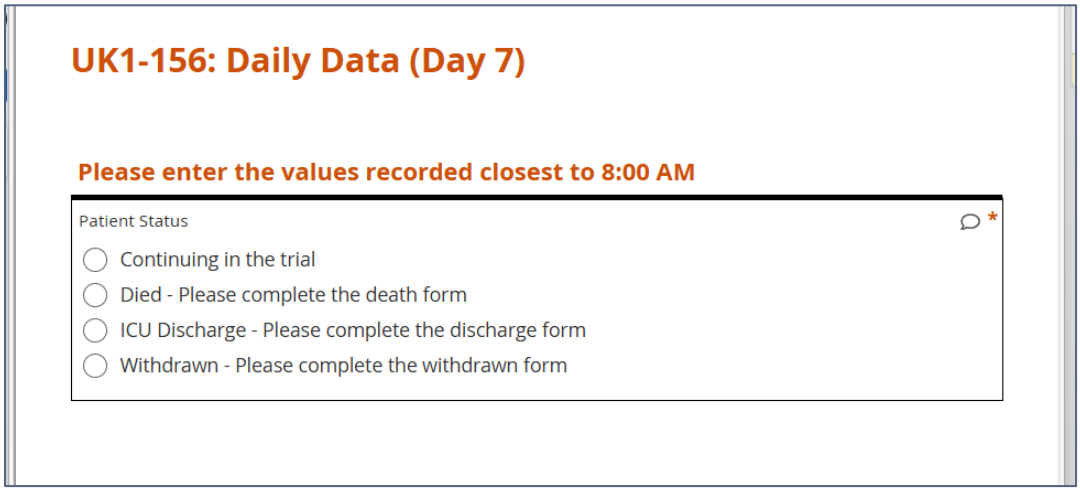
Next answer the remaining questions on the form:

- Indicate whether the samples were placed directly in -80 freezer for storage. If not applicable, please select.
- Indicate whether the samples were placed directly in -20 freezer for storage. If not applicable, please select.
- Any further information that should be known please enter in the comments field.

Click on 'Close' or 'Complete' to save the data

9.27 Daily data day 7

This form should be used to record Daily Data for Day 7
And must be completed when the patient is in ICU.



This form should be used to record Daily Data at Day 7 Visit, Any values entered on this form should be those that were done closest to time 8:00 am

- Complete the Patient Status

If patient status is **Continuing in the trial,** please complete the remaining questions on the form

- Enter the date of visit day
- Indicate **Yes or No** whether the patient is receiving respiratory support, If Yes, please select type of respiratory support

If O2 Therapy is selected:

- Select one of the following modes of O2 therapy:-
  - o FM: Face mask
  - o NP: Nasal Prongs
  - o TM: Trach mask
  - o T-piece

If CPAP/NIV is selected:

- Select the Mode of ventilation: CPAP

*Please note that BiPAP is listed as an IMV

If IMV is selected:

Select from the following:-

- A/C: Assist control (also known as V/C or AC/VC)
- SIMV (Vol): Synchronized intermittent mandatory ventilation (volume)
- SIMV (Pressure): Synchronized intermittent mandatory ventilation-pressure
- PRVC: Pressure regulated volume control
- APRV: Airway pressure release ventilation
- PCV: Pressure control ventilation (also known as P/C or AC/PC)
- PSV: Pressure support ventilation
- VSV: Volume support ventilation

- HFO: High frequency oscillation
- Jet: Jet ventilation
- BiPAP: Bilevel positive airway pressure (non-invasive ventilation [NIV])
- PAV: Proportional assist ventilation
- NAVA: Neurally adjusted ventilatory assist
- ASV: Adaptive Support Ventilation

If HFNC ≥30L/min is selected:

- Select the Mode of ventilation: HFNC (Optiflow)

Enter the results closest to 8am for each test, if a test was not performed select 'Not Done' for that test.

PaO_2

Arterial pressure of Oxygen, select the preferred units:- kPa, mmHg.

FiO2

Enter the percentage of oxygen delivered when the arterial blood gas was obtained. This value should only be obtained from the ABG, (%) value

PaO2/FiO2 ratio

This is an automatically calculated field derived from PaO2/FiO2

Flow rate L/min

Enter the flow rate, the volume of gas/air delivered per minute, this option will only appear for HFNC

Mean airway pressure

The airway pressure measured at the airway opening during the administration of positive airway pressure, averaged over an entire ventilatory cycle, please enter in cmH_20

Inspiratory positive airway pressure (IPAP)

Record the set Inspiratory Positive Airway Pressure in cmH2O.

Absolute neutrophils

Enter the absolute neutrophils result in $x10^9/L$

Bicarbonate

Select the units either mmol/L or mEq/L and enter the lowest/worst result for this test

Steroid Treatment

Indicate **Yes or No** whether the patient has received any steroid in the 24hrs prior to randomisation. Enter the total daily dose and route of administration.

Is the patient receiving any vasopressors or inotropes?

- Indicate **Yes which one or No** whether the patient is receiving vasopressors or inotropes, if yes, select which Vasopressors/Inotropes was received.
- you will be required to choose which one from the following:
    - Highest Dopamine (mcg/kg/min) value.
    - Highest Dobutamine (mcg/kg/min) value
    - Highest Adrenaline (mcg/kg/min) value - *Please Note: This value is not accounted for in the calculation, e.g. If MAP Score and this value are added it will take the score of MAP into account.*
    - Highest Noradrenaline (mcg/kg/min) value
    - Highest dose Epinephrine (mcg/kg/min) value
- Indicate **Yes or No** whether the patient received Vasopressin, Levosimendan; Milrinone.

Renal

- Indicate **Yes or No** whether the patient is receiving Renal Replacement Therapy.
- Indicate **Yes or No** whether the patient received continuous Neuromuscular Blocking Agent.
- Indicate **Yes or No** whether the patient received Extracorporeal Membrane Oxygenation (ECMO)

MMST, Maximal Inspiratory pressure and hand grip

- Enter the results for each test, if a test was not performed select '**Not Done'** for that test
- Enter Hand grip strength dynamometry *kg of force* value
- Enter Maximal inspiratory pressure *cmH20* value
- Select the grade (0-5) for Manual Muscle Strength Testing (MMST)

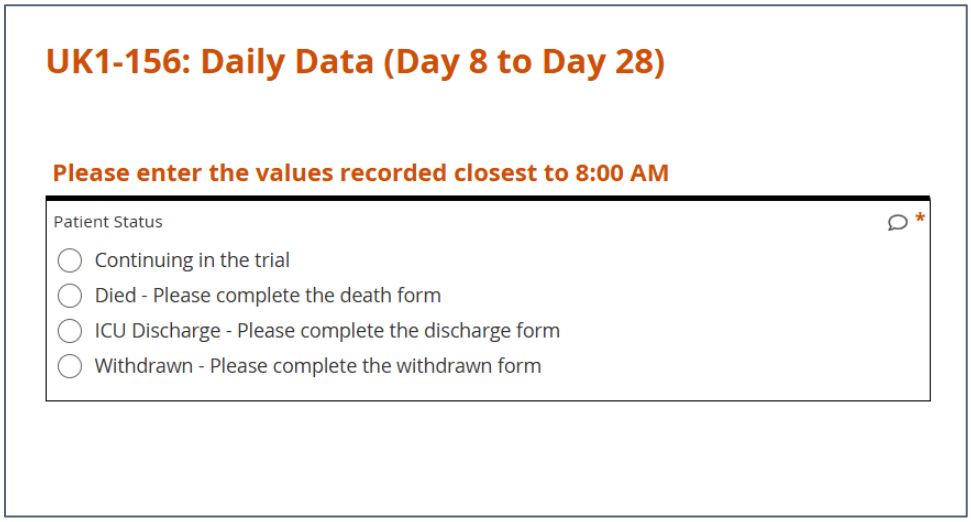
For the remaining Patient Status questions

If Patient died, ensure a Death form has been completed.
If patient has been discharged from ICU – Please complete the discharge form.
If patient withdrew - Please complete the study withdrawal form.

Click on 'Close' or 'Complete' to save the data

9.28 Daily data Day 8 to Day 28

This form should be used to record Daily Data for Day 8 to Day 28 and must be completed when the patient is in ICU.



This form should be used to record Daily Data at Day 8 through to Day 28 Visit, any values entered on this form should be those that were done closest to time 8:00 am

- Complete the Patient Status

If patient status is **Continuing in the trial** please complete the remaining questions on the form

- Enter the date of visit day
- Indicate **Yes or No** whether the patient is receiving respiratory support, If Yes, please select type of respiratory support

If O2 Therapy is selected:

- Select one of the following modes of O2 therapy:-
  - o FM: Face mask
  - o NP: Nasal Prongs
  - o TM: Trach mask
  - o T-piece

If CPAP/NIV is selected:

- Select the Mode of ventilation: CPAP

*Please note that BiPAP is listed as an IMV

If IMV is selected:

Select from the following:-

- A/C: Assist control (also known as V/C or AC/VC)
- SIMV (Vol): Synchronized intermittent mandatory ventilation (volume)
- SIMV (Pressure): Synchronized intermittent mandatory ventilation-pressure
- PRVC: Pressure regulated volume control
- APRV: Airway pressure release ventilation
- PCV: Pressure control ventilation (also known as P/C or AC/PC)

- PSV: Pressure support ventilation
- VSV: Volume support ventilation
- HFO: High frequency oscillation
- Jet: Jet ventilation
- BiPAP: Bilevel positive airway pressure (non-invasive ventilation [NIV])
- PAV: Proportional assist ventilation
- NAVA: Neurally adjusted ventilatory assist
- ASV: Adaptive Support Ventilation

If HFNC ≥30L/min is selected:

- Select the Mode of ventilation: HFNC (Optiflow)

Enter the results closest to 8am for each test, if a test was not performed select 'Not Done' for that test.

PaO_2

Arterial pressure of Oxygen, select the preferred units:- kPa, mmHg.

FiO2

Enter the percentage of oxygen delivered when the arterial blood gas was obtained. This value should only be obtained from the ABG, (%) value

PaO2/FiO2 ratio

This is an automatically calculated field derived from PaO2/FiO2

Flow rate L/min

Enter the flow rate, the volume of gas/air delivered per minute, this option will only appear for HFNC

Mean airway pressure

The airway pressure measured at the airway opening during the administration of positive airway pressure, averaged over an entire ventilatory cycle, please enter in cmH_20

Inspiratory positive airway pressure (IPAP)

Record the set Inspiratory Positive Airway Pressure in cmH_2O.

Absolute neutrophils

Enter the absolute neutrophils result in $x10^9/L$

Is the patient receiving vasopressors or inotropes

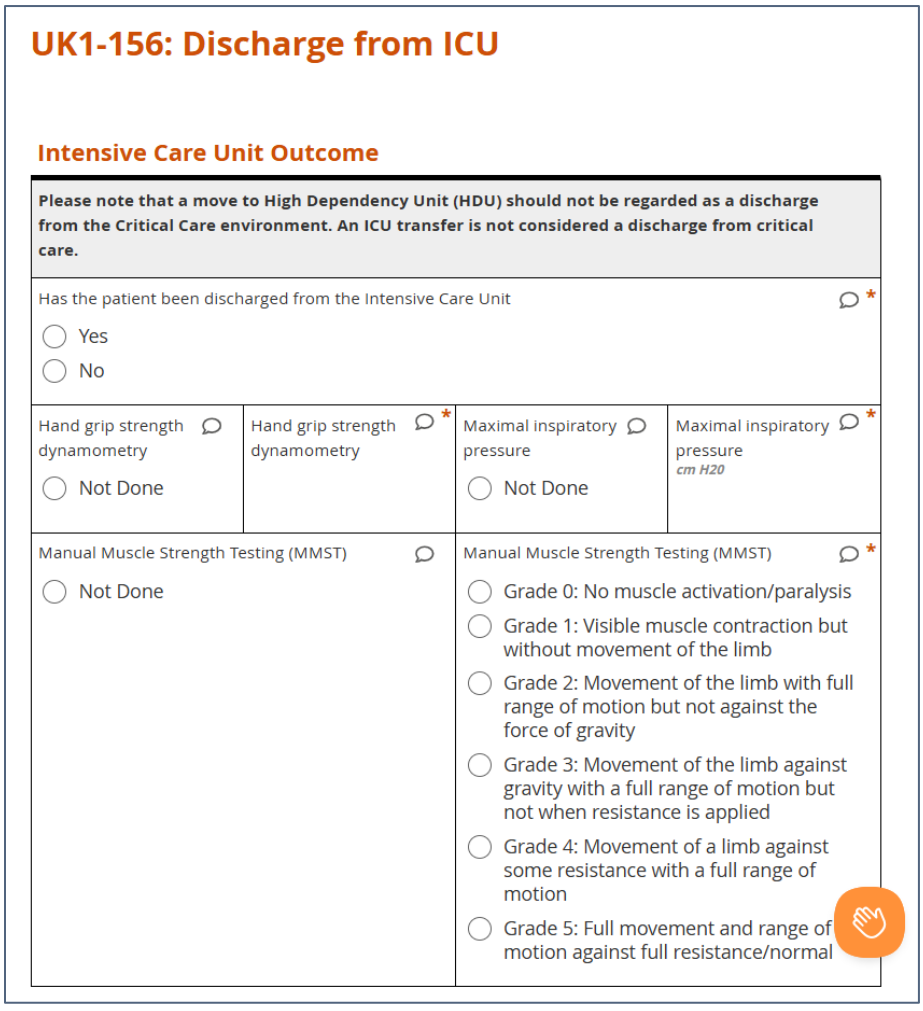
Indicate **Yes or No** whether the patient is receiving vasopressors or inotropes.
Is the patient receiving Renal Replacement Therapy
Indicate **Yes or No** whether the patient is receiving Renal Replacement Therapy.

Did the patient receive continuous Neuromuscular Blocking Agent.
Indicate **Yes or No** whether the patient is received continuous Neuromuscular Blocking Agent.

Did the patient receive Extracorporeal Membrane Oxygenation (ECMO)
Indicate Yes or No whether the patient is receiving Extracorporeal Membrane Oxygenation (ECMO).

Click on 'Close' or 'Complete' to save the data

9.29 Discharge from ICU



This form should be completed if the patient is being discharged from ICU, it should not be used if the patient is transferring to another critical care environment e.g. High Dependency Unit

Intensive Care Unit Outcome

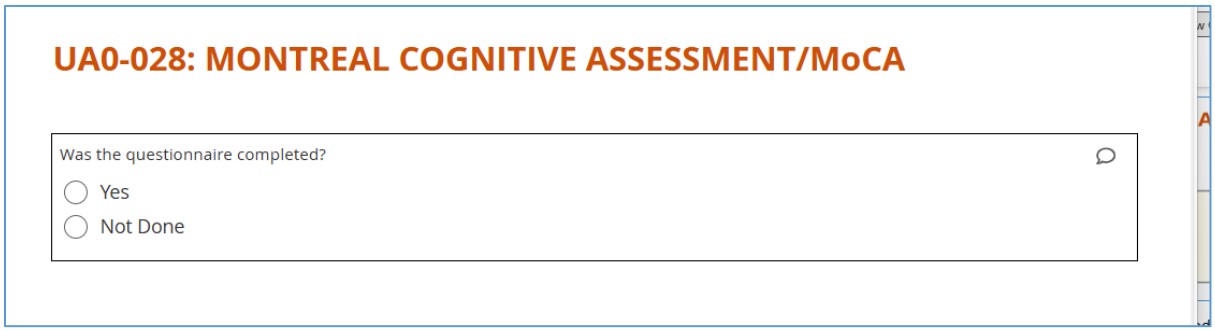
- Indicate **Yes or No** whether the patient has been discharged from the Intensive Care Unit
- Enter the Date of First Intensive Care Unit Discharge (if applicable)
- Enter the Time of First Intensive Care Unit Discharge (24 hour clock) (if applicable)
- Enter the results for each test, if a test was not performed select '**Not Done'** for that test
- Enter Hand grip strength dynamometry value *kg of force*
- Enter Maximal inspiratory pressure value *cmH20*
- Select the grade (0-5) for Manual Muscle Strength Testing (MMST)

Length of ICU Stay

- Length of ICU Stay – this is auto-calculated from the date entered for ICU Admission on the hospital admission form

Click on 'Close' or 'Complete' to save the data

9.30 MOCA



- Indicate **Yes, or Not Done** whether the questionnaire was completed.
- If Not Done – Select Reason it was not done

MONTREAL COGNITIVE ASSESSMENT/MoCA Answer ALL questions
Memory/Attention – Was this completed Indicate **Yes, or No** whether Memory/Attention was completed

Verbal Fluency - If 0-2 words select 0 points; If 3-5 words select 1 point; If 6-9 words select 2 points; If 10-13 words select 3 points; If 14 words or more select 4 points Select the score given for this question (0 - 4) or select 'Not Done'
Orientation Select the score given for this question (0 - 6) or select 'Not Done'
Memory Select the score given for this question (0 - 5) or select 'Not Done'
Total Score **Read-only field.** The total score is automatically calculated by the system according to the scores given in previous questions.

Click on 'Close' or 'Complete' to save the data.

9.31 Discharge from Hospital

Hospital discharge will be the first date that the patient is discharged to home/community/rehab/hospice. A transfer between hospitals is not considered as a hospital discharge.

Hospital Outcome

- Indicate **Yes or No** whether the patient been discharged from Hospital
- If Yes, Enter the date of first hospital discharge (if applicable)
- Enter Time of First Hospital Discharge (if applicable)

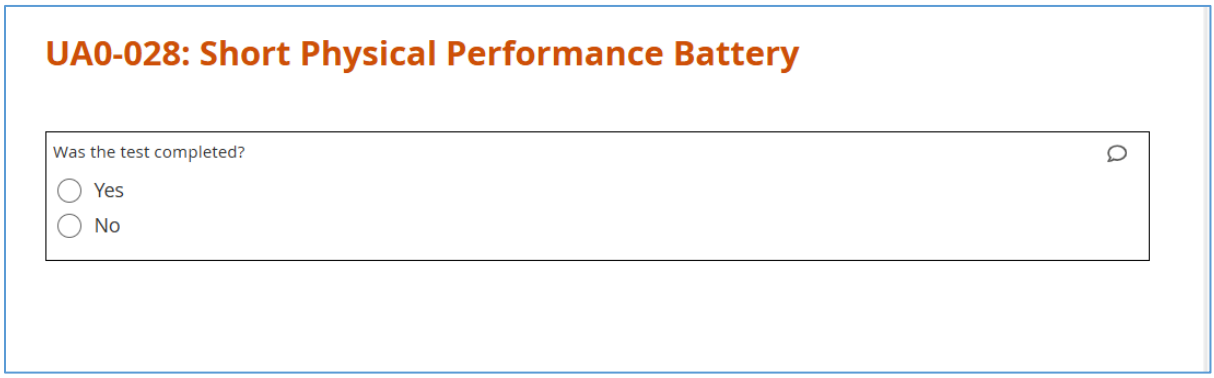
Length of Stay

Length of Hospital Stay – this is auto-calculated from the date entered for Hospital Admission on the Hospital Admission form

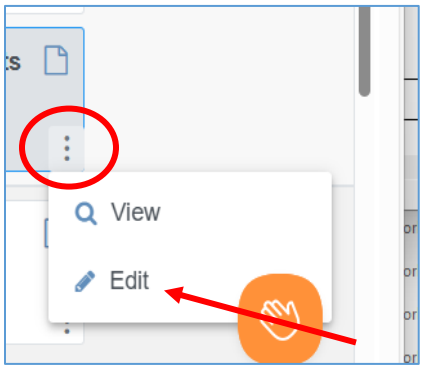
Click on 'Close' or 'Complete' to save the data.

9.32 Short Physical Performance Battery

Please note: This form may be hidden/not required depending on your jurisdiction



- To complete the questionnaire please click the **Actions** tab these are the 3 dots located on the right side of form and then select **Edit**

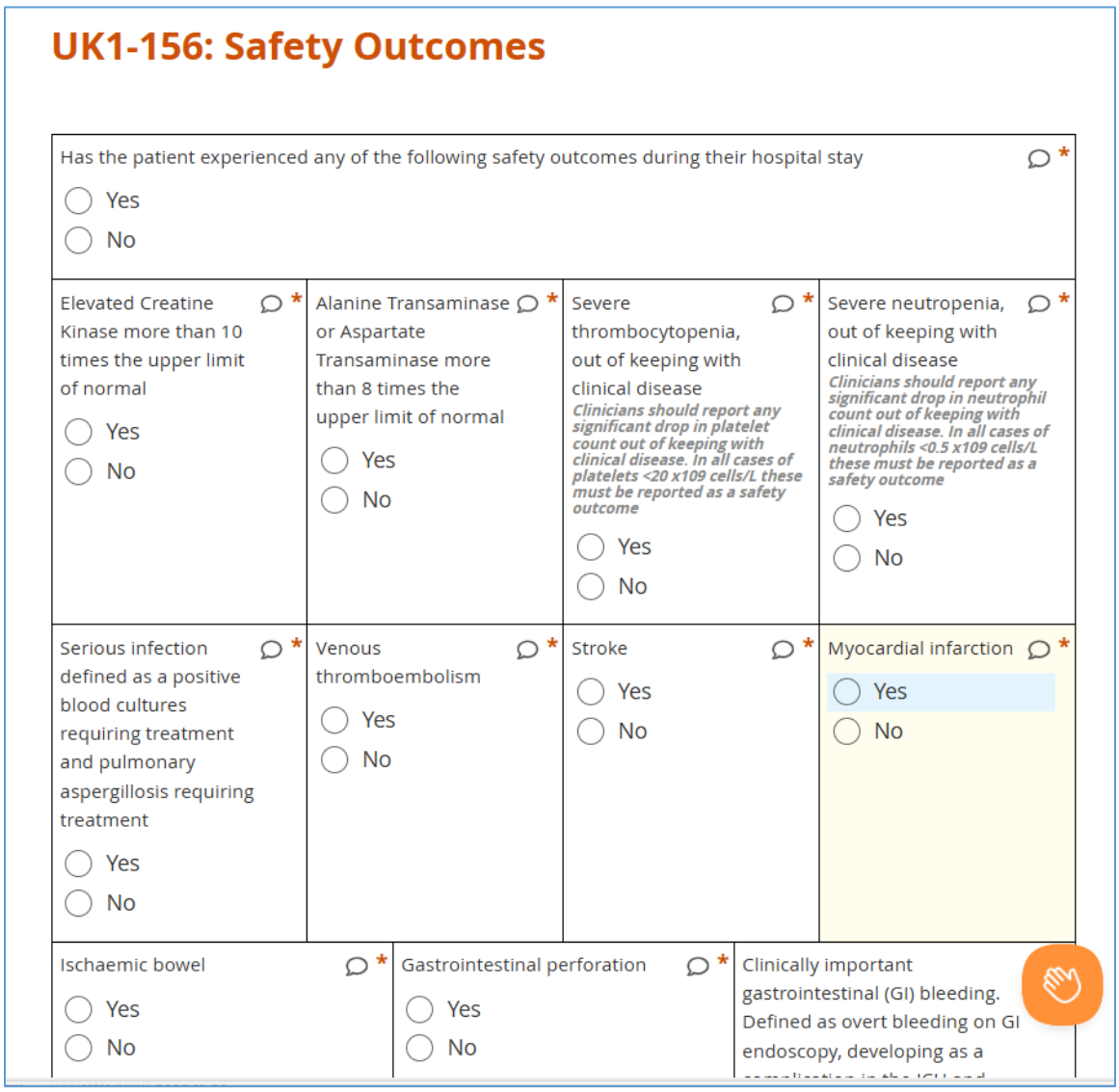


SHORT PHYSICAL PERFORMANCE BATTERY Answer ALL questions
Indicate **Yes, or No** whether the test was completed if Yes, complete the remaining questions
Chair Stand Test Select the score given for this question (0 - 4)
Balance Test Select the score given for this question (0 - 4)

Gait Speed Test
Select the score given for this question (0 - 4)

Click on ‘Close’ or ‘Complete’ to save the data.

9.33 Safety Outcomes



- Indicate **Yes or No** whether the patient has experienced any of the following safety outcomes during their hospital stay.

<u>If Yes,</u>

- Indicate **Yes or No** for question **Elevated Creatine Kinase was more than 10 times the upper limit of normal**
- if Yes Enter the description of the event and Date of occurrence
- Indicate **Yes or No** if event was ongoing, If no, enter the end date of the event

- Indicate **Yes or No** for question **Alanine Transaminase or Aspartate Transaminase was more than 8 times the upper limit of normal more than 10 times the upper limit of normal**.
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event

- Indicate **Yes or No** for question **Severe thrombocytopenia, out of keeping with clinical disease.**
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event

- Indicate **Yes or No** for question **Severe neutropenia, out of keeping with clinical disease.**
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event.

- Indicate **Yes or No** for question **Serious infection defined as a positive blood cultures requiring treatment and pulmonary aspergillosis requiring treatment.**
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event.

- Indicate **Yes or No** for question **Venous thromboembolism**
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No. enter the end date of the event.

- Indicate **Yes or No** for question **Stroke**
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event.

- Indicate **Yes or No** for question **Myocardial infarction**
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event.

- Indicate **Yes or No** for question **Ischaemic bowel**
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event.

- Indicate **Yes or No** for question **Gastrointestinal perforation**
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event

- Indicate **Yes or No** for question **Clinically important gastrointestinal (GI) bleeding. Defined as overt bleeding on GI endoscopy, developing as a complication in the ICU and accompanied by 1 or more of the following features within 24 hours**
  - Spontaneous drop of systolic, mean arterial pressure or diastolic blood pressure of 20mmHg or more
  - Start of vasopressor or a 20% increase in vasopressor dose
  - Decrease in haemoglobin of at least 2 g/dl
  - Transfusion of 2 units of packed RBC or more
- If Yes Enter the description of the event and Date of occurrence
- Indicate Yes or No if event was ongoing, If No, enter the end date of the event

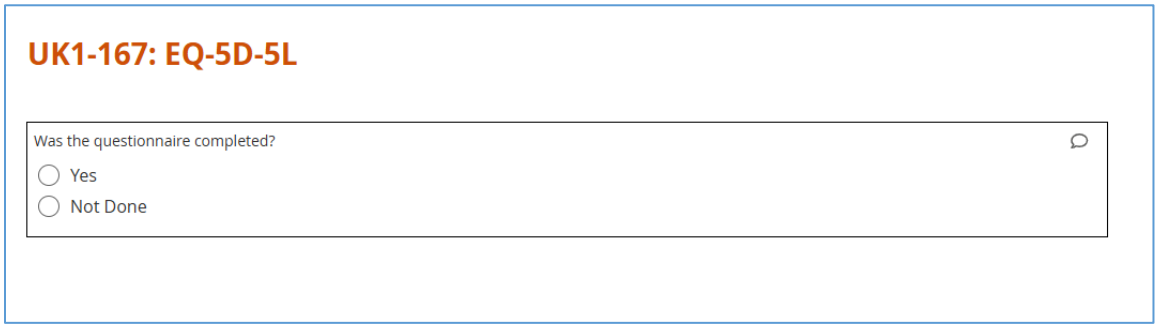
Click on 'Close' or 'Complete' to save the data.

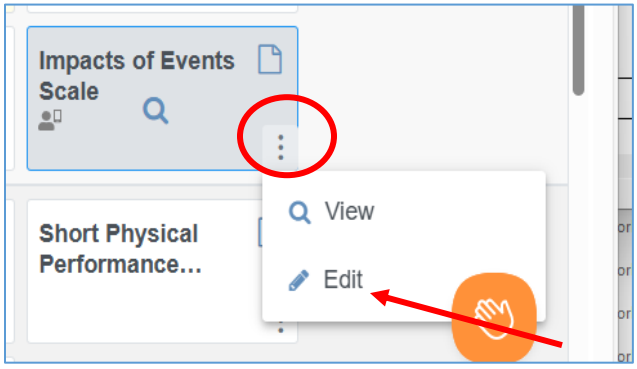
9.34 Follow Up data - Day 90

- Indicate **Yes, No or Unknown** whether the patient is alive 90 days after randomisation
- If Yes, Enter date this was confirmed.
- If No, Enter date patient died.

Click on 'Close' or 'Complete' to save the data.

9.35 EQ-5D-5L





- To complete the questionnaire please click the **Actions** tab these are the 3 dots located on the right side of form and then select **Edit**

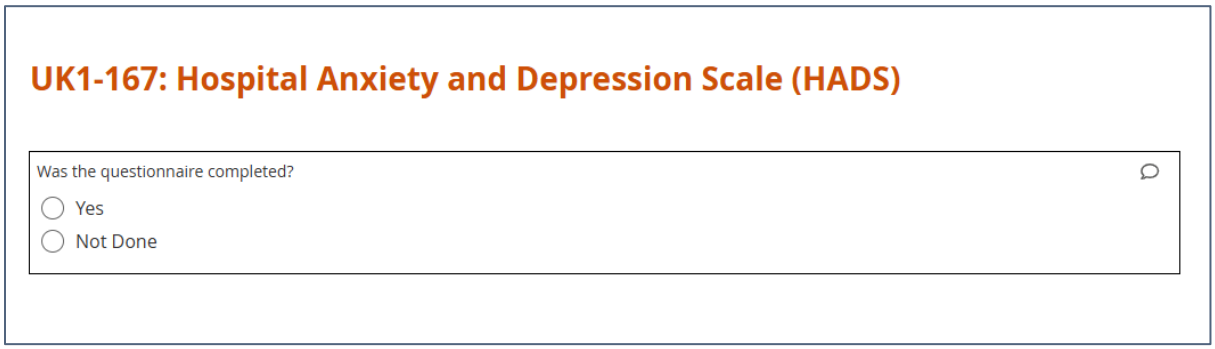
- Please note that Quality of Life (QoL)/ health related questionnaires may be completed centrally in your jurisdiction.
- If the patient has died please select 'not done' and 'unable to contact patient'.
- Indicate **Yes, or Not Done** whether the questionnaire was completed
- If Not Done – Select Reason it was not done
- Enter the Date the questionnaire was completed

EQ-5D-5L This Questionnaire should be completed within **+14 Days of Follow Up Visit**. Answer ALL questions.
MOBILITY Select the option that the patient has described/selected
SELF-CARE Select the option that the patient has described/selected
USUAL ACTIVITIES Select the option that the patient has described/selected

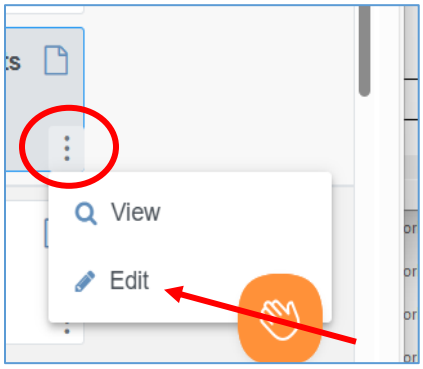
PAIN/ DISCOMFORT Select the option that the patient has described/selected
ANXIETY/ DEPRESSION Select the option that the patient has described/selected
We would like to know how good or bad your health is TODAY. Please indicate on the scale (0-100) to indicate how your health is TODAY. Enter the number that the patient has stated

Click on 'Close' or 'Complete' to save the data.

9.36 Hospital Anxiety and Depression Scale (HADS)



- To complete the questionnaire please click the **Actions** tab these are the 3 dots located on the right side of form and then select **Edit**



- Please note that Quality of Life (QoL)/ health related questionnaires may be completed centrally in your jurisdiction.
- If the patient has died, please select 'not done' and 'unable to contact patient'.
- Indicate **Yes, or Not Done** whether the questionnaire was completed
- If Not Done – Select Reason it was not done

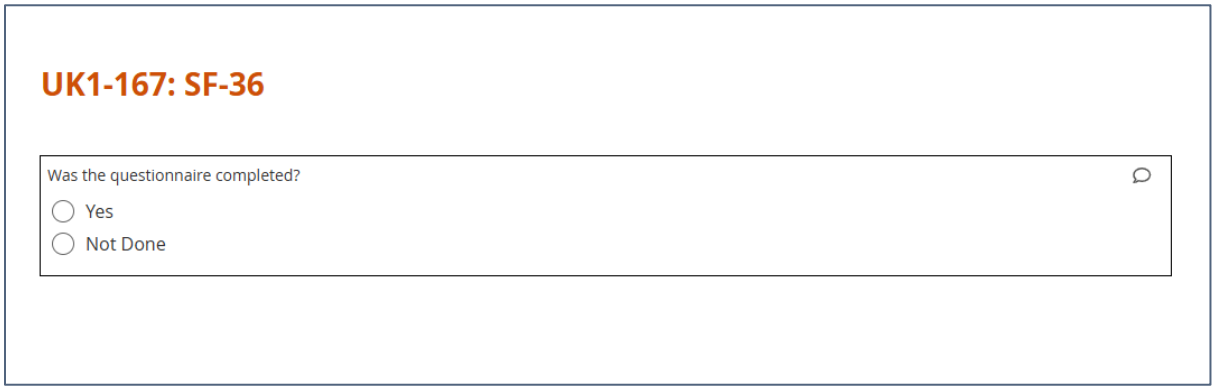
- Enter the Date the questionnaire was completed

Hospital Anxiety and Depression Scale (HADS) This Questionnaire should be completed within **+14 Days of Follow Up Visit**. Answer ALL questions
I feel tense or 'wound up': Select the option that the patient has described/selected
I still enjoy the things I used to enjoy: Select the option that the patient has described/selected
I get a sort of frightened feeling as if something awful is about to happen: Select the option that the patient has described/selected
I can laugh and see the funny side of things: Select the option that the patient has described/selected
Worrying thoughts go through my mind: Select the option that the patient has described/selected
I feel cheerful: Select the option that the patient has described/selected
I can sit at ease and feel relaxed: Select the option that the patient has described/selected
I feel as if I am slowed down: Select the option that the patient has described/selected
I get a sort of frightened feeling like 'butterflies' in the stomach: Select the option that the patient has described/selected
I have lost interest in my appearance: Select the option that the patient has described/selected
I feel restless as I have to be on the move: Select the option that the patient has described/selected
I look forward with enjoyment to things: Select the option that the patient has described/selected
I get sudden feelings of panic: Select the option that the patient has described/selected
I can enjoy a good book or radio or TV program: Select the option that the patient has described/selected

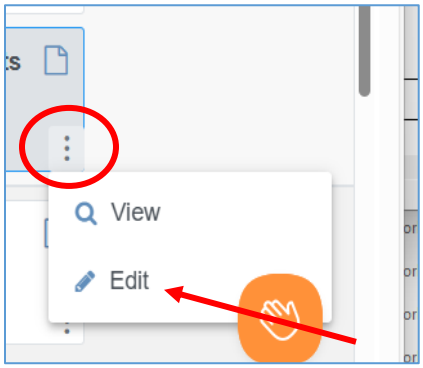
Total Score: Depression **Read-only field.** The total sum of all Depression Questions is automatically calculated by the system according to the scores given in previous questions.
Total Score: Anxiety **Read-only field.** The total sum of all Anxiety Questions is automatically calculated by the system according to the scores given in previous questions
Total Score: **Read-only field.** The total sum of all Anxiety Questions and all Depression Questions are automatically calculated by the system according to the scores given in previous questions

Click on 'Close' or 'Complete' to save the data.

9.37 Social and Wellbeing SF-36



- To complete the questionnaire please click the **Actions** tab these are the 3 dots located on the right side of form and then select **Edit**



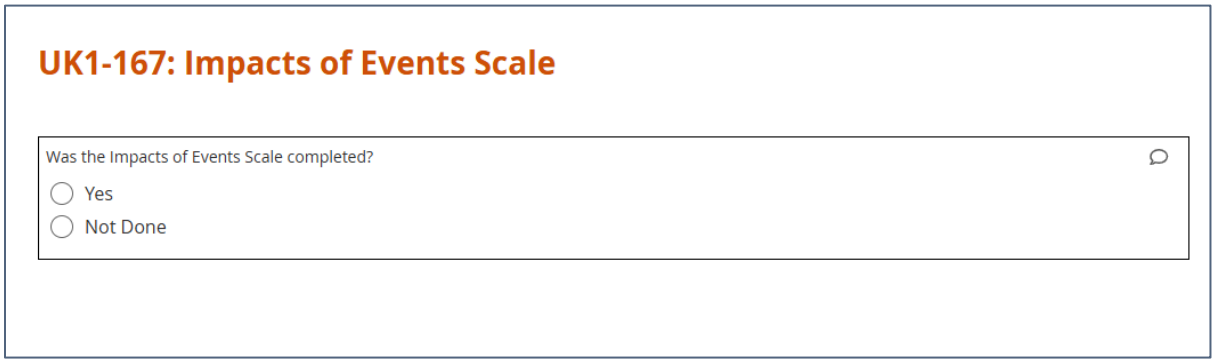
- Please note that Quality of Life (QoL)/ health related questionnaires may be completed centrally in your jurisdiction.

- If the patient has died, please select ‘not done’ and ‘unable to contact patient’.
- Indicate **Yes, or Not Done** whether the questionnaire was completed
- If Not Done – Select Reason it was not done
- Enter the Date the questionnaire was completed

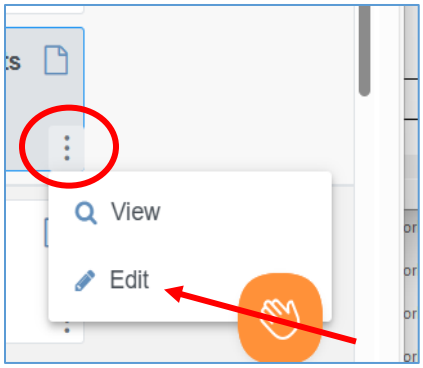
SF-36 This Questionnaire should be completed within **+14 Days of Follow Up Visit**. Answer ALL questions
During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health? Select Yes or No that the patient has described/selected for all questions in this section.
During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? Select Yes or No that the patient has described/selected for all questions in this section.
Welfare Benefits Question Set Select Yes or No that the patient has described/selected for all questions in this section.
Care Needs (adapted from Griffiths et al (2013) Indicate Yes or No for Q. Do you receive care (depend on other people for help) to undertake to undertake your normal activities? Is ‘Yes’ is selected answer all the questions in this section. Select the option that the patient has described/selected.

Click on ‘Close’ or ‘Complete’ to save the data.

9.38 Impact of Events Scale



- To complete the questionnaire please click the **Actions** tab these are the 3 dots located on the right side of form and then select **Edit**

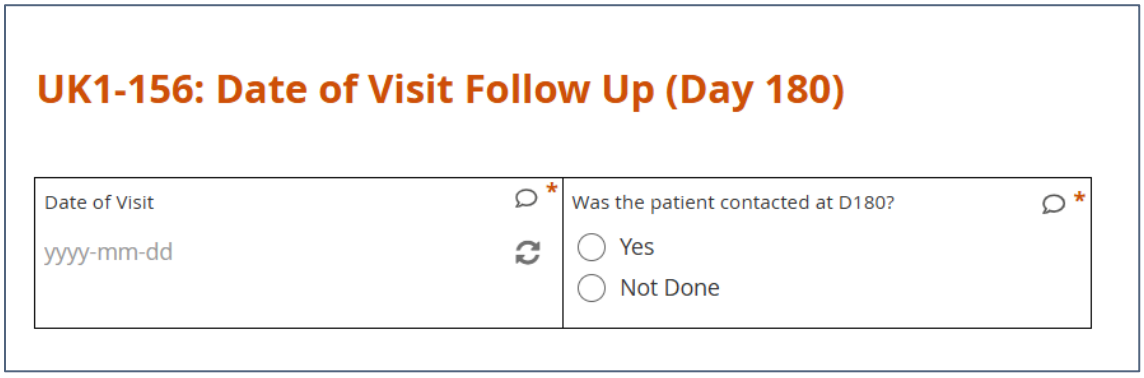


- Please note that Quality of Life (QoL)/ health related questionnaires may be completed centrally in your jurisdiction.
- If the patient has died, please select 'not done' and 'unable to contact patient'.
- Indicate **Yes, or Not Done** whether the questionnaire was completed
- If Not Done – Select Reason it was not done.
- Enter the Date the questionnaire was completed.

Impact of Events Scale
This Questionnaire should be completed within **+14 Days of Follow Up Visit**. Answer ALL questions
DURING THE PAST SEVEN DAYS with respect to (the event). How much were you distressed or bothered by these difficulties? Select the option [0 – 4] that the patient has described/selected for **each** question on the form. 0 - Not at all; 1 - A little bit; 2 – Moderately; 3 - Quite a bit; 4 – Extremely]

Click on 'Close' or 'Complete' to save the data.

9.39 Follow Up data - Day 180

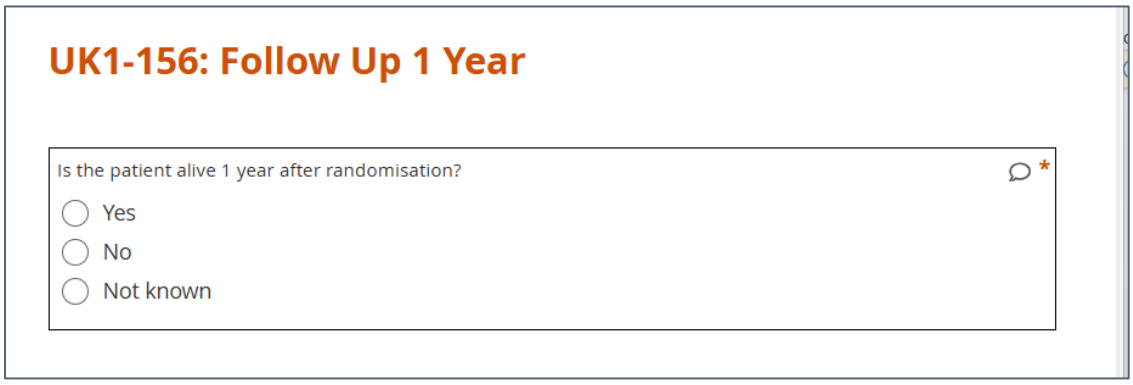


- Enter Date this visit was performed
- Indicate **Yes or Not Done** whether the patient contacted at Day 180
- If Not Done – Select Reason it was not done.

- Note if the patient has died before this date, then please enter the date of death as the date of visit, this will flag a query, please answer the query explaining that the patient has died. Then for 'was the patient contacted' select 'not done' and 'unable to contact patient'.

Click on 'Close' or 'Complete' to save the data.

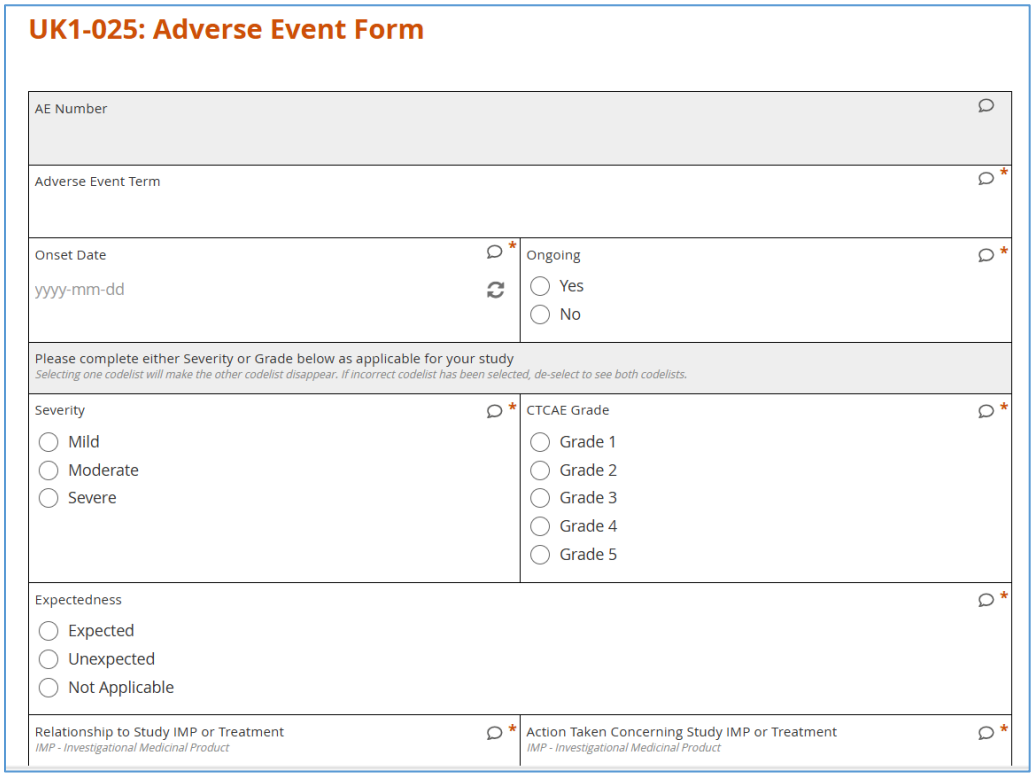
9.40 Follow Up data - 1 year



- Indicate **Yes, No or Unknown** whether the patient is alive 90 days after randomisation.
- If Yes, Enter Date this was confirmed.
- If No, Enter Date patient died.

9.41 Adverse Event Form

Please note: This form may be hidden/not required depending on your jurisdiction.



Section 7.9 details the location of adverse event and how to Add New.

Answer all questions on the form

- The AE number will be auto populated by the system.
- Enter the description/name of the adverse event in the “Adverse Event Term” field and complete the rest of the form.

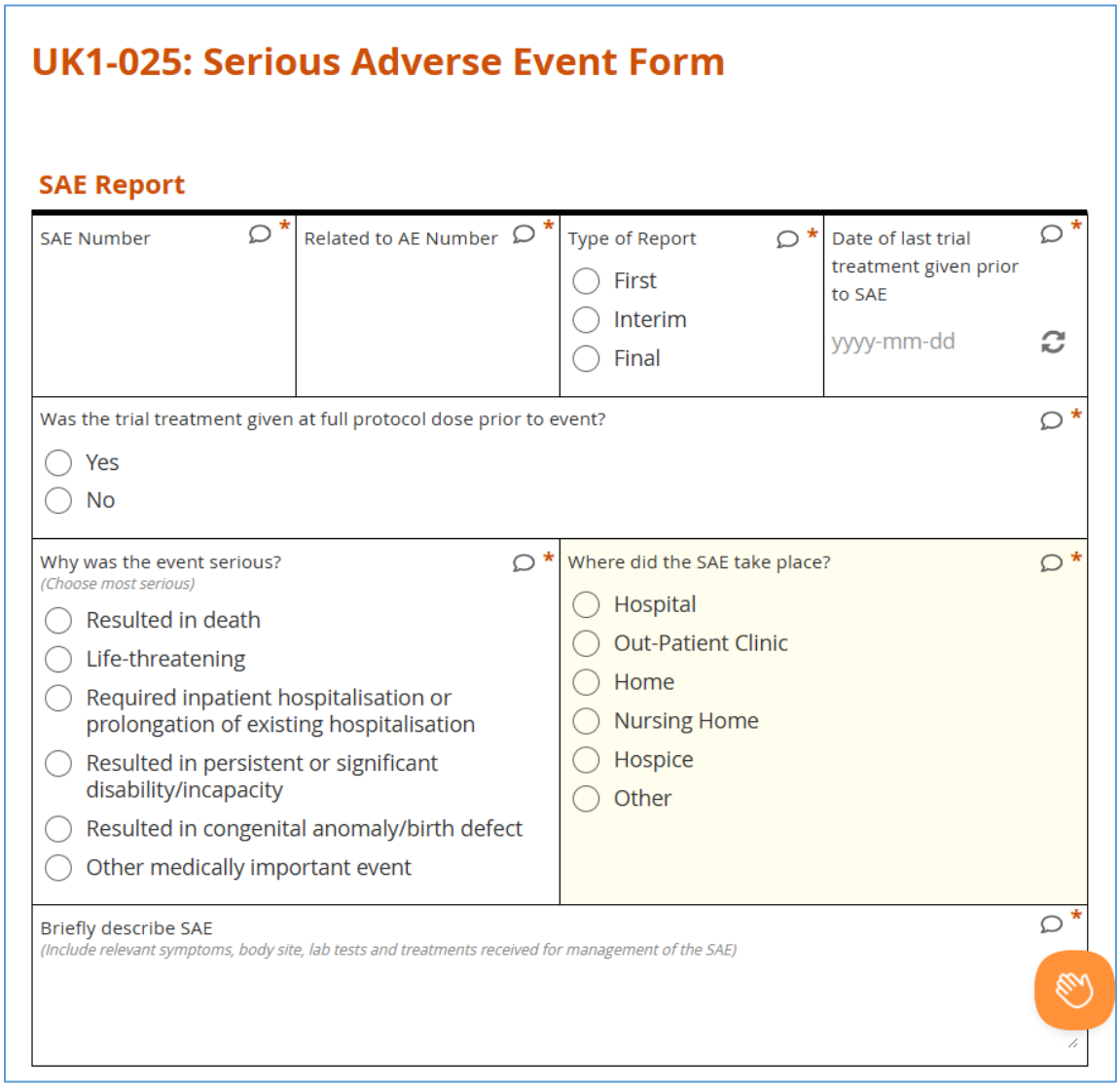
- Only one event should be reported per page

- If AE is not ongoing, enter End date and ensure Outcome has been completed.
- If action taken is “Medication”, ensure that the medication is recorded on the Concomitant Medication form.

- If “Does this adverse event meet the criteria for a Serious Adverse Event?” question is yes, complete a SAE form.
- Use the “Comments” field to record any additional information that has not previously been recorded on the eCRF regarding this AE.
- The Medical Coding section is not applicable for site staff to complete please leave blank.

Click on ‘Close’ or ‘Complete’ to save the data.

9.42 Serious Adverse Event Form



UK1-025: Serious Adverse Event Form

SAE Report

SAE Number *	Related to AE Number *	Type of Report *	Date of last trial treatment given prior to SAE *
		○ First ○ Interim ○ Final	yyyy-mm-dd

Was the trial treatment given at full protocol dose prior to event? *

○ Yes
○ No

Why was the event serious? * (Choose most serious)	Where did the SAE take place? *
○ Resulted in death ○ Life-threatening ○ Required inpatient hospitalisation or prolongation of existing hospitalisation ○ Resulted in persistent or significant disability/incapacity ○ Resulted in congenital anomaly/birth defect ○ Other medically important event	○ Hospital ○ Out-Patient Clinic ○ Home ○ Nursing Home ○ Hospice ○ Other

Briefly describe SAE *
(Include relevant symptoms, body site, lab tests and treatments received for management of the SAE)

Section 7.9 details the location of adverse events and how to Add New

Once an SAE has been added you will see a summary of the SAE on this page.

Answer all questions on the form by completing each section.

- The SAE reference number will be auto-populated by the system
- State whether related to an AE by entering the AE number*

**For UK Sites only – Please enter '0' for AE number*

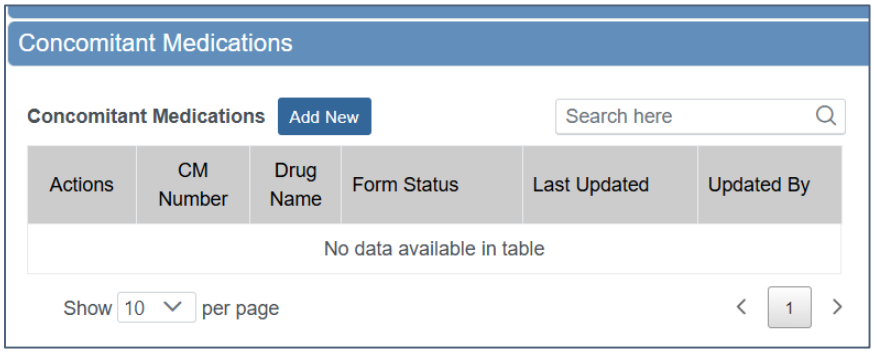
- Select Type of Report
- Enter Date of last trial treatment given prior to SAE
- Enter the Event seriousness

- If place of SAE occurrence is Other, please specify.
- Enter a narrative description of the event that occurred in the 'Briefly describe SAE' field.
- Only one event should be reported per page
- Enter the description/name of the event in the "Serious Adverse Event term" field and complete the rest of the page.
- Enter Date of Notification
- Enter Date SAE started, If AE is not ongoing, enter 'End date' and ensure SAE status has been completed.
- Enter the severity of SAE – Mild, Moderate or Severe
- If SAE Status is selected as "Recovered/Resolved", "Resolved with sequelae" or "Fatal" enter End date.
- Enter Trial Treatment, if additional trial treatment was given click '+' details in the 'Trial Treatment/IMP (blinded' section and enter details.
- Enter any Other Treatment if additional treatment was given click '+' details in the 'Other Treatments at Time of Event' section and enter details.
- Enter any Protocol Required Treatment (NIMPS), if additional treatment was given click '+' details in the 'Protocol Required Treatment (NIMPS)' section and enter details
- Complete 'Other Relevant Information' section.

Click on 'Close' or 'Complete' to save the data.

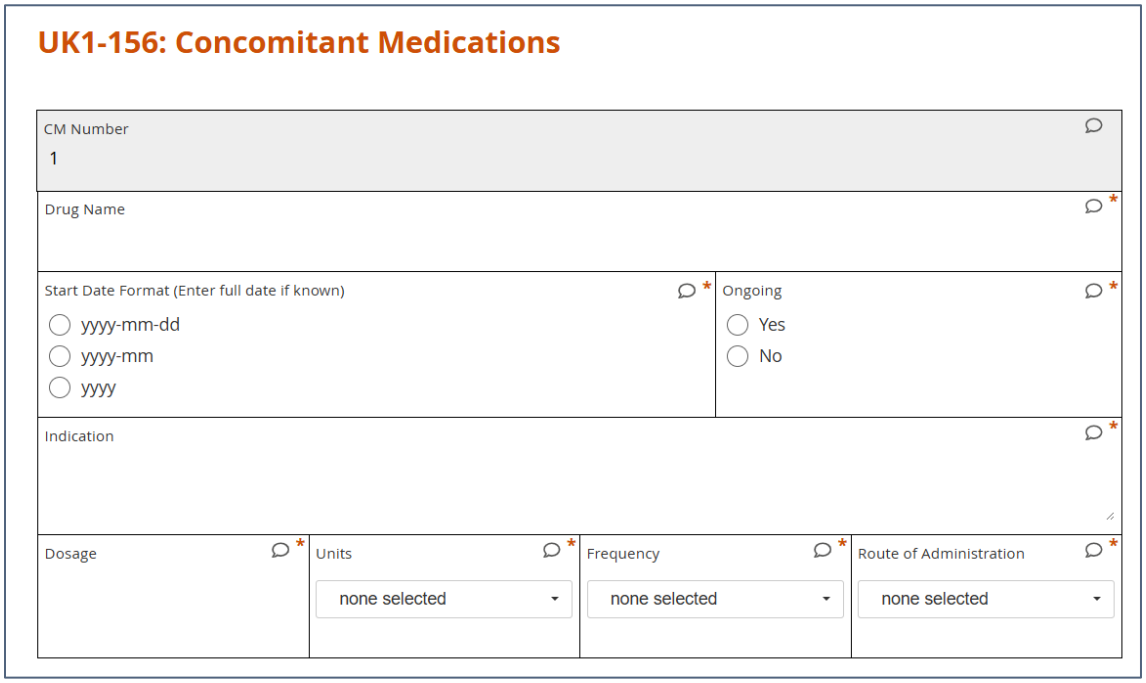
9.43 Concomitant Medications

Please note: This form may be hidden/not required depending on your jurisdiction.



- To add a new medication, click on the 'New' button and a new Concomitant Medication page (see below) will open

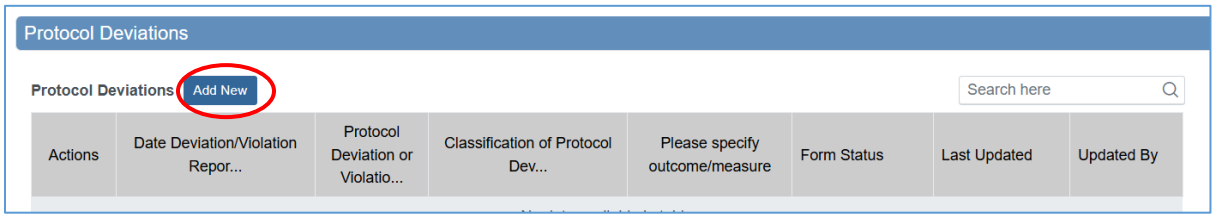
- Once a medication has been added you will see a summary of the concomitant medication on this page



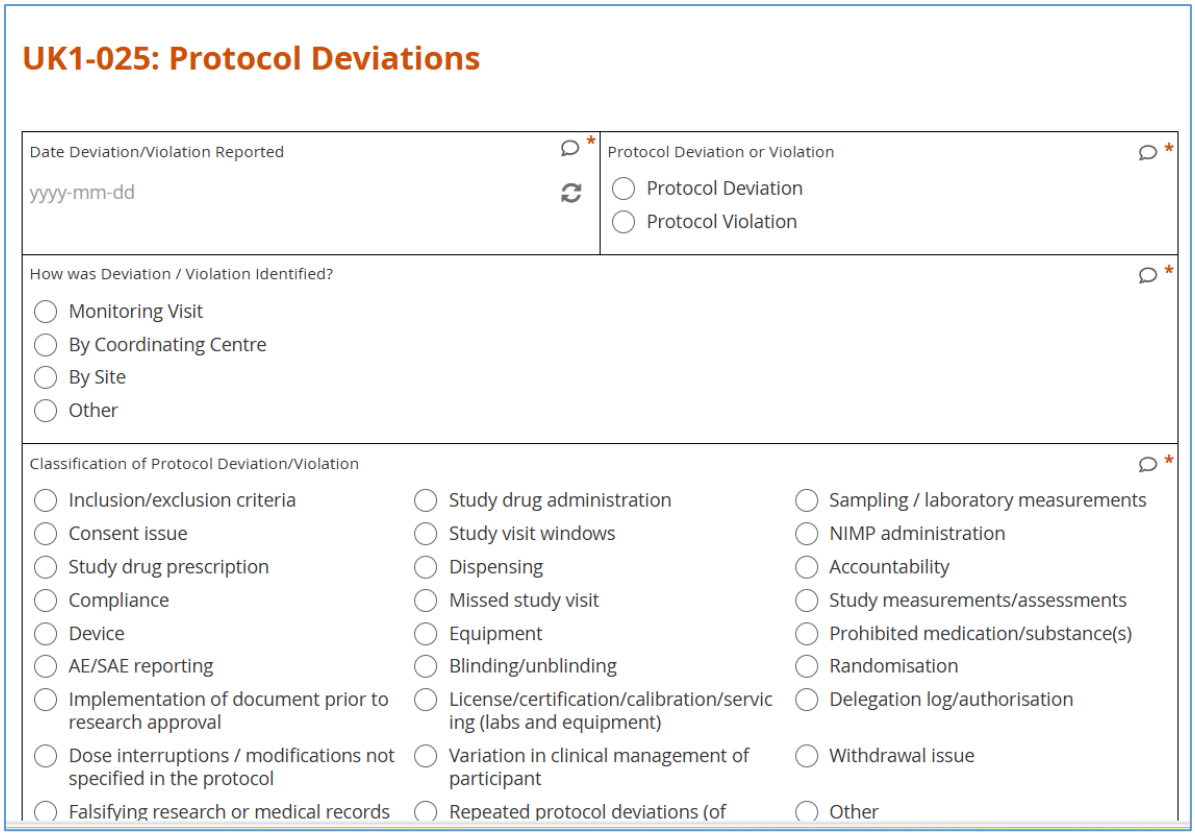
- Enter only one medication per line.
- If start date is unknown; use the “unknown” field to select the part of the date that is unknown (day or month).
- Enter ‘Stop Date’ or select ‘Ongoing’ if the medication is still being taken by the subject.
- Record the indication. If indication is an adverse event, ensure that the description is the same as what is recorded on the AE page
- Enter ‘Dose’ If ‘Other’ provide specification. and select ‘Dose Unit’ from the list. If unit is not in the list, select ‘Other’ and specify.
- Select frequency from the list. If not on the list, select “Other” and specify details.
- Select Route from the list. If Route is not on the list, select “Other” and specify details.

Click on ‘Close’ or ‘Complete’ to save the data

9.44 Protocol Deviations



To add a Protocol Deviation/Violation form, click on the 'Add New' button for the Protocol Deviation page will open



- Enter the date the protocol deviation/violation has been reported.
- Select whether this was a protocol deviation or violation:
  Deviation: a protocol deviation occurs when a process or criteria has not been actioned in line with the approved protocol.

  Violation: a protocol violation occurs when there is a consistent variation in practice from the defined protocol. Non-compliance with the inclusion and exclusion criteria is always classed as a significant protocol violation.

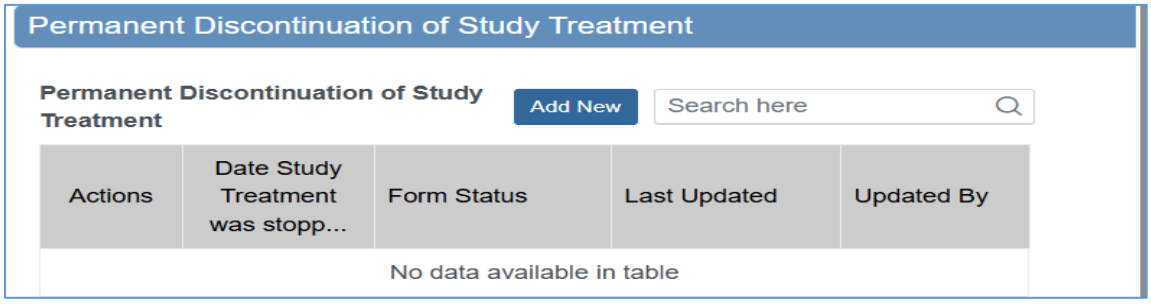
  Please refer to the relevant Study Manuals or the study team for guidance.
- Select how the deviation/violation was identified, if none apply, select 'Other' and specify in the 'Please specify' box
- Select one of the classifications. Only one can be selected.
- Describe in detail the deviation/violation.
- Select how the deviation/violation was identified, if none apply, select 'Other' and specify in the 'Please specify' box
- Enter the date the deviation/violation occurred.
- Enter any Corrective Action Preventive Action that have been taken/implemented as a response to this deviation/violation.

- Select ‘Yes’ or ‘No’ to confirm if deviation/violation was a serious breach question
- Select ‘Yes’ or ‘Not applicable for Study Manager Review

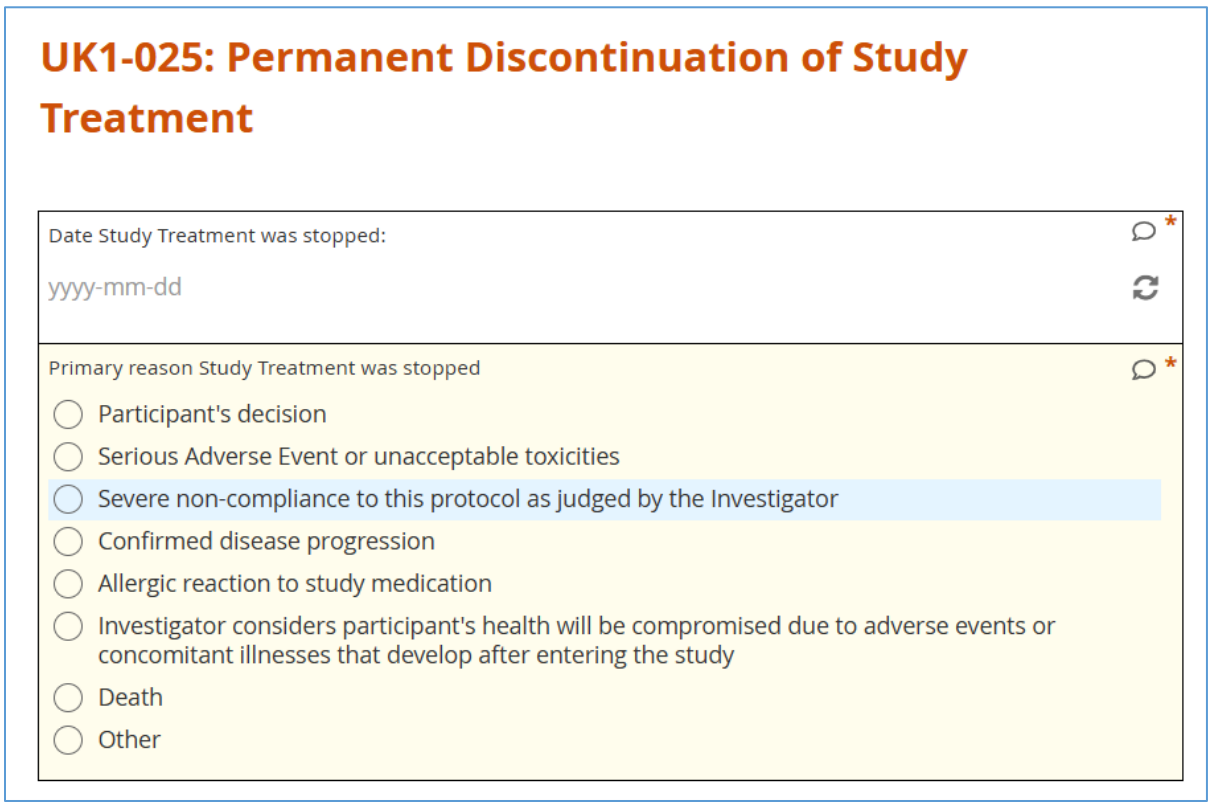
If multiple deviations are being entered at once, you can add another form automatically by selecting ‘Add another Protocol Deviations’ above the ‘Close’ form button.

Click on ‘Close’ or ‘Complete’ to save the data

9.45 Permanent Discontinuation of Study Treatment



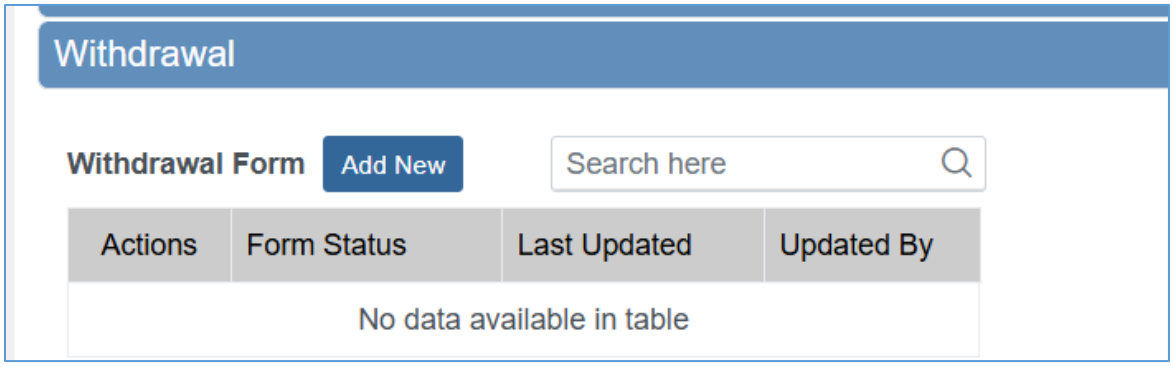
To add a Permanent Discontinuation of Study Treatment form, click on the ‘Add New’ button for the Permanent Discontinuation of Study Treatment page will open



- This form should only be completed if it is evident that a participant has permanently discontinued Study Treatment before the end of the study
- Enter date participant permanently discontinued study treatment
- Select Reason for discontinuation
- If reason is due to Significant Adverse Event or unacceptable toxicities (not captured via safety outcomes) please complete a Serious Adverse Event form.

Click on 'Close' or 'Complete' to save the data.

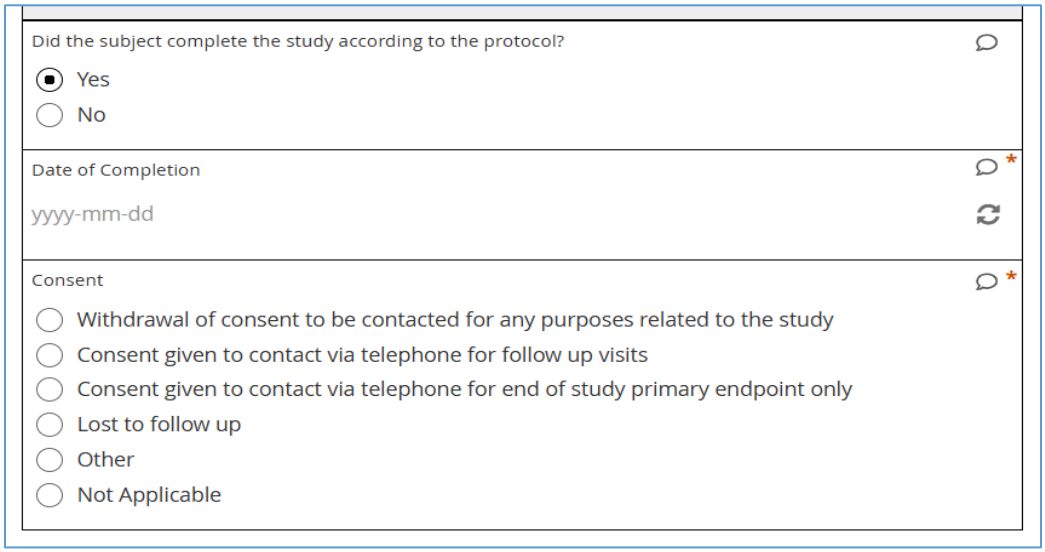
9.46 Withdrawal Form

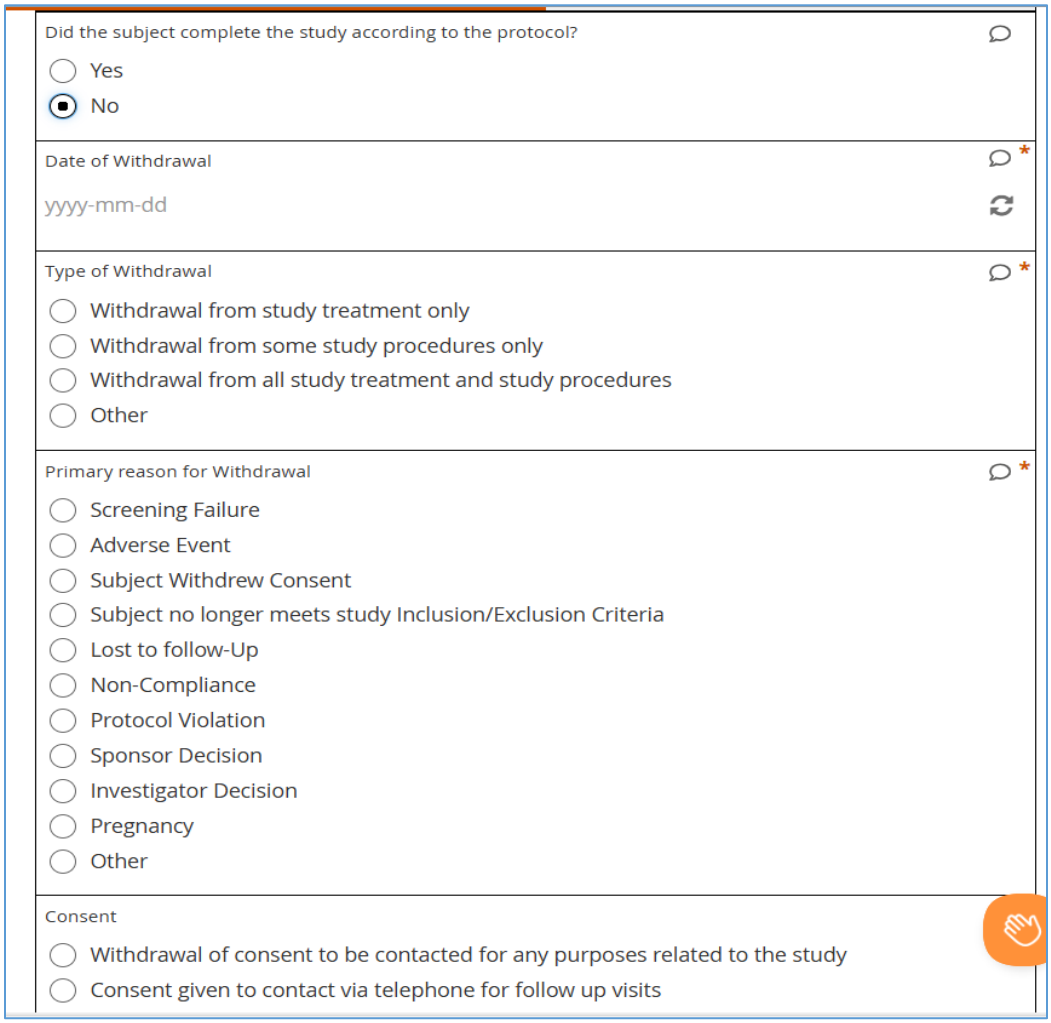


To add a Withdrawal form, click on the ‘Add New’ button for the Withdrawal page will open

Answer all questions

- This form should be also completed for patient who withdraw from the study prior to end of study, a permanent discontinuation from study treatment form should also be completed.
- Otherwise, this form should be completed for all patients who complete the study.
- If the participant died, please select yes, as the participant completed the study according to the protocol
- First, confirm whether the participant completed the study. If Yes, enter the ‘Date of Completion’ and the ‘Consent’ question

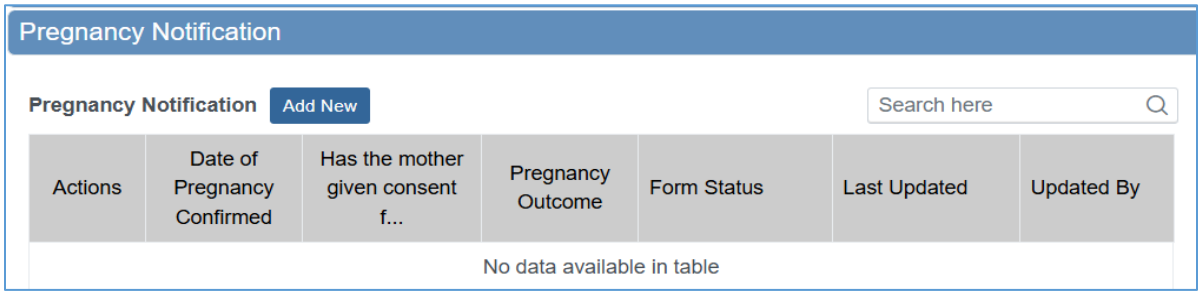




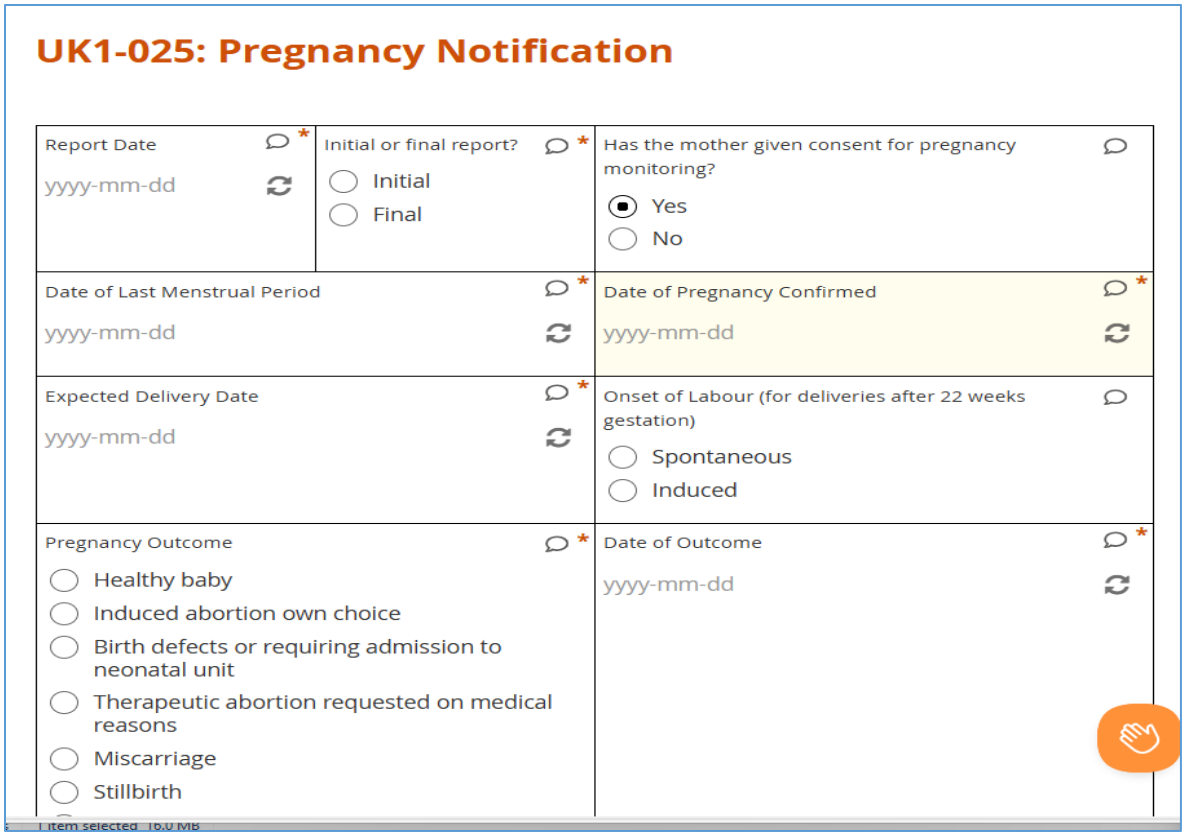
- If "No," please enter the ‘Date and Type of Withdrawal’, along with the Primary reason for the Withdrawal.
- If Primary Reason for Withdrawal is selected as ‘Other’, please specify details in the box provided.
- The Consent question on the form should also be completed to confirm participant consent.

Click on ‘Close’ or ‘Complete’ to save the data.

9.47 Pregnancy Notification



• Complete this form to report details of any pregnancy from the time of informed consent experienced by trial participant where such reporting is required by the trial protocol.
• To add a Pregnancy Notification form, click on the 'Add New' button for the Pregnancy Notification page will open

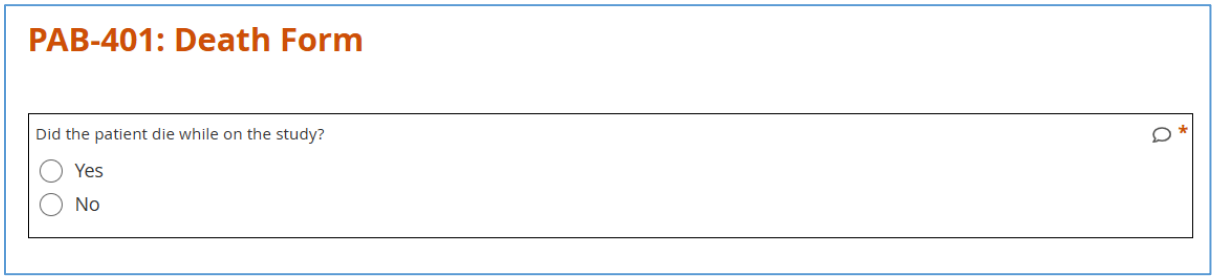


- Enter Date of report
- Indicate whether report is Initial or final report.
- Indicate **Yes or No** whether the mother has given consent for pregnancy monitoring
- Enter the Date of Last Menstrual Period
- Enter the Date pregnancy was confirmed
- Enter the Date of Expected Delivery

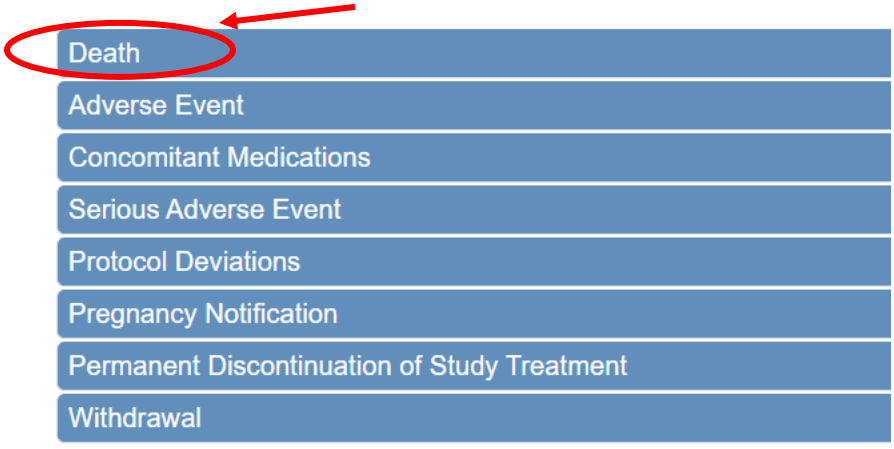
- Indicate whether onset of Labour was Spontaneous or Induced
- Select the Pregnancy Outcome from the list
- Enter Date of Outcome
- Provide any additional information related to the pregnancy in the comments field provided.

Click on ‘Close’ or ‘Complete’ to save the data.

9.48 Death Form



Death Form is located after ‘Visits’ tab



- Complete this form when a participant has died. Answer all questions
- If Participant died during the study enter the Date & Time of death.

Click on ‘Close’ or ‘Complete’ to save the data.

10. CRF Completion Queries

If you have any questions, please contact your trial management team.

11. Version History

Version Number	Date	Author	Description
1.0	17-Oct-2025	Vivienne Okona-Mensah	New document

12. Amendments

Section	Amendment