sealed envelope™

Red Pill

Version 13

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Chapter 1

Overview

Red Pill is an online application for collecting and managing data on subjects recruited to a clinical trial or other study.

Note that all data shown in this help is fictional and for illustrative purposes only.

This documentation applies to version 13, released January 2017. The version number is shown in the footer of every page when logged into Red Pill.

Chapter 2

Accessing the system

The Access application is the gateway for Red Pill systems. Systems set up before 2015 have Access URLs that are specific to a client - e.g. *www.sealedenvelope.com/abc_trialsunit*. Systems set-up after 2015 generally have the same common URL: *www.sealedenvelope.com/access*. In either case the URL will be contained in automated emails sent out when a new user account is created.

Users are requested to authenticate themselves by providing their log-in credentials. See the Access help for more information.

Chapter 3

Getting started

Investigator accounts

If you will be entering CRF data on subjects, an administrator for your trial will create your user account. Administrators are usually staff at the trial coordinating centre. The login details will be sent to your email address. This user account will normally be associated with your site and you will be able to view and add data for subjects at this site. Depending on a trial-wide setting controlled by administrators you may also be able to edit data.

When you login, you will normally first arrive at a summary page showing the trials you have access to. You can also manage your account details and change your password here. You can get to the summary page at any time using the **Home** link.

Once you access a trial you will be able to see enrolled subjects at your site and enter data yourself.

Administrator accounts

When a Red Pill system is set up, the first administrator account is created by Sealed Envelope and the login details are sent to that person's email address. The administrator should log in and create the trial sites, unless the sites have been pre-coded by Sealed Envelope.

You do not need to add all your sites at once - you can come back later and add more sites as needed.

Next you should add some investigator accounts for each site so that data entry can be performed by staff at the sites. You do this through the Access application. Check the settings page and make any adjustments to suit your trial.

Finally check the specification page and case report forms and report any discrepancies or errors to Sealed Envelope.

Chapter 4

Subjects

Subject records can be viewed by clicking on the **Subjects** link in the top menu. This shows a list of all subjects entered into the study to date. An amber question mark in the status column of the subject listing indicates that there is an open query for that subject.

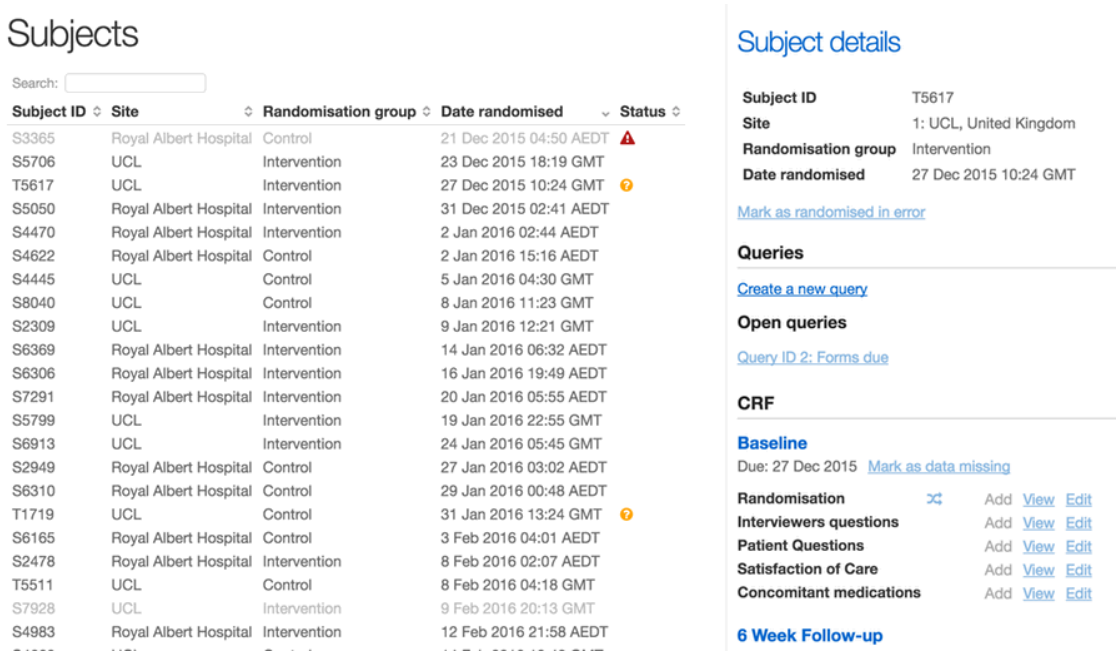


Figure 4.1: Viewing an individual subject record

Adding subjects

New subjects may be added to the list at any time by clicking on the **Add a subject** link in the top menu. This opens the study entry form which requests a subject identifier and date of study entry. Note that at least one site must be created before any subjects can be added.

Some trials may be configured such that subjects are randomised into the trial. If this is the case a subject can be added via the **Randomise** link in the top menu. Check the specification page to see if this is the case.

Deleting subjects

Subjects may be deleted by administrative users providing the delete subject setting is enabled. A delete subject option is shown in the 'Subject details' section. The user will be asked to confirm they wish to go ahead. Deleting the subject will also delete all associated forms and queries. This cannot be undone so administrators should think carefully before deleting.

Searching

The search box filters the subject list to match the entered terms. Note that form data is not searched. Multiple search terms narrow the focus, e.g. `1 2` finds rows that match `1` *and* `2`. Putting search terms in brackets performs a wider search for any matches, e.g. `(1, 2, 3)` or `(1 2 3)` finds rows that match `1` *or* `2` *or* `3`.

Subject details

Clicking on a subject in the list shows subject details from the study entry form, any queries and provides links to add, view and edit the forms for that subject grouped by visit.

Schedule

For visits at specific timepoints (for instance 30 days after study entry) the due date is shown. Overdue forms are highlighted in red. If the Withdrawal form has been completed and the subject

marked as withdrawn from follow-up, then any visits due after the date of withdrawal will not be shown as overdue. All uncompleted forms in these visits will become inaccessible. Forms that were completed before the subject was marked as withdrawn will remain accessible and may be viewed and edited in the normal way.

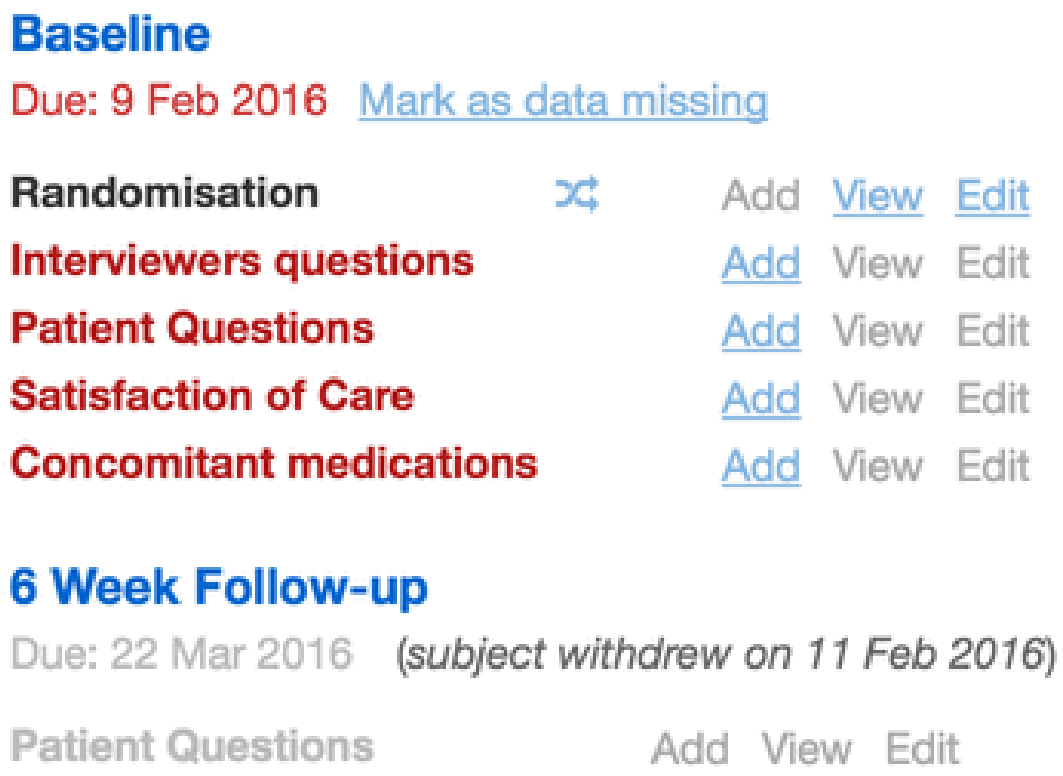


Figure 4.2: A follow-up visit due after subject withdrew

Missing forms

Sometimes forms within a visit are not available because, for instance, the subject did not attend a follow-up appointment, the data was not collected or was lost. Forms within visits can be marked as missing using the **Mark as data missing** links. Marking the data as missing in this way causes all uncompleted forms in the visit to become inaccessible and they will not be shown as overdue.

Forms that were completed before a visit was marked as missing will remain accessible and may be viewed and edited in the normal way.

Figure 4.3: A follow-up visit marked as missing

Subject-entered forms

A subject invitations section may be displayed to invite the subject to self-complete some forms in the CRF if subject entered forms are enabled.

Form status

A green tick next to a form name indicates that it has been marked as validated. An amber question mark symbol next to a form name indicates that the form has an open query.

Chapter 5

Data entry of forms

Forms can be completed by clicking on the **Add** link shown on the subject details section next to the name of the form. At the top of every form is a banner reminding the user of which subject they are entering data on. Date fields can be completed manually or by using the date-picker that appears when a user clicks on the calendar icon.

> Tip: When entering dates or times manually, just type the numbers – the / or : will be filled in automatically.

Validation

Validation (e.g. range checking) is carried out on the form to reduce errors. There are two types of error messages - those in the form of popup warning messages and those displayed in red on the form. The popup message alerts may warn the user of a value that may be incorrect (such as a high blood pressure) or give some other message. The user must dismiss the alert before proceeding.

Red error messages require either a change to the value entered or providing a justification for overriding the validation check before proceeding. Validation checks may not be overridden on subject entered forms.

Some fields are always required - these are displayed with an adjacent red asterisk - whilst others may become required or not applicable depending on the answers to previous questions. Other fields are optional and may be left blank if desired.

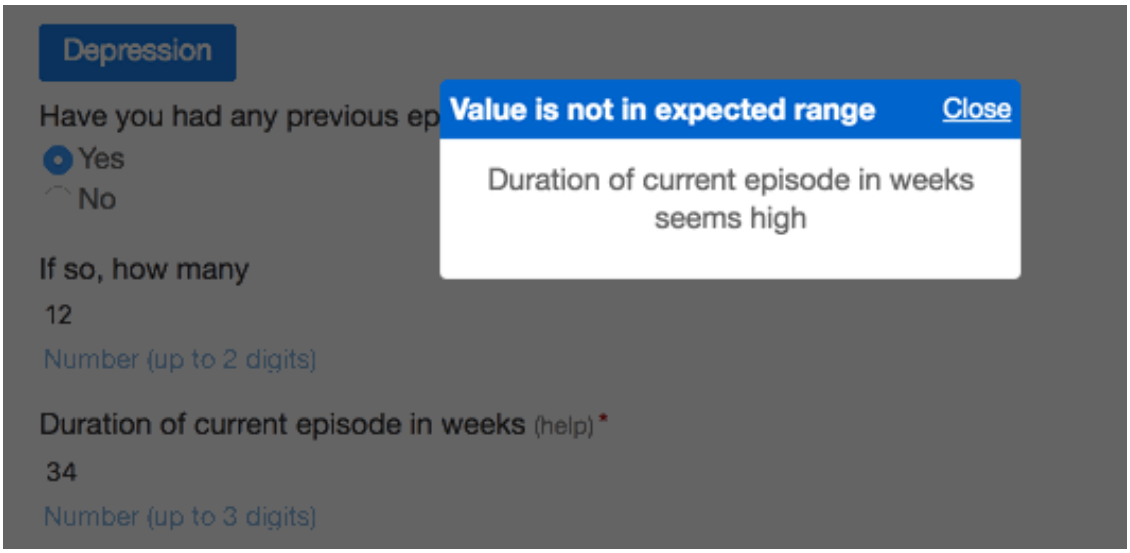


Figure 5.1: Popup warning message

Repeating sections

Some sections of a form can be added multiple times. This is used, for instance, to record all the hospital admissions for a subject. A button, such as **Add hospital admissions** will be shown on the parent form. Clicking this button goes to a subform which can be added as many times as necessary. The subforms are saved along with the parent form.

Likert scales

Sections that capture Likert scale responses are laid out in a grid. Validation and overriding work in the same way as for other sections.

Encrypted PII fields

Fields containing personally identifiable information (PII) that have been configured in the CRF builder to be stored in an encrypted format are shown with a small padlock symbol below. PII fields can be viewed and edited through the web interface like any other field, but they will be in

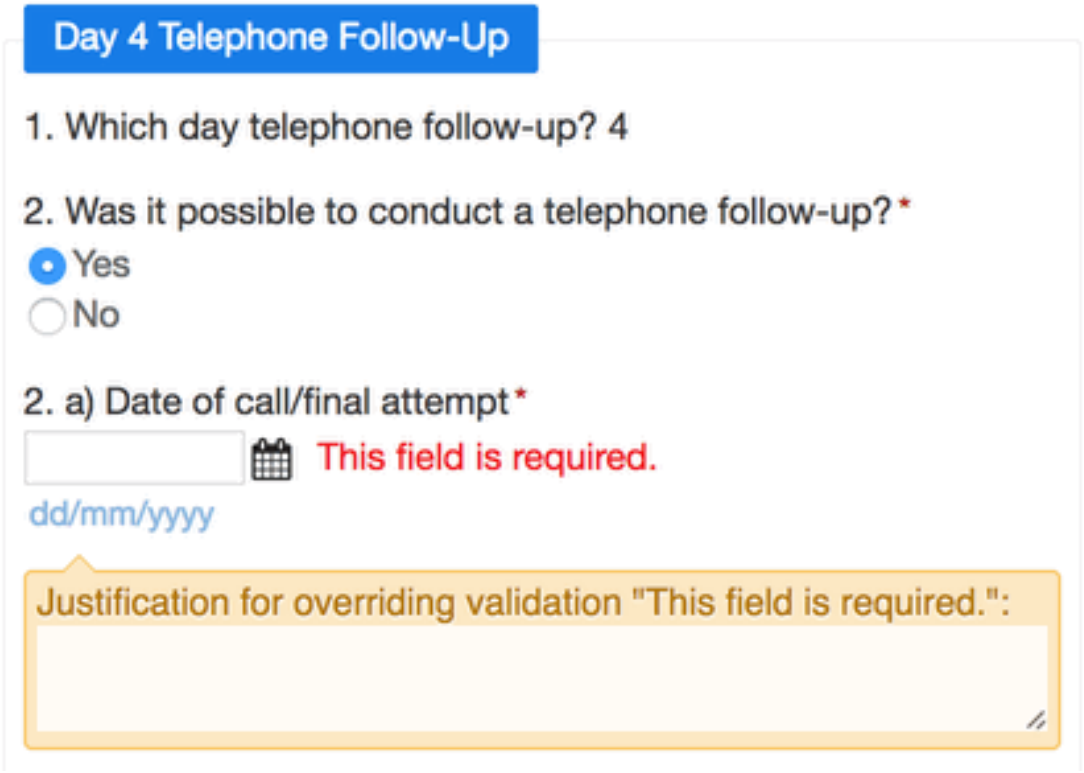


Figure 5.2: Overriding form validation

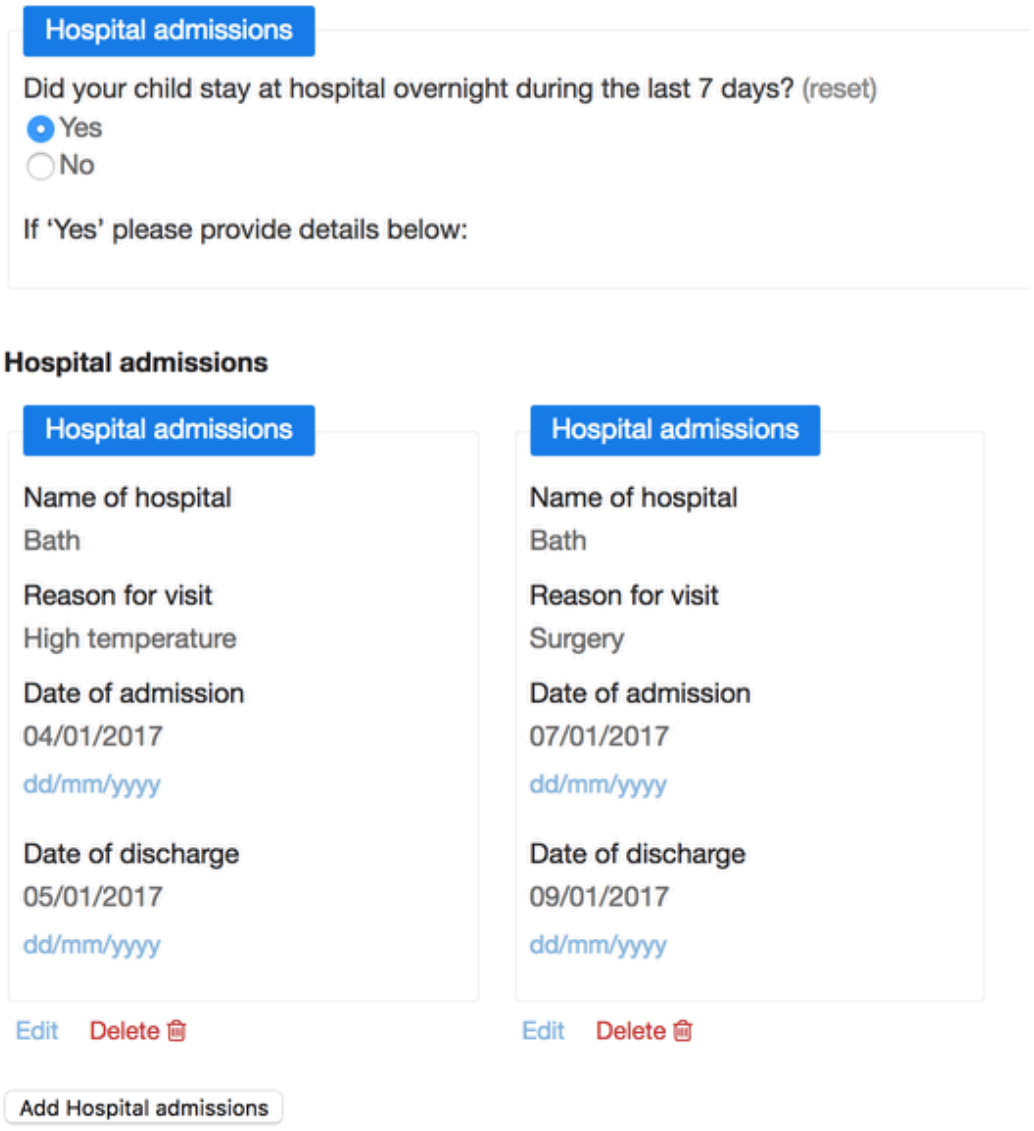


Figure 5.3: A form with subforms

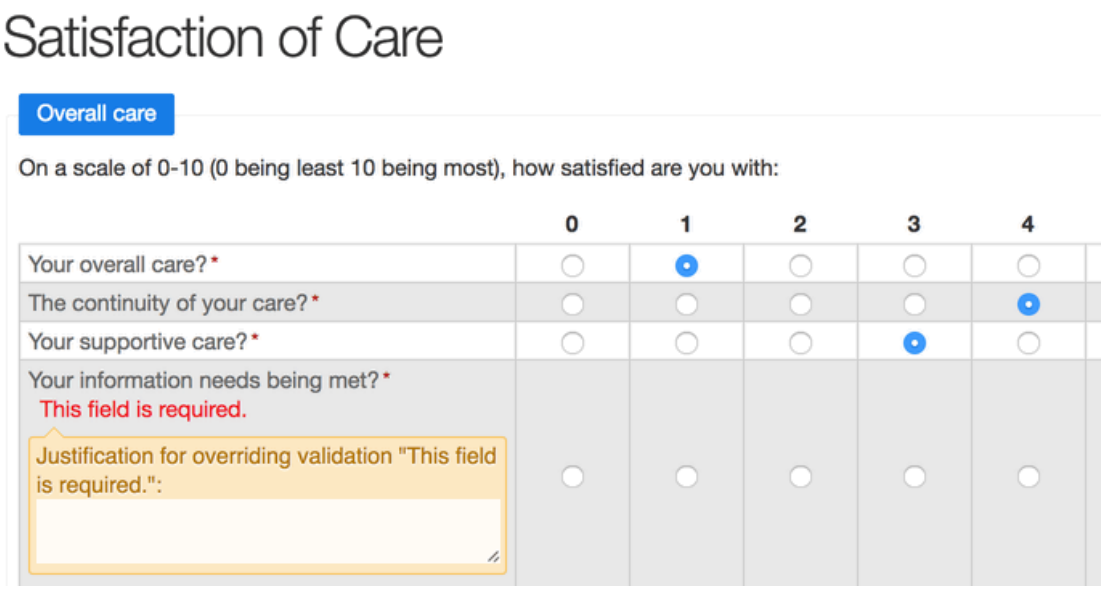


Figure 5.4: A Likert scale section

encrypted format when downloaded. Sealed Envelope support can provide instructions on how to decrypt this data after download if necessary.

Review step

Once the form has been completed without errors the **Save form** button will usually present the user with a review page. Here the user can visually check that the data entered is correct and, if satisfied, complete the declaration by entering their password to save the form.

> This review step may be disabled for some systems, in which case the data is saved immediately.

If there are errors the user may return to the previous page to make changes. Once the declaration has been successfully completed the form is saved to the database.

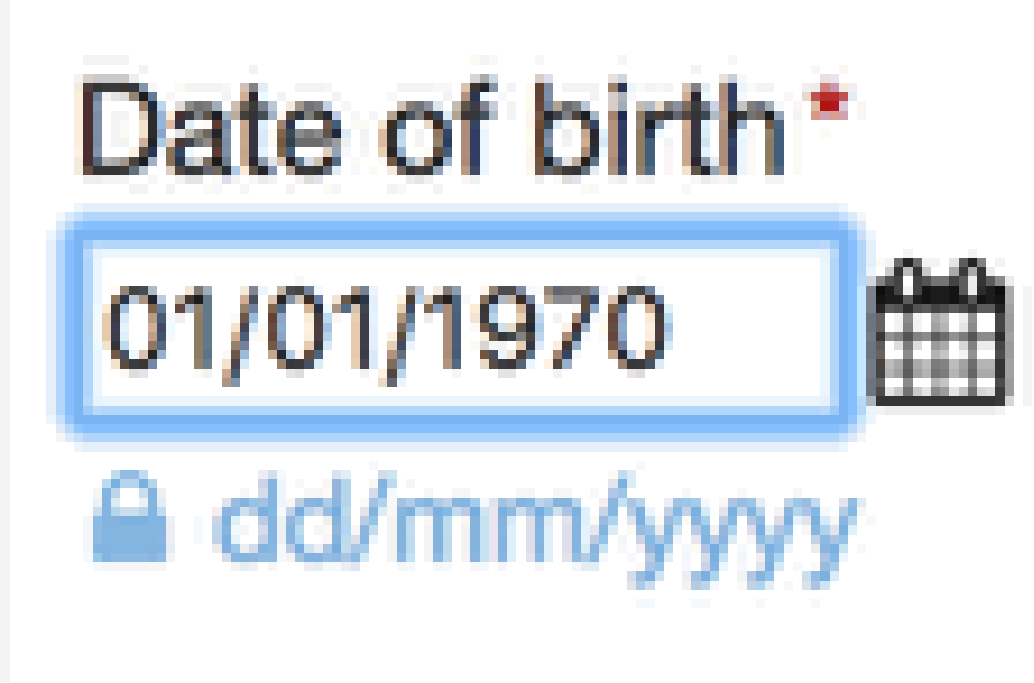


Figure 5.5: An encrypted field

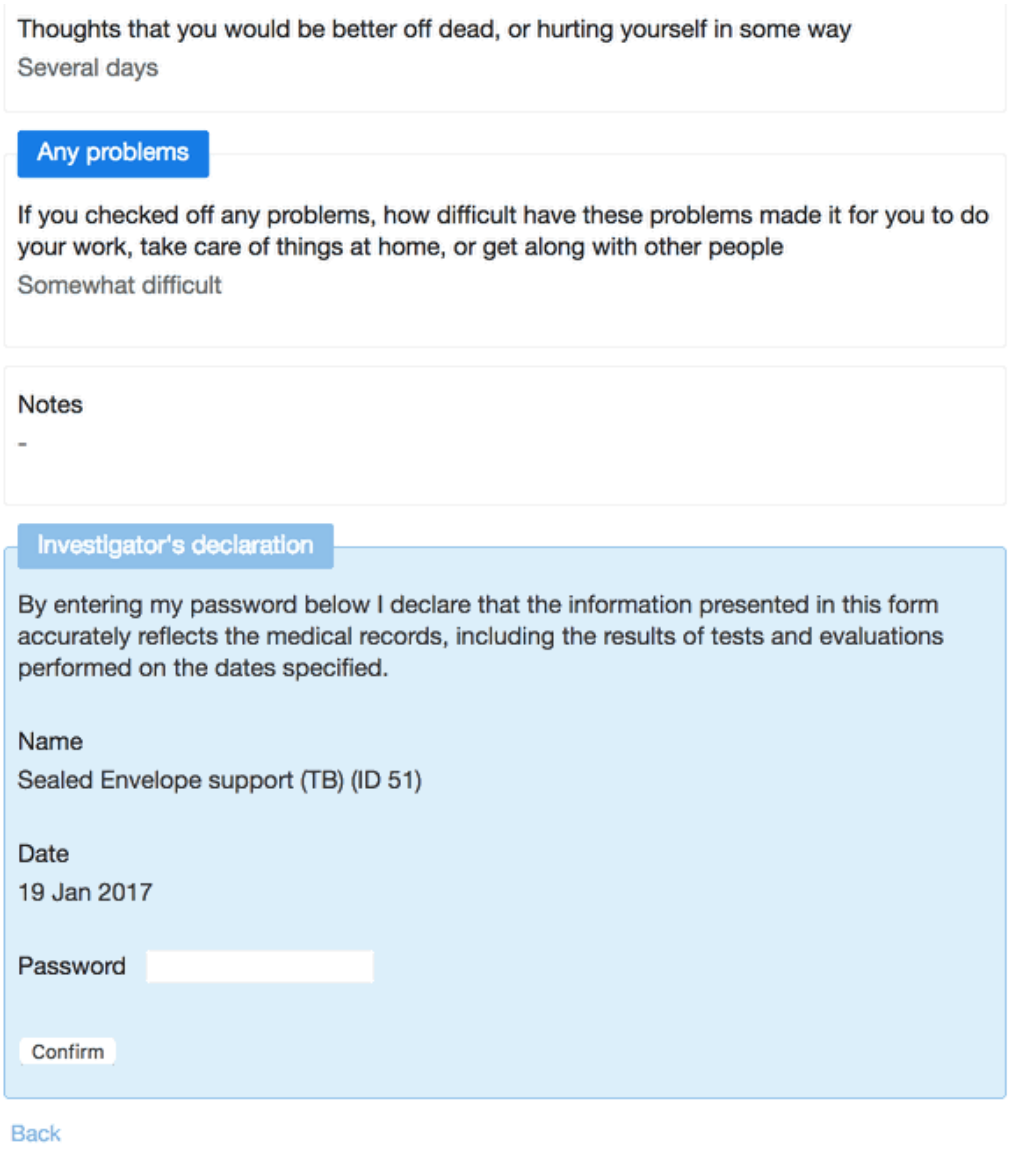


Figure 5.6: Reviewing a form before saving

Auto-saved drafts

Once data entry is commenced most forms are auto-saved periodically.

> Study entry forms (or the randomisation form when subjects are randomised into the study) are never auto-saved.

> Edits to existing forms are not auto-saved.

A message indicating a draft has been saved is shown periodically at the top of the form. This allows the user to navigate away from the form and return to it later without losing data. When returning to a form that has a saved draft, the user is shown a message and given the option to load the draft data or ignore it. If the draft is ignored and data-entry started again the original data will no longer be available.

> There is only one draft per form/subject and it is accessible to all users (not just the author of the draft).

If the user navigates away from the page before saving the data, a pop-up message is shown to warn the user that the data has not been permanently saved yet. This is because, even though a draft may exist, it could be lost by the actions of another user.

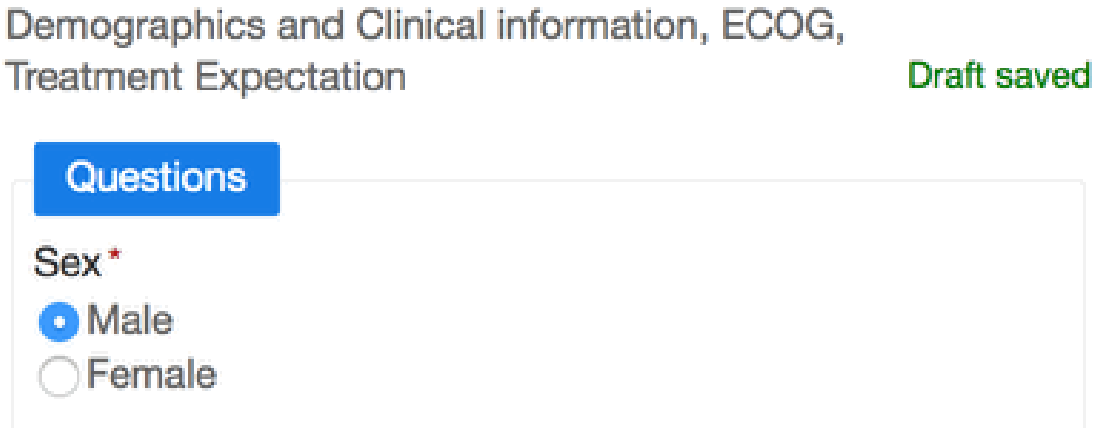


Figure 5.7: Saved draft message

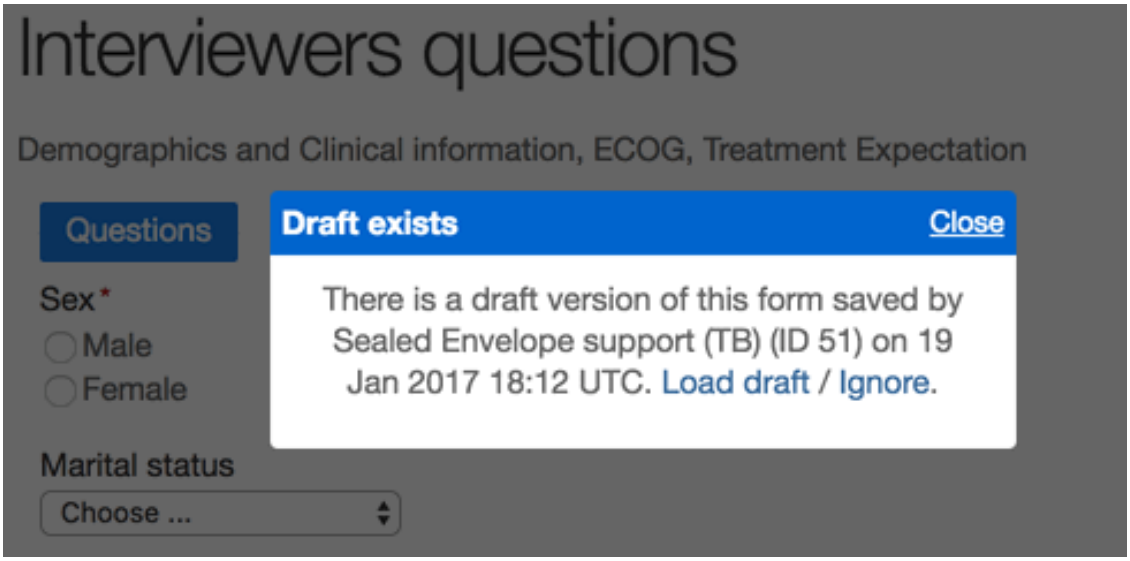


Figure 5.8: Load draft dialogue

Form completion messages

After a form has been saved, the user may be prompted to complete other forms based on the answers they have given. For instance, an event form may be required if a stroke has been recorded. If the form contains any of these rules and they are triggered by the data recorded, the user will see a message asking them to complete the related forms. A query will also be automatically opened to remind the user to complete the required forms.

Repeating forms

Most forms can only be completed once per subject, but some can be entered multiple times. Repeating forms are normally used for events (like SAEs) that can occur multiple times per subject. As repeated forms are entered, they are listed in the subject view with a sequence number.

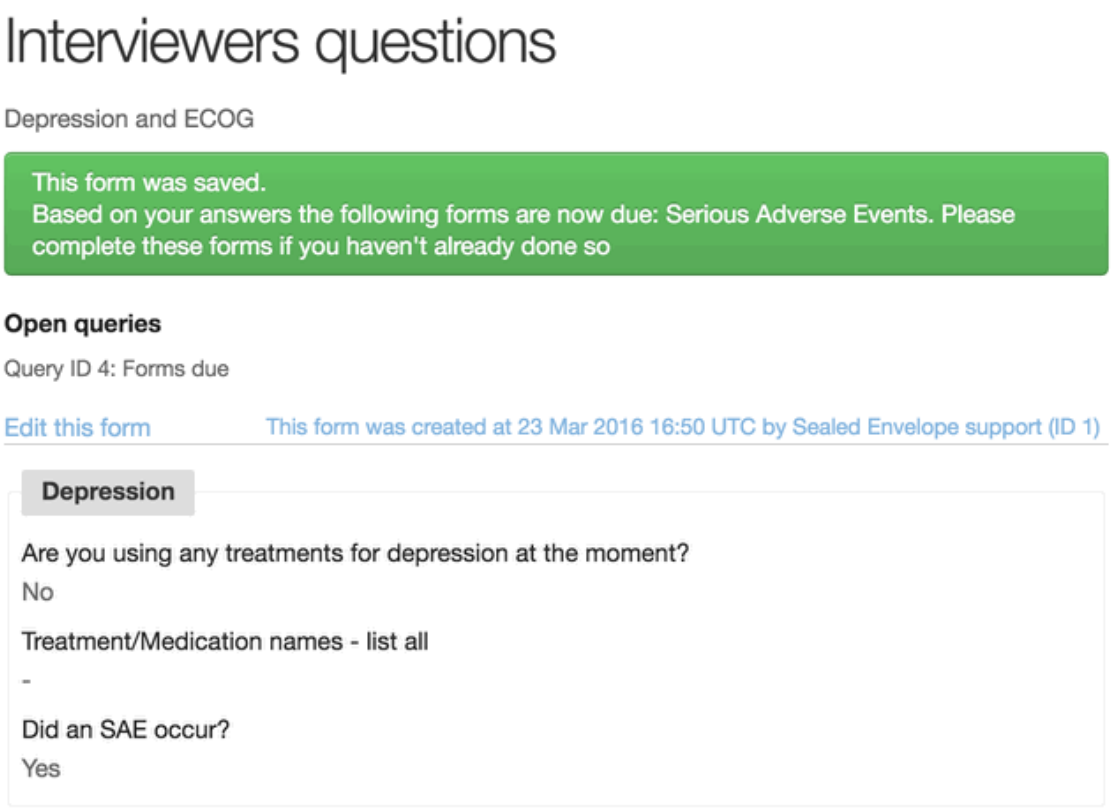


Figure 5.9: Reminder to complete related forms

Figure 5.10: Repeat entry forms

Chapter 6

Editing forms

Completed forms may only be edited by users with administrator accounts. Forms are edited by clicking on the **Edit** link next to the selected form shown on the patient details screen, or by clicking on the **Edit this form** link shown when viewing a form. The form is displayed in the same way as when adding the form but with some extra fields for recording validation status and reason for editing. The user may change any of the values in the form and they must complete the reason for editing field before reviewing and saving the form.

Validation status

When editing a form, the validation status can be set to 'Validated' provided there are no open queries for the form. Once a form is marked as validated, a green tick appears next to the form name in the patient details. If a query is added to the form after the form has been marked as validated, the validation status will automatically be changed to 'Not validated'. It is up to the trial coordinating team to decide what constitutes a validated form. It may, for instance, be as a result of a formal monitoring visit, or alternatively visual check against the source data by someone who did not enter the data.

Completed forms may not be deleted. However, the validation status may be set to 'Data unusable' to indicate that the whole form should be disregarded.

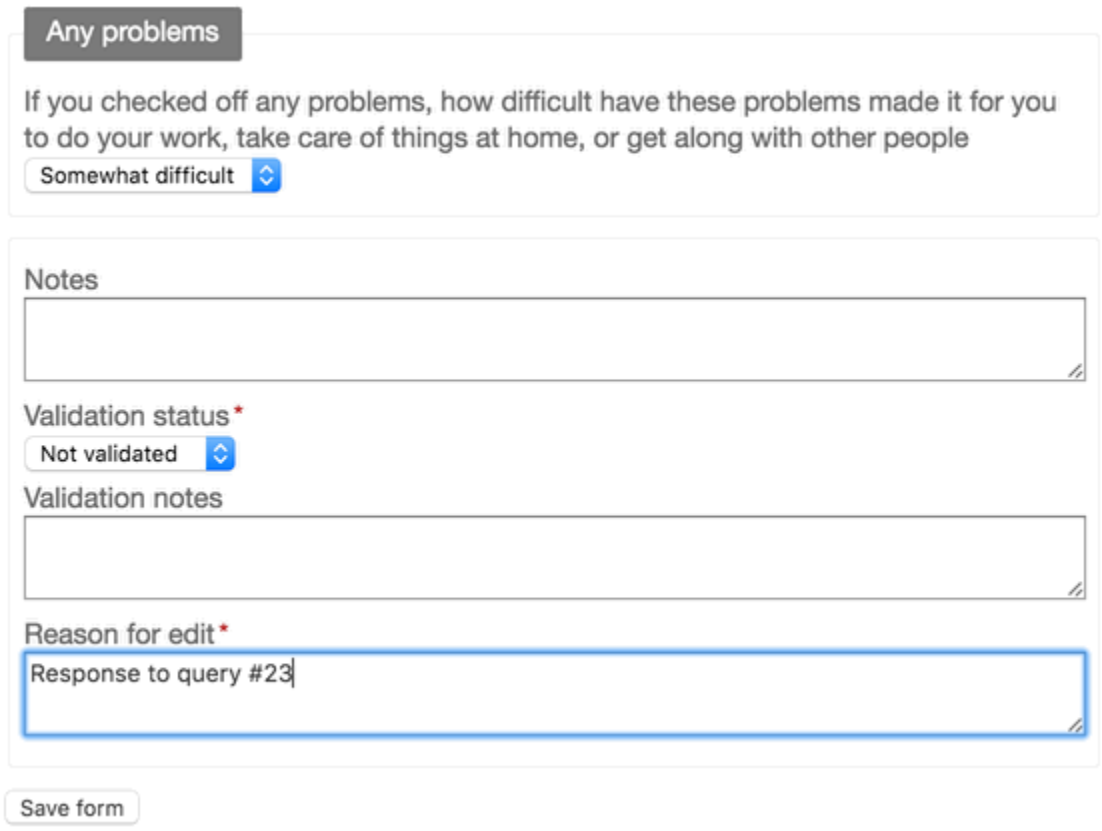


Figure 6.1: Editing a form

Chapter 7

Subject entered forms

Subject entered forms are forms which can be self-completed by the subject. See the specification page to see if this feature is enabled and information on email templates, reminders and information shown to subjects when logging in.

Inviting subjects

Subjects must be invited to complete their forms by completing a subject invitation form. To do this the subject must be selected from the subject list and the **Invite subject to complete forms** link used. This link will only be shown to investigators and not administrators or other roles as it leads to a page that potentially contains personally identifiable information (subject email and, optionally, mobile number).

Completing the subject invitation form enrols the subject and allows them to complete certain forms themselves. The form to invite the subject requires their personal email address and, optionally, mobile number. These fields are stored in an encrypted format in the database. Invitations and reminders will be sent by email and also by SMS if a mobile number is given. Unique links to complete forms online are included in both emails and SMS messages. These links expire after a set time period which is configurable for a study. Links can be turned off so that notification emails and texts act as simple reminders to complete paper forms. The number of reminders sent if forms are not completed and time delay between reminders is also configurable for a study. These details can be viewed on the specification page.

An optional memorable word can be entered which will be required by the subject to enter their

forms. The time of day at which automatic invites and reminders will be sent can also be customised for each subject. Deactivating a profile prevents further invitations and reminders from being sent and subjects will not be able to enter forms, even using an unexpired link.

Invite schedule

Once the subject invitation form has been completed the invite schedule is displayed. This shows when invites and reminders will be automatically sent. It shows whether a subject has logged in and how many forms they have completed. If a subject completes all forms due at the visit any remaining reminders will be cancelled. Links are provided to manually trigger invitations, which is useful to invite a particular subject earlier or later than scheduled. The invite schedule can be viewed by administrators but links for manual invitations are not displayed.

Note that invitations are still sent out and forms can be entered by subjects for visits that have been marked as missing.

Subject list

Subjects with an active invitation to complete forms are denoted by a green icon of a person in the status column of the subject list. Subject entered forms are also shown with this icon in the subject details section.

Report

A subject invitation report is available to administrators. This shows for each invited subject when each visit is due, whether the subject has logged in and the number of forms they have completed out of the total due.

What the subject sees

Once a subject goes to the URL in their email or SMS invitation and, optionally, enters their memorable word they will see a list of forms to complete. Clicking on the name of the form takes them to that form where they can complete their answers. Unlike data entry of forms by investigator

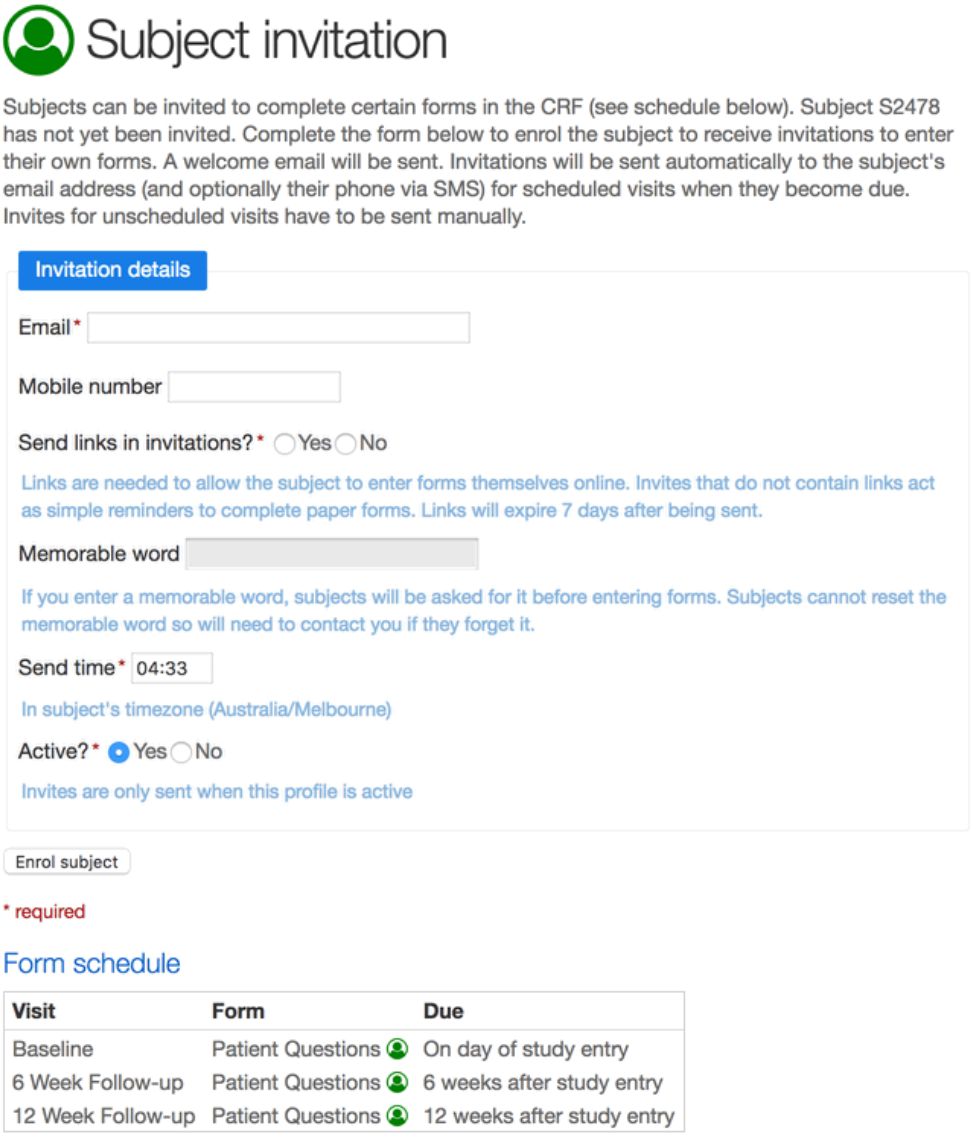


Figure 7.1: Subject invitation form

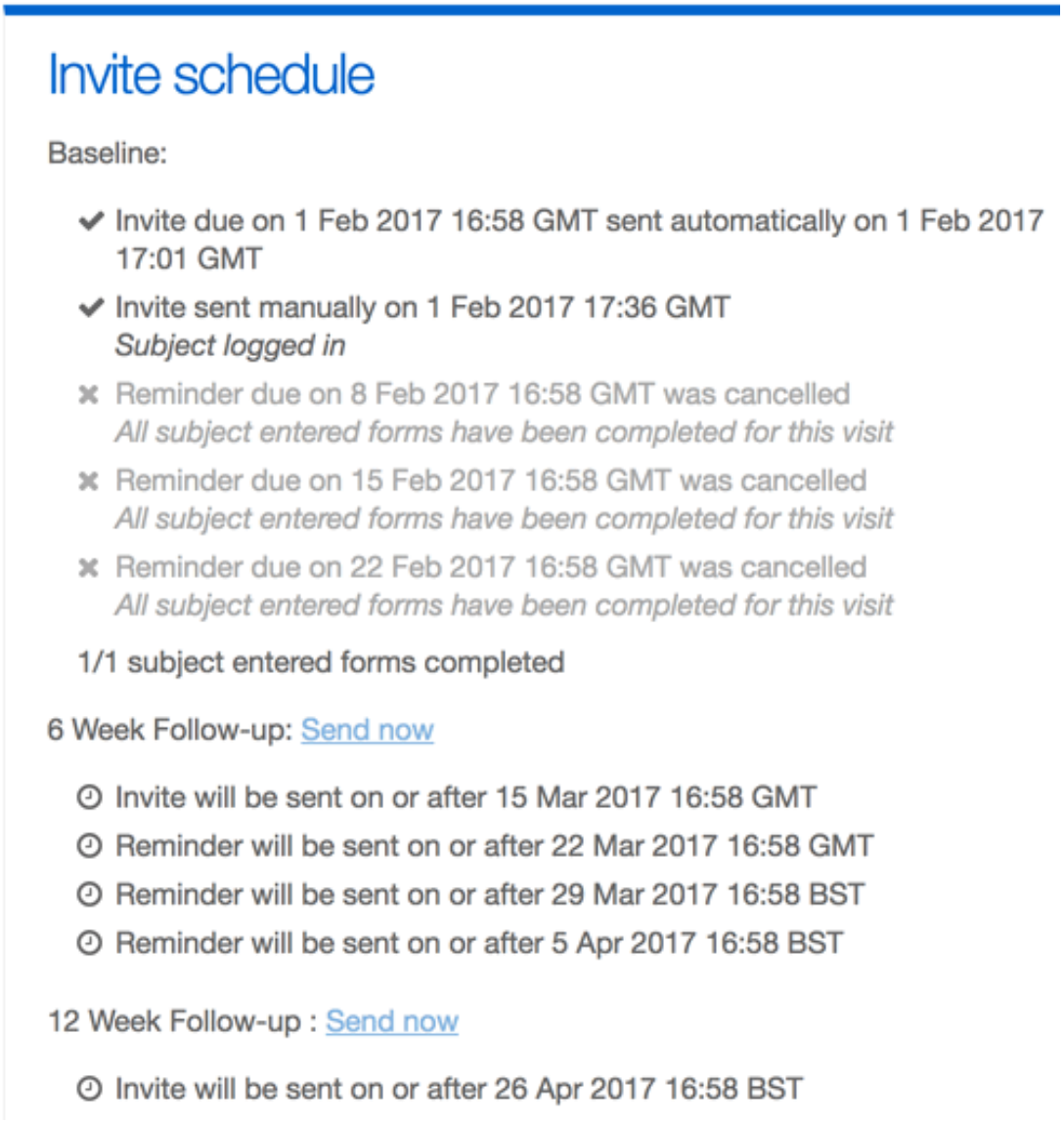


Figure 7.2: Subject invitation schedule

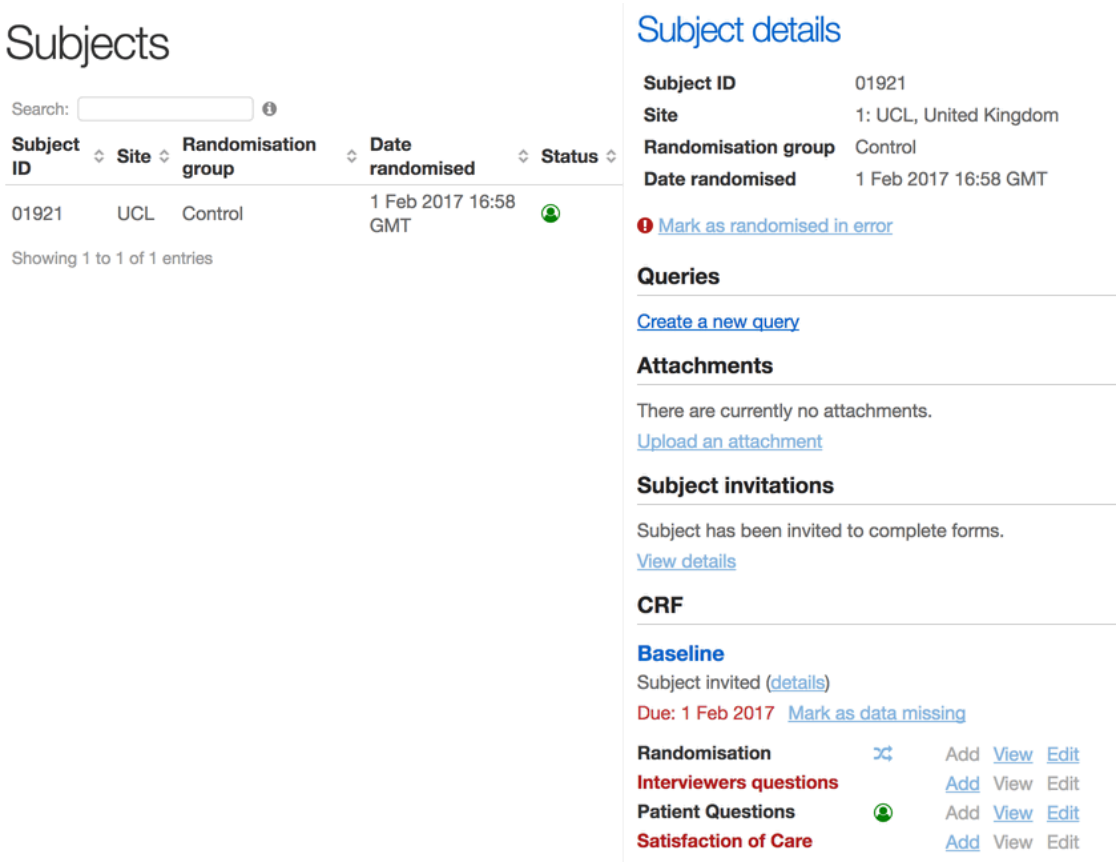


Figure 7.3: Subject list

and administrator accounts, subjects cannot override the validation checks on fields. They also will not see the review step - once they press the save button the form is saved immediately and cannot be viewed or edited by the subject. Entered forms are shown as completed in the list of forms.

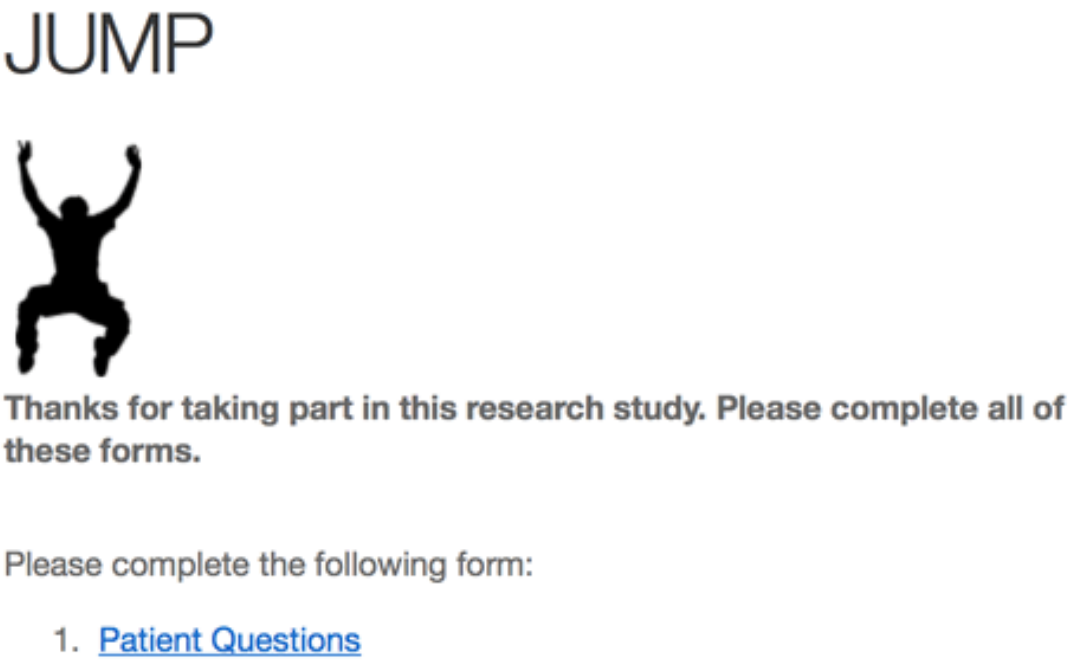


Figure 7.4: List of forms as seen by the subject

The subject can return to complete the forms at any time until the unique link in their email expires. Once all the forms are completed a thank you message is displayed.

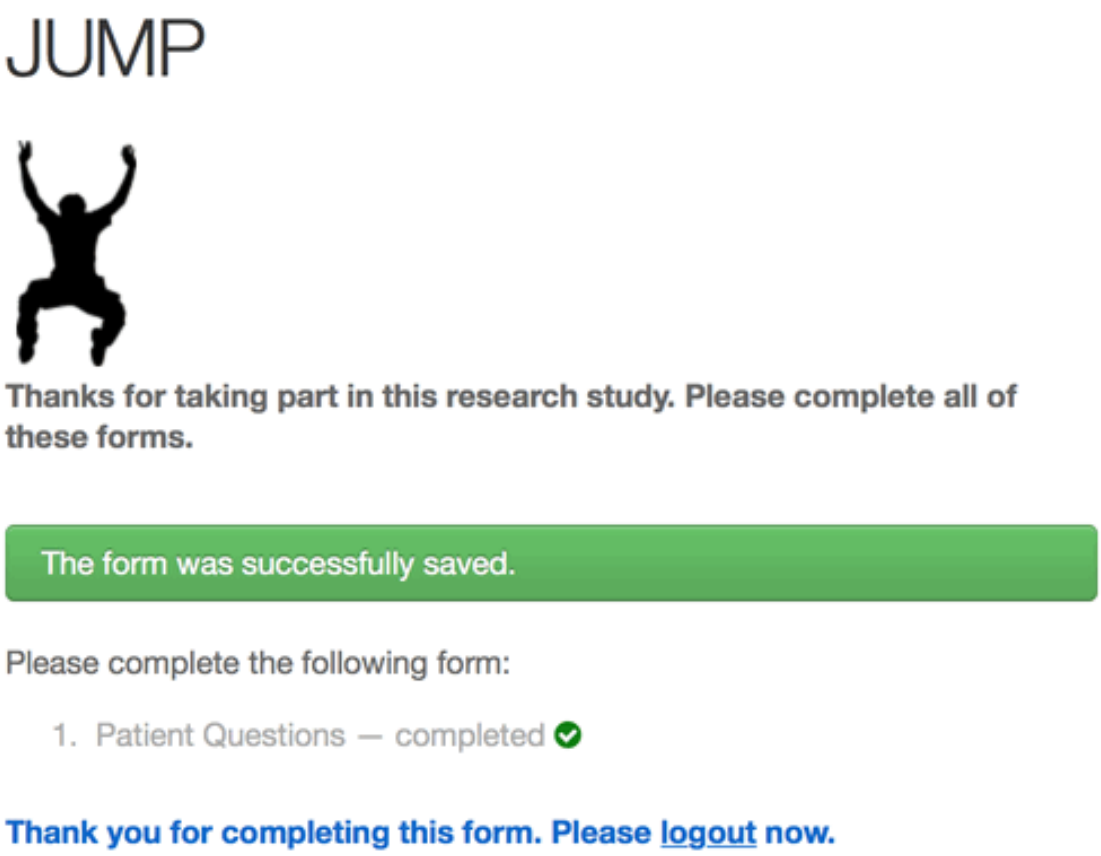


Figure 7.5: Completed forms as seen by the subject

Chapter 8

Overdue forms

An overview of overdue forms for all subjects may be viewed by clicking the **Overdue forms** link in the left-hand side bar. Each subject is shown as a row in the table, with a cell for each form in a visit with a time-point.

> Note that visits without time-points are not shown

Completed forms are shown in green, overdue forms in red. Forms that will never be completed because the subject withdrew or did not attend a visit are shown in grey. Blue cells indicate that the form is not applicable to that subject - for instance because a form is only collected on subjects with a baseline abnormality. Clicking on a cell displays the name of the associated form. The table may be filtered by entering terms in the search box.

The percentages of forms completed, overdue etc are shown in the summary by site and overall. Note that percentages are calculated excluding forms that are not yet due in the denominator. So although 100% of forms may be shown as done today, this may change in the future as forms become due.

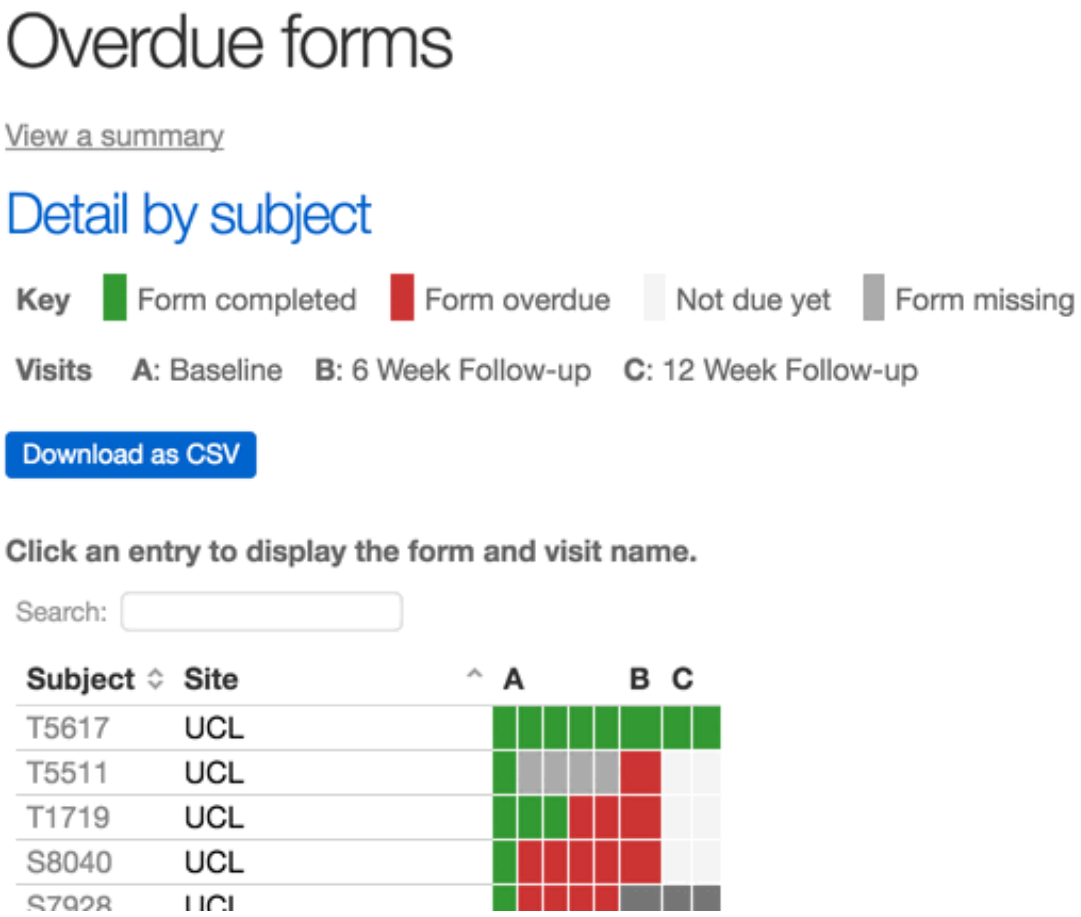


Figure 8.1: Overdue forms detail

Summary by site

Key Form completed | Form overdue | Form missing | Subject withdrew

Number and percentage of forms by status excluding forms not yet due.

Site					
UCL	21 *30%*	43 *61%*	4 *6%*	3 *4%*	0 *0%*
Royal Albert Hospital	16 *19%*	62 *73%*	4 *5%*	3 *4%*	0 *0%*
Total	37 *24%*	105 *67%*	8 *5%*	6 *4%*	0 *0%*

Figure 8.2: Overdue forms summary

Chapter 9

Viewing forms

Forms are viewed by clicking on the **View** link next to the selected form shown on the patient details screen. The most recent version of the form is displayed. If the form has been edited a history bar will be shown, allowing past versions of the form to be displayed. Changes to the form compared to the previous, older, revision are highlighted in yellow when navigating through the history. The exception to this is repeating sections within forms - changes to these are not highlighted.

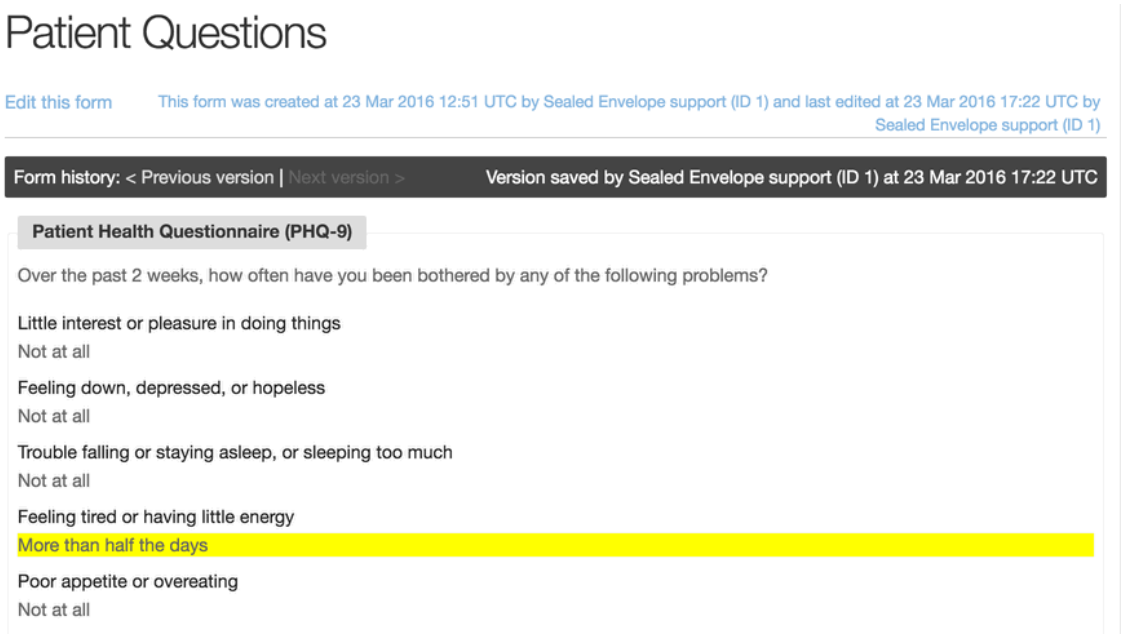


Figure 9.1: Viewing a form that has been edited

Chapter 10

Sites

Trial sites (centres) must be added to the system before adding or randomising a subject, updating a code list, or creating investigator accounts. Sites must also be set to **Recruiting** before subjects can be added.

Administrators can add sites by clicking on the **Sites** link in the top menu, followed by the **Create a new site** link.

Site identifier

The site identifier can be any alphanumeric text and may be used in some trials to create a subject identifier of the form `SNNN` where `S` is the site identifier and `NNN` is a sequential number (either within or across sites).

Note it is not possible to change the site identifier if a site has associated records, such as user accounts, subjects, kits in the code list or allocations in a randomisation list stratified by site.

Timezone

The timezone of a site affects the display of randomisation dates and times generated by the system, such as date/time of randomisation, unblinding and marked in error. It is also used by validation rules such as checking whether a date is in the past. Other date/times, such as timestamps on forms, are usually displayed in GMT timezone (UTC).

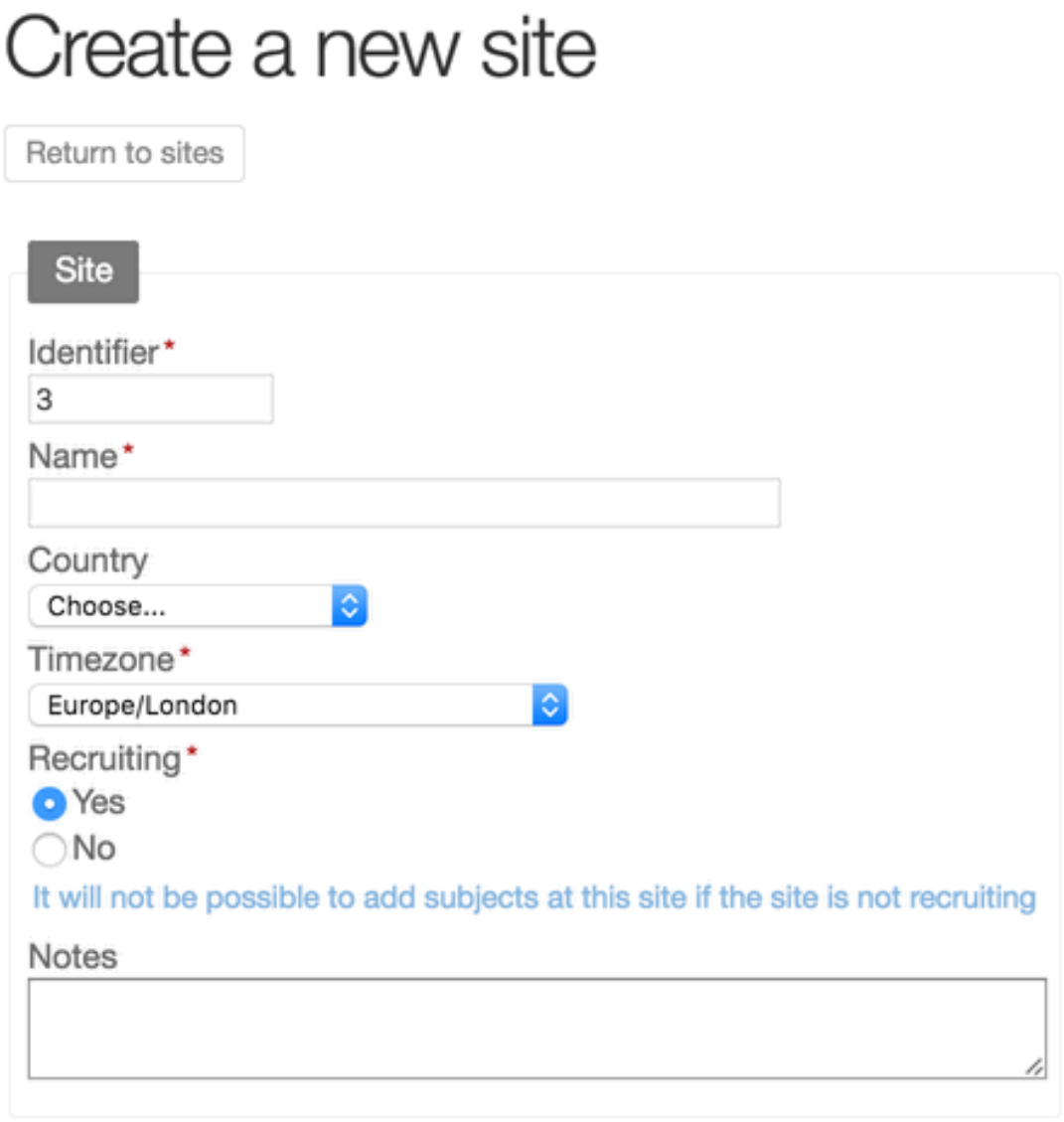


Figure 10.1: Adding a new site

Note that sites **cannot be deleted** if they have associated records, such as user accounts, subjects, kits in the code list or allocations in a randomisation list stratified by site.

Chapter 11

Queries

Queries are intended to be used by administrators to raise questions about the form data for investigators to answer and for investigators to notify administrators of any issues they are aware of in completed forms. Queries can be linked generally to a subject, or more specifically to a particular form for a subject. Queries may only be closed by administrator users. Investigators can create new queries and add messages to existing queries.

Opening queries

A query can be opened either on the subject details section or when viewing a form, by clicking on the **Create a query** link. The query must be given a title and an initial message. To link the query to a specific form in the CRF, choose the appropriate form from the related form drop-down control. Once it has been created, the query will be shown on the subject details panel and form specific queries will also be shown when viewing the form. In addition, if a form has an open query attached, an amber question mark symbol appears next to the form name in the subject details panel.

> Note that creating a query or re-opening a closed query linked to a form will cause the form to be marked as not validated.

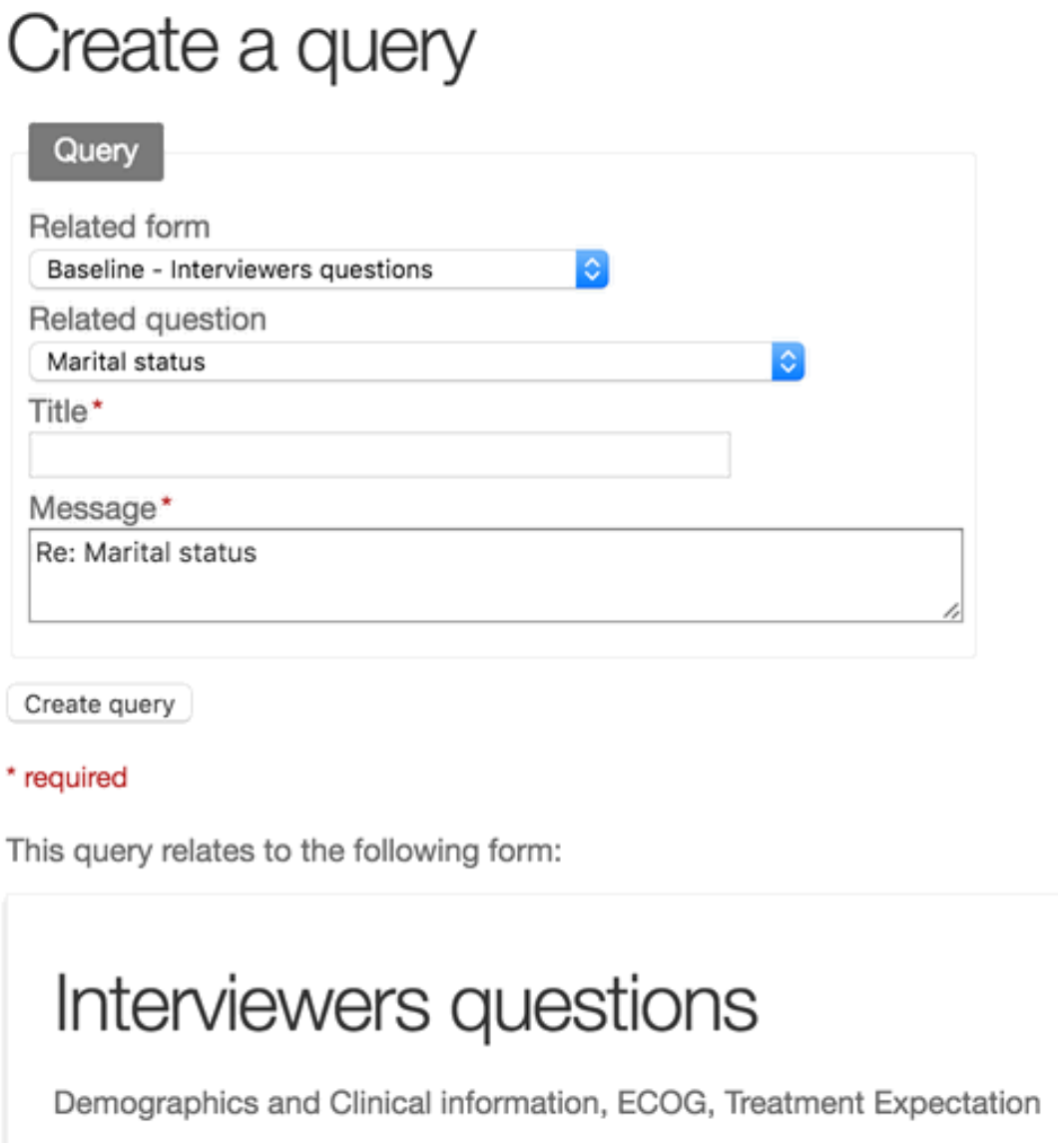


Figure 11.1: Creating a new query

Adding messages

Messages may be added to queries by investigators or administrators, forming a conversation thread. Administrators can close a query when the issue has been resolved. Administrators may also re-open a closed query by setting the action to 'Reopen' when adding a new message to it.

When viewing a query, printing the web-page will display an extra box that asks the investigator to write their response, with signature and date. This may be useful for the site's own records or workflow.

Email notifications

When a query is created or updated an email notification is sent out to:

- On creation: all administrators, and all investigators at the same site as the subject the query relates to;
- On update: all users who have participated in the query - that is the user who created the query and any user who has added a message to the query.

The format of the notification email is:

```
From: Sealed Envelope
Subject: [Trialname] Query updated
Date: Thu, 22 Oct 2015 15:43:22 +0100
To: joe@trialsite.org,admin@trialcentre.org

A query "Confirm date of birth" has just been updated by Joe Bloggs (ID 8). You can view
    the query here:

   https://www.sealedenvelope.com/Trialname/query/view/3

Note, this message was auto-generated on Thu 22 Oct 2015 15:43 Europe/London (GMT +0100).
```

Listing queries

A list of queries grouped by site is displayed by clicking on the **Queries** link in the top menu. The conversation thread for a query can be viewed by clicking on the query in the list. This view also

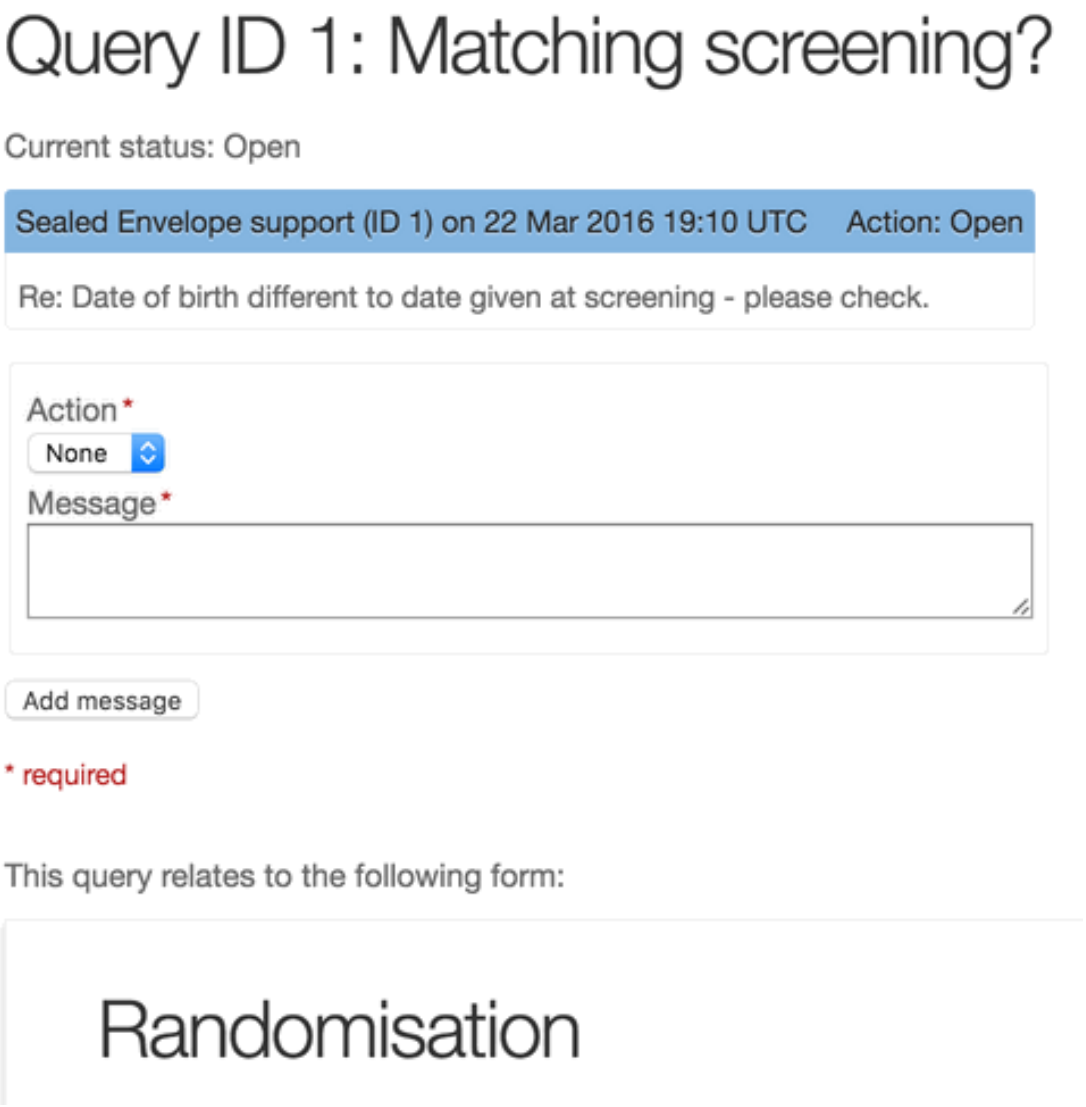


Figure 11.2: Viewing an open query

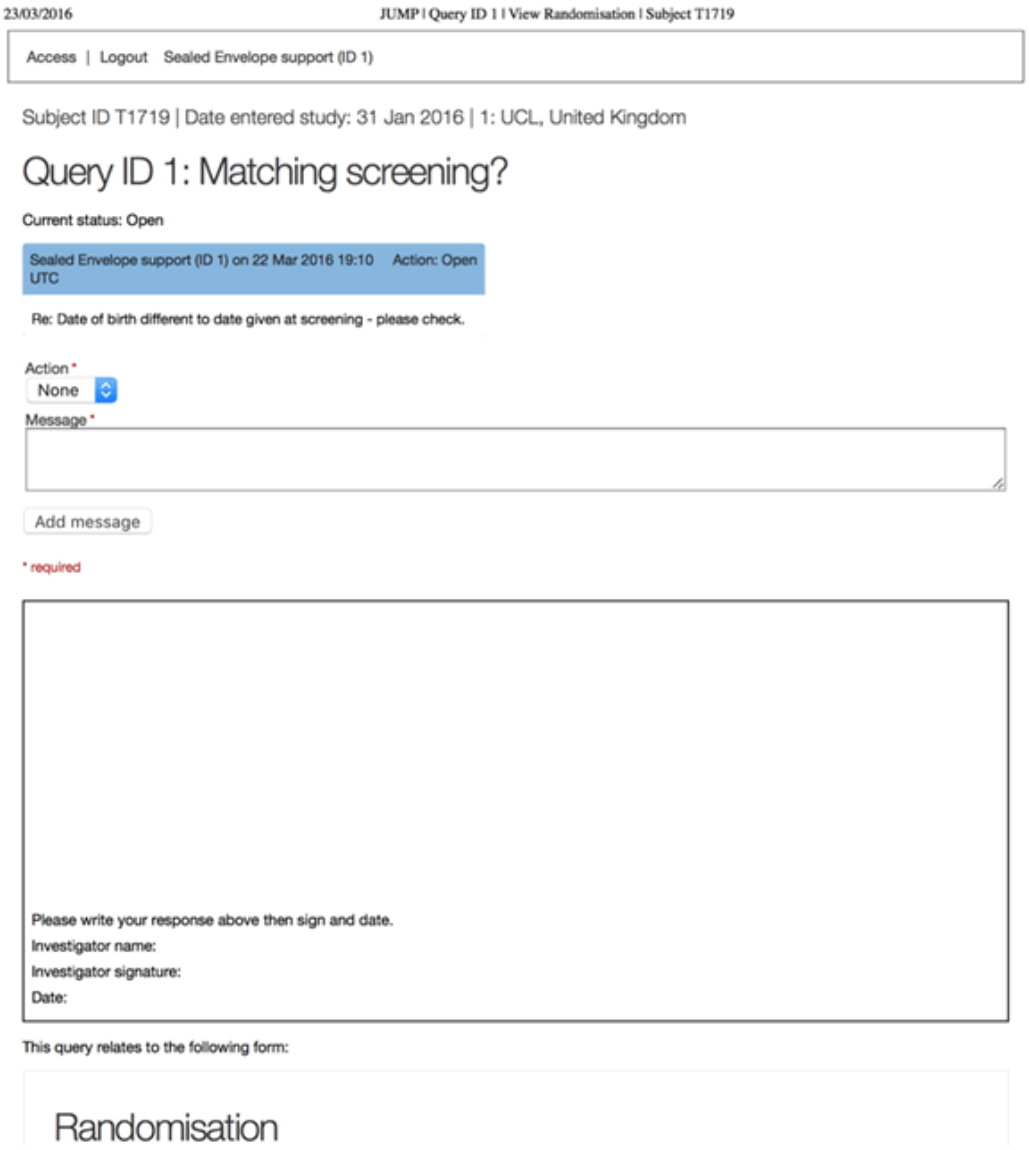


Figure 11.3: Response box shown when printing a query

displays links for editing the query or viewing the related subject or form.

Chapter 12

Subject attachments

If subject attachments are enabled, documents associated with a subject can be uploaded for storage in the subject's CRF.

> Note: It is **essential** that documents containing personally identifiable subject information are not uploaded.

The specification page will list details of the maximum file size allowed for an individual attachment and the remaining the space available for attachments.

Permissions

Every role with access to the subject view may download the attachments. Investigators can upload new attachments, and Administrators can delete existing attachments.

Uploading attachments

The subject record will have an Attachments section with a link to **Upload an attachment**. Following the link leads to the Attachments page for that subject, and a form where the file to be uploaded and an optional description can be specified.

Submitting the form will store the attachment in the subject's CRF.

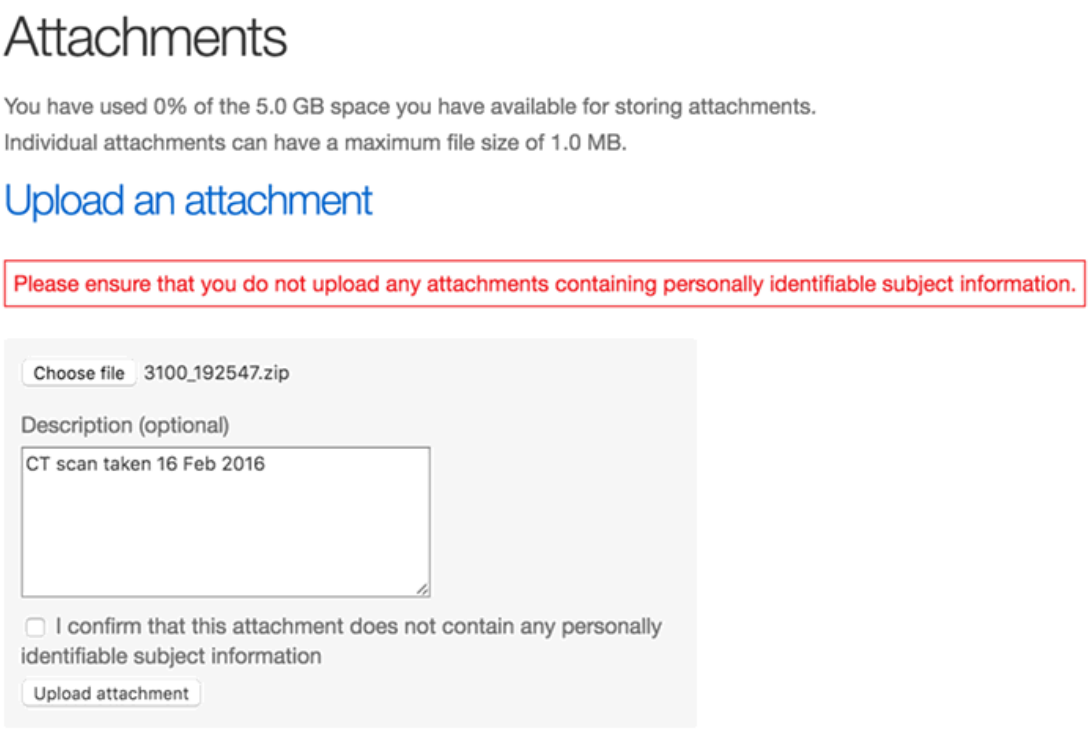


Figure 12.1: Uploading an attachment

Viewing and downloading existing attachments

Once attachments have been uploaded for a subject the subject view will display a link to download the attachment.

The Attachments page will contain a table detailing the attachments for that subject.

Deleting an attachment

Administrators can delete existing attachments. To delete an attachment follow the **Delete** link from the table on the Attachments page. This leads to a confirmation page where clicking the **Delete attachment** button will remove the attachment from the subject's CRF.

> Note: Deleted attachments are removed from the filesystem so this action cannot be undone.

Running out of space

Contact support@sealedenvelope.com to increase the space available for storing attachments.

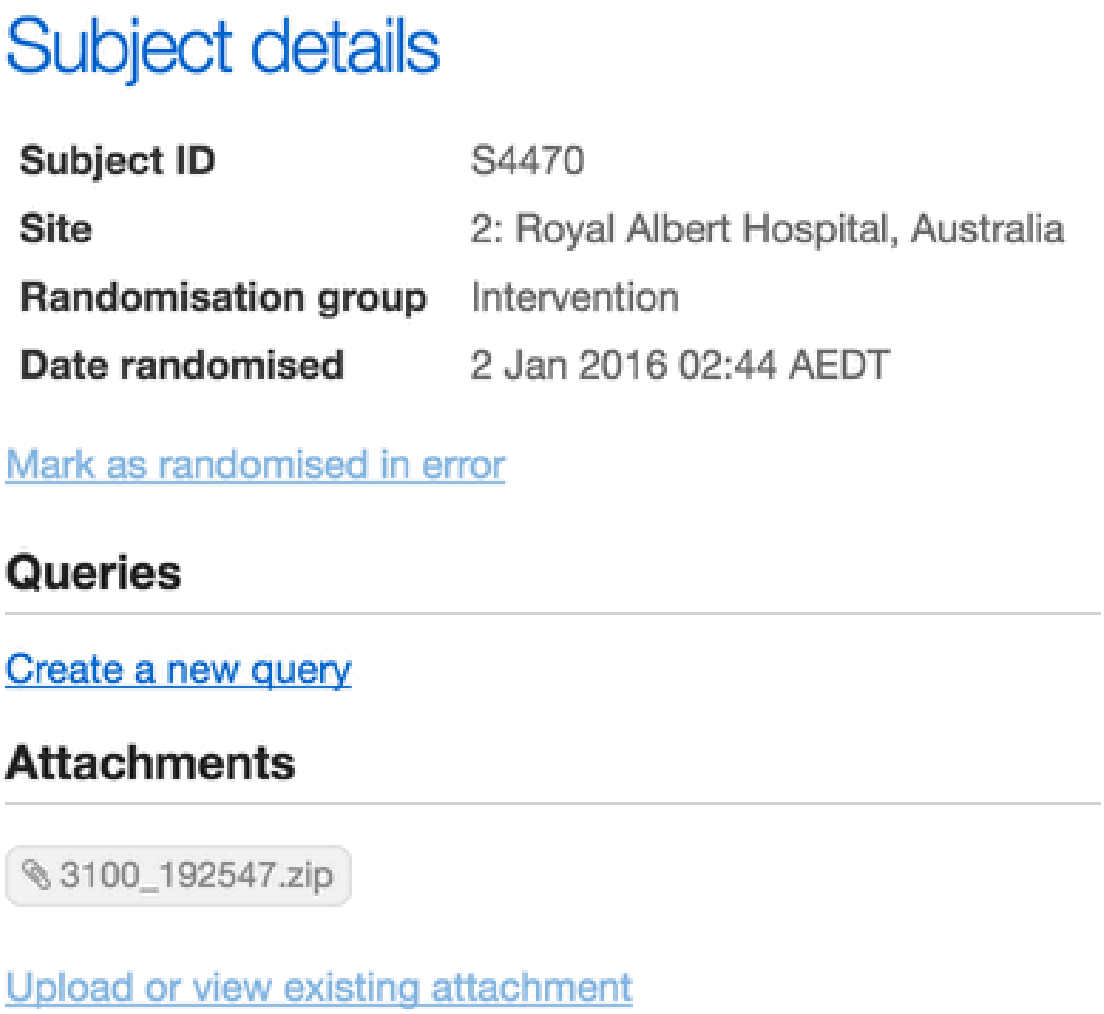


Figure 12.2: An attachment listed in the subject view

Figure 12.3: Table of attachment details

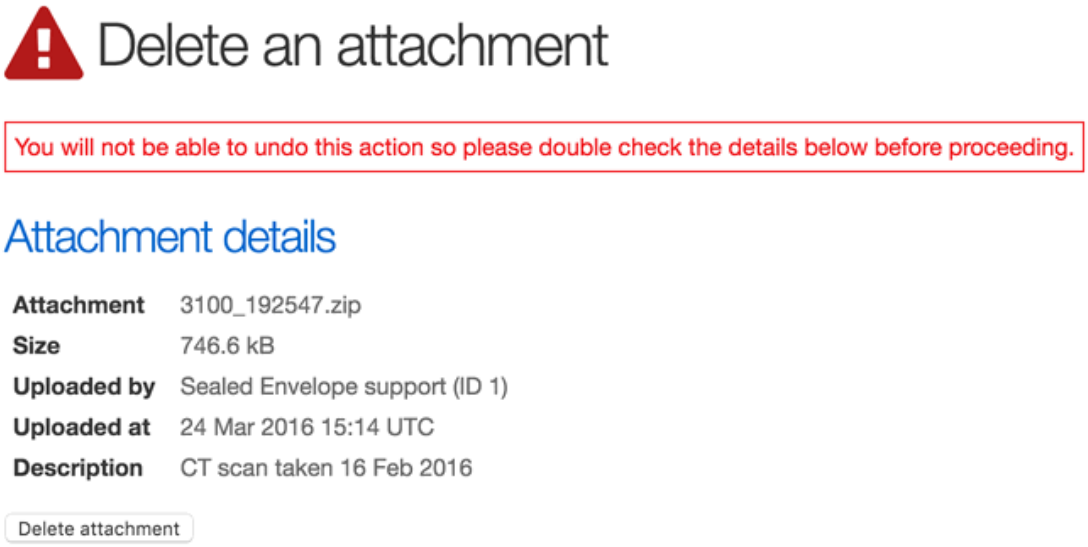


Figure 12.4: Deleting an attachment

Chapter 13

Reports

Various reports summarising data-entry and randomisation activity and site status are available by clicking on the **Reports** link in the top menu. Clicking on a report title displays the report compiled from the live database so that it is always up to date. Report data can be downloaded as a plain text comma separated value file by clicking on the **Download as CSV** link. Reports may also be sorted by clicking on a column heading or filtered by entering search terms into the search box.

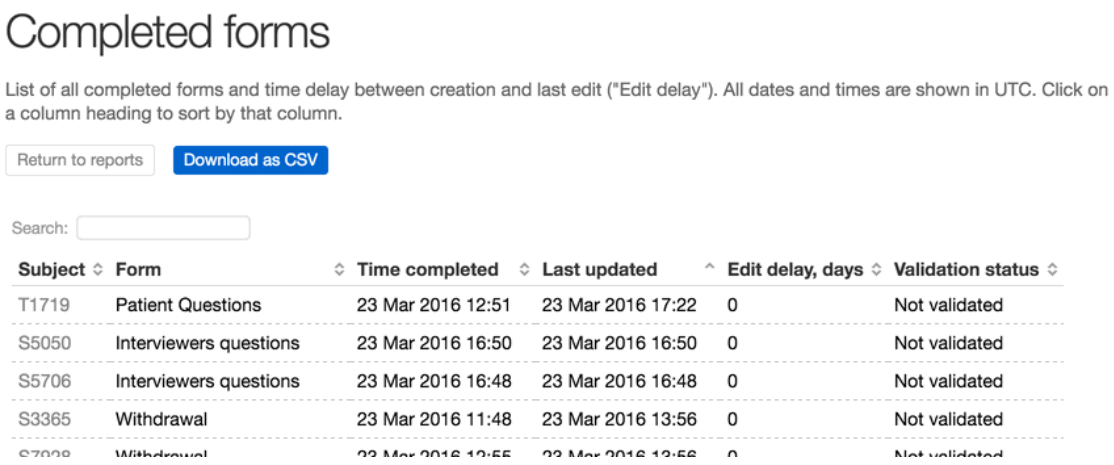


Figure 13.1: Viewing a report

Chapter 14

Downloads

CRF data may be downloaded in either CSV or Stata fixed format via the **Download** link in the top menu. The download page shows a list of forms in the CRF and provides links to download the data for each form individually or for all forms (as a zip file).

Data dictionary

A data dictionary can be viewed which shows the fields for each table (there is one table per form). The field name, data type and label are displayed.

Encrypted PII fields

Fields containing personally identifiable information (PII) that have been configured in the CRF builder to be stored in an encrypted format will be downloaded with AES-256 encryption applied. This means these fields cannot be viewed or analysed without decryption. Decryption can be carried out using common decryption tools such as OpenSSL. Contact Sealed Envelope support for further instructions.

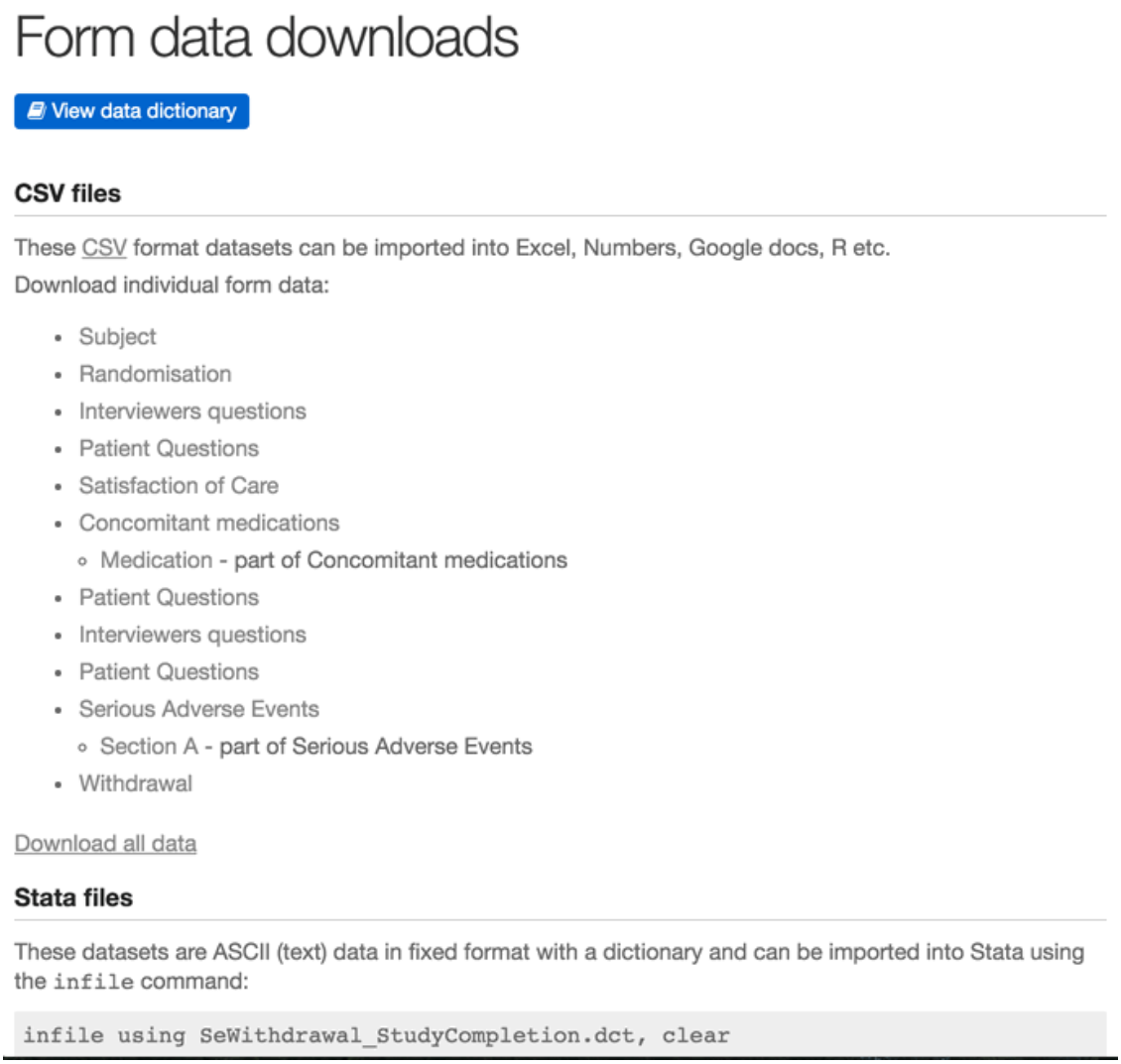


Figure 14.1: Form data download page

Form data dictionary

Download form data

Data types are specified as MySQL data types.

Subject

Database table name is **patient**.

Field name	Data type	Additional information
identifier	varchar(255)	Patient identifier
id	int(10) unsigned	
patientId	int(10) unsigned	Subject id
userIdentifier	varchar(255)	User who created row
lastUserIdentifier	varchar(255)	User who last updated row
invNo	int(10)	Telephone randomisation investigator number
dateEnteredStudy	date	Date of study entry yyyy-mm-dd
dateRandomised	datetime	Date & time of randomisation (UTC)
code	enum('Control','Intervention')	Randomised group
blockNumber	int(10) unsigned	Block number
blockSize	int(10) unsigned	Block size
blockSequence	int(10) unsigned	Sequence number within block
forced	enum('Control','Intervention')	First choice randomised group that was unavailable

Figure 14.2: Form data dictionary

CSV format

The data for each form is provided in comma separated value format, which is a plain text file that can be opened in many spreadsheet or Statistical programs. The first row contains a header with the question labels for each column.

Patient identifier	id	Subject id	User who crea	Timestamp for row creation (UTC)	Sex - Questions	Marital status - Questions	If
T5617	1	1	Sealed Envelo	2016-03-23 11:36:19	Male	Partner - Living with	
T1719	2	2	Sealed Envelo	2016-03-23 12:51:18	Female	Married	

Figure 14.3: Viewing CSV file in spreadsheet

Every file contains a patient identifier field (`identifier`) and subject ID field (`patientId`) so that data stored on the same subject in different forms can be linked together.

Stata format

The data for each form is provided in Stata fixed format, which is a plain text file format with a dictionary 'header' that describes the format of the rows. Each row contains information from one saved form with a subject identifier field to identify the subject record it belongs to. The data can be easily imported into Stata using the infile command.

For example, to import the data from a baseline form called *Interviewers questions*, the following infile command would be used in Stata:

```
infile using InterviewersQuestionsVER1_Baseline.dct, clear
compress
```

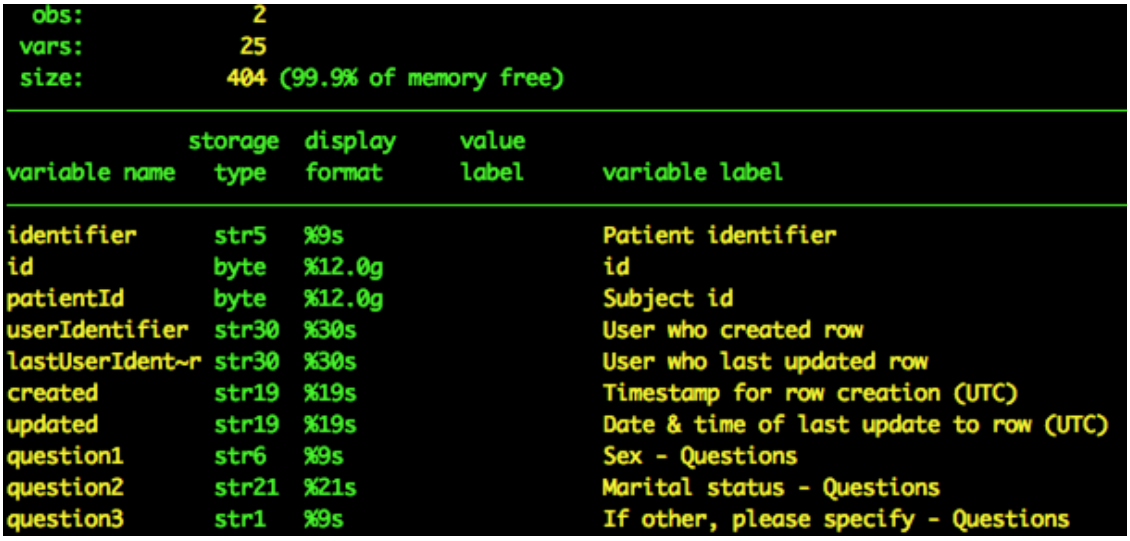
where `InterviewersQuestionsVER1_Baseline.dct` is the full filesystem path to the downloaded file. The `compress` command is recommended to reduce the storage space allocated to each variable.

Example

Some interview data has been downloaded in Stata fixed format. There are two rows below the dictionary header because only data on two subjects have been entered so far:

```
dictionary {
  str244 identifier `"Patient identifier"'
  long id `"id"'
  long patientId `"Subject id"'
  str244 userIdentifier `"User who created row"'
  str244 lastUserIdentifier `"User who last updated row"'
  str244 created `"Timestamp for row creation (UTC)"'
  str244 updated `"Date & time of last update to row (UTC)"'
  str244 question1 `"Sex - Questions"'
  str244 question2 `"Marital status - Questions"'
  str244 question3 `"If other, please specify - Questions"'
  str244 question4 `"Have you had any previous episodes of depression? - Depression"'
  str244 question5 `"If so, how many - Depression. Number (up to 2 digits)"'
  str244 question6 `"Duration of current episode in weeks - Depression. Number (up to 3
    digits)"'
  str244 question7 `"Are you using any treatments for depression at the moment? -
    Depression"'
  str244 question8 `"Treatment/Medication Name - Depression"'
  str244 reasonForEdit `"Reason for editing row"'
  str244 notes `"Notes"'
  str244 validationOverrides `"Justifications for overriding validation"'
  str244 validationStatus `"Validation status"'
  str244 validationNotes `"Validation notes"'
  str244 _dateEntered `"Date of study entry yyyy-mm-dd"'
  str244 _dateWithdrew `"Date of withdrawal from follow-up - Withdrawal."'
  str244 _site `"Site"'
  str244 _country `"Country"'
  str244 _visit `"Visit"'
}
"T5617" 1 1 "Sealed Envelope support (ID 1)" "Sealed Envelope support (ID 1)" "2016-03-23
    11:36:19" "2016-03-23 11:36:19" "Male" "Partner - Living with" "" "Yes" "3" "3" "No"
    "" "" "" "{}" "Not validated" "" "2015-12-27" "" "1: UCL" "United Kingdom" "Baseline"
"T1719" 2 2 "Sealed Envelope support (ID 1)" "Sealed Envelope support (ID 1)" "2016-03-23
    12:51:18" "2016-03-23 12:51:18" "Female" "Married" "" "No" "" "2" "No" "" "" "" "{}" "
    Not validated" "" "2016-01-31" "" "1: UCL" "United Kingdom" "Baseline"
```

The data is imported and compressed, and the output from Stata's `describe` command can be seen in the screenshot. The variable names and variable descriptions have been picked up automatically from the dictionary header.



```
  obs:             2
 vars:            25
 size:           404 (99.9% of memory free)
-------------------------------------------------------------------------------
              storage  display     value
variable name   type   format      label      variable label
-------------------------------------------------------------------------------
identifier      str5   %9s                    Patient identifier
id              byte   %12.0g                 id
patientId       byte   %12.0g                 Subject id
userIdentifier  str30  %30s                   User who created row
lastUserIdent~r str30  %30s                   User who last updated row
created         str19  %19s                   Timestamp for row creation (UTC)
updated         str19  %19s                   Date & time of last update to row (UTC)
question1       str6   %9s                    Sex - Questions
question2       str21  %21s                   Marital status - Questions
question3       str1   %9s                    If other, please specify - Questions
```

Figure 14.4: Form data imported into Stata

Category variables are stored as strings so can be tabulated without needing variable labels. Category variables can be encoded if storage space is an issue.

Conversion notes

During conversion into Stata download format, note the following changes that are made to the data:

- All strings are truncated at 244 characters
- Newlines are replaced by spaces
- Double quotes are replaced by single quotes

Stata with .do file format

This format provides a pair of Stata files per form: the raw data and a **.do** file to process the data. The data is imported by running the **.do** file within Stata. There are some differences to the Stata format described above to make analysis more convenient: categorical variables are stored as numeric values with value labels attached, and additional numeric variables are created for date fields.

```
. tab question2

    Marital status -
           Questions |      Freq.     Percent        Cum.
---------------------+-----------------------------------
             Married |          1       50.00       50.00
Partner - Living with |          1       50.00      100.00
---------------------+-----------------------------------
               Total |          2      100.00
```

Figure 14.5: Tabulating imported form data

Chapter 15

Audit trail

Clicking the **Log** link in the top menu bar displays the audit trail. The most recent 100 lines are shown by default; click the 'Show all' button to see the entire log. The audit trail is a plain text file which can be downloaded if required using the **Download** button. The log records all significant events and changes to the data including:

- Data entry and editing of forms
- Creation and adding messages to queries
- Creation and editing of sites
- Randomisations
- Movement of blocks within code lists
- Unblinding
- Downloads from the system such as reports in CSV format, CRF data, code list and the audit trail itself

An example extract from a log is shown below. The items shown in each row of the log are (from left to right):

- IP address of the user who initiated the event
- Name and user ID of the user
- URL
- Server date and time (including GMT offset)
- Notice level - usually this will be "INFO (6)"
- Message

Where applicable, the message contains information on the data before and after the event. Some events might generate several related messages - such as an explanatory note

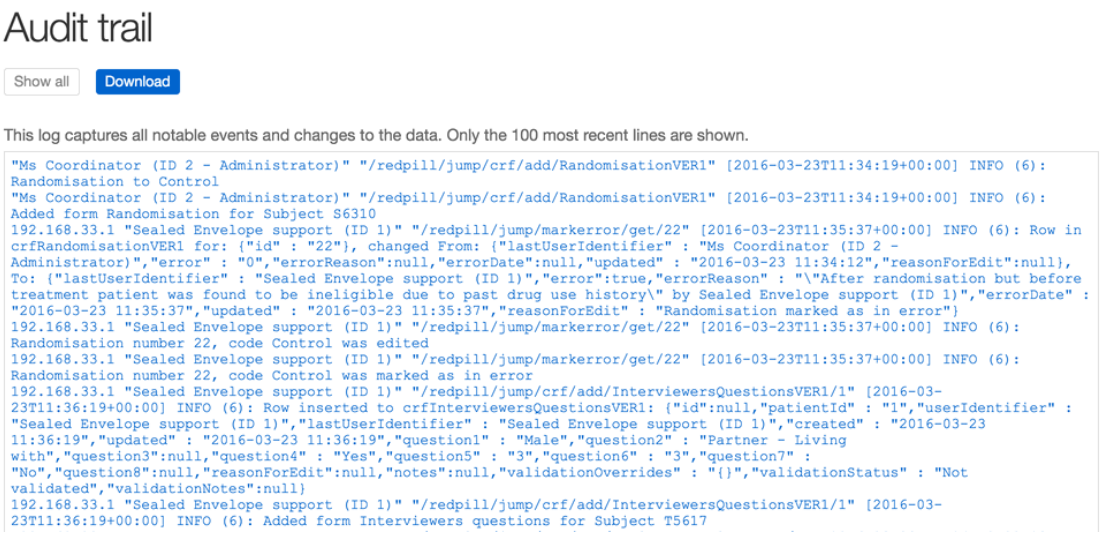


Figure 15.1: Audit trail

```
"Edited form Eligibility Criteria Check At Recruitment for Patient SDN01"
```

plus a change in the data:

```
"Row in crfBaselineEligibilityCriteria for: {"id" : "1"}, changed From: {"updated" :
    "2015-10-22 17:45:47","reasonForEdit":null ..."
```

Example extract

```
100.2.3.4 "Simon Admin (ID 2)" "/redpill/trialname/crf/reviewadd/
    BaselineEligibilityCriteria/1" [2015-10-22T17:45:47+01:00] INFO (6): Row inserted to
    crfBaselineEligibilityCriteria: {"id":null,"patientId" : "1","userId" : "1","
    lastUserId" : "1","created" : "2015-10-22 17:45:47","updated" : "2015-10-22
    17:45:47","reasonForEdit":null,"notes":null,"diagnosisOfIpfOrNsip" : "No","rhcMeanPap"
     : "Yes","ageRange" : "No","dateWrittenInformedConsentGiven" : "10\/08\/2008","
    validationStatus":null,"validationNotes":null}
100.2.3.4 "Simon Admin (ID 2)" "/redpill/trialname/crf/reviewadd/
    BaselineEligibilityCriteria/1" [2015-10-22T17:45:47+01:00] INFO (6): Added form
    Eligibility Criteria Check At Recruitment for Patient SDN01
```

```
100.2.3.4 "Simon Admin (ID 2)" "/redpill/trialname/crf/reviewedit/
    BaselineEligibilityCriteria/1" [2015-10-22T17:48:40+01:00] INFO (6): Row in
    crfBaselineEligibilityCriteria for: {"id" : "1"}, changed From: {"updated" :
    "2015-10-22 17:45:47","reasonForEdit":null,"unstableUnderlyingLungDisease":null,"
    anySeriousComorbidity":null,"systolicBp":null}, To: {"updated" : "2015-10-22
    17:48:40","reasonForEdit" : "Adding some more answers","unstableUnderlyingLungDisease"
     : "No","anySeriousComorbidity" : "Yes","systolicBp" : "No"}
100.2.3.4 "Simon Admin (ID 2)" "/redpill/trialname/crf/reviewedit/
    BaselineEligibilityCriteria/1" [2015-10-22T17:48:40+01:00] INFO (6): Edited form
    Eligibility Criteria Check At Recruitment for Patient SDN01
100.2.3.4 "Simon Admin (ID 2)" "/redpill/trialname/contact/add/Individual" [2015-08-13T10
    :37:45+01:00] INFO (6): Row inserted to contact: {"id":null}
1.2.3.4 "Simon Admin (ID 2)" "/redpill/trialname/contact/add/Individual" [2015-08-13T10
    :37:45+01:00] INFO (6): Row inserted to individual: {"id" : "52","title":null,"
    lastName" : "Kinnear","firstName" : "James","jobTitle" : "Layman","responsibility":
    null,"notes":null,"type" : "individual","qualifications":null,"regNo":null,"cv" :
    "0","cvDate":null,"delegationLogReceived" : "0","delegationLogReceivedDate":null}
100.2.3.4 "Simon Admin (ID 2)" "/redpill/trialname/contact/add/Individual" [2015-08-13T10
    :37:45+01:00] INFO (6): Added contact James Kinnear
```

Chapter 16

Settings

A settings page is available to administrators that allows some features to be turned on or off to suit the requirements of a trial. Changes to settings are recorded in the audit trail. There are some common settings (see below) and there may also be some trial specific settings.

Review step

The review step is turned on by default and introduces an intermediate step when saving forms. The user is required to review the form data and enter their password to confirm the information is correct before the data is saved to the database. The process is described in the data entry section. Since investigator accounts normally do not have privileges to enter data once it is saved, the review step can help to prevent errors which would then require a query to resolve.

However, administrators may prefer to turn this review step off. In this case the form is saved immediately with no intermediate review page. This could be preferable, for instance, if data entry staff are entering paper CRFs into a Red Pill database.

> Note the review step is always enabled for randomisation forms

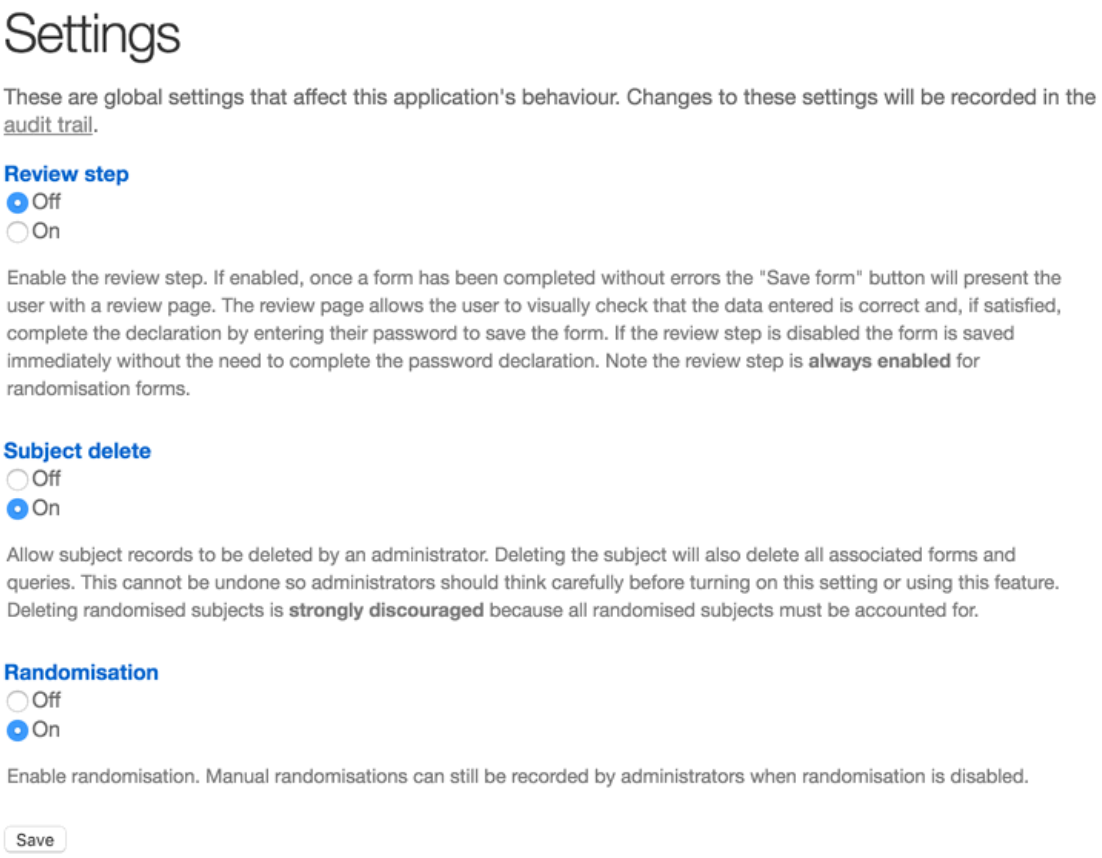


Figure 16.1: Settings page

Investigator edit

By default investigators cannot edit forms - only add them and view them. This setting enables investigators to also edit forms after they have been saved. In addition it allows investigators to mark forms in a visit as missing.

Subject delete

The ability to delete subjects is turned off by default. Deleting a subject will also remove all their CRF data, randomisation data and queries. The deleted data is shown in the audit trail but the action cannot be undone. Administrators should consider very carefully whether to turn this feature on and use it. We recommend it is used only in exceptional circumstances.

> We **strongly discourage** using the delete feature on randomised subjects because all randomised subjects must be accounted for.

If a subject was randomised in error mark them as such rather than deleting the record.

Form delete

Allows an administrator to delete forms. The deleted data is shown in the audit trail. Randomisation forms cannot be deleted - the randomised in error feature should be used instead. Study entry forms may not be deleted either - the subject must be deleted to remove this form.

> The form delete setting will not be shown for randomisation only systems

Randomisation

Randomisation systems and Red Pill systems with a randomisation form can turn randomisation on or off. When randomisation is disabled, administrator accounts can still record manual randomisations. This may be useful, for instance, if offline randomisations have been carried out due to the Sealed Envelope website being unavailable.

This is a global setting - to stop randomisation at a specific site, edit the site and set *Recruiting* to **No**.

Chapter 17

Specification

The specification for a Red Pill or randomisation application can be viewed by clicking the **Specification** link in the top menu. The specification is only accessible to administrator users. It shows the following information where relevant:

- Names of forms that can be completed multiple times per patient.
- The timetable used by the form scheduling feature, showing when visits are due and the forms within each visit.
- Whether any of the forms can be self-completed by subjects, and information about custom text shown to the subject in invitation emails and after logging in.
- Details on randomisation method used, treatment groups, allocation ratio, strata, blinding, code list length, randomisation limit, data collected at randomisation (where relevant).
- Format of randomisation, unblinding and kit assignment email notifications.
- If attachments are enabled, the maximum file size allowed and percent of storage allowance used.
- User account privileges for different roles.
- Library version numbers.
- Server type (staging/production), database version, current value of settings.

There may also be extra custom information specific to the study.

Specification

Multiple forms

The following forms can be completed as many times as required.

- Serious Adverse Events

Form schedule

Visit	Form	Due
Baseline	Randomisation	On day of study entry
	Interviewers questions	On day of study entry
	Patient Questions	On day of study entry
	Satisfaction of Care	On day of study entry
	Concomitant medications	On day of study entry
6 Week Follow-up	Patient Questions	6 weeks after study entry
12 Week Follow-up	Interviewers questions	12 weeks after study entry
	Patient Questions	12 weeks after study entry
Other forms	Serious Adverse Events	at any time
	Withdrawal	at any time

Subject entered forms

Subjects may be invited to complete the following forms:

- Baseline visit: Patient Questions
- 6 Week Follow-up visit: Patient Questions
- 12 Week Follow-up visit: Patient Questions

Figure 17.1: Specification page

Chapter 18

Making changes to the specification

Once a Red Pill or randomisation system is in production, changes to the forms or other aspects of the system can only be done through a documented change control process. To initiate this process please download and complete a Change Request spreadsheet [Excel file].

The Change Request Log will require you to complete the following information:

Change # Sequential change number 1, 2, 3, …
Visit Name of visit, e.g. *Baseline*
Form Name of form, e.g. *ECG results*
Item / Question The question to be added or changed, eg. *1. ECG - Has a baseline ECG been taken?*
Change type One of:

- New form
- New field
- Change field
- Other change

New or revised forms and fields might be required due to a change in the protocol or a mistake in the original specification. Other changes include changes to validation rules or user permissions etc.

If new field, please record response required When adding new fields, please list what type of response is expected. Please choose from:

- Single line text
- Paragraph text - a text box allowing long text entries
- Encrypted text - a text box whose value will be stored in an encrypted format

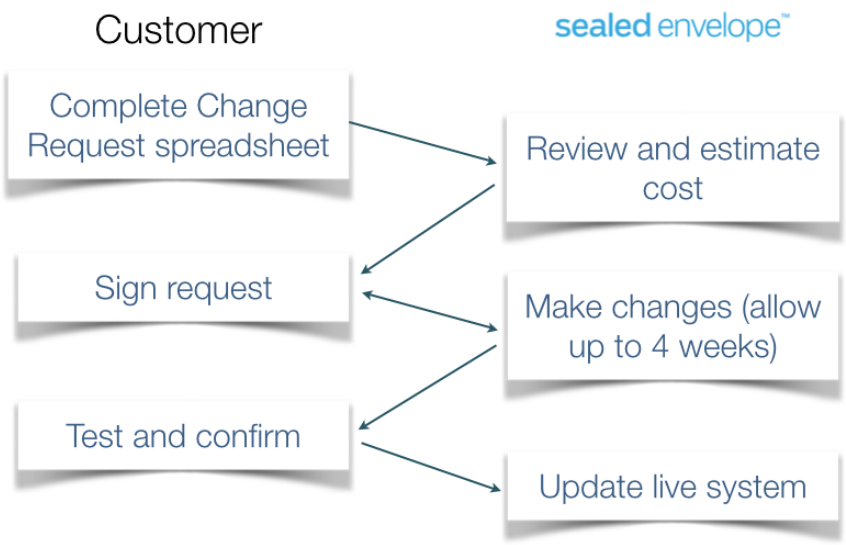


Figure 18.1: Flowchart for change request process

- Number
- Date
- Yes/No
- Category - please list all categories eg, Mild; Moderate; Severe
- Clock time - the time of day in 24hr clock format (e.g. 13:15)
- Elapsed time - a duration in hours and minutes (e.g. 30:50)
- Explanation - explanatory text (e.g. The following questions are about your health)

Change description The actual change that is required in the eCRF. e.g. *The drop down menu is missing a category and should be updated to include new option in drop down menu*

Once you have completed the form, please send it to Sealed Envelope for review. Sealed Envelope will review your list of changes and provide you with an estimate of how long it will take to configure these changes and provide you with a cost estimate to fulfil your request.