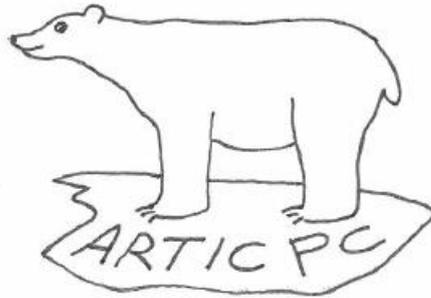


Research online manual



ARTIC-PC

**Antibiotics for lower Respiratory Tract Infection in
Children presenting in Primary Care**

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1 CONTACTS

The following persons of the Julius Center data management department are involved in this study:

Name	Function	Email	Telephone
Joost Schotsman	Project Coordinator	jschotsm@umcutrecht.nl	+31 88 75 69426
Chantal Hendriks	Data Manager	c.hendriks-4@umcutrecht.nl	+31 88 75 68207

2 INTRODUCTION eCRF

Research Online (RO) is an electronic data capture (EDC) system that enables the data collection for clinical studies. Web-based Case Report Forms form the basis of the system to facilitate the study specific data collection. By using internal data validation checks within these forms, only data of high quality can be submitted to the study database. The forms can easily be accessed by all standard web browsers (see 3.1). Pre-defined programmed workflows make it possible to show particular forms only after a particular answer or event.

Project management of the study is facilitated by the integrated live study progress reports. After data of the last participant is entered, the database can be closed and data can be made rapidly available for further analysis and publication purposes. The system meets all requirements according to ICH-GCP standards (International Conference on Harmonisation (ICH) on Good Clinical Practice (GCP)) for electronic data entry with respect to safeguarding data integrity and data security regulations. Users will have role-based access* to the platform after they have logged-in using their own username and password. The system will log all data entry steps with timestamps and user information, so creating an audit trail. The role-based access to the system will avoid unauthorised data access and actions. Data traffic with RO over the internet is encrypted using secured data communication protocols. The central databases and web servers are hosted in a secure data centre. The database is backed up every day.

All studies are accessible from the website: <https://www.researchonline.org/>

* Based on their role definition programmed by the data management department, a person can or cannot perform certain tasks (e.g. randomise participants, enter data, answer queries etc).

3 LOGIN INTO RESEARCH ONLINE

3.1 Browsers

RO works with all standard modern web browsers, but Chrome  gives the best performance.

Note: for old versions of internet explorer  (version 8 or older) the performance is not optimal, please update to a more modern browser.

3.2 Account request and login

The local network coordinator is responsible for account requests to the central data management team in Utrecht. The requests can be sent to the following mail address: C.Brugman@umcutrecht.nl

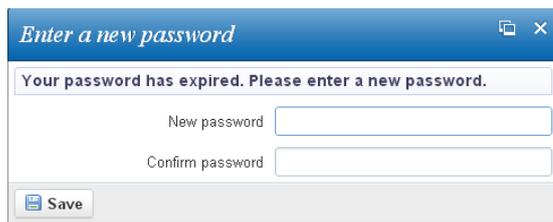
The data management team will create the requested account within two working days and will send the account details to the local network coordinator or account owner.

Once account details are received take the following steps to login:

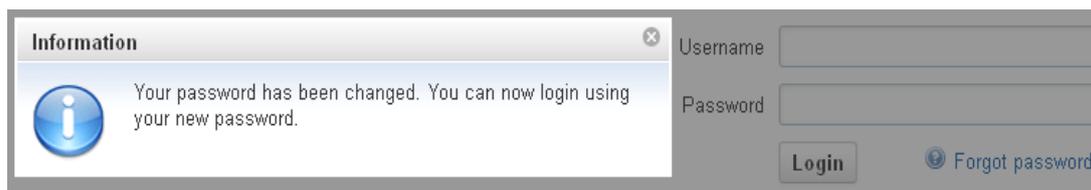
- 1) Open your browser and surf to the study specific website:

<https://www.researchonline.org/>

- 2) Enter your account name and password and click 'Log in'.
- 3) The system will prompt you to change your password immediately.



- 4) Enter a new strong password (see paragraph 3.3) and log in.



- 5) Log in again with your new password.

3.3 Password policy

The new password must contain at least three of the following:

- 7 characters
- At least 1 letter lower case (a,b,c,...)
- At least 1 letter upper case (A,B,C,...)
- At least 1 number (0,1,2,...)

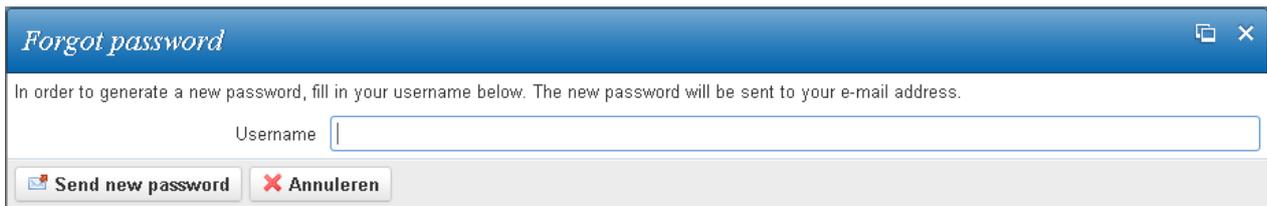
Your password must be changed yearly.

Note: After 15 minutes of inactivity you are logged out automatically.

3.4 Forgotten password

A password can easily be reset by RO using the 'Forgot password' option.

Click the 'Forgot password' link and type in your username. An email will be sent to the email address that belongs to that account name.



The screenshot shows a web form titled "Forgot password" in a blue header bar. Below the header, there is a text instruction: "In order to generate a new password, fill in your username below. The new password will be sent to your e-mail address." Underneath this instruction is a text input field labeled "Username". At the bottom of the form, there are two buttons: "Send new password" with an envelope icon and "Annuleren" with a red 'X' icon.

3.5 Account locked

After 3 invalid login attempts with the same username, the account will be locked for ten minutes. During this period it is not possible to login anymore. After ten minutes the account will automatically be unlocked. All login attempts are logged by the system and will be monitored closely by data management.

4 CHECK PERSONAL DATA

1. Click on 'My Account' and check your personal data.

[Home](#) [Switch active study](#) [My Account](#) [Administration](#) [Study configuration](#) [Research](#) [Reporting](#)

User name

Full name

First name

Preposition

Last name

Email

Language

Time zone

2. Change the relevant data if necessary.

5 WORKFLOW ARTIC PC

CRF baseline	Sample logistics	Diary day 1	Chest X-ray	Diary week 1	Diary week 2
- CRF 1	- Blood samples - Swabs	- Diary received? * - General questions - Health status ***	- Chest X-ray	- Daily Symptoms Diary week 1 - Health status *** - Weekly questions - Weekly questions part 2	- Diary week 2 completed? ** - Daily Symptoms Diary week 2 - Health status *** - Weekly questions - Weekly questions part 2

Diary week 3	Diary week 4	Diary final questions	Spirometry	Withdrawal	SAE
- Diary week 3 completed? ** - Daily Symptoms Diary week 3 - Health status *** - Weekly questions	- Diary week 4 completed? ** - Daily Symptoms Diary week 4 - Health status *** - Weekly questions	- Final questionnaire	- Spirometry ****	- Withdrawal form	- Serious Adverse Event (SAE) *****

* When the Diary is received, this will activate the rest of the forms in visit Diary day 1, Diary week 1 and Diary final questions. Also, the forms 'Diary week ... completed' will be made available.

** When 'Diary week ... completed' is Yes, the forms of that week will appear.

*** The Health status forms will only be available for subjects with age 4+ (based on age in CRF1)

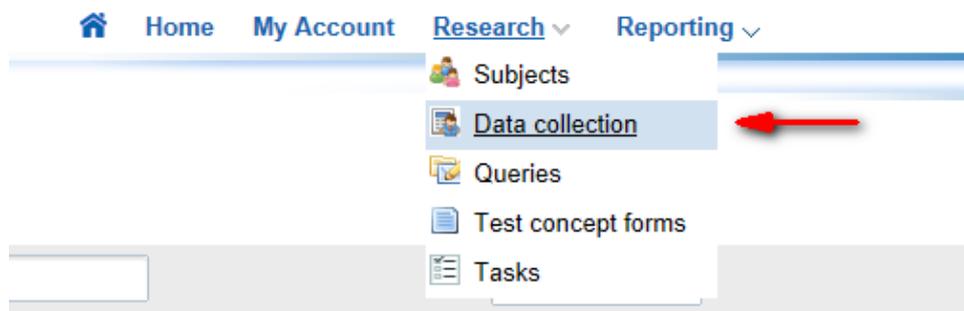
**** Spirometry form will only be available for subjects with age 6+ (based on age in CRF1)

***** The SAE form can be filled out more than once. Each time a SAE form is submitted, a new empty form will be made available.

On page 10 of this manual data collection using Research Online is described in detail. After a participant has been added as a new subject in RO he/she automatically appears in the "Data collection overview". This overview shows all forms that have to be completed (CRF, diary, sample tracking forms etc) for the participant and data entry can start.

6 ADDING A NEW SUBJECT TO RESEARCH ONLINE

1. Click 'Research' and select 'Data collection'.



2. An overview of the included participants is displayed.

Data collection overview



Search filter: Subject nr Site Sort by

Inclusion date from Inclusion date to

Subject	CRF Baseline	Sample logistics	Diary day 1	Chest X-ray	Diary week 1	Diary week 2	Diary week 3	Diary week 4	Diary final questions	Spirometry	Withdrawal	SAE
0002												
0001												

3. Click 'Add new subject' in the left upper corner to include a new participant.

Data collection overview

Search filter: Subject nr

Inclusion date from

Make sure you only add participants who fulfill the inclusion and do not meet the exclusion criteria.

4. Enter the following information:
 - a. Subject no: The unique participant ID number (e.g. 010003) from the CRF/informed consent/labels used for this participant.
 - b. Inclusion date: **IMPORTANT** this is the **date that the patient was enrolled in the study** (Day 1). Today's date is shown by default, but it will be necessary to change this date if entering data from paper CRFs at a later date.
 - c. Site will be automatically selected, but can be changed, if necessary, using the drop-down list on the right.

Edit subject ✕

Subject no format 6 digits

➔ Subject no

➔ Inclusion date ➔ 

➔ Site ➔ 

5. Click 'Save' to save the data of this participant.
6. The participant is now shown in the Data collection overview.

As the RO TEST site was used, only the last 4 digits (..0003) are shown in the Data collection overview. After inclusion of a real ARTIC PC participant all 6 digits (010003) of the unique participant ID number will be shown.

Data collection overview

Add new subject

Search filter:

Subject nr

Inclusion date from 

Site 

Inclusion date to 

Sort by 

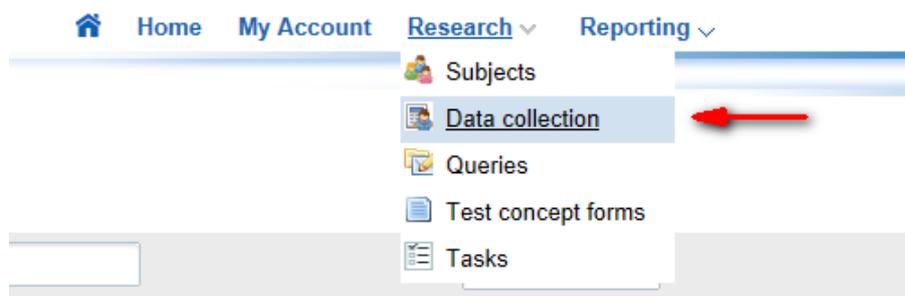
Subject	CRF Baseline	Sample logistics	Diary day 1	Chest X-ray	Diary week 1	Diary week 2	Diary week 3	Diary week 4
➔ 0003	 	 						
0002	 	 						
0001		 						

7 DATA COLLECTION

7.1 Data collection overview

After a participant has been included in RO and appears in the data collection overview, you can start entering data:

1. Click on 'Research' and select 'Data collection'.



2. The data collection overview appears. The first step is to complete the CRF baseline.

Data collection overview



Search filter: Subject nr

Inclusion date from  Inclusion date

Subject	CRF Baseline	Sample logistics	Diary day 1
0003	 *		
0002	 *		
0001			

The symbol* shown on the button in the 'CRF Baseline' column for participant 0003 tells you there is a new CRF1 for this participant to complete.

 * This symbol means 'New': data entry has not yet started.

- Click on the 'New' button to show the CRF 1 form.

Fill out forms

Subject

Visit/Form group

Overview Deleted

 Edit  Print form

Form	Status	Open Query	ID1	ID2
CRF 1 	New	No		

[← Back to data collection overview](#)

Double click on this form to open and complete it. Below you see the start of the ARTIC PC CRF1.

Eligibility if all of Inclusion Criteria

	Yes	No
Age 6m - 12y	<input checked="" type="radio"/>	<input type="radio"/>
Presenting with infective acute LRTI	<input checked="" type="radio"/>	<input type="radio"/>

 Exclusion criteria if any of

	Yes	No
Infective cough	<input type="radio"/>	<input checked="" type="radio"/>
Immune compromised	<input type="radio"/>	<input checked="" type="radio"/>
Antibiotics in last 30 days	<input type="radio"/>	<input type="radio"/>
Non infective asthma exacerbation	<input type="radio"/>	<input type="radio"/>
Severe, clinician judged, tachypnoea	<input type="radio"/>	<input type="radio"/>
Sibling enrolled in this project	<input type="radio"/>	<input type="radio"/>

- Fill in the questions. Click 'next' to go to the next page, all data will be saved automatically.

- Click 'Submit form' on the last page of the form.



- After a successful submission, you will get the message: 'The form has been received, thank you'. Close the information-box to go back to the forms.
- Complete other forms, if applicable, or click the button 'Back to data collection overview' to return to the overview showing per participant the forms that have to be completed (CRF, diary, sample tracking forms etc).
- When the forms are filled in and submitted completely and correctly, the forms will be marked completed.

Subject	CRF Baseline	Sample logistics	Diary day 1	Chest X-ray
05120				
03143				
01433				
05117				

- If you want to fill in forms of another participant, use the search filters at the top of the screen to find the participant you need.



Search filter: 

Subject nr

Site

Inclusion date from 

Inclusion date to 



- You can also use the TaskManager to fill in outstanding forms. Select the option from the menu 'Research' → 'Tasks' and it will show an overview of all forms/tasks still to be completed.

TaskManager

Subject Form

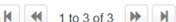
Site

Form date 

Status

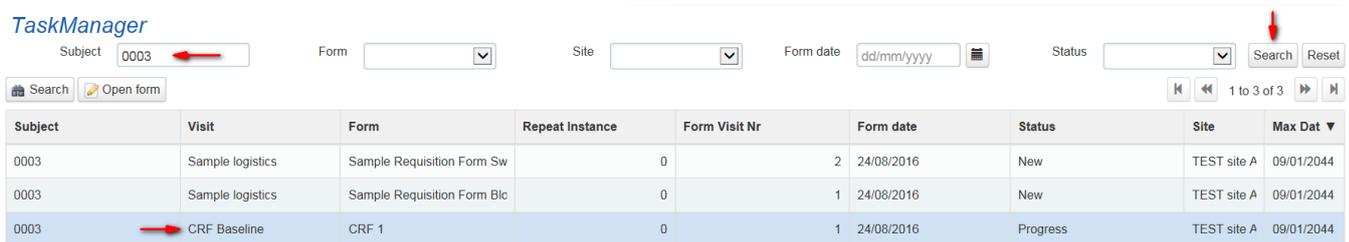
 1 to 3 of 3

Subject	Visit	Form	Repeat Instance	Form Visit Nr	Form date	Status	Site	Max Dat ▼
0003	Sample logistics	Sample Requisition Form Sw	0	2	24/08/2016	New	TEST site A	09/01/2044
0003	Sample logistics	Sample Requisition Form Blc	0	1	24/08/2016	New	TEST site A	09/01/2044
0003	CRF Baseline	CRF 1	0	1	24/08/2016	Progress	TEST site A	09/01/2044

Overview of outstanding forms/tasks for participant 0003 using the TaskManager.

11. From this overview, forms for individual participants can also be opened and filled in (select form and click 'open form' button).

The 'search' button can be used to find the form you want to access.



The screenshot shows the 'TaskManager' interface. At the top, there are search filters: Subject (0003), Form (dropdown), Site (dropdown), Form date (dd/mm/yyyy), and Status (dropdown). A red arrow points to the 'Search' button. Below the filters are 'Search' and 'Open form' buttons. A table displays the search results:

Subject	Visit	Form	Repeat Instance	Form Visit Nr	Form date	Status	Site	Max Dat
0003	Sample logistics	Sample Requisition Form Sw	0	2	24/08/2016	New	TEST site A	09/01/2044
0003	Sample logistics	Sample Requisition Form Blc	0	1	24/08/2016	New	TEST site A	09/01/2044
0003	CRF Baseline	CRF 1	0	1	24/08/2016	Progress	TEST site A	09/01/2044

After a search for the outstanding forms from participant 0003, and selection of the CRF 1 (marked blue now), click 'open form' to enter data.

7.2 Form/visit Status

Each form can have the following status:

	New	Progress	Completed
			
Query			
Late			
Late + query			
Locked			

New: data entry has not yet started

Progress: data entry has started, but one or more mandatory items are unanswered

Query: one or more queries have been raised for the form

Complete: all mandatory items are answered and no queries are present on the form

Locked: it is not possible to change data of locked forms

The status of an entire visit is determined by the status of the forms within the visit.

7.3 Mark item as Missing or Pending

Most items are mandatory; this means that the question must be answered in order to be able to submit the form. For some questions an escape option is present, making it possible to indicate that the answer is missing, unknown, or still pending. If the escape option is available, the following symbol is present on the right hand side of the question:



Click on this button and select the correct option from the scroll down menu.

If the option 'missing', 'unknown' or 'not done' is chosen, data will never be known. If the option 'pending' is chosen, data is considered to be temporarily missing and to be entered at a later stage. In that case a query is generated when the form is submitted. The form status will change to 'completed' once this data has been entered.

Does anybody in the household where the child usually lives smoke?

No
 Yes
 Don't know



Above a mandatory questions in the CRF 1. If the answer is not (yet) known, click on the button on the right and select the correct option from the scroll down menu.

Attention

Why can't you fill in the answer?

Missing
 Unknown
 Not Done
Pending
 Other

7.4 Override

Numerical fields may contain ranges, for example, Temperature (°C) must be between 35 and 43. Some fields can be overruled in case the entered value is correct, but out of range.

Temperature (°C)

Enter a number in the range 35.0 - 43.0

 **Override**

A comment must be entered to explain why the entered value is out of range.

Override validation errors

Comment

To overrule a check, click the 'Override' button, add a comment and click the 'Save' button to overrule and be able to proceed.

7.5 Change participant number (subject number)

If an incorrect participant number is entered by mistake, ask the data manager in Utrecht to change this (see section 13 for contact details).

7.6 Delete subject

As soon as data is entered for a participant it is not possible to delete this participant. Erroneously entered participants can only be removed by the data manager in Utrecht (see section 13 for contact details).

8 CHANGING DATA

Once the data form is submitted to the database, the audit trail keeps track of all changes (see section 12). If an item needs to be changed, go to the data collection overview, locate the form that needs changing open the form, locate the data that needs changing and press the pencil button on the right of the item that requires changing.

A pop up appears in which the answer can be changed. A reason for change can be selected from a predefined list, or another reason can be typed in. Click the 'Save' button to confirm the modification.

Change answer

Gender

Male

Female

Select a reason for this change

Or type a reason

Male

Female

9 QUERIES

9.1 Mandatory fields and ranges

A mandatory question (see orange asterix) must be answered during data entry (unless a missing option is present and used). If the question is not answered, and you try to submit the form, a red error message appears below, explaining why submission failed. If an escape option is available the following symbol is present on the right hand side of the question:

 Smoking

Never smoked regularly

Stopped smoking but used to smoke regularly

Current smoker (=> 1 cigarette per day)

  This question is required

To use the missing option, click on this button and select the suitable option from the scroll down menu shown (see also page 14). Only chose the option 'missing', 'unknown' or 'not done' if the data is not known and never will be. If the option 'pending' is chosen,

data is considered to be temporary missing and to be entered at a later stage. In that case a query is generated when the form is submitted. The form status will only change to 'completed' once this query has been answered.

For dates and numeric fields, an error message will appear when an entered value is outside the predefined range. Sometimes an overrule option is available, so that it is still possible to enter a value outside the range. Then a reason must be entered to clarify why the range is exceeded (section 7.4).

9.2 Validation rules

To prevent data inconsistencies or missing data, an error message in red will be

generated during data entry for each question that does not meet the specified

entry does

Date Informed Consent signed Query

08 APR 2014

Date patient questionnaire send/given

02 APR 2013

Date can not be before IC date, please verify

Messages

the
shown

Message text

Close query by researcher?

Save Cancel

validation rules, or when an answer is considered mandatory. An example is below:

It is possible to overrule the validation rule if your answer is correct. Therefore click the overrule button and give a reason for overrule (see section 7.4):



9.3 Manual queries

Monitors and data managers can create manual queries based on visual checks. Forms with queries can be identified on the data collection overview. These forms are marked with a question mark symbol:

Monitors and data managers will enter the query message and check whether the researcher is allowed to close/sign off the query after an answer is given or not. If not, the monitor or data manager will formally close the query after the answer is checked (see section 9.5).

9.4 Answering queries

Forms with queries can be identified on the data collection overview. These forms are marked with the question mark symbol.

To answer the queries open the form and go to the query. Below an example of a query:

Date patient questionnaire send/given

02 APR 2013

Date can not be before IC date, please verify

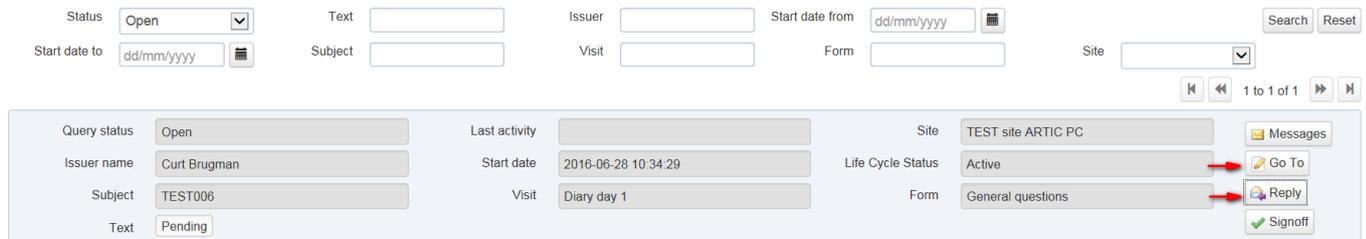
Messages

By clicking on the Messages link it is possible to see who has raised the query and when. It is possible to answer (reply) to the query directly, but it is also possible to use the Query overview for this.

All queries will be collected in the Query overview: 'Research' → 'Query'.

When you open this overview, it automatically shows all queries having the status 'open'.

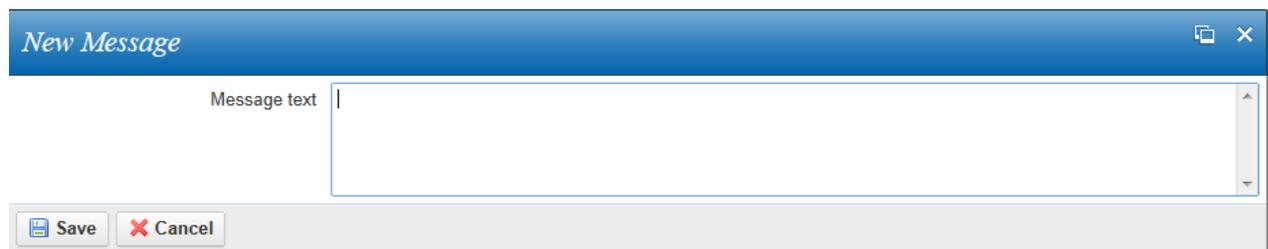
Query overview



You can filter for specific queries by status, query text, issuer, subject, visit, site or form to find a particular query.

The 'Go To' button links to the form item that contains the query.

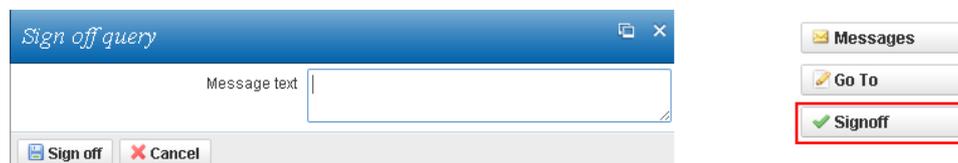
The 'Reply' button gives the opportunity to answer the query. Enter the reply and click 'Save'.



9.5 Close queries (Sign off)

If the query response answers the query correctly then the query can be closed by the researcher (if applicable), or by the data manager/monitor.

Click the 'Sign off' button to close the query. A reason for closing must be given.



9.6 Query answering and closing timelines and responsibilities

Each generated query must be answered within ten working days. The monitor will contact the sites in case they do not adhere to these timelines. The monitor is also responsible for closing (signing off) the answered monitor queries in case of a valid response. Data management is responsible for



closing (signing off) all (non-monitor) answered queries in case of a valid response. A query must be closed or reissued within a week after the response.

10 PRINTING COMPLETED FORMS

To print completed forms navigate to: 'Research' → 'Data Collection', select the participant and visit/form from the data collection overview and click on the 'Print form' button. A pdf file will be created which you can print and/or save.

Fill out forms

Subject

Visit/Form group

Overview Deleted

 Edit  Print form ←

Form	Status	Open Query	ID1	ID2
CRF 1 ←	Completed	No		

[← Back to data collection overview](#)

The selected form is marked blue, click the 'Print form' button to create the pdf.

11 CREATING REPORTS

Reports show real live data available at the moment of running the report. Only the data that is accessible to the user is incorporated. The following default reports are available to users in RO:

- Inclusions: total number of inclusions
- Filled forms: total number of forms and their status (new, progress, completed)
- Queries: total number of queries

[Home](#) [Switch active study](#) [My Account](#) [Research](#) ▾ **Reporting** ▾

Reporting ▾

■ Inclusions

■ Filled forms

■ Queries

The numbers in the following report only describe data which you are actually allowed to see. Possibly there is more data available.

[↓ Export data to CSV](#) [📄 Export report to CSV](#)

To create a report showing the number of inclusions, click on 'reporting' and select 'Inclusions' (see above). A report is generated and shown automatically (see below).



The numbers in the following report only describe data which you are actually allowed to see. Possibly there is more data available.

Export data to CSV Export report to CSV

Study	Site	Number of inclusions
ArticPc	[All sites]	0

To export data or the report into excel click the 'Export data to CSV' or 'Export report to CSV' button.

12 AUDIT TRAIL

RO has an extensive audit trail that keeps track of all operations performed within the system. Per operation a date/time stamp, event type and the username are stored.

There are three levels of audit trailing:

- Subject level: e.g. inclusion date
- Form level: initial entry date, lock date related to database closure
- Item level

To see the audit trail on **subject level** navigate to: 'Research' → 'Subject'

Select the subject and press the 'View changes' button.

Subjects per site

Search Import subjects Lock all forms...

Site	Organization
UMC_G	
UMC_U	

Search New Edit Delete View changes

Subject no	Signed	Inclusion date	Start treatment	Site
UMC_G003	Yes	12/18/2012	12/18/2012	UMC_G
UMC_G004	No	12/18/2012	12/18/2012	UMC_G
UMC_G005	No	12/18/2012	12/18/2012	UMC_G
UMC_G006	No	2/7/2013	2/7/2013	UMC_G

Changes for subject

Subject UMC_G011

1 to 2 of 2

Entry date	Username	Event type
2013-03-25 10:19:09	jnurse2	Subject included
2013-03-25 10:19:51	jnurse2	Subject signed

Close

To see the audit trail on **form level** navigate to: 'Research' → 'Data Collection', select the subject and visit/form from the data collection overview and click on the 'View all changes' on the bottom of the form (for item level changes), or click on the spy glass button top right (for query, form status and lock/unlock changes).

Close View all changes

Status Query

Subject number U001

✖
Audit trail status

Last saved by

Last saved on

Status history

🔍 Search
1 to 6 of 6

Start date	End date	Username	Status	Locked	Delete
2013-04-11 03:35:22		jschotsman	Query	No	No
2013-04-11 03:34:50	2013-04-11 03:35:22	jschotsman	Completed	No	No
2013-03-24 01:19:30	2013-04-11 03:34:50	jschotsman	Completed	Yes	No
2013-03-20 04:25:25	2013-03-24 01:19:30	jnurse1	Completed	No	No
2012-12-18 07:58:16	2013-03-20 04:25:25	jschotsman	Progress	No	No
2012-12-18 07:57:55	2012-12-18 07:58:16	jschotsman	New	No	No

✖ Close

To see the audit trail on **item level** navigate to: 'Research' → 'Data Collection', select the subject and visit/form from the data collection overview and go to the item of interest.

Click on the 'Spy glass' sign to see the details of the history.

Gender 

Male 

Female 

Select the event type 'Changed Answer' to show the detailed audit trail.

✖
Audit trail question

🔍 Search
1 to 2 of 2

Entry date	Username	Event type
2013-03-26 09:23:25	jnurse2	Changed Answer
2013-03-22 09:47:32	jnurse2	Initial Data Entry

Previous value (if applicable)

Gender

Male

Female

Changed value

Gender

Male

Female

Reason for change

Reason

Explanation

✖ Close

13 HELPDESK

During working hours (Amsterdam, GMT+1) the data management department of the Julius Center in Utrecht will be available by email for all (technical) questions concerning the website and RO.

Response time will be within 24 hours and resolution time of easy fixable problems will be as soon as possible, and within 48 hours. The time to fix more difficult problems will be discussed with the issuer for each case separately.

In case of questions or problems concerning the eCRF, please e- mail: Chantal Hendriks:
C.Hendriks-4@umcutrecht.nl

The website has 24/7 monitoring tools implemented. In case the website is down an automated message will be generated to inform you and it will be fixed as soon as possible.