MRC Clinical Trials Unit

Smarter studies
Global impact
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UCL

UPLOADING TRIAL RESULTS TO EudraCT

VERSION 1.0

APPROVALS

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[redacted]	Statistician	[redacted]
Reviewer(s)	**Position**	**Signature**
[redacted]	Medical Statistician	[redacted]
Approver	**Position**	**Signature**
[redacted]	Senior Statistician	[redacted]

All appropriate approvals must have been completed prior to uploading to SOPbox.

UPLOAD TO SOPBOX

Name	Position	Signature	Date uploaded to SOPbox
[redacted]	SOPbox Administrator	[redacted]	14 Nov 2017

The effective date of this Working Instruction is the day on which it is uploaded to SOPbox and is available to use. This is the date associated with the signature of the SOPbox Administrator.

For the Revision History please see the Version History Summary in SOPbox.

UPLOADING TRIAL RESULTS TO EUDRACT

TABLE OF CONTENTS

Note: Glossary of terms, acronyms and abbreviations will be provided in a separate document for all SOPs and associated documents

The following symbols may be used in this WI:

Indicates a link to a related document

Indicates instructions to document trial-specific processes elsewhere

Throughout this document the MRC Clinical Trials Unit at UCL will be either referred to as, 'MRC CTU at UCL' or 'the unit'. In instances where neither read well in the sentence, 'the CTU' may be used.

1 BACKGROUND AND RATIONALE

Following the completion of a trial with a Clinical Trials Authorisation (CTA) within the European Union (MRC CTU SOP 003 – Regulatory Approval), results must be uploaded to the European Clinical Trials Database (EudraCT). Results must be uploaded within one year of the end of the trial as defined in the protocol (six months for paediatric trials). The amount of time required to obtain permission from EudraCT to upload results and the time needed to upload them should not be underestimated, and sufficient time for this to be completed within these timelines should be allowed. Obtaining permission to upload results should be done as far in advance as possible so as not to delay uploading results. Once uploaded and made public, results will be publicly available through the European Union Clinical Trials Register (clinicaltrialsregister.eu).

2 PURPOSE

The purpose of this WI is:

- To define the MRC CTU roles and responsibilities involved in uploading results to EudraCT.
- To outline the procedures for obtaining permission to upload results to EudraCT and enter results from a clinical trial on to the system.

This working instruction does not provide information on which results to upload as this will be trial-specific (decided by the Trial Statistician) but instead provides practical guidance on the process of uploading results.

3 RESPONSIBILITY AND ROLES

The following table lists the roles relevant to this WI and a brief description of their responsibilities.

ROLE	RESPONSIBILITIES

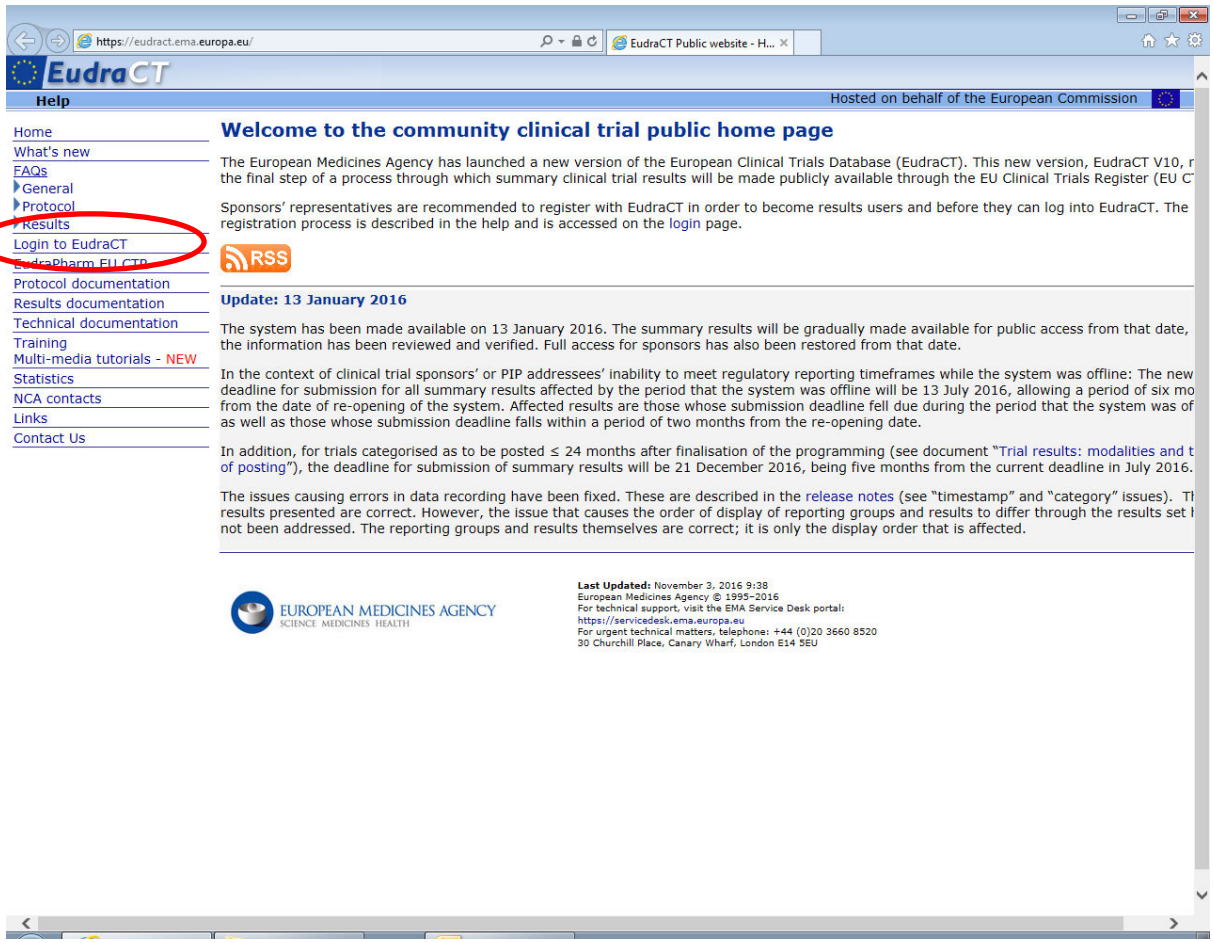
Trial Statistician	• Ensuring permission to upload results to EudraCT is obtained (by Sponsor, themselves or other TMG member)
	• Posting results
	• Circulating the PDF for checking by
	  ○ Trial manager/data manager (trial information)
	  ○ An appropriately experienced statistician other than the statistician who uploaded the results against the final statistical report
	• Approving making results public

Trial Manager/Data Manager	• Check trial information section of the PDF circulated by statistician. Raise any discrepancies with the statistician. The Trial/Data Manager is not responsible for checking results. This is the responsibility of an appropriately experienced statistician other than the statistician who uploaded the results

Throughout this document, Trial Statistician can be replaced with Delegated Statistician as appropriate.

4 PROCEDURES

The EudraCT system can be accessed at https://eudract.ema.europa.eu. Click "Login to EudraCT" (top left of screen):

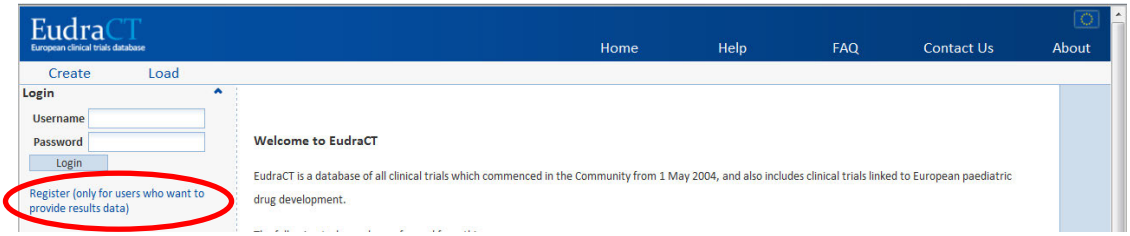


4.1 REGISTRATION AND BECOMING A RESULTS USER

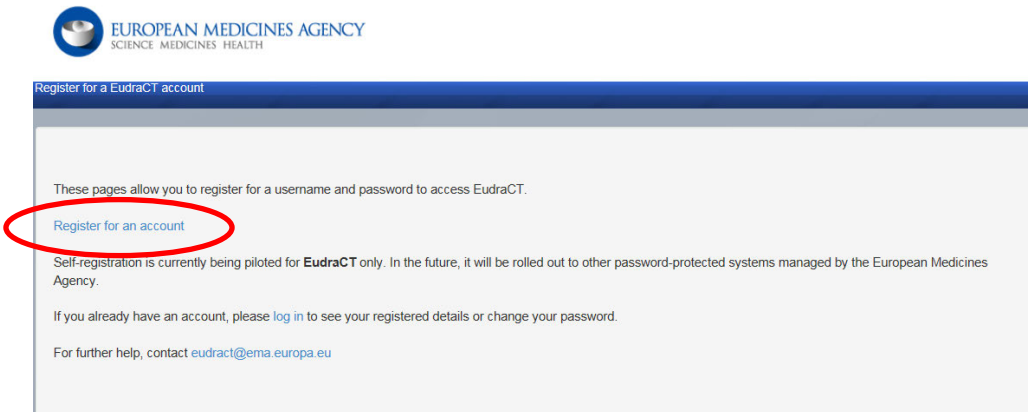
First time users need to register (section 4.1.1) and become a results user (section 4.1.2).

4.1.1 REGISTRATION

1. Click "Register" (top left of screen).



2. Click “Register for an account”.



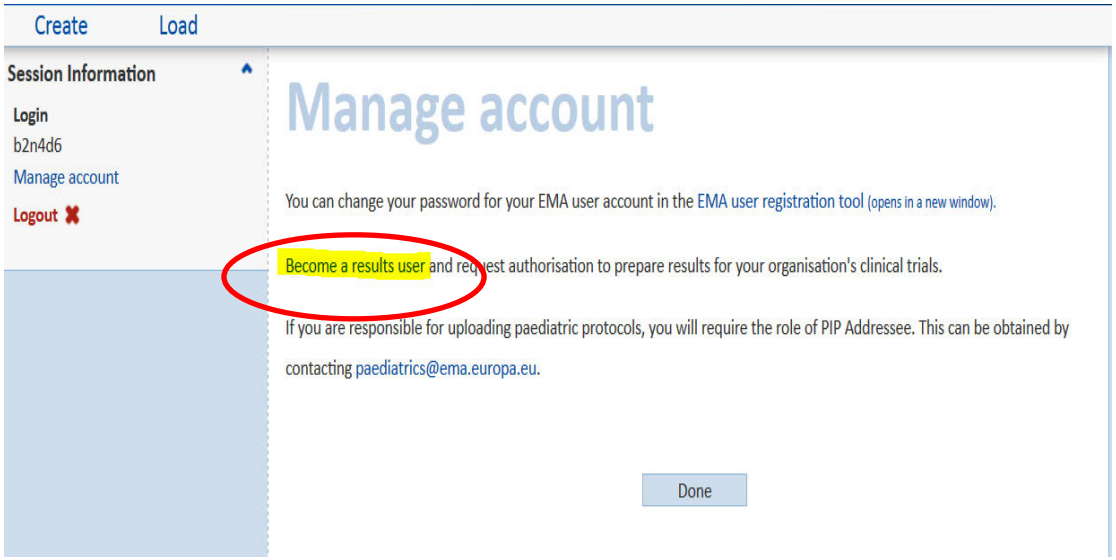
3. Accept terms and conditions.

4. Enter your MRC CTU at UCL details.

5. You will receive an email from the European Medicines Agency. Click the link, then you will receive a username and password.

4.1.2 BECOME A RESULTS USER

1. Login to EudraCT, using the username and password you acquired from section 4.1.1.
2. Click “Manage account”.
3. Click “Become a results user”.



4. Accept the terms and conditions.
5. Log out and back in for changes to take place.

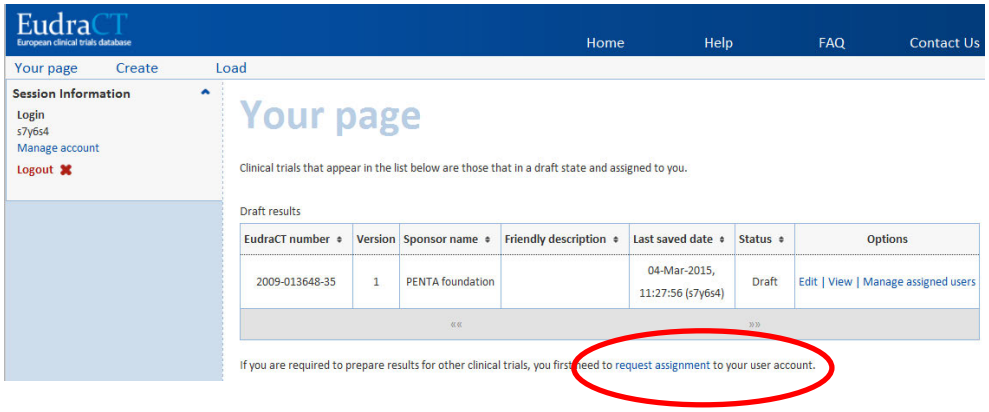
4.2 OBTAINING PERMISSION TO UPLOAD RESULTS FOR A SPECIFIC TRIAL

Once you are registered with EudraCT and a "results user," (if not, you need to complete Section 4.1 first) obtain permission to upload results for the specific trial:

1. The simplest way to obtain this permission is to upload a letter from the Sponsor of the trial. You will need this letter before logging on. A template letter can be found in MRC CTU TT 0416 – Letter to Obtain Permission from EudraCT to Upload Trial Results. The trial name in the letter must be the same as that registered with EudraCT at the beginning of the trial (this is usually as given in version 1.0 of the protocol). The letter must be **signed by hand** (for trials sponsored by MRC, this can be signed by the CTU Director) and converted to .pdf ready for uploading.

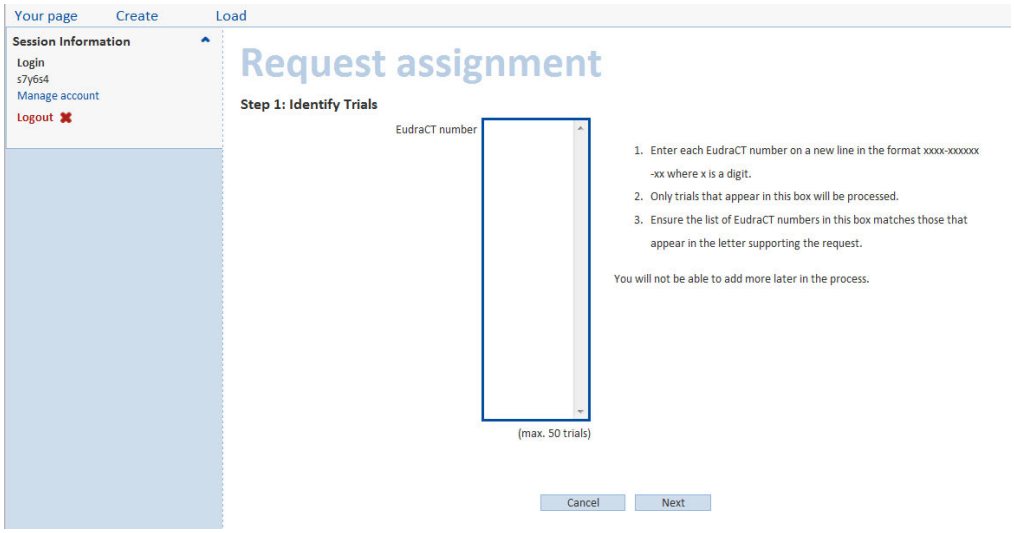
2. Log on.

3. You should see the following page (if not, click on "Your page" at the top of the page):



4. Click "request assignment".

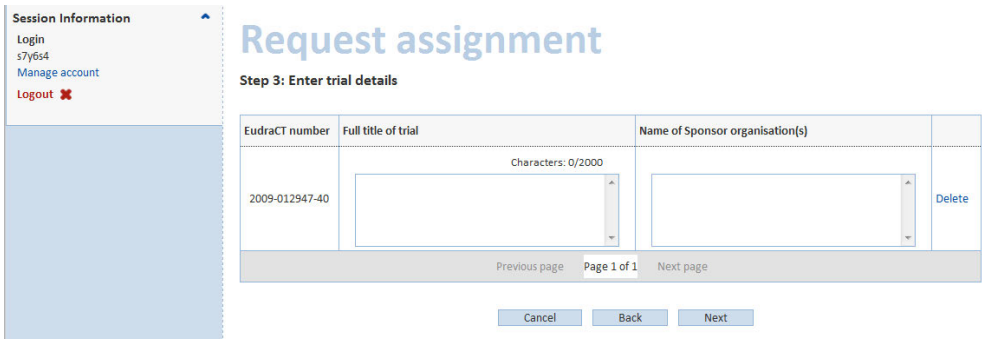
5. Enter the EudraCT number of the trial you need to upload results for:



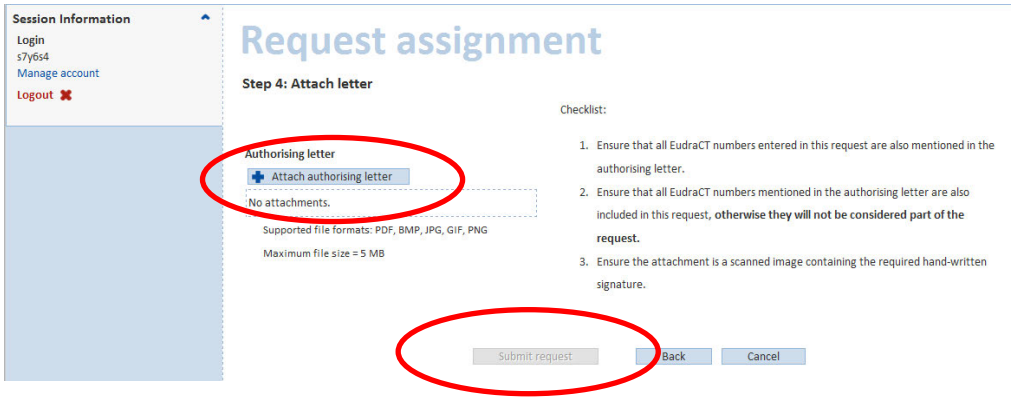
6. Click "Next".

7. Click “Request assignment to trials via letter”.

8. Enter the full title of the trial and the name of the Sponsor. Ensure the title of the trial is exactly that which the trial was registered with (usually the same as in version 1.0 of the protocol):



9. Attach the letter (in .pdf format) from (1) above:



10. Click “Submit request”.

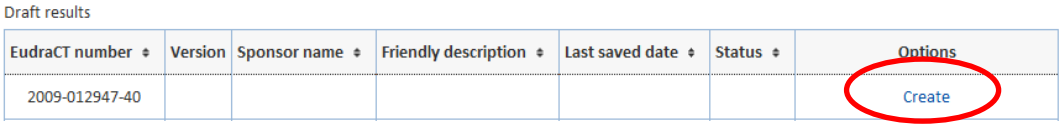
11. In due course you should receive an email from EudraCT letting you know your application to upload results has been successful.

12. Each user can assign one backup user and multiple delegated results preparers and posters for each trial. It is standard CTU practice not to use this facility, but to have one user for each trial. This user usually obtains permission to upload results towards the end of the trial (but in sufficient time), as staff can change over the course of a trial.

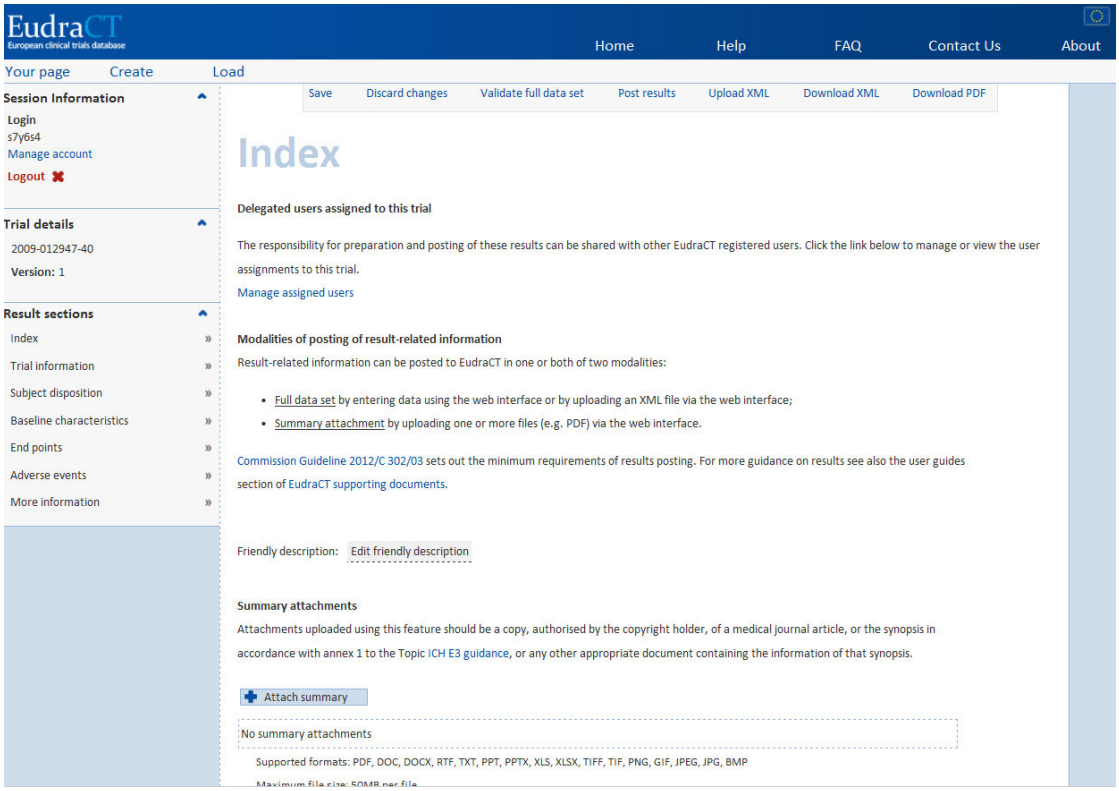
4.3 UPLOADING RESULTS

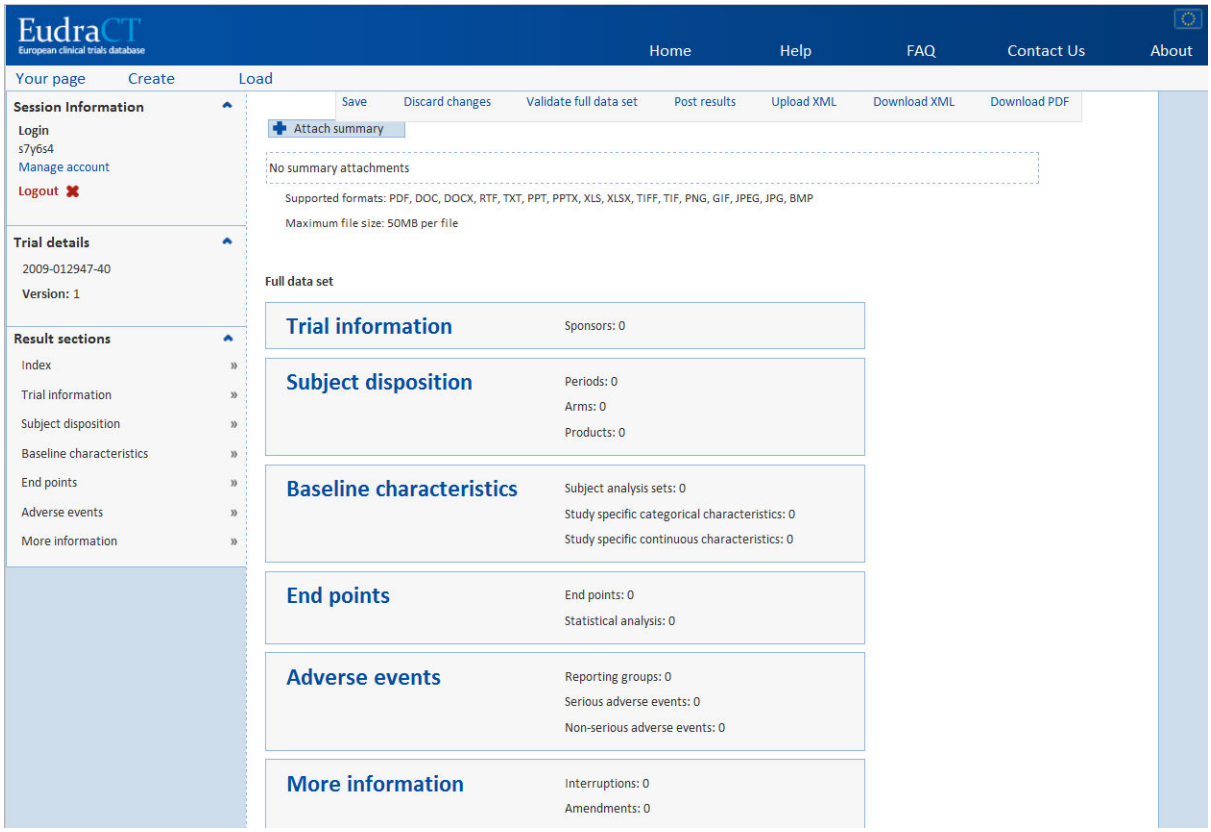
The data to be entered should be similar in breadth and depth to that reported in a final publication.

If you are not registered with EudraCT (Section 4.1.1), not a "results user" (Section 4.1.2) or do not have permission to upload results for the relevant trial (Section 4.2), you need to do this first. If you are registered with EudraCT, a "results user" and have permission to upload results for that trial, when you first log on you will see a screen like the following:



To add results, click on "Create". You will then enter the index page:





This is where trial information and results are uploaded, in the following sections: trial information, subject disposition, baseline characteristics, end points, adverse events and more information. Each of these will be described in the following sections of this working instruction.

On the index page, you have the option to enter a friendly description of the trial and also to attach a summary. It is usual CTU practice to NOT attach a summary, as the results to be included in this summary would be similar in breadth and depth to those requiring uploading separately in the following sections of this working instruction.

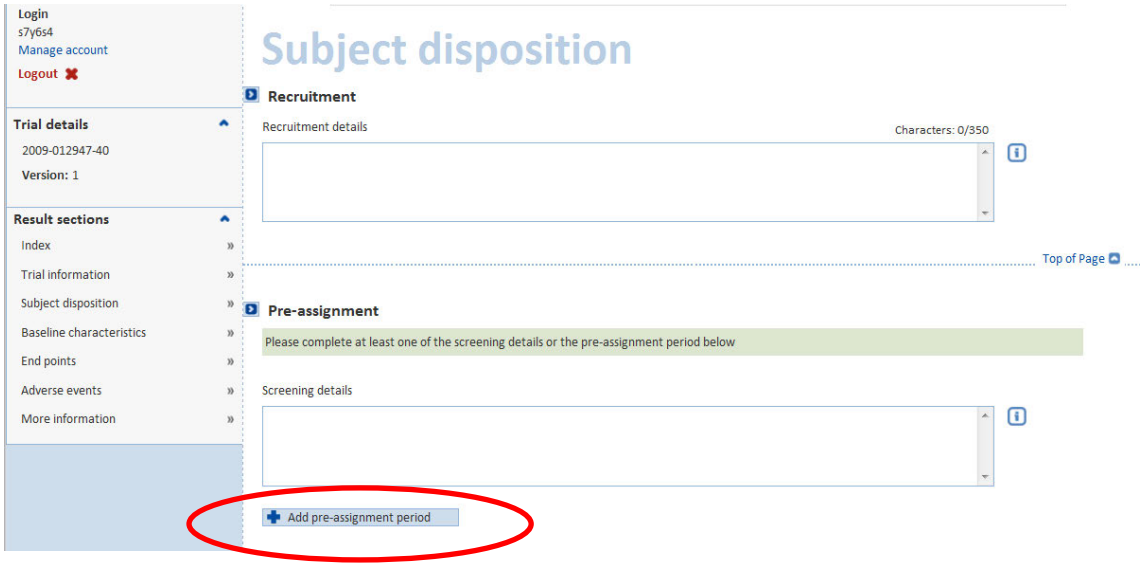
4.3.1 TRIAL INFORMATION

Some trial information, entered when the trial was being set up, may already be present in this section. Ensure all information is up-to-date.

4.3.2 SUBJECT DISPOSITION

In the EudraCT system, trials are composed of periods (e.g. screening/pre-assignment, main trial).

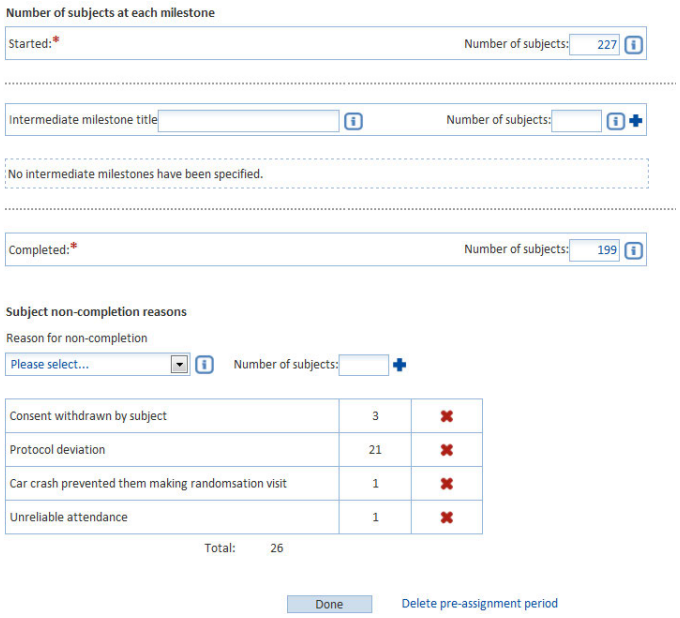
1. First of all, enter details of the screening period. In the EudraCT system, this is referred to as the pre-assignment period, so click on “Add pre-assignment period”:



a. Enter the number of patients screened in the "Started" section.

b. If there are any intermediate milestones in the screening-randomisation period, then you can enter what they were and how many subjects completed follow up until each milestone (usually not applicable at CTU).

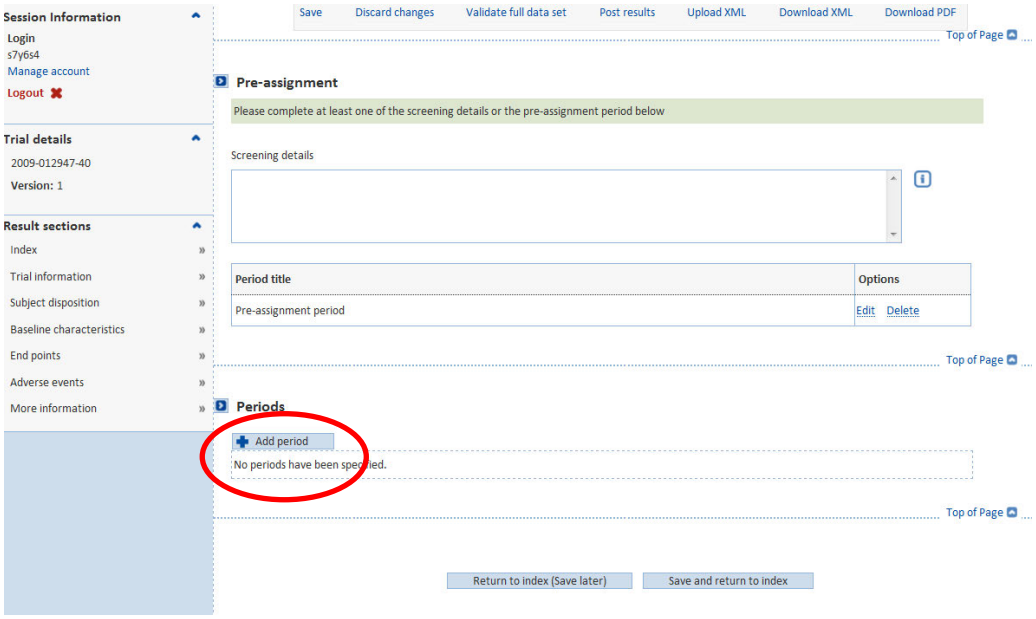
c. "Completed" is the total number randomised, so enter the total number randomised, as well as any reasons for not randomising. For example for a trial that screened 227 patients and randomised 199:



d. Click "Done".

2. Enter subsequent periods (e.g. main trial) by repeating (a) – (f) below:

   a. Click “Add period”:

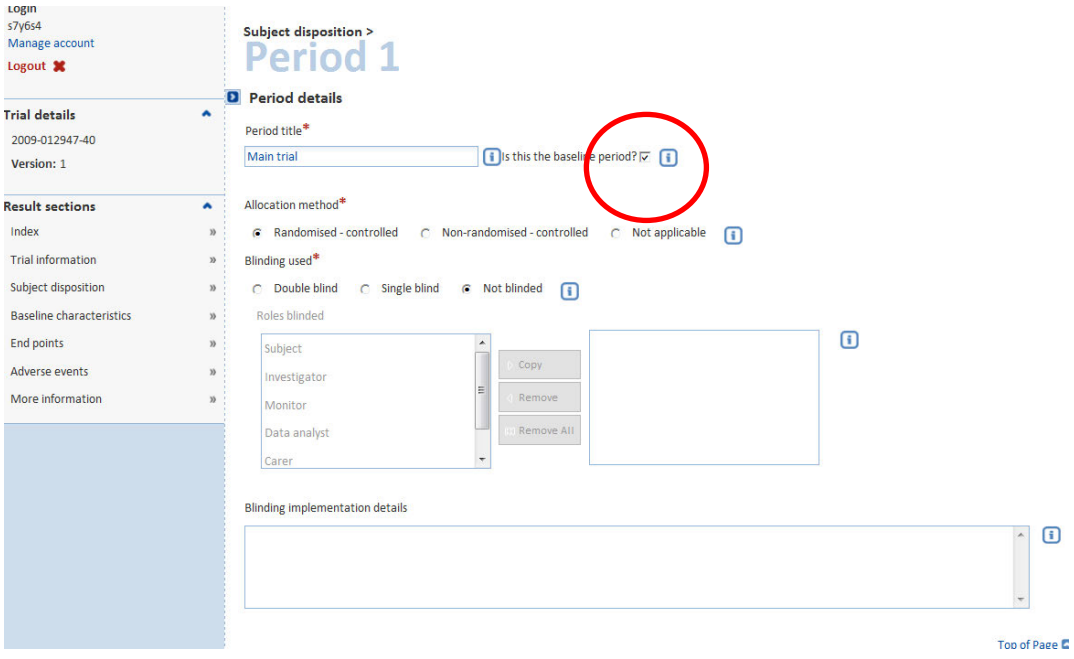


   b. Enter the name of the period that you are defining (e.g., “Main trial”).

   c. If this is the first/only period (excluding the screening/pre-assignment period), tick “Is this the baseline period”. The baseline period is the period for which baseline characteristics will be reported.

   d. Enter allocation method (usually, “Randomised - controlled,” at CTU).

   e. Enter details on blinding.



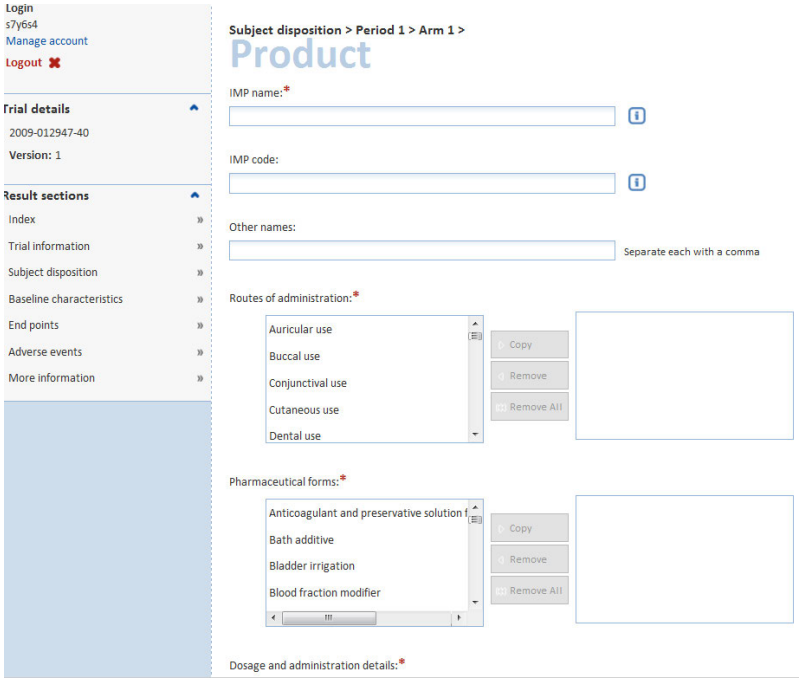
f. Enter arms by repeating (i) – (iv) below:

i. Click “Add arm”:

ii. Add the name and description of the arm, as well as specifying whether it is an intervention arm or otherwise.

iii. Enter medicinal products by repeating (i) – (iii) below:

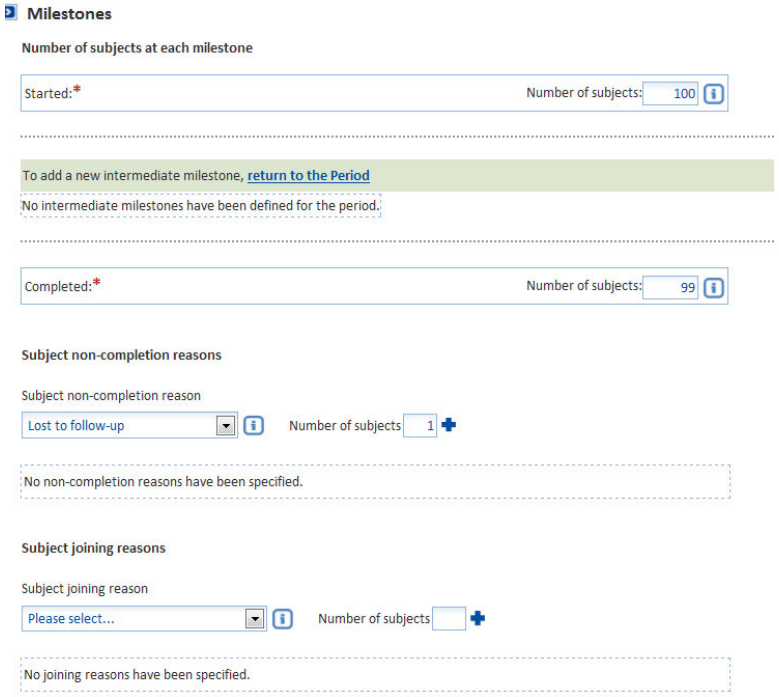
i. Click “Add product”, which will take you to the following screen:



ii. Fill in as much information as possible. Take particular care with route(s) of administration, pharmaceutical form(s) and dosage.

iii. Click on “Done”.

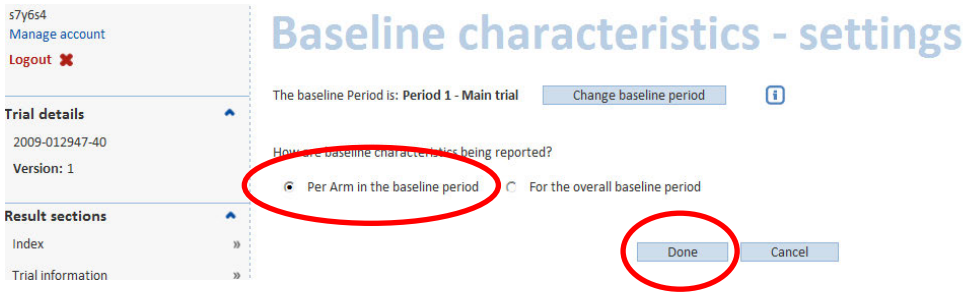
iv. Scroll down to “Milestones” where you can enter the number of patients that started the arm, how many finished it and non-completion reasons (e.g. lost to follow up/withdrew consent). For example for an arm which had 100 people randomised but had one lost to follow up by the end of the period:



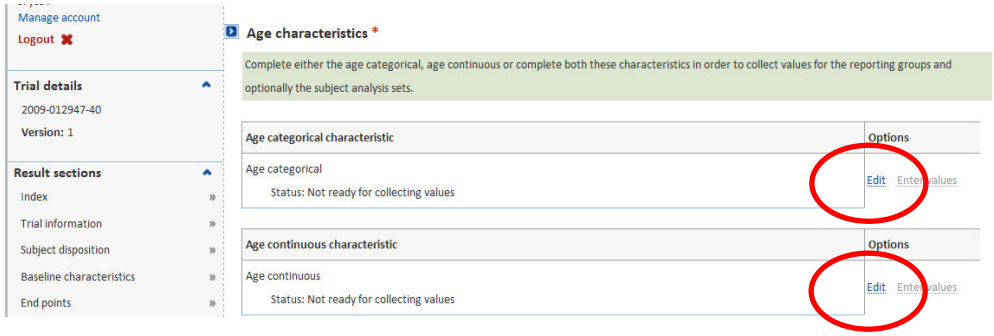
4.3.3 BASELINE CHARACTERISTICS

Baseline characteristics are reported for the baseline period defined in Section 4.3.2.

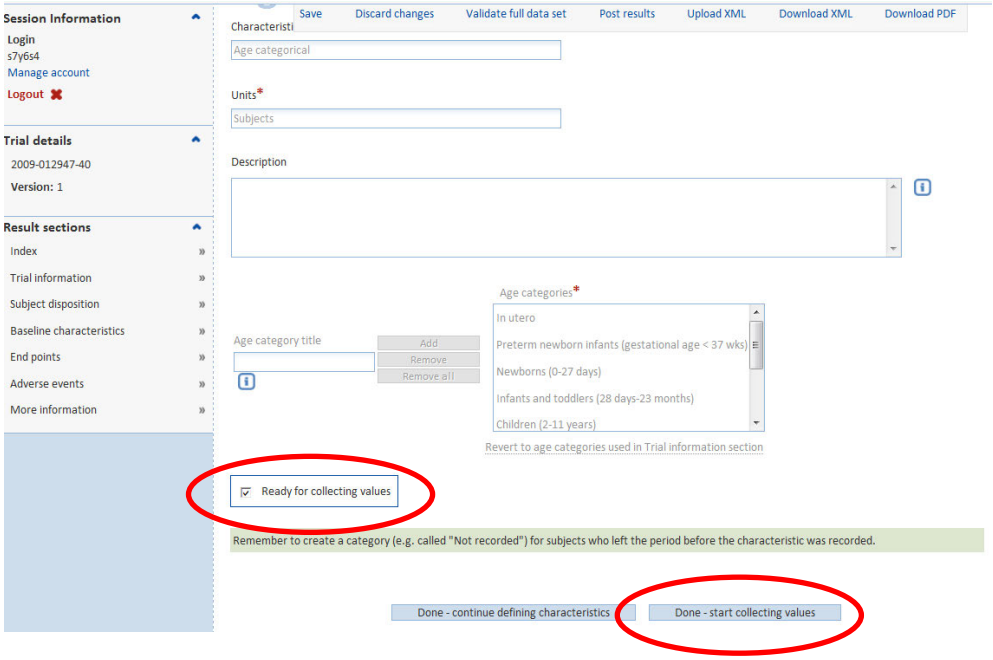
1. Choose whether you would like to report the baseline characteristics by arm or overall (it is usual CTU practice to report baseline characteristics by arm):

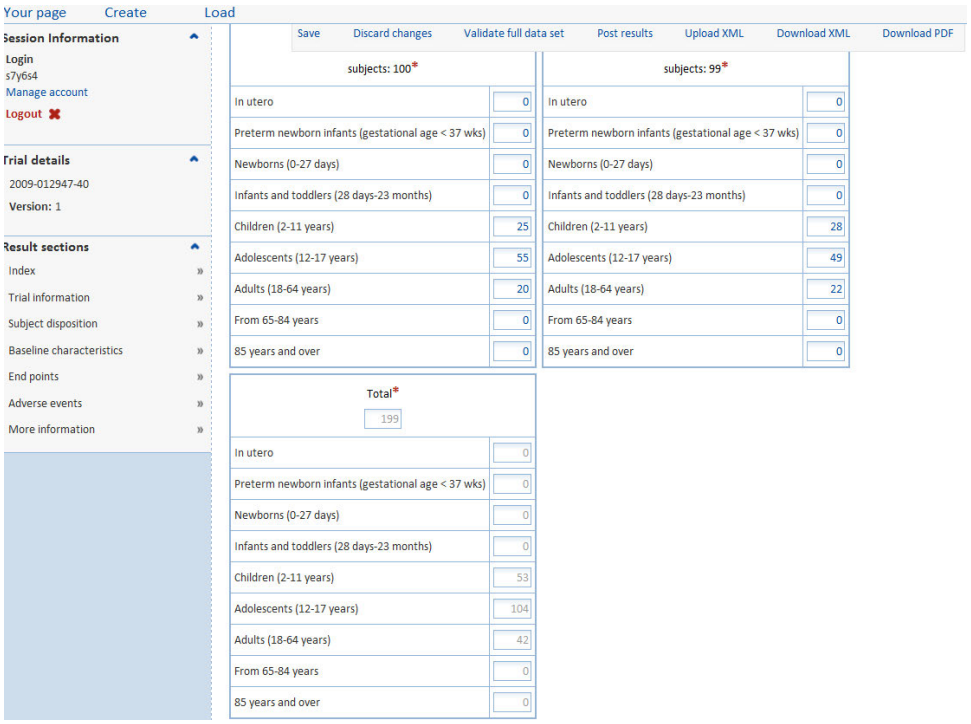


2. Age characteristics:

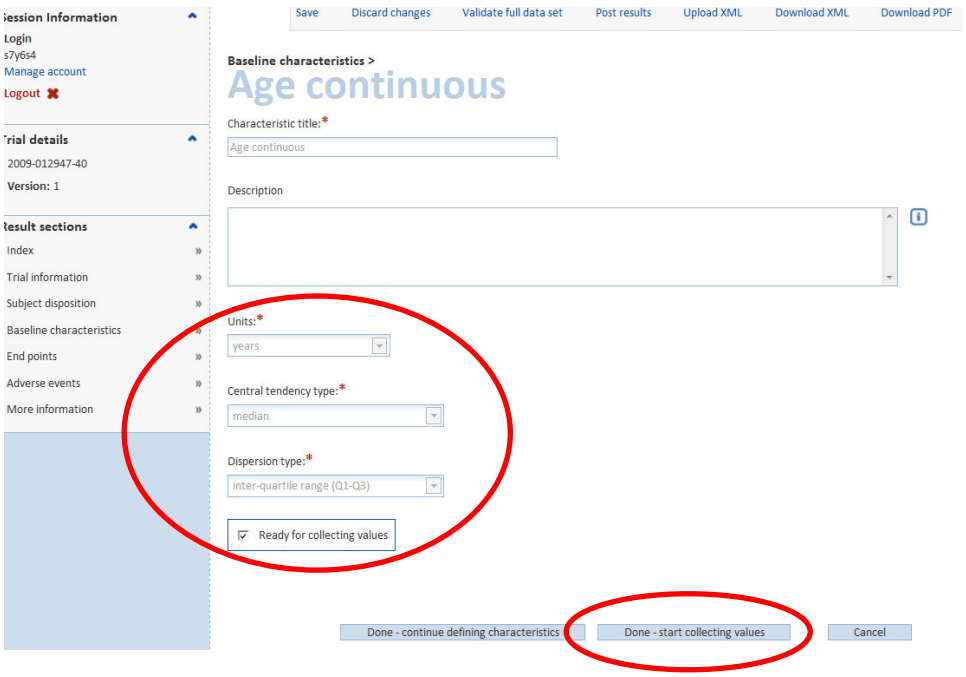


a. Age categorical characteristics: you will see a list of specific age categories (in utero, preterm newborn infants, newborns, infants and toddlers, children (2 – 11 years), adolescents (12 – 17 years), adults, from 65-84 years, 85 years and over). Tick "Ready for collecting values" and click "Done – start collecting values". Enter values carefully:





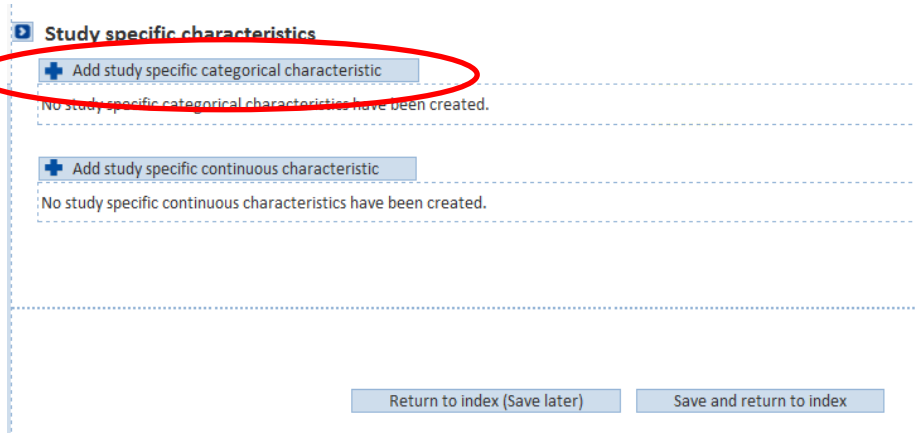
b. Age continuous characteristic: select which units (years), the summary statistic (central tendency type, e.g. median) and measure of spread (dispersion type, e.g. inter-quartile range) you are reporting. As before, tick "Ready for collecting values" and click "Done – start collecting values"

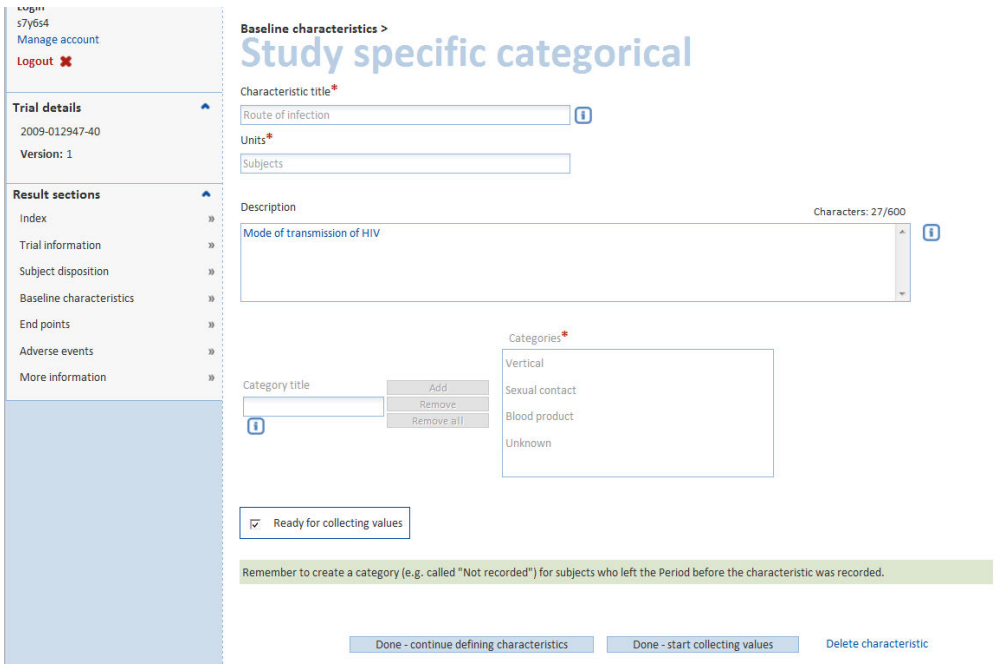


3. Gender characteristics (categorical). As per age categorical characteristics, tick "Ready for collecting values" and click "Done – start collecting values".

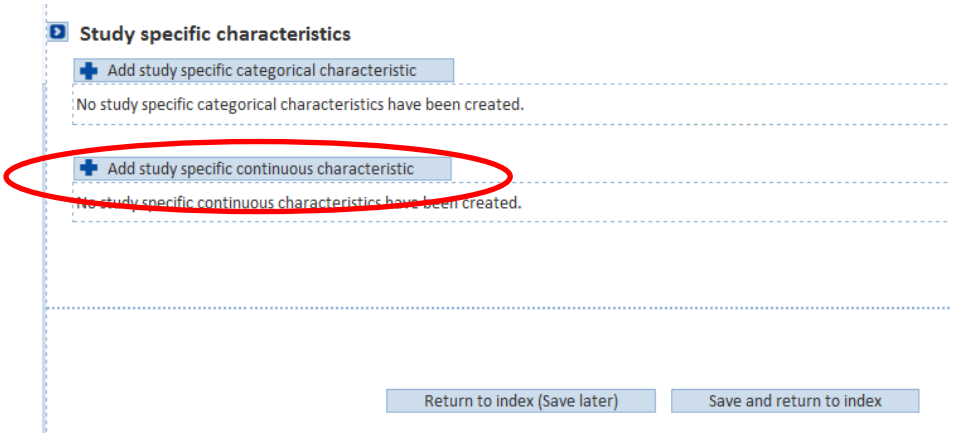
4. You should then add study specific characteristics, for example, those in the overall baseline table for the study. There are likely to be many of these.

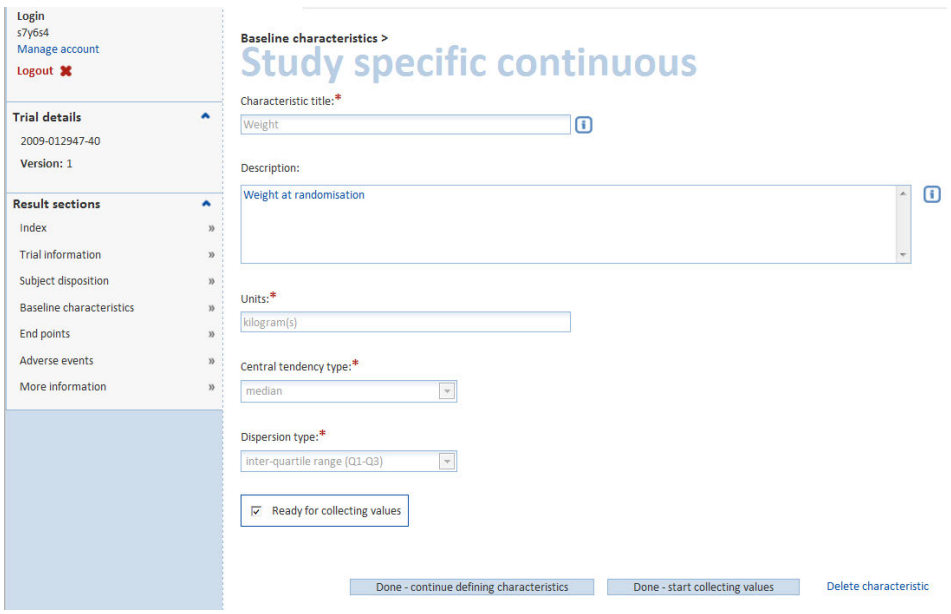
    a. For a categorical variable, click "Add study specific categorical characteristic". Add categories (remember to create a category – e.g. called "Not recorded" – for any subjects for whom the characteristic was not recorded), tick "Ready for collecting values" and click "Done – start collecting values":





b. For a continuous variable, click “Add study specific continuous characteristic”. Select the summary statistic (central tendency type) and measure of spread (dispersion type) you will be reporting, tick “Ready for collecting values” and click “Done – start collecting values”

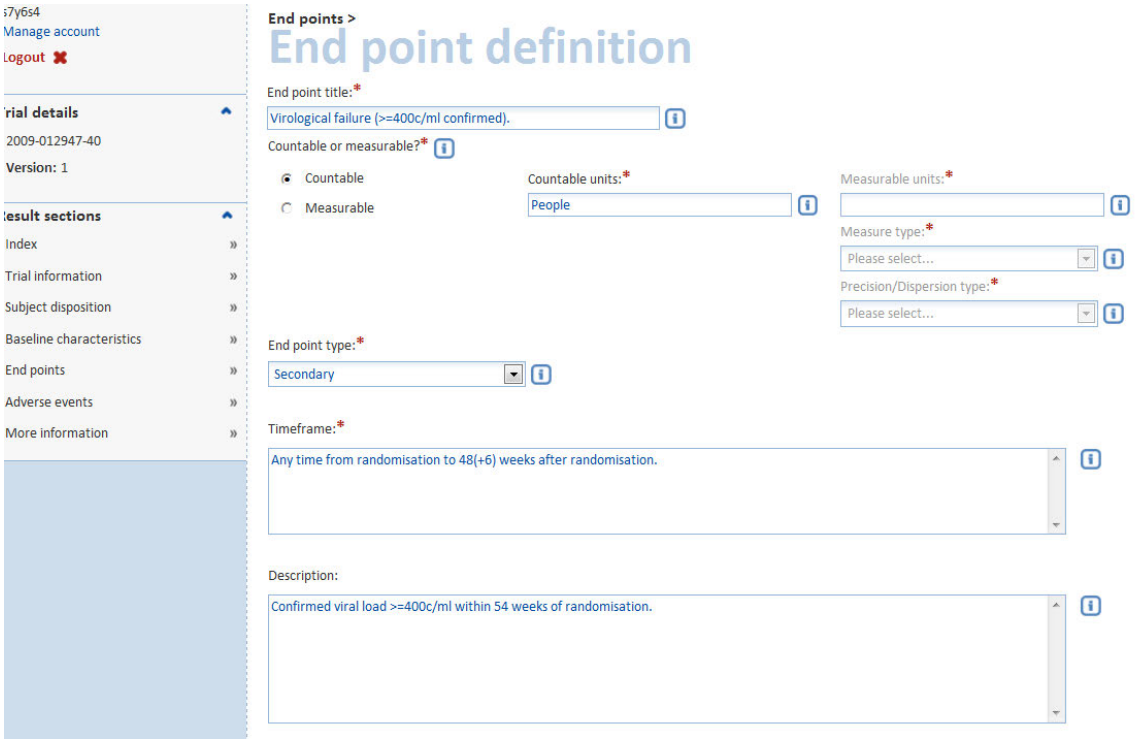




4.3.4 END POINTS

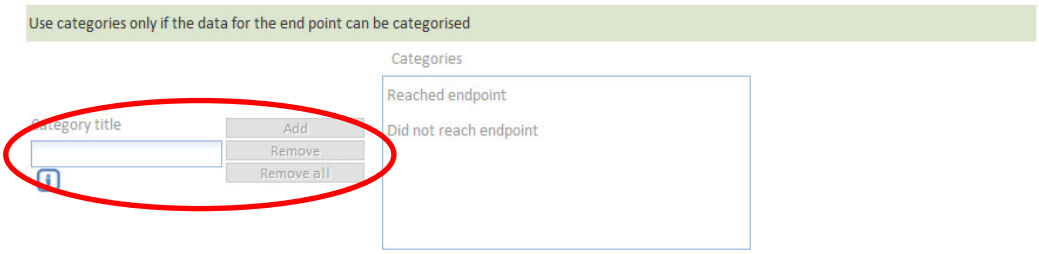
1. Click “Add end point”.

2. Enter endpoint title, whether it is countable or measurable (*either* countable *or* measurable must be selected), units (if measurable, measure and precision/dispersion types must also be selected), whether it is primary/secondary/other/post-hoc and the time frame (e.g. “any time from randomisation to 48 weeks after randomisation”). The optional description field should be used if the full definition of the endpoint is not completely clear from the other details entered.



3. If the data for the end point can be categorised, add categories (e.g. “Reached endpoint”, and “Did not reach endpoint”, but more descriptive names can also be used). Create a

category – e.g. called “Not recorded” – for any subjects for whom the end point was not recorded.

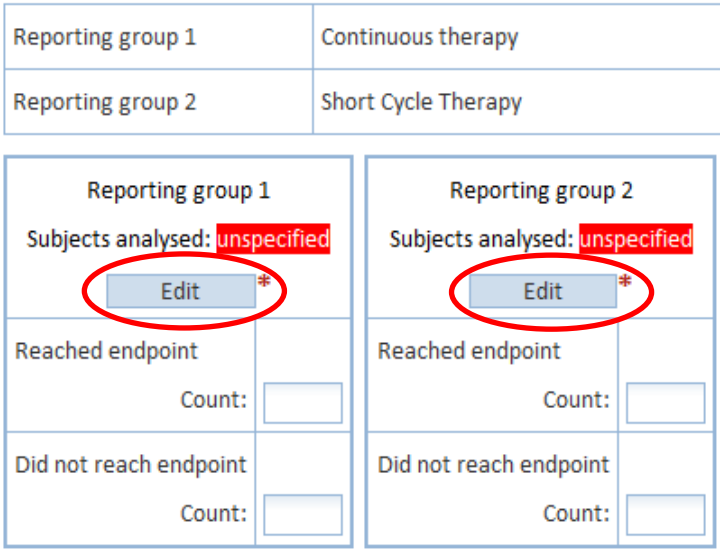


4. Select the periods and arms (as defined in Section 4.3.2 – Subject Disposition) you will be reporting for:

5. Tick “Ready for collecting values”.

6. Click “Done – start collecting values”

7. Enter values carefully. For each period/arm, first specify the number of subjects analysed. For a countable end point, enter the number of individuals in each period/arm that are in each category defined in (3) above:

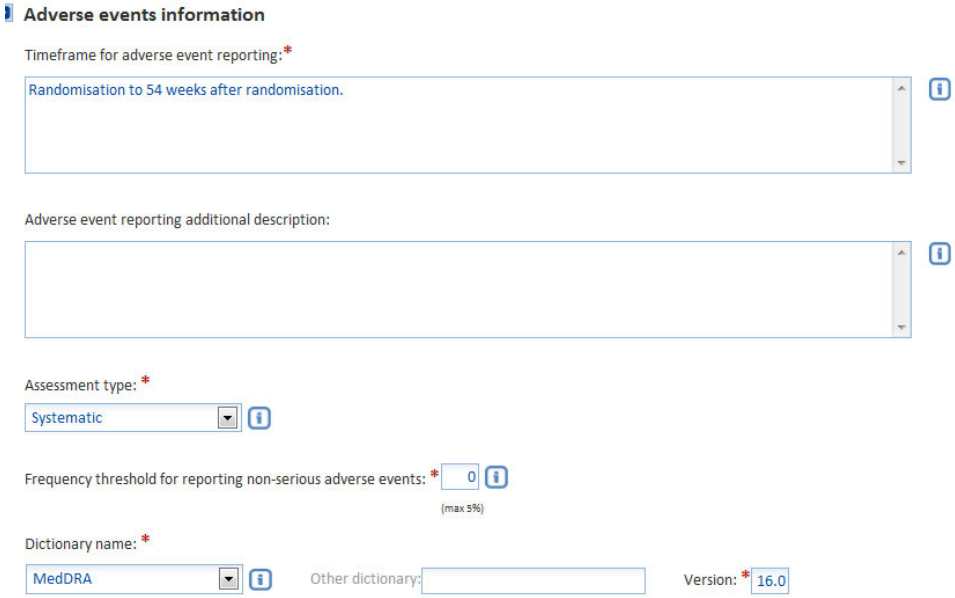


8. You will then have the option to add some statistical analyses for the endpoint. You must add one at a time and follow the self-explanatory guidance after clicking in “Add statistical analysis”.

4.3.5 ADVERSE EVENTS

Serious adverse events (SAEs) and non-serious adverse events are reported separately.

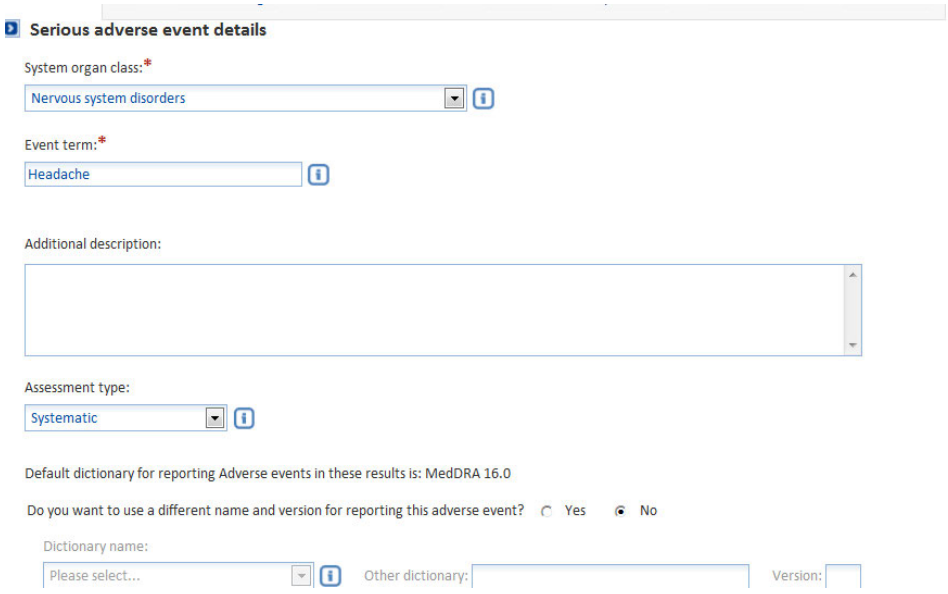
1. Enter in the overall timeframe for adverse event reporting in the trial (e.g. “any time from randomisation to 48 weeks after randomisation”), assessment type (systematic/non-systematic), threshold frequency for reporting non-serious adverse events (all = 0), dictionary name (e.g. MedDRA) and version:



2. Serious adverse events:

   a. Click “Add serious adverse event”.

   b. For example for the serious adverse event of headache, enter the system organ class and event term (e.g. as per MedDRA dictionary) and assessment type (systematic/non-systematic):



c. Subjects affected = number of subjects with one or more event; subjects exposed = number of subjects; occurrences = number of events; occurrences causally related to treatment = number of events causally related to treatment; fatalities = number of fatalities; fatalities causally related to treatment = number of fatalities causally related to treatment. For example, 3 events in 2/100 subjects would be entered as 2 subjects affected, 100 subjects exposed and 3 occurrences. If 0/3 occurrences were causally related to treatment, occurrences causally related to treatment would be entered as 0. 0 fatalities would be entered as 0 fatalities and 0 fatalities causally related to treatment.

Values for serious adverse event per reporting group *

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number	Occurrences causally related to treatment number	Fatalities number	Fatalities causally related to treatment number
Continuous therapy	0	100	1	0	0	0
Short Cycle Therapy	1	99	0	0	0	0

3. Non-serious adverse events:

a. Click “Add non-serious adverse event”.

b. For example for the non-serious adverse event of measles, enter the system organ class and event term (e.g. as per MedDRA dictionary) and assessment type (systematic/non-systematic):

Non-serious adverse event details

System organ class:*

Infections and infestations

Event term:*

Measles

Additional description:

Assessment type:

Systematic

Default dictionary for reporting Adverse events in these results is: MedDRA 16.0

Do you want to use a different name and version for reporting this adverse event? Yes No

Dictionary name:

Please select... Other dictionary: Version:

c. Subjects affected = number of subjects with one or more event; subjects exposed = number of subjects; occurrences = number of events. For example, 3 events in 2/100 subjects would be entered as 2 subjects affected, 100 subjects exposed and 3 occurrences.

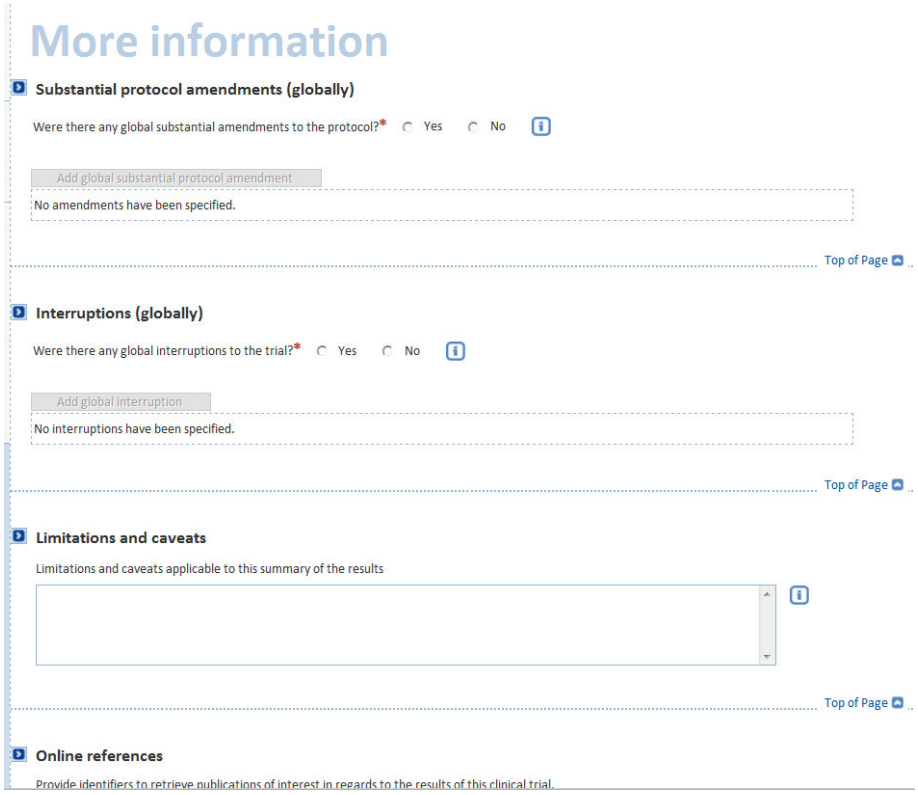
Values for non-serious adverse event per reporting group *

Threshold for non-serious adverse event reporting is: 0%

Reporting groups	Subjects affected number	Subjects exposed number	Occurrences all number
Continuous therapy	0	100	0
Short Cycle Therapy	1	99	1

4.3.6 MORE INFORMATION

Enter whether there were any global substantial amendments to the protocol, interruptions to the trial, limitations and caveats applicable to this summary of results and references to publications of interest in regards to the results of this clinical trial.



4.4 CHECKING TRIAL INFORMATION AND RESULTS

Return to the index page (Section 4.3) and download a PDF of all the trial information and results (in the top-right hand corner of the screen). As per Section 3 (responsibility and roles), an appropriately experienced statistician other than the statistician who uploaded the results is responsible for checking results from the PDF against the final statistical report (raising any discrepancies with the statistician who uploaded the results). The Trial Manager/Data Manager is responsible for checking the trial information section of the PDF (raising any discrepancies with the statistician who uploaded the results). The Trial/Data Manager is not responsible for checking results.

4.5 APPROVING MAKING RESULTS PUBLIC

Every effort should be made to ensure the main trial results are published (in the public domain) prior to posting the results on the EudraCT website. When the uploaded results have been checked and amended as necessary, go to the index page (Section 4.3) and click, “post results,” (top of the screen). Follow the instructions.

Once the results have been uploaded, ask your Trial Manager to send a short confirmatory email to CT.Submission@mhra.gsi.gov.uk, with ‘End of trial study report: EudraCT XXXX-XXXXXX-XX’ as the subject line (MRC CTU SOP 014 – Trial Reporting and Communication).