Title	2R2 website: site user's manual
SOP Code	2R2 SOP20_08Sep2020
Effective Date	15 September 2020

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1.0 Purpose(s)

The objective of this standard operating procedure (SOP) is to ensure users at study sites and at the coordinating center can correctly use the study website, for collection of study participants' data.

The SOP will ensure:

- data are collected in compliance with the standards of Good Clinical Practice and the study protocol;
- the safety and protection of study participants, as communication of adverse events is also done through the use of the study website;
- the quality of the data produced by the study.

2.0 Scope: Persons affected

This SOP concerns: coordinating center, site principal investigators, site coordinators and site research teams involved in conducting research with human subjects for the study entitled -$2R^2$ *Higher dose Rifampin for 2 months vs Standard dose Rifampin for Latent TB: a 3-arm randomized trial.*

3.0 Responsibilities.

The trial coordinating center is responsible for developing and maintaining this SOP and for making it available at the clinical research site. At the clinical trial site, the site principal investigator is responsible for adoption of the processes described in the SOP.

4.0 Definition(s) and abbreviations

I. **AE:** Adverse event

II. **ATB:** Active TB

III. **Case Report Form (CRF)**: A printed, optical, or electronic document designed to record all of the protocol required information to be reported to the coordinating center on each trial participant in this research study.

IV. **Coordinating centre:** research staff involved in running the $2R^2$ study who are based at Research Institute of McGill University Health Centre (RI-MUHC)

V. **CXR:** Chest x-ray

VI. **eCRF**: the electronic version of CRF. eCRFs are in the 2R2 website.

5.0 Procedures

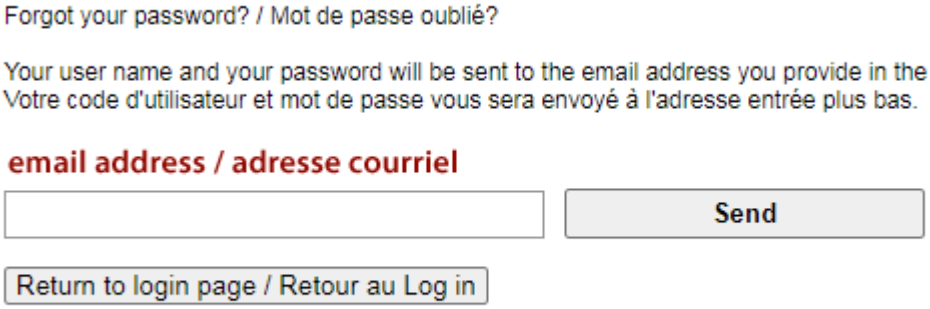
5.1. Procedures to access the 2R2 online database

Access the database using an internet browser.

1. Open an Internet browser. Please use **Google Chrome**, as this is the preferred browser for 2R2 database.
2. Enter the URL https://2r2.crc.chus.qc.ca/

At the first access:

1. Enter your username. Your username have been assigned to you by the coordinating center. Please contact the coordinating center if you do not have an username.
2. Click on "Forgot your password? / Mot de passe oublié?" (**figure 1**)



This window will appear,
Type your work email (the one the coordinating center uses to contact you) and you will receive an email with your password.

For all subsequent accesses:

1. Open an Internet browser. The preferred browser for 2R2 database is Google chrome, please use this one if possible.
2. Enter the URL https://2r2.crc.chus.qc.ca/
3. Type your username
4. Type your password
5. Click on the "Log in" button

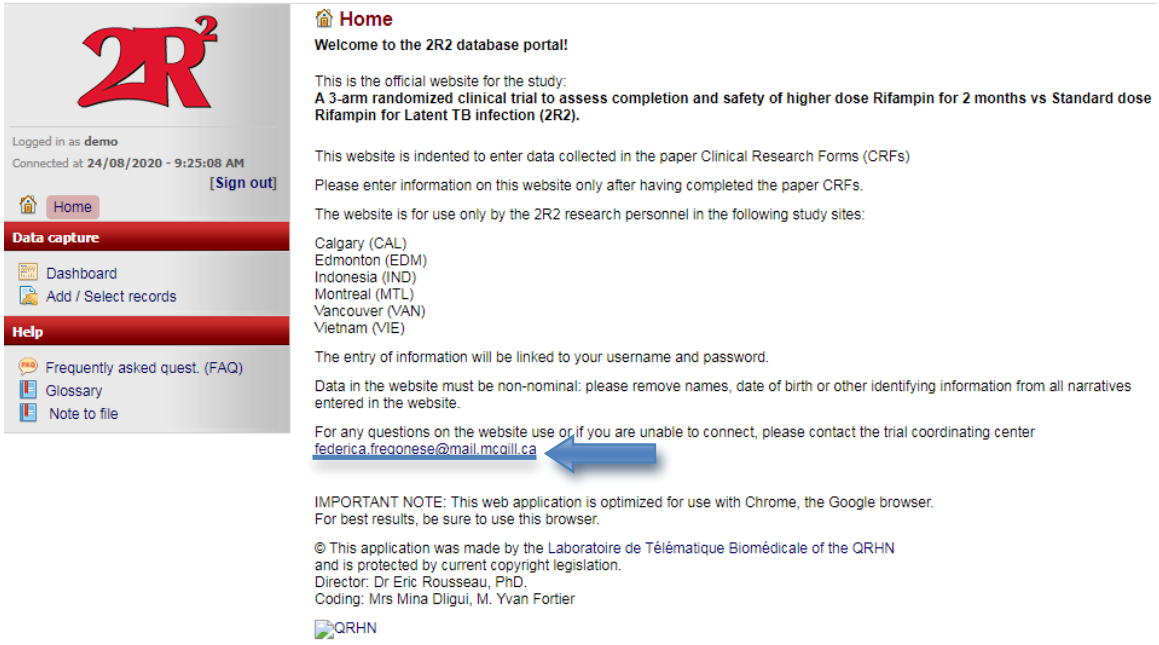
Figure 2

Note: data entered in the 2R2 website are linked to the username of person entering that case report form for the first time. Please do not share your password with anyone.

5.2 General information on the main page

Once you completed the login to the website, you will see the home page (**figure 3**)
From that page you can also have access to the contact for the coordinating center.

Figure 3



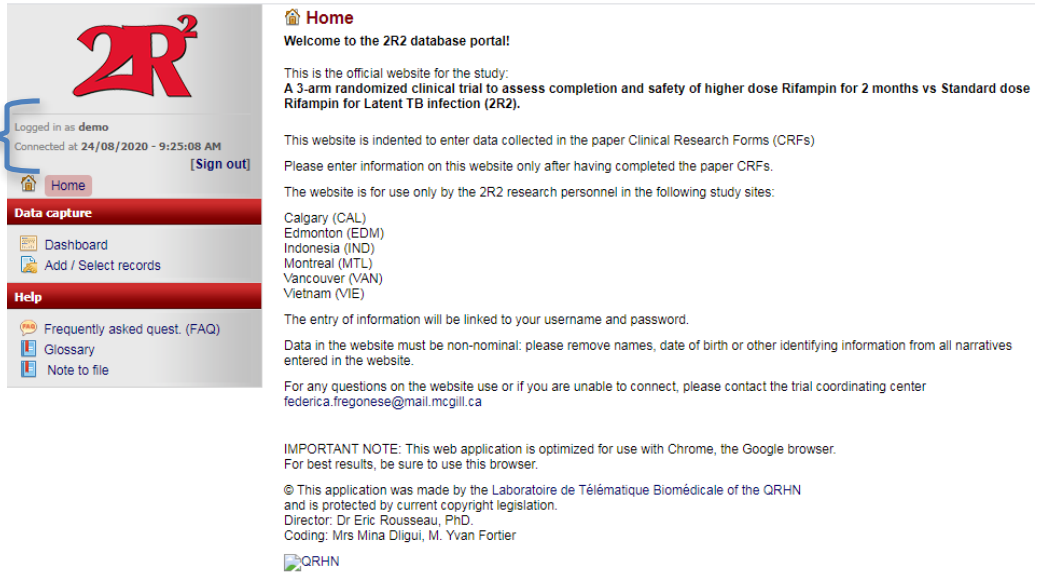
Once you are into the website, you will see on the top left menu, under the study logo, your name, date and time. You can also sign out/disconnect at any time. You will be disconnected form the website after 20 minutes of inactivity. (figure 4)

Figure 4

-Name of the person who is connected

-date and time of connection

-sign out-disconnect



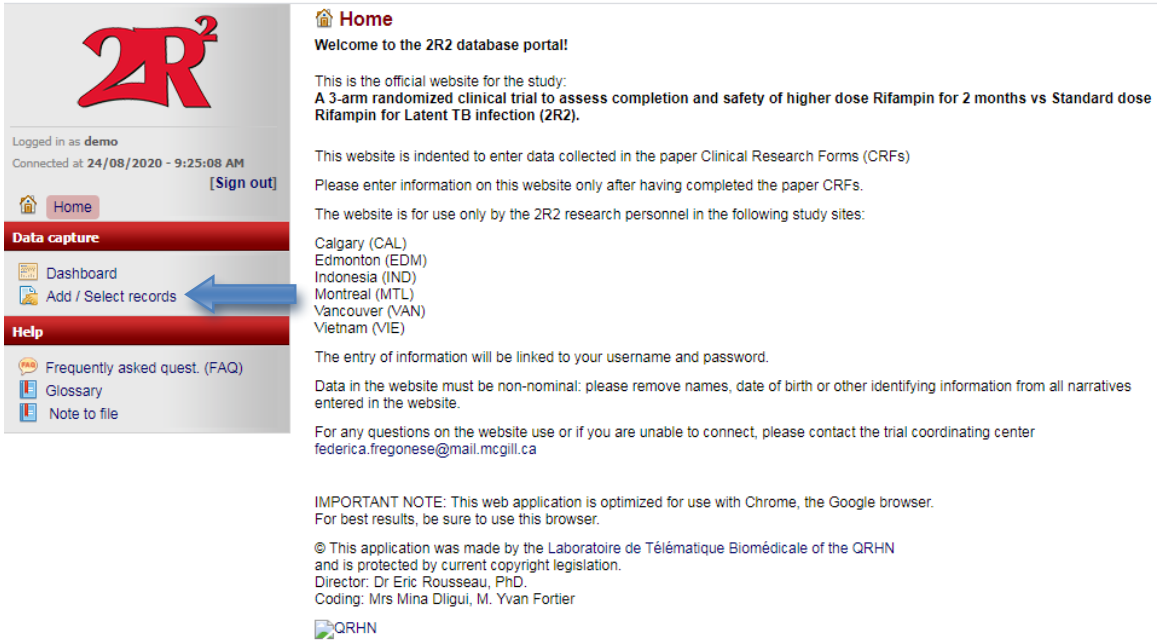
5.3 Use of the website for site user

Site users are the site research coordinators at each study site, unless not differently agreed between site PI and coordinating center.
A site user can enter, review and modify only information for participants of that study sites.
Note: remind to fill in the CRF in the 2R2 website only after having completed the paper CRFs.

5.3.1 Access to the main participant table

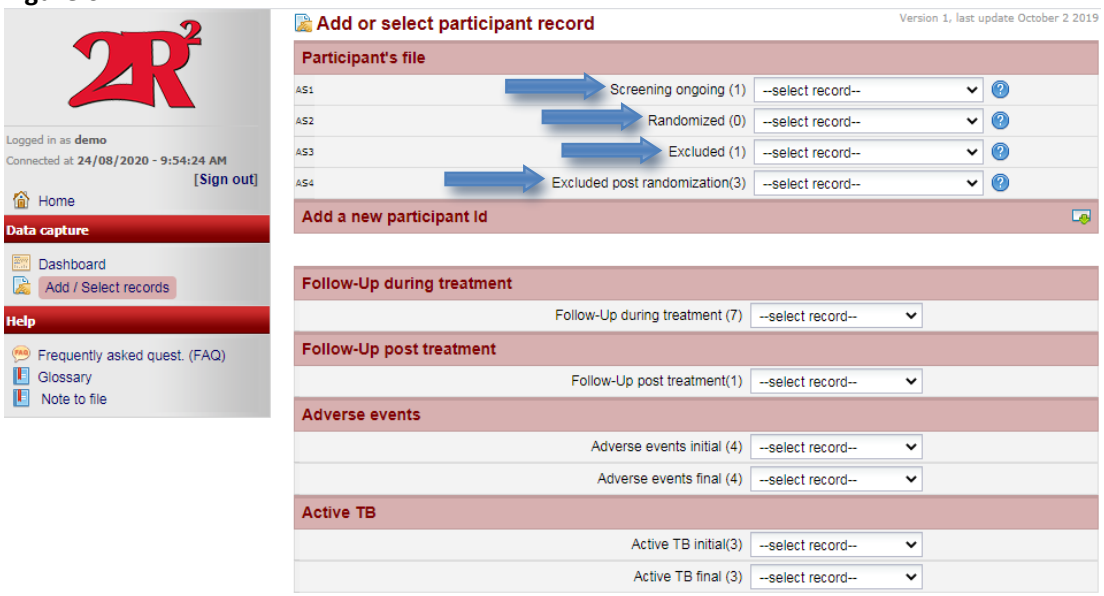
If you want to review a participant's file or if you want to add a new participant, click on "**Add/select records**" in the left menu (**figure 5**)

Figure 5



It will bring you to the main table to have access to the following lists of all participants' files of your site: (**figure 6**)

Figure 6



Participants are here classified as

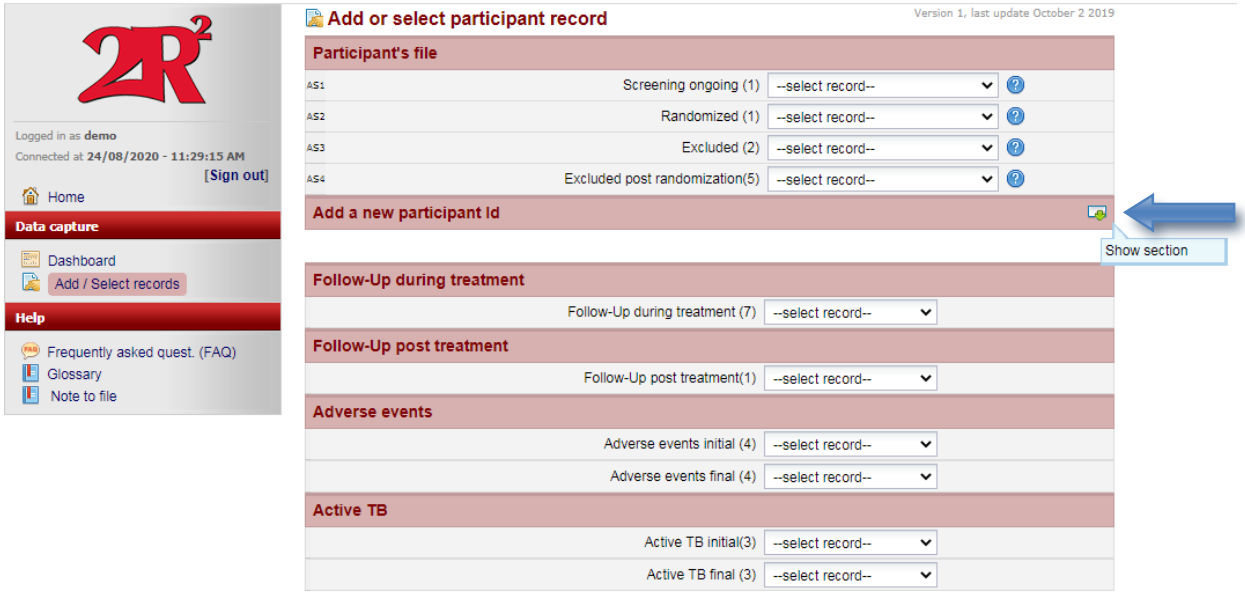
- Screening ongoing - if they have started screening but did not complete it yet (i.e. they have started any parts of **CRF1**, **2** or **3** but they are not ready to be randomized yet);
- Randomized;
- Excluded (i.e. **CRF1**, **2** or **3** clearly met one of the exclusion criteria before randomization);
- Excluded post randomization (i.e. one of the exclusion criteria have been known after randomization took place and coordinating center has agreed to consider the participant "excluded after randomization").

You can click on the questions marks to see the meaning of these categories.

5.3.2 How to create a new participant ID

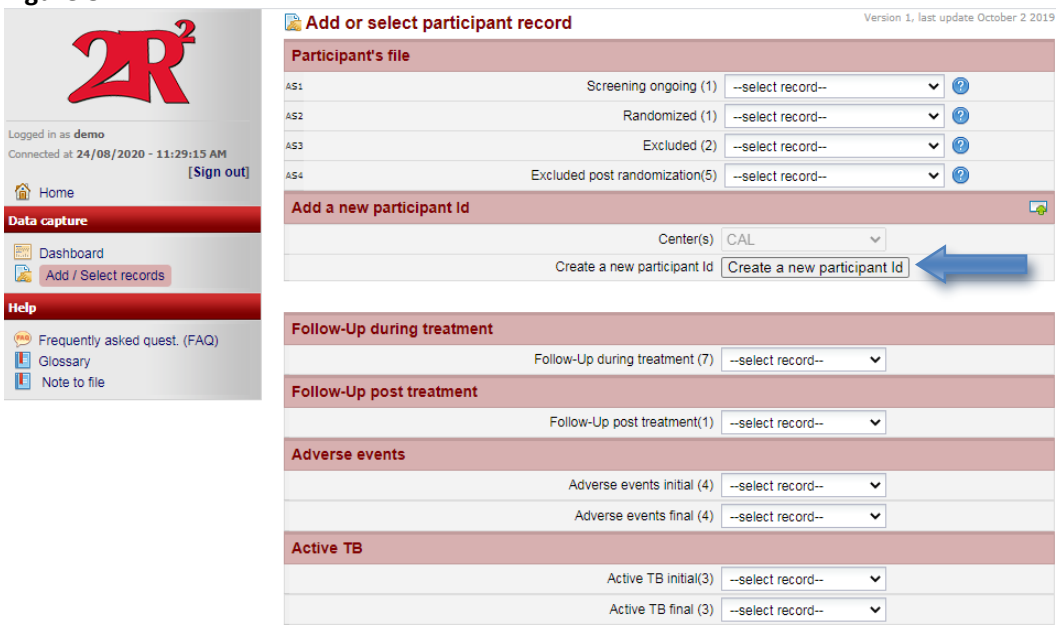
To add a new participant, click on "**show section**". You will have access to create a new participant ID (**figure 7).**

Figure 7



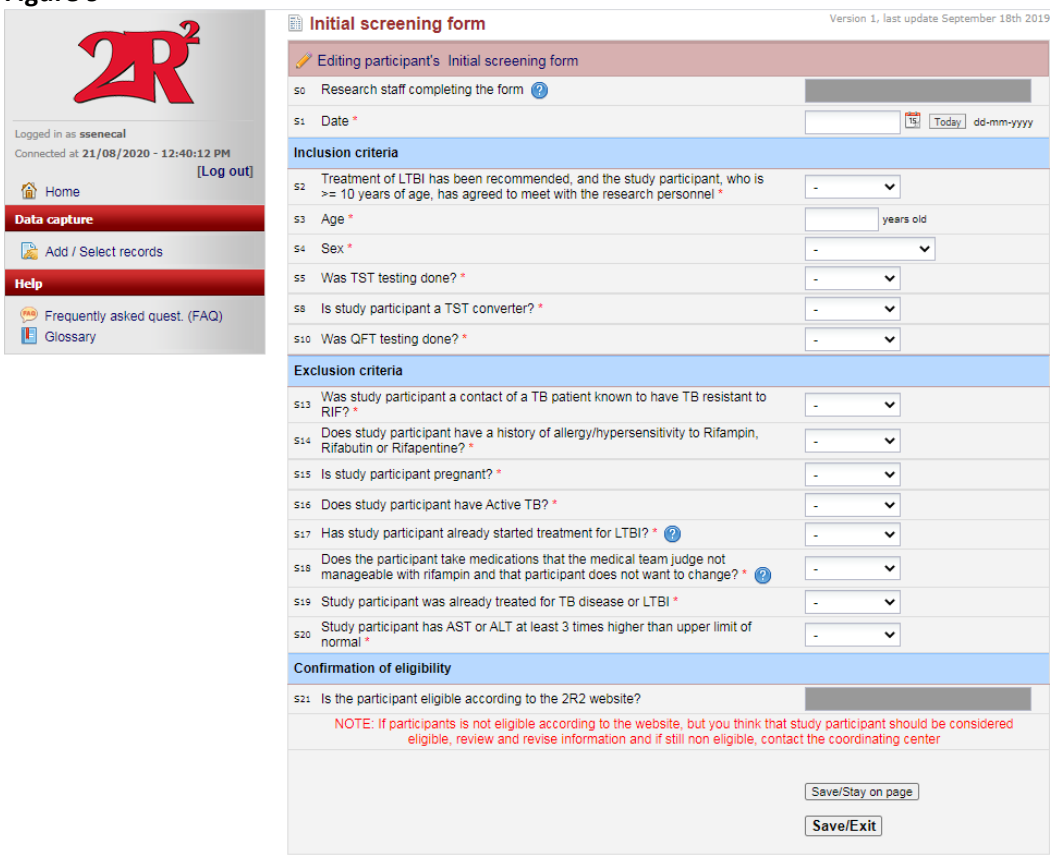
Then click on the "**Create a new participant ID**" button to have access to the **CRF1**: Initial screening form (**figure 8).**

Figure 8



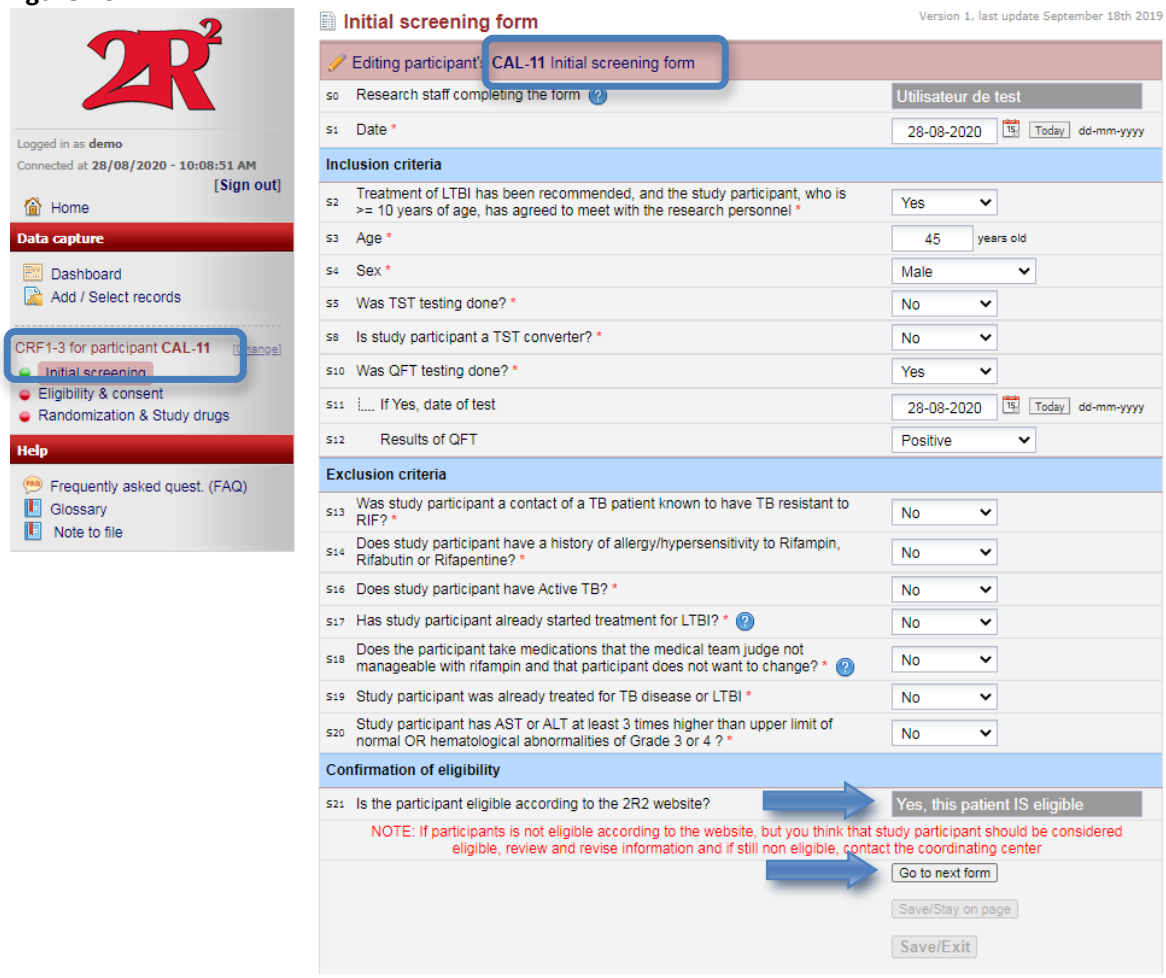
The CRF-1: Initial screening form will appear, and you can transcribe all the data that you already have on your paper copy of **CRF1**. (**figure 9**)

Figure 9



Once you click on "**Save/Stay on page**" at the bottom of the page, an ID number for the participant is created and appear in the left menu and on the top of the form. (**figure 10**)

Figure 10



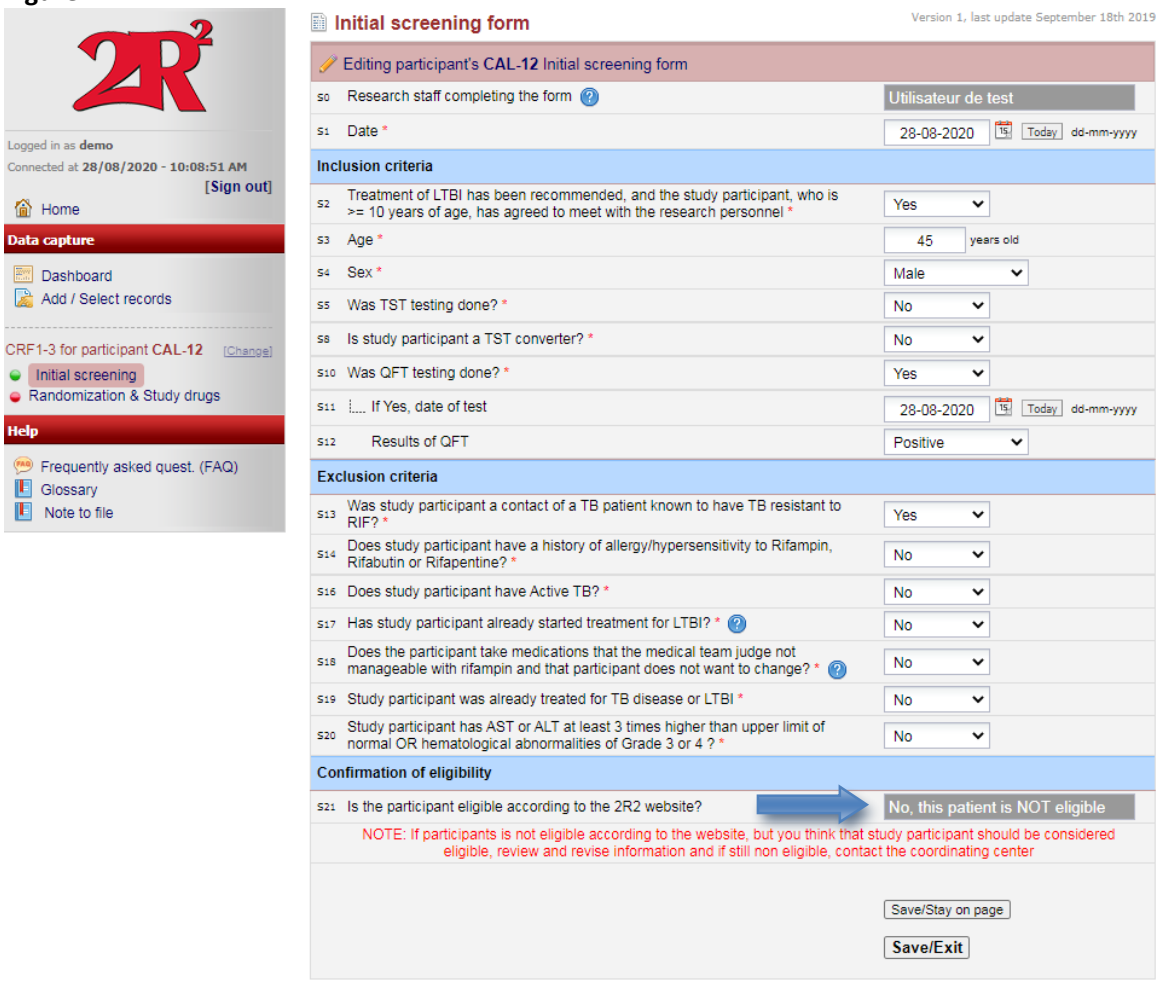
Note: an ID will be created for all participant you enter data for, independently if this participant will be eligible or not.

Once you have clicked on "**Save/stay on page**", if a patient is eligible, S21 will show the answer automatically. If for 2R2 website the participant is eligible, the answer to S21 will be "Yes, this patient is eligible" .

You can then continue by clicking on **"Go to next form"**.

If the 2R2 Websites considers that the patient is NOT eligible, then answer to question S21 will appear to be "**No, this patient is not eligible**". (**figure 11**)

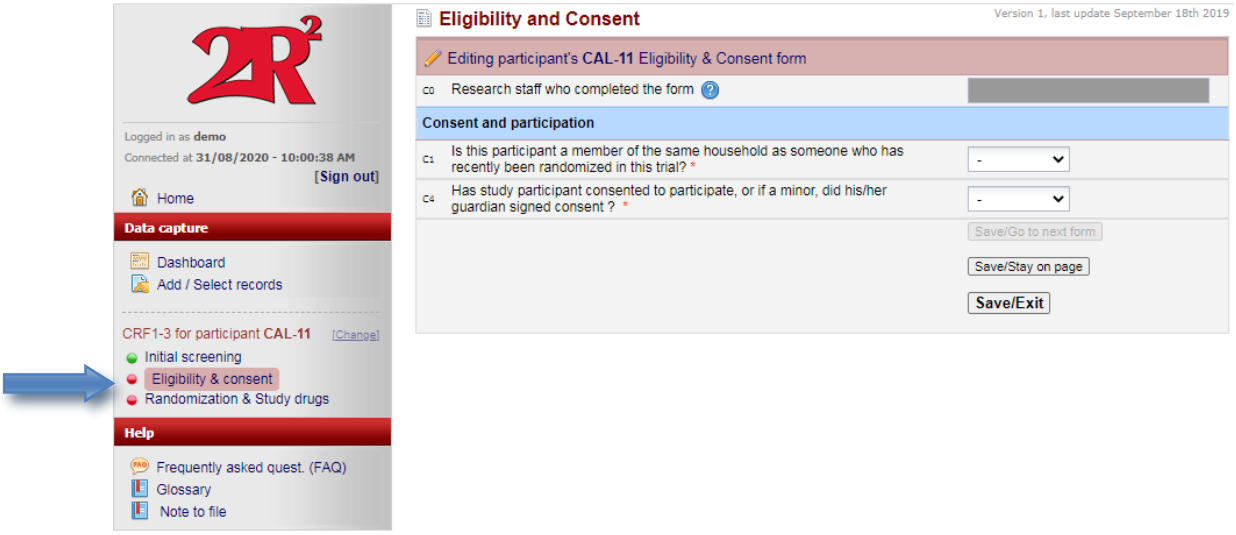
Figure 11



If you think that this patient should be consider eligible, review and revise information entered and if still non-eligible, contact the coordinating center.

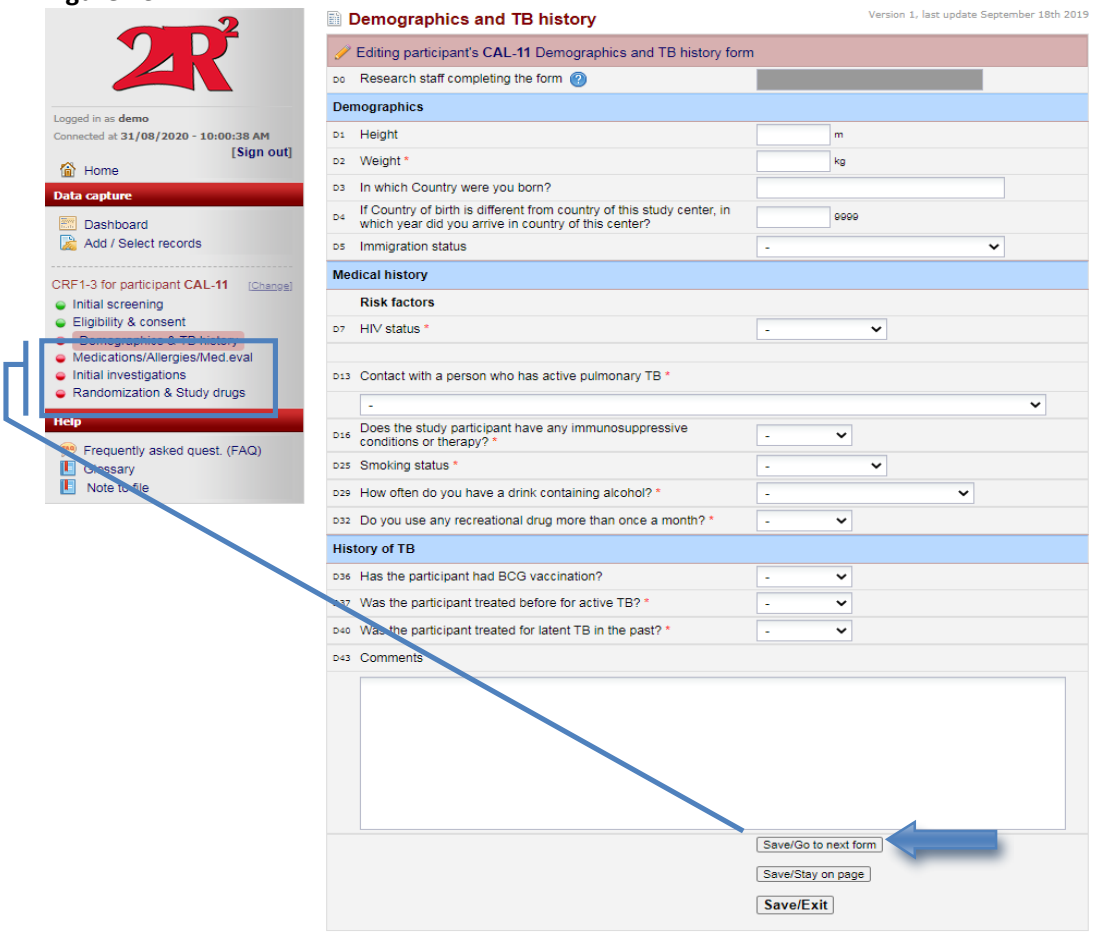
5.3.3 How to randomize a new participant

If participant is eligible, continue to the Eligibility & Consent page and transcribe in this page the data you have collected in paper **CRF2**, then "**save/stay on the page**" (**figure 12**)



Continue with the Demographics & TB history, Medication/allergies/Med. Eval., Initial investigations and Randomization & Study drugs pages from **CRF3** then "**save/go to next form**" (**figure 13**).

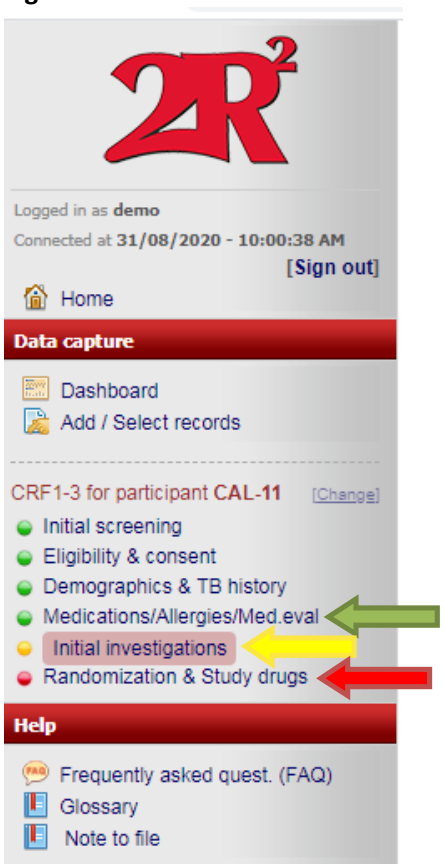
Figure 13



Note: In "Initial investigations" page, under variable L2 there is the possibility to upload the CXR. DO NOT upload the CXR done at randomization for all participants. The CXR upload will be required ONLY for participants who will develop an Active TB during follow-up. The upload of CXR done at enrolment will then be required only once you have completed **CRF11** and **CRF12** (see **5.3.11 CRF12 Active TB Final** for more information) for participants with active TB.

While completing the forms you will see small coloured dots in the left menu, beside each page of the CRF. The dots indicate if a CRF (or a CRF page) is **"completed"**, **"ongoing"** or **"not yet started"**. (**figure 14**)

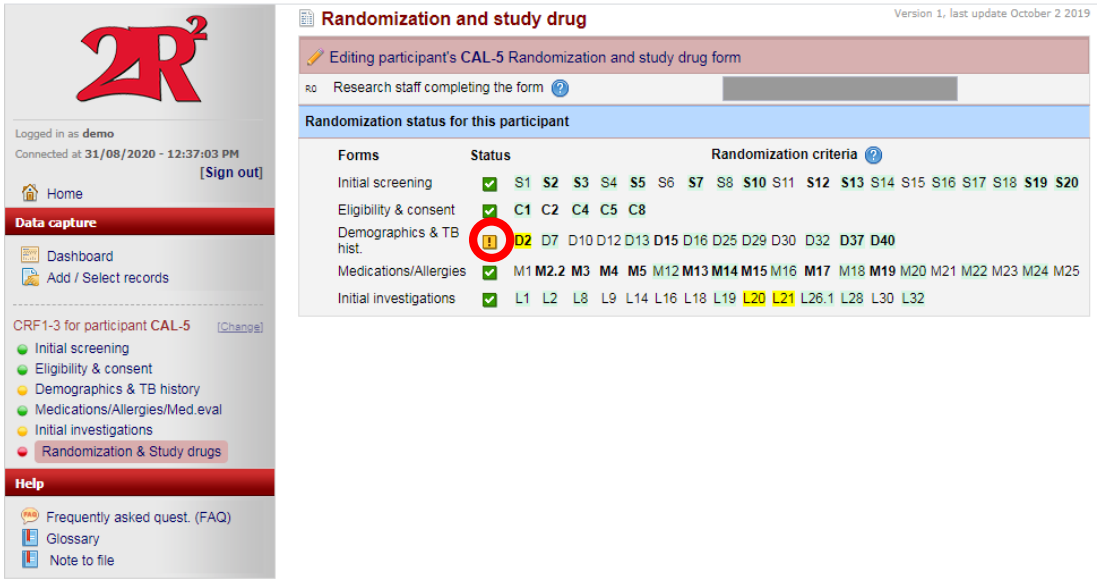
Figure 14



Green dots = form is completed;
Yellow dots = form is ongoing, information is still missing;
Red dots = form is not started yet, no information entered

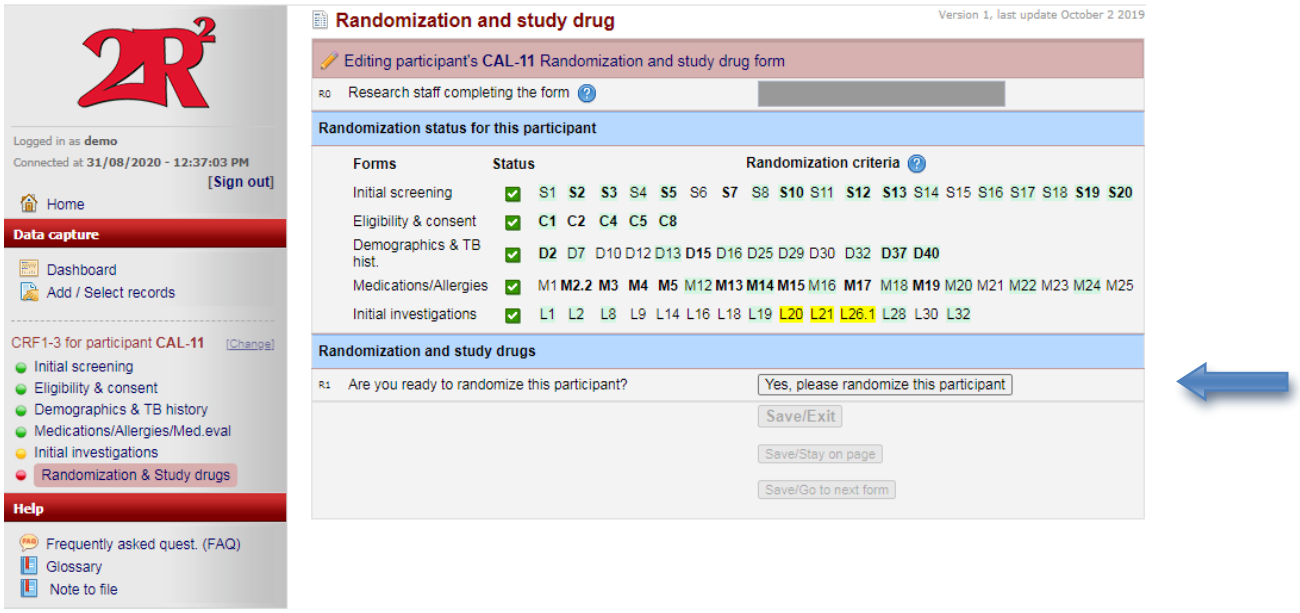
You will not be able to randomize a participant if one of the forms is in yellow or red. You will see an exclamation mark under "Status" for the incomplete form, in the Randomization page (**figure 15**)

Figure 15



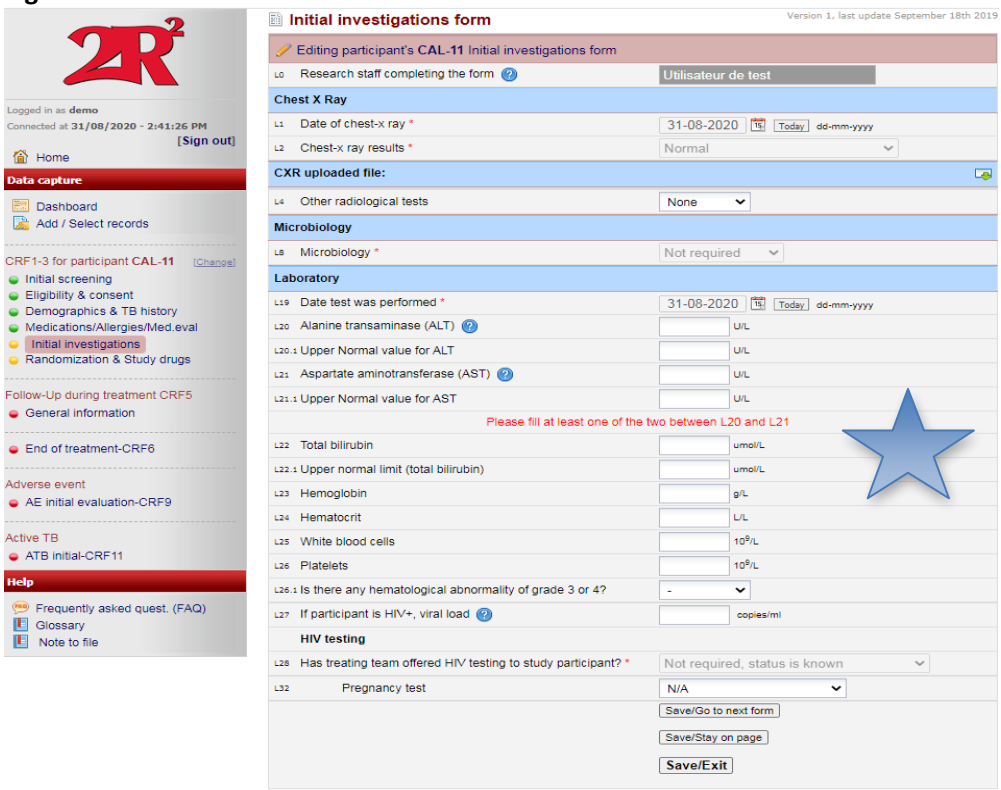
Once all the forms are completed, they have a green dot on the menu on the left, and you can randomize the participant, by clicking on "**Please randomize this participant" (figure 16)**

Figure 16



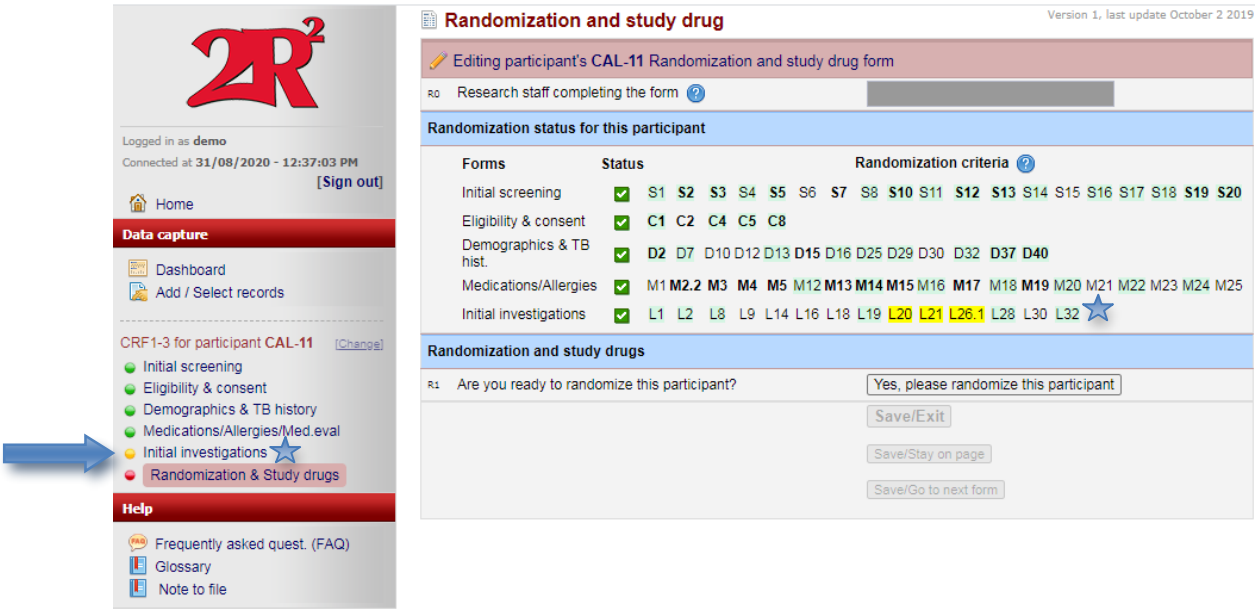
Exception : You can randomize a participant even if you have not completed the part reporting the results of the blood test, but you must enter a date for the lab test done. Fill in the results as soon as you have them (i.e. in the next 1-2 days after enrolment (**figure 17**).

Figure 17



Until you do not complete all the information required in the forms, the dot beside the form in the left menu will remain yellow (**figure 18**).

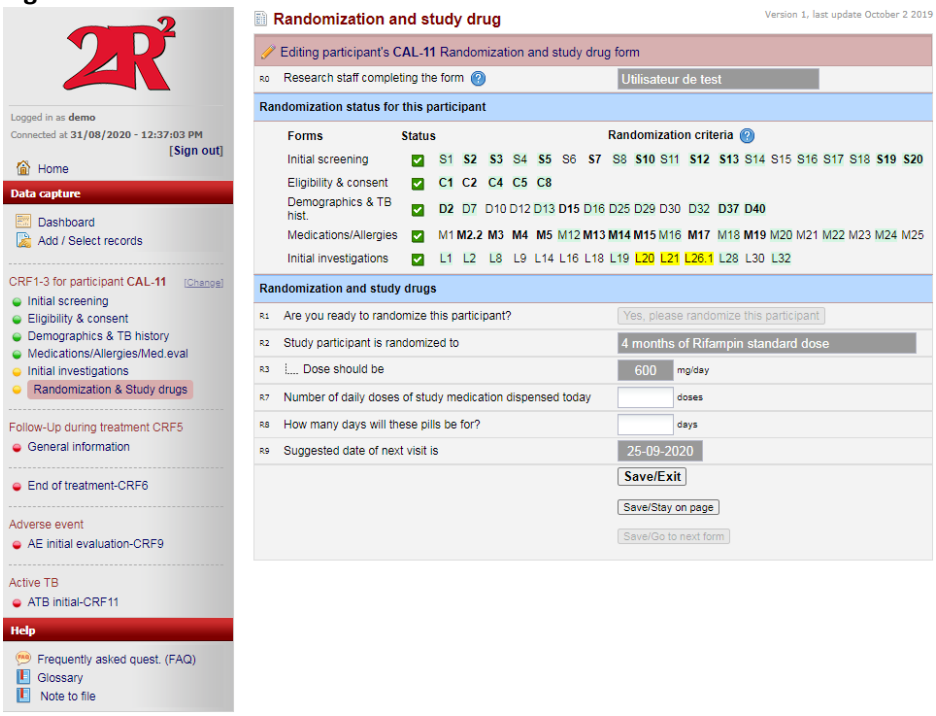
Figure 18



Note: Yellow dots will require review by the coordinating center if not resolved within 2 weeks.

Once the participant is randomized, the website will assign the duration of treatment at question R2 (i.e. 4 months of standard dose or 2 months of high dose rifampin) **(figure 19)**

Figure 19



If participant is not randomized once you click on "**Yes, please randomize this participant**" but you think that he/she should be randomized, review and revise information and if still NOT able to randomize, contact the coordinating center.

5.3.4 CRF5: Follow-up during treatment

General notes for CRF5:

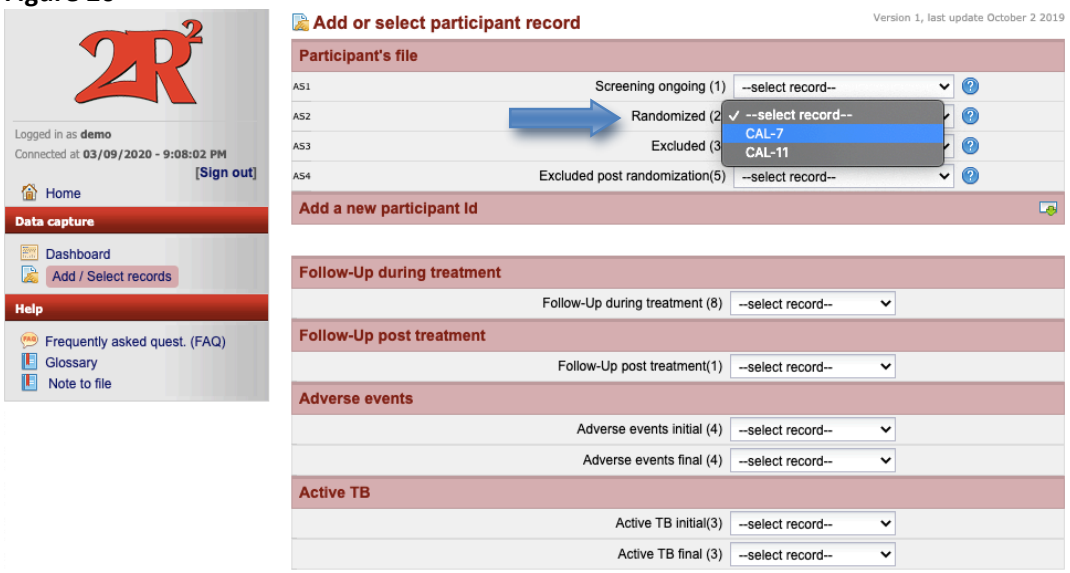
1. In the website, **CRF5** has been divided in 4 pages: "General Information", "Symptoms and physical exam", "Investigations during follow-up" and "Treatment Plan".

2. As each participants has more than one follow-up, different follow-ups for each participants are named and sorted by date of the follow-up. You can see all the follow-up forms done for one participant by scrolling down the window in the section "Follow-up during treatment" once the participant ID has been selected in the **"Add/Select record"** page (**figures 20-21**).

When you are ready to enter the data from the paper **CRF5** into the website, select the participant for whom you want to add the follow-up form by clicking on **"Add/Select records"** in the menu of the left.

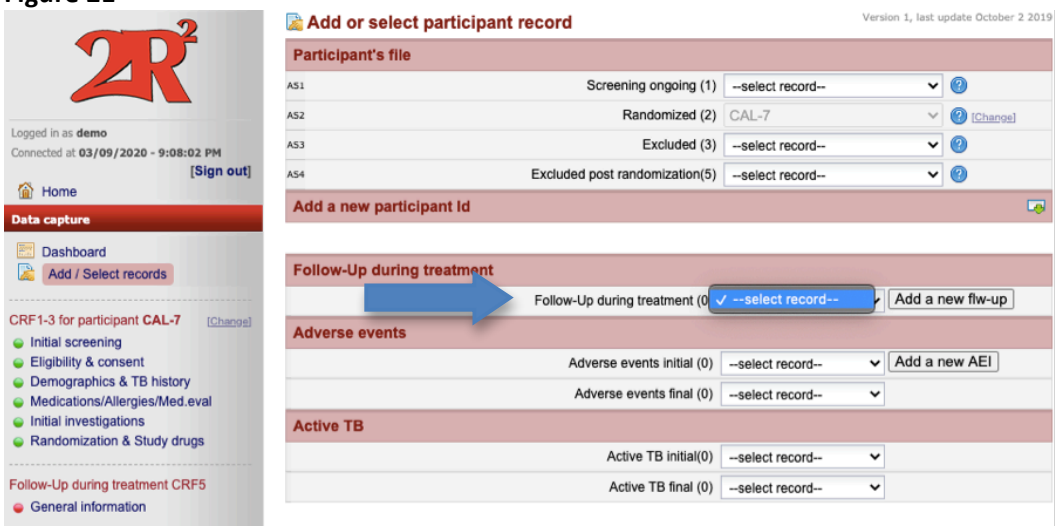
Click on a participant who has been already randomized (by opening the scroll down list at "Randomized") and for whom you want to enter the follow-up form (**figure 20**)

Figure 20



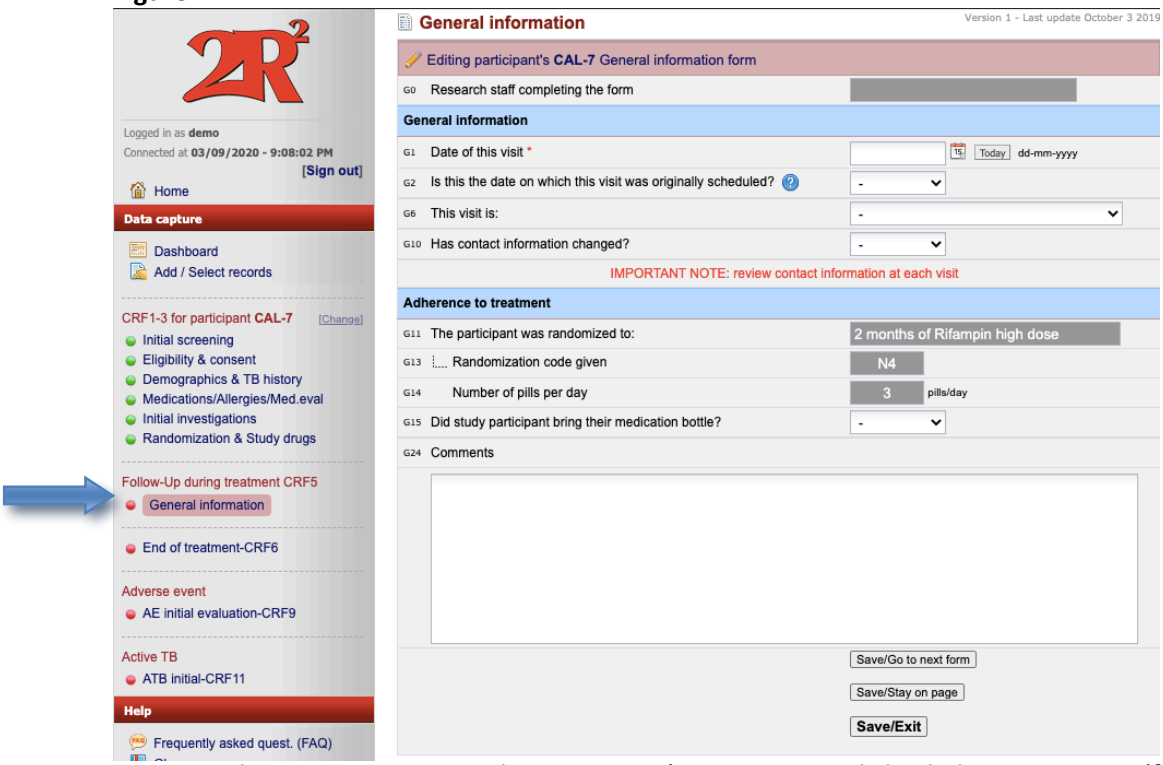
You can choose to complete a follow-up form already started (selecting the date of follow-up form you want to complete, by opening the scroll down window) or you can choose to add a new follow-up form, by clicking on **"Add a new flw-up"**. (**figure 21**)

Figure 21



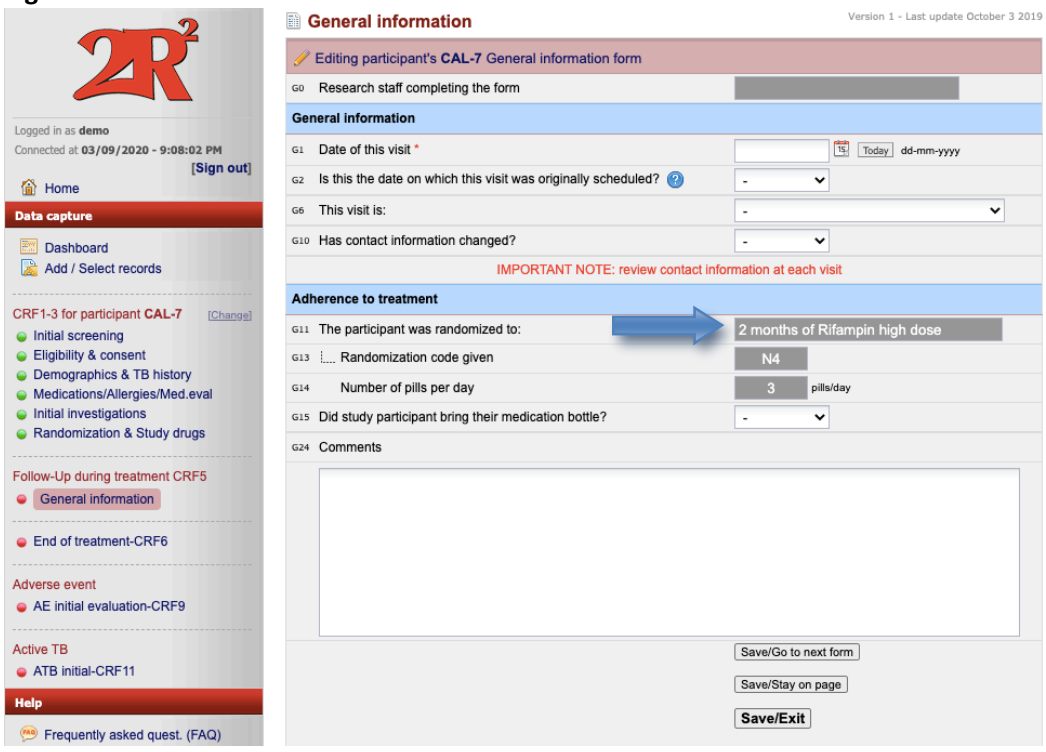
You will be directed to the first page (General Information) **(figure 22)**

Figure 22



Note: On this page you can see the participant's treatment and check that it is correct (**figure 23**).

Figure 23



Once you finish completing the "General Information" page, click on **"Save/Go to next form"** and complete "Symptoms and physical exam" (**figure 24**) and "Investigations during follow-up" (**figure 25**). Click on **"Save/Go to next form"** at the end of each page once done.

Figure 24

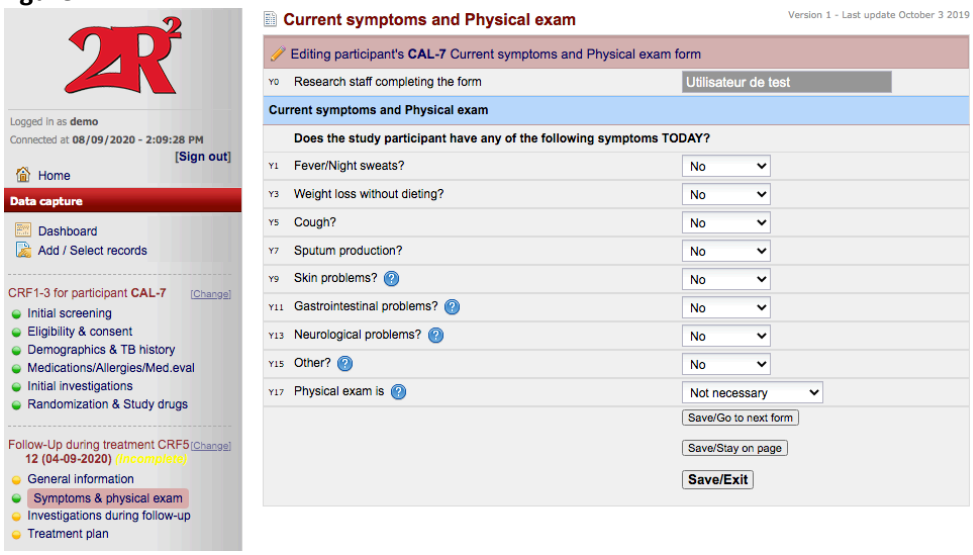
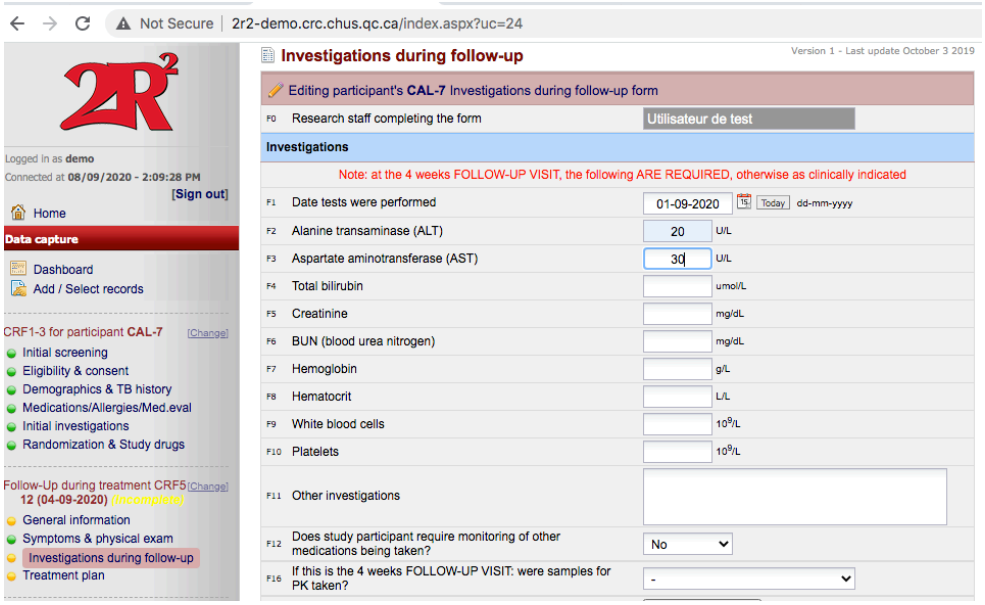


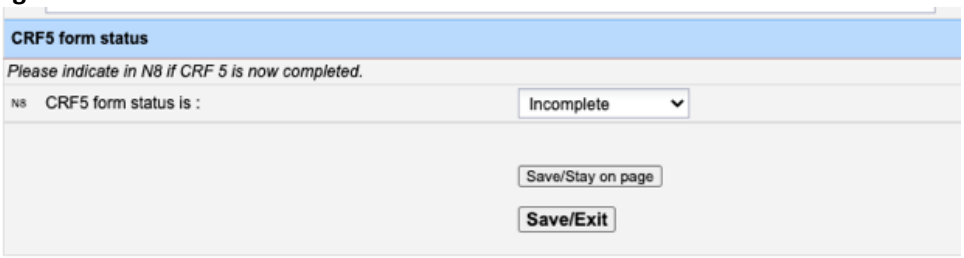
Figure 25



Note: There may be different types of follow-up appointments that participants can have, for example: in-person visits with a blood test done, in-person visits without blood test, phone calls, medication pick-ups, etc. For this reason, the follow-up form **CRF5** can be completed in all its parts (in visits in which all follow-up components are carried out) or just partially (for example during a call follow-up). The judgment if the form is completed or not will be based on a) final statement done by the site user; b) confirmation given by the coordinating center. At this purpose, there is a question at the end of **CRF5** in the 2R2 website (in page "Treatment plan") asking the site user if data entered for this specific follow-up appointment have to be considered completed or if are still pending.

This is question N8 (in the last page of **CRF5**, "Treatment Plan") which asks if the form has to be considered as "Complete" or "Incomplete". Choose incomplete if there are still information pending (in any part of **CRF5**) which will be entered as soon as they will become available to you. (**figure 26**)

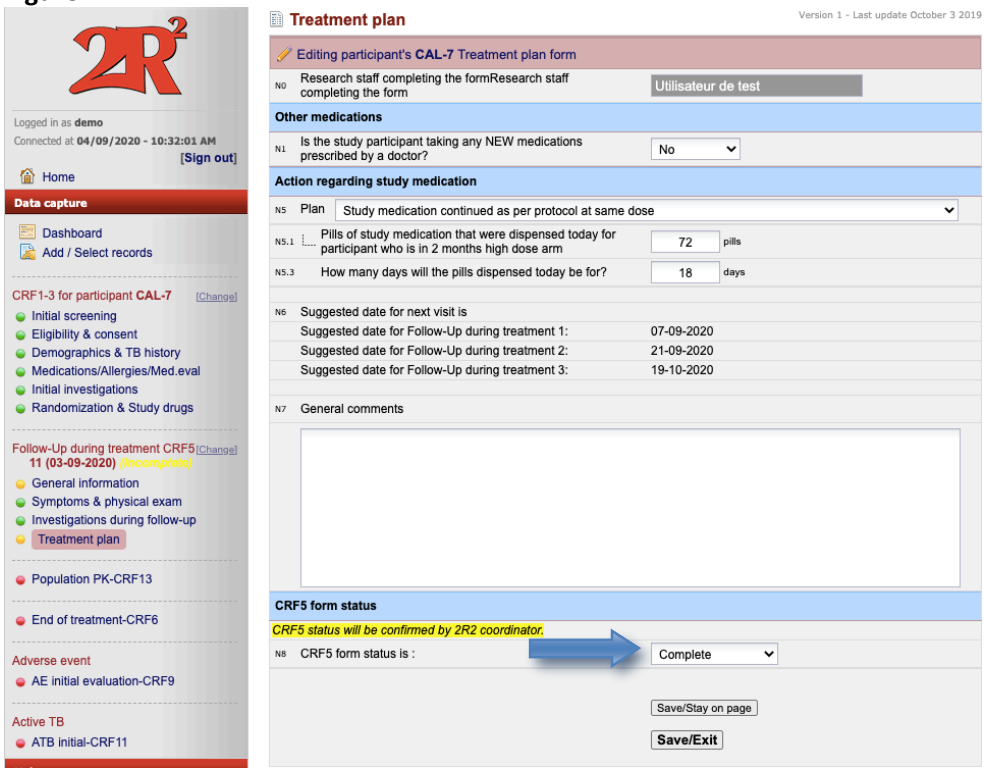
Figure 26



This can be, for example, if at a 1 month visit, blood test has been done and results are still pending when **CRF5** is entered in the website. By choosing "Incomplete", in this case, the site user can go back and fill in the pending information once available.

Once all information you can enter have been entered, choose "Complete". a message will appear above the question N8: "**CRF5** status will be confirmed by 2r2 coordinator". (**figure 27)**

Figure 27



Note: you can choose complete for forms where all variables are entered or for forms which are not all filled out, but that have all the information that were expected to be collected for that appointment. For example: in a follow-up visit at 2 months after treatment started, where there is no routine blood test required, a **CRF5** form in which "Investigation during follow-up" remains blank (and therefore has a red dot) is still to be considered a complete follow-up form (as lab test were not requested and not done).

Figure 28

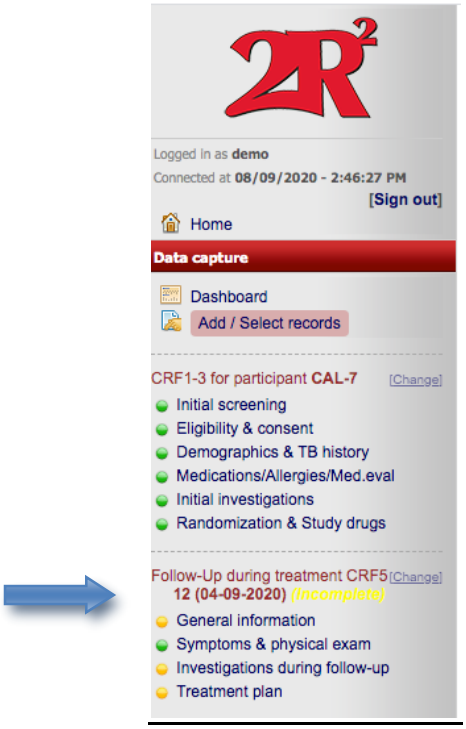


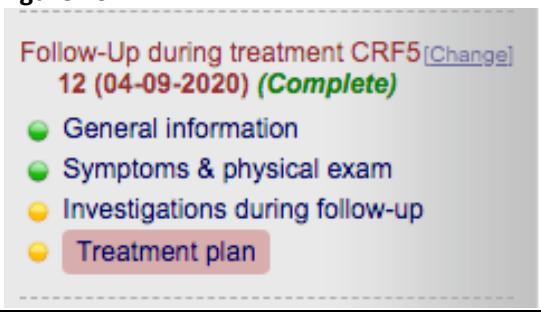
Figure 28

At this point, the word "incomplete" (in yellow) beside the name of this specific form (Follow-up During treatment (**CRF5**)), <date> in the left menu will remain, until the coordinating center confirms that this follow-up form in indeed considered completed.

If the coordinating center does not agree with classifying the form as complete, site user will be contacted for more information.

If the coordinating center agrees and confirms that this **CRF5** is to be considered completed, then the world beside the follow-up form will become "complete" (in green). (**figure 29**)

Figure 29

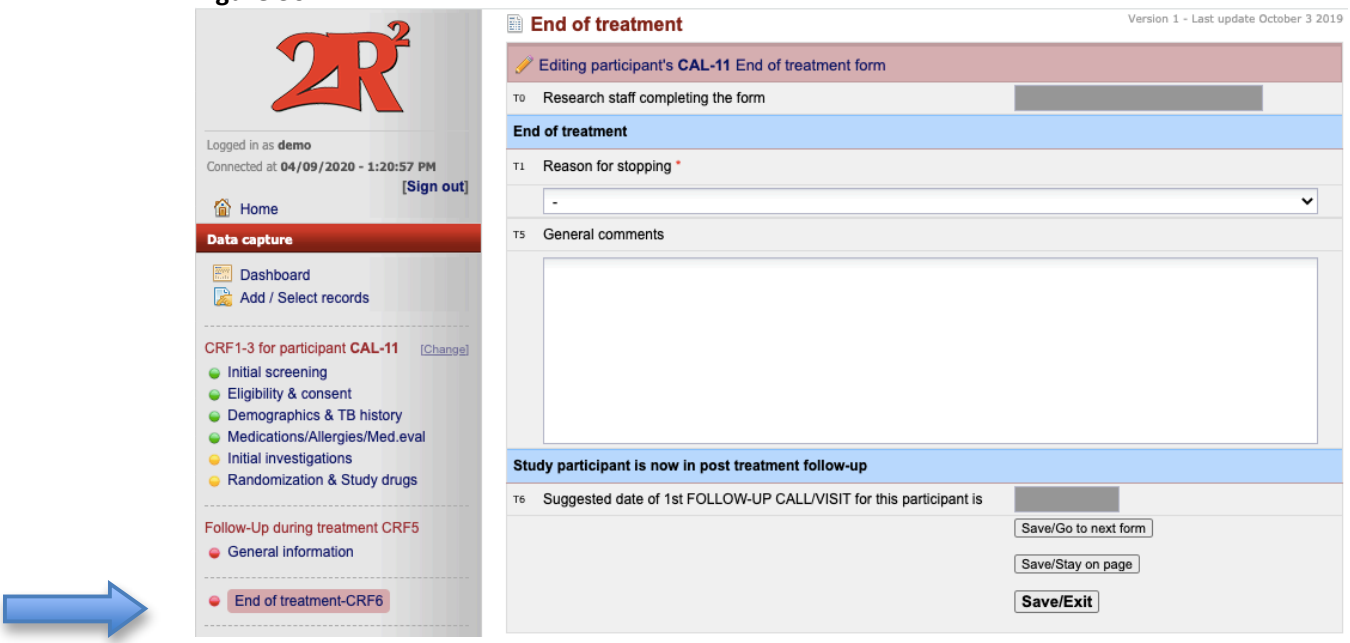


Note: the dots on the left menu, besides the pages of **CRF5** which have not filled in all their variables, will remain yellow even when the **CRF5** is considered completed (as they reflect the status of all variables and will not be modified). These yellow dots will not require any further action, if the **CRF5** is classified as "complete" by the word in green beside the CRF name.

5.3.5 CRF6 End of treatment

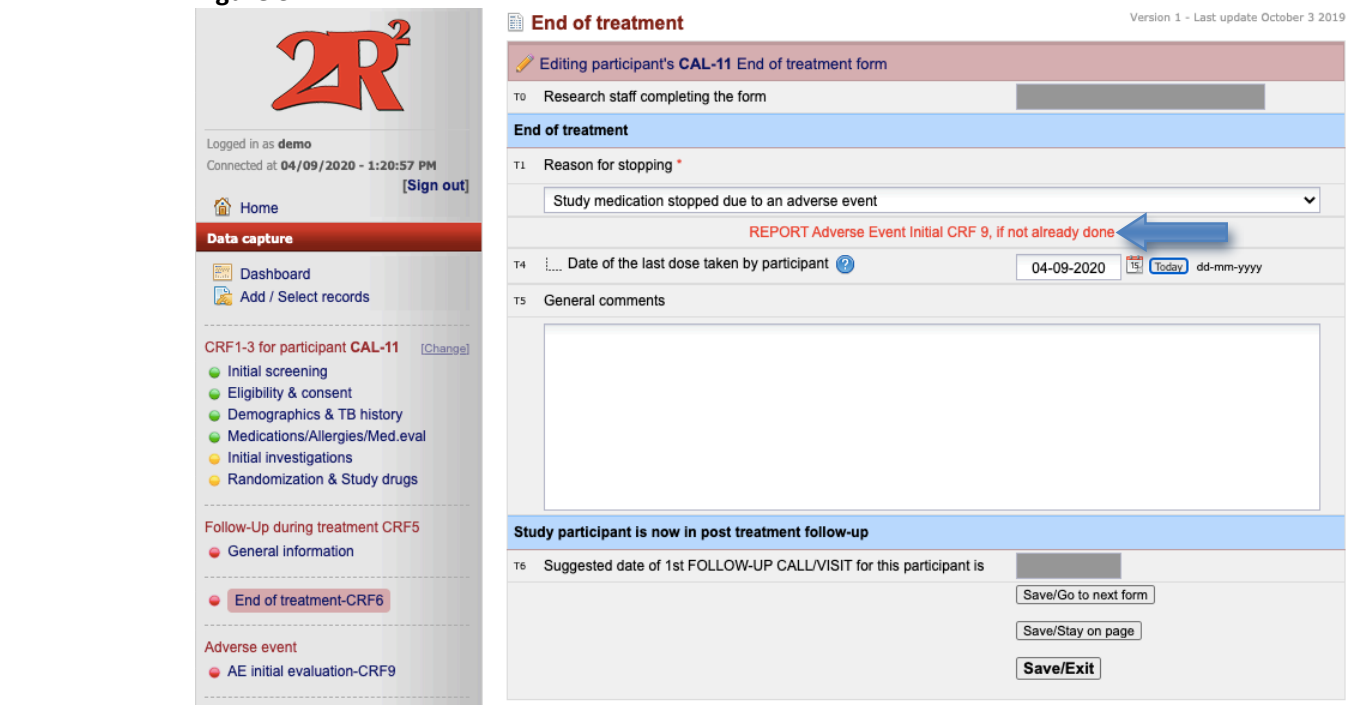
The form End of treatment is visible at all times in the menu on the left when you select a randomized participant. You must click on "End of treatment **CRF6**" to fill out the **CRF6** form. (**figure 30**)

Figure 30



Note: while completing **CRF6**, if a sentence in RED appears when you select a Reason for stopping (T1), **pay attention!** This means that you must fill out another form, if not already done, beside completing the end of treatment form (see example in **figure 31**)

Figure 31

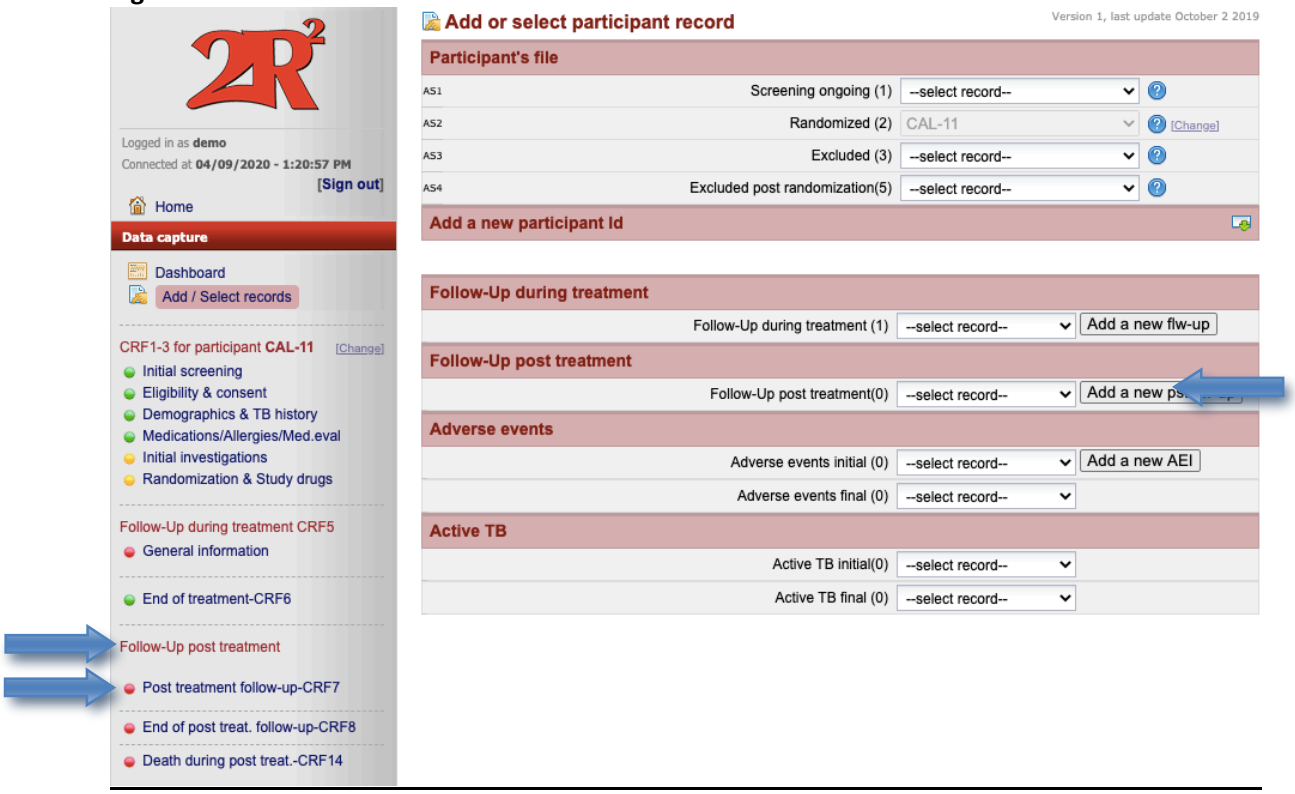


Complete **CRF6** only when you are sure participant stopped treatment permanently and you know the date of last dose taken (T4).

5.3.6 CRF7 Follow-up evaluation post treatment

Once you have completed a form "End of treatment" and you did **"Save/Exit"**, the section "Follow-Up post treatment" will appear. Then you can click on Post treatment follow-up-CRF7 on the left menu or click on **"Add a new pst flw-up"** in the "**Add/select participant record**" page. (**figure 32**)

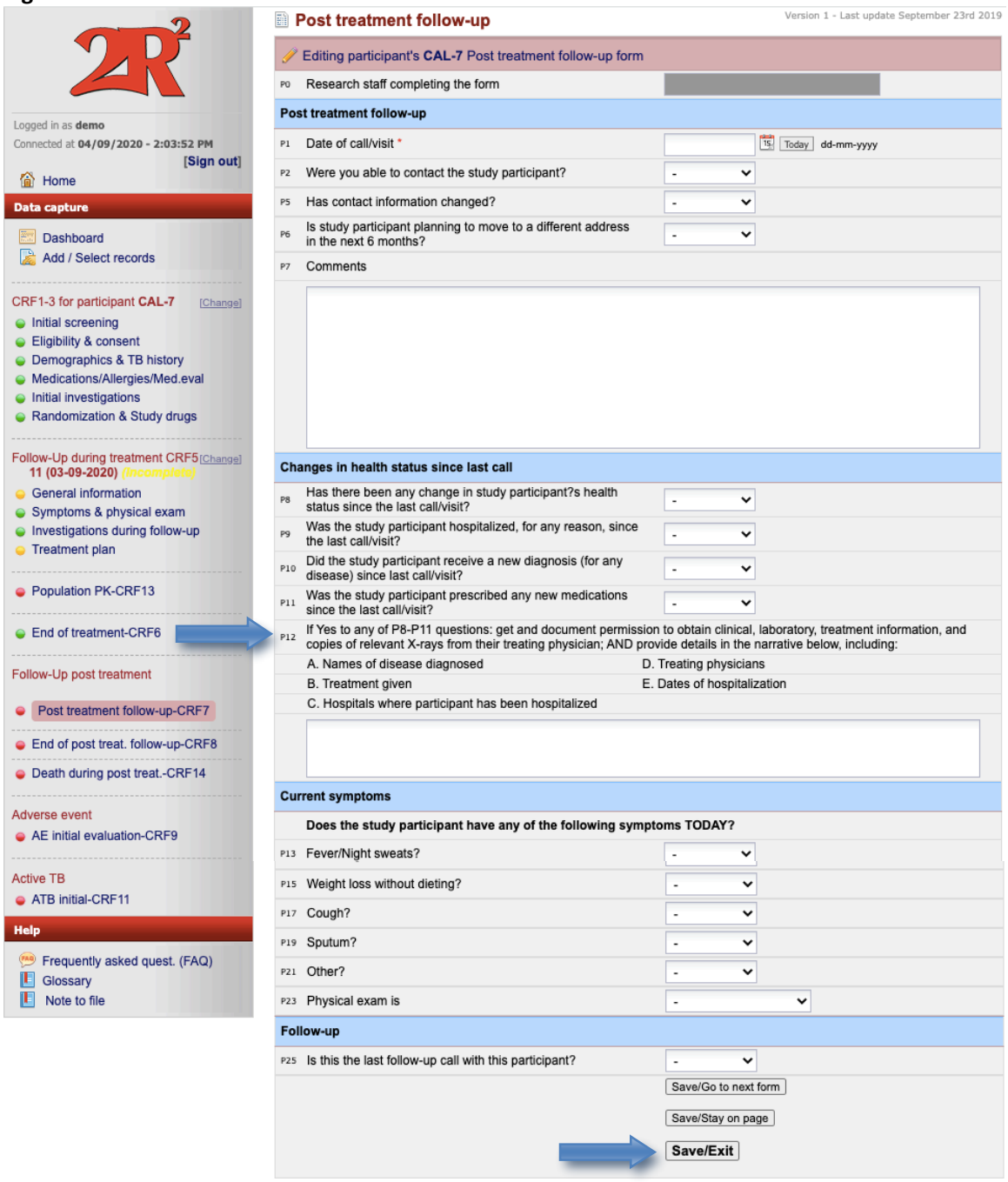
Figure 32



The form post treatment follow-up **CRF7** will appear (**figure 33**), fill out the form and click **"Save/Exit"** when it's complete.

Note: Don't forget to fill out the question P12 if you said yes to any of P8-P11.

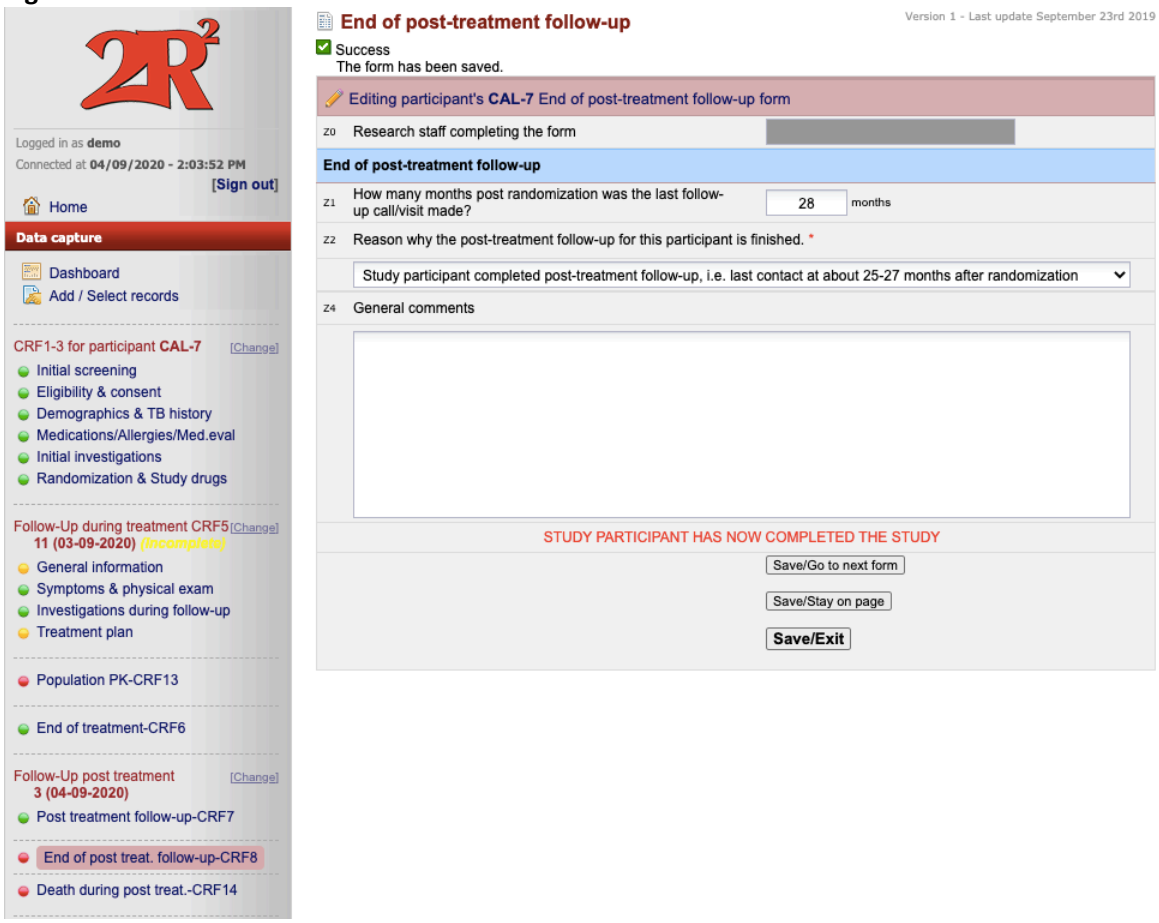
Figure 33


Logged in as demo
Connected at 04/09/2020 - 2:03:52 PM
[Sign out]
Home
Data capture
Dashboard
Add / Select records
CRF1-3 for participant CAL-7 [Change]
Initial screening
Eligibility & consent
Demographics & TB history
Medications/Allergies/Med.eval
Initial investigations
Randomization & Study drugs
Follow-Up during treatment CRF5 [Change]
11 (03-09-2020) (Incomplete)
General information
Symptoms & physical exam
Investigations during follow-up
Treatment plan
Population PK-CRF13
End of treatment-CRF6
Follow-Up post treatment
Post treatment follow-up-CRF7
End of post treat. follow-up-CRF8
Death during post treat.-CRF14
Adverse event
AE initial evaluation-CRF9
Active TB
ATB initial-CRF11
Help
Frequently asked quest. (FAQ)
Glossary
Note to file
Post treatment follow-up
Version 1 - Last update September 23rd 2019
Editing participant's CAL-7 Post treatment follow-up form
P0 Research staff completing the form
Post treatment follow-up
P1 Date of call/visit *
Today
dd-mm-yyyy
P2 Were you able to contact the study participant?
P5 Has contact information changed?
P6 Is study participant planning to move to a different address in the next 6 months?
P7 Comments
Changes in health status since last call
P8 Has there been any change in study participant?s health status since the last call/visit?
P9 Was the study participant hospitalized, for any reason, since the last call/visit?
P10 Did the study participant receive a new diagnosis (for any disease) since last call/visit?
P11 Was the study participant prescribed any new medications since the last call/visit?
P12 If Yes to any of P8-P11 questions: get and document permission to obtain clinical, laboratory, treatment information, and copies of relevant X-rays from their treating physician; AND provide details in the narrative below, including:
A. Names of disease diagnosed
B. Treatment given
C. Hospitals where participant has been hospitalized
D. Treating physicians
E. Dates of hospitalization
Current symptoms
Does the study participant have any of the following symptoms TODAY?
P13 Fever/Night sweats?
P15 Weight loss without dieting?
P17 Cough?
P19 Sputum?
P21 Other?
P23 Physical exam is
Follow-up
P25 Is this the last follow-up call with this participant?
Save/Go to next form
Save/Stay on page
Save/Exit

5.3.7 CRF8 End of post treatment follow-up

The form "End of post treatment follow-up **CRF8**" is only visible once you have completed "End of treatment form **CRF6**". **CRF8** will appear in the menu on the left. Once the post-treatment follow-up is completed, you must click on "End of post treatment follow-up **CRF8**" and fill out the form (**figure 34**)

Figure 34

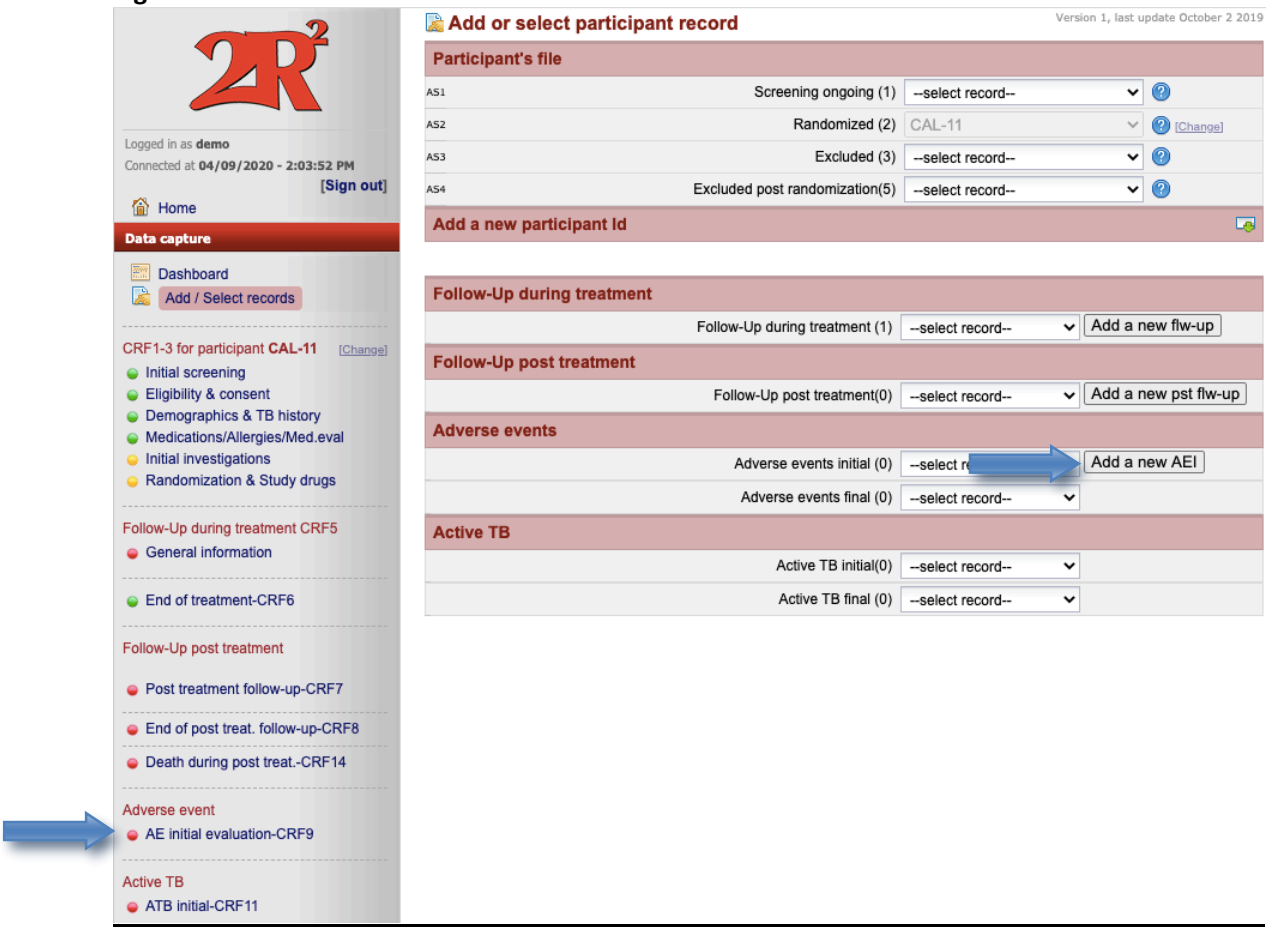


Click on **"Save/exit"** when it's complete.

5.3.8 CRF9 Adverse event Initial evaluation

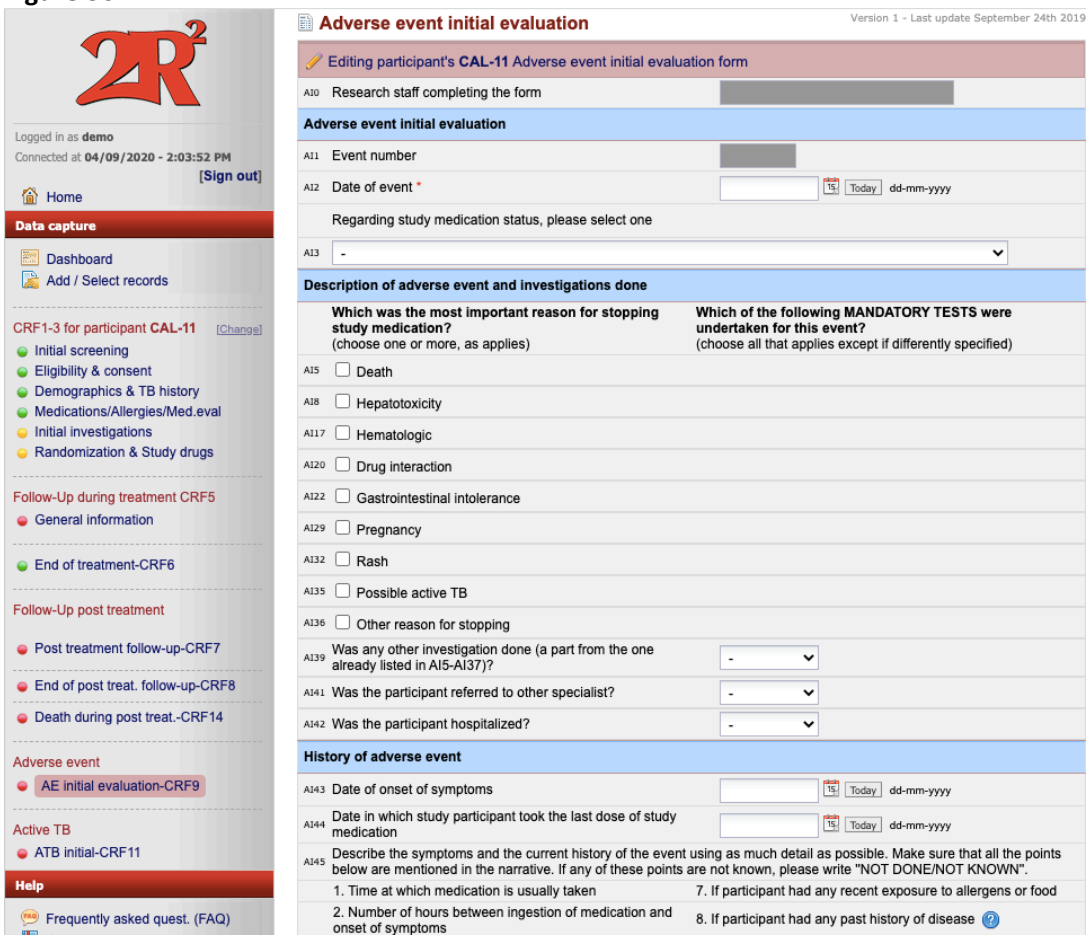
The form Adverse Event Initial **CRF9** is visible at all times in the menu on the left when you select a randomized participant. To enter a **CRF9**, click on **"AE Initial evaluation CRF9"** on left menu or click on **"Add a new AE"** in **"Add/Select participant record"** page. (**figure35**)

Figure 35



The **CRF9** form will appear, then you can fill it out, transcribing from the paper form (**figure 36**)

Figure 36

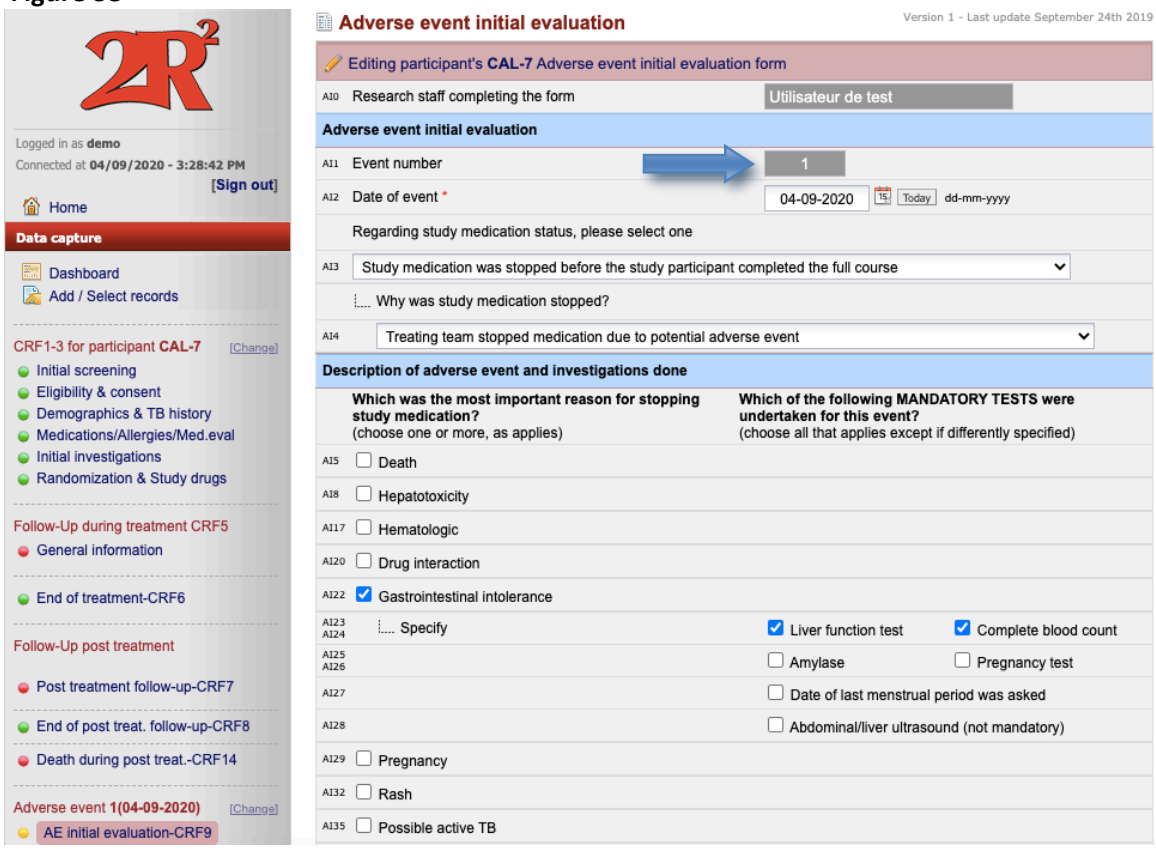


When you entered the information needed in **CRF9**, click first on "**Save/stay on page**"(**figure 37**)

Figure 37

You will see an Event number appearing on the top of the form (**figure 38)**. Use this number to add as event number on your paper form **CRF9**.

Figure 38



When you are sure that your **CRF9** is complete, click on **"SAVE & CLOSE"** in the space reserved for site user (see **figure 37** above).

This action will submit the **CRF9** (AE Initial evaluation form) to coordinating center and will serve as an alert that a new AE has occurred in the trial. You will not be able to modify a **CRF9** once the **"SAVE & CLOSE"** button has been chosen.

The coordinating center will review the **CRF9** and get back to you if more information is needed. If no additional information is needed for the **CRF9**, you will have to complete the **CRF10** (AE Final evaluation form) for this AE once the event is resolved.

Figure 39

As each participant can have more than one AE, each **CRF9** is named with the date in which is generated (**figure 39**)

Once a **CRF9** has been saved, an **"AE final evaluation CRF10**" will appear below the **"AE initial evaluation CRF9"** on the left menu. (**figure 39**)

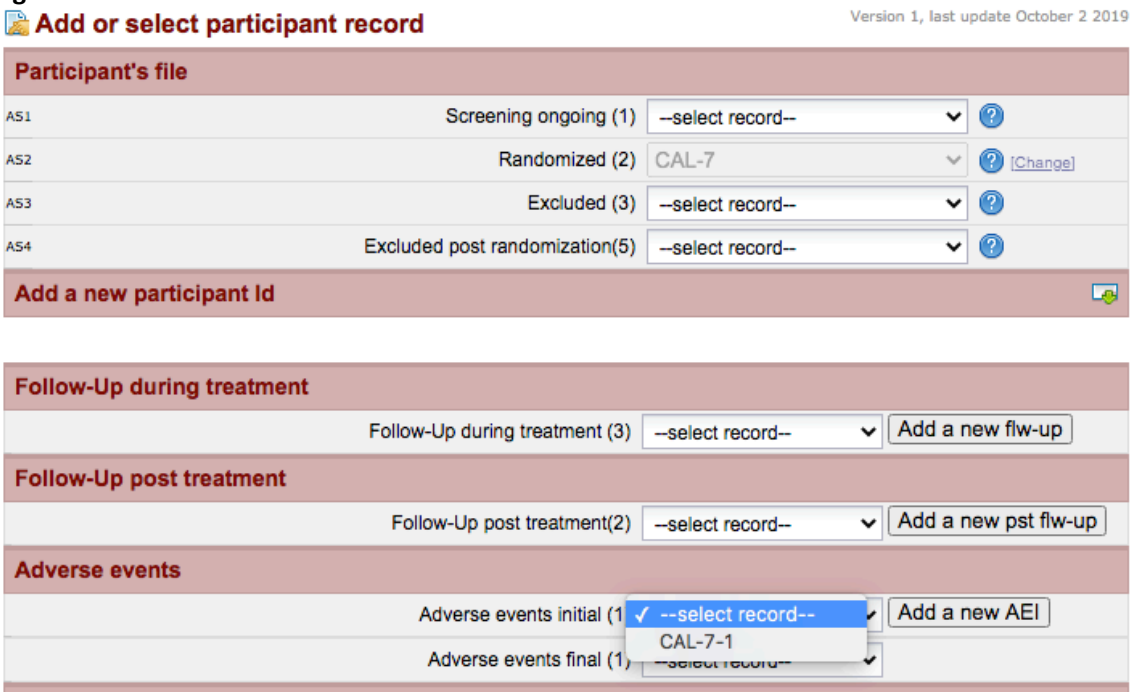
The dot in the left menu for **CRF9** will remain yellow until the coordinating center reviews and approves the **CRF9** form. Once approved the dot will become green.

5.3.9. CRF10 Adverse Event Final evaluation

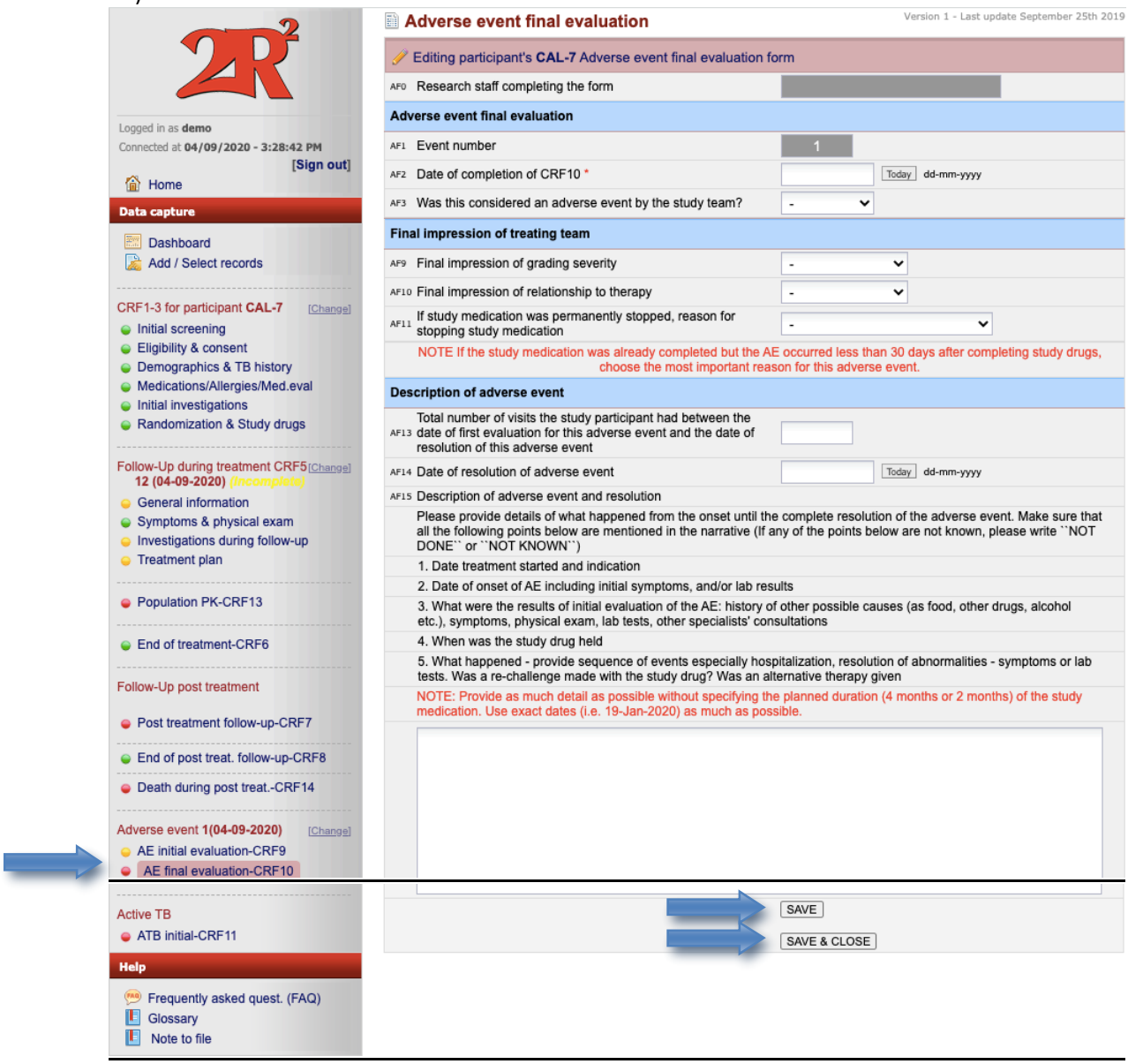
For each **CRF9** that has been entered in the website, a **CRF10** must be completed, as soon as all information needed are available.
A **CRF10** can be completed only after a **CRF9** has been completed (i.e, you have clicked on "**SAVE & CLOSE"**) and the coordinating center has approved it (i.e. the dot beside **CRF9** is green).

To complete a **CRF10**: select the participant you want to add a **CRF10** for, from the "**Add/Select participant record"** page, then select the AE initial evaluation for which you want to add a Final AE form in the section **"Adverse Events"** of the same page**,** in this example, AE #1 is selected for participant CAL-7 (**figure 40).**

Figure 40



You can now open **CRF10** from the left menu (**CRF10** will be below **CRF9**), and fill CRF10 (**figure 41**)



Once you are sure to have entered all the information, click on **"SAVE & CLOSE"**, at the bottom of the form. **Note**: If you want just to save the form, to work on it later, click on **"SAVE"**.

Once you clicked on **"SAVE&CLOSE"**, the from is submitted for review to the coordinating center and cannot be modified. The coordinating center will contact you if more information are needed.

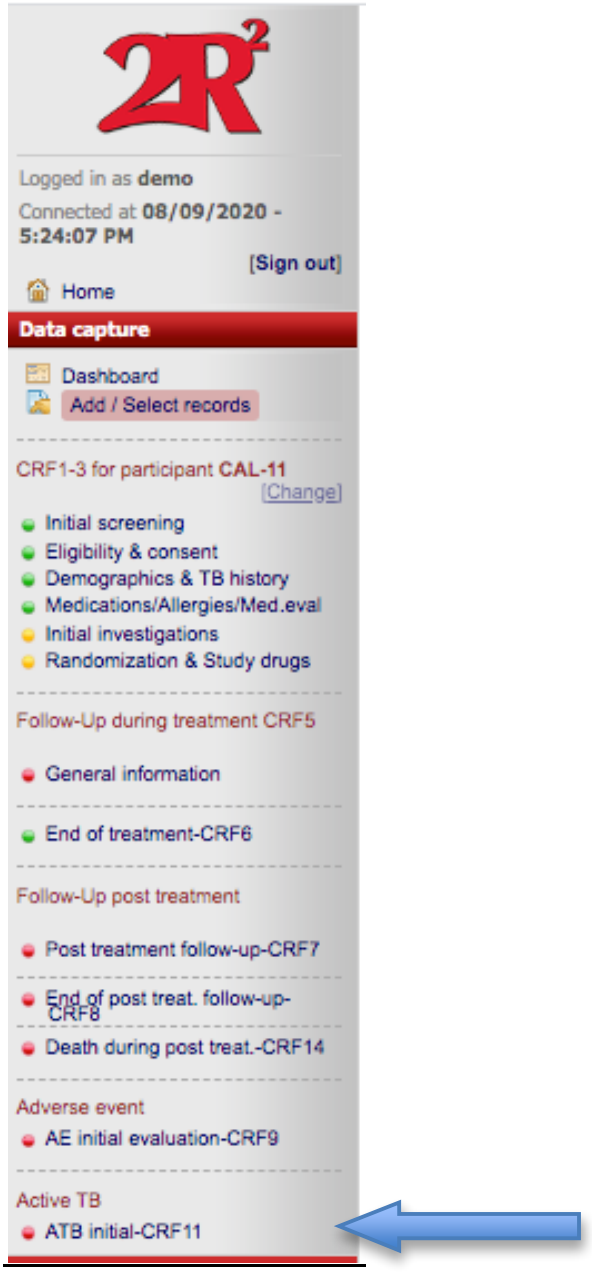
Note: the dot in the left menu will be yellow until the coordinating center will approve the form. Once approved the dot will be green. If a **CRF9** and **CRF10** for an AE are approved, they are sent automatically to the AE panel for review. If the AE panel does not find agreement in the review, the coordinating center will contact you for more information. In that case the **CRF10** will be "reopen" for you to modify and add the additional information needed. Once modifications have been made, you can click on **"SAVE&CLOSE"** and then whole process will be repeated (i.e.

the coordinating center will approved or ask for more info, once approved, the new **CRF10** will be sent to review to AE panel until an agreement is found).

5.3.10 CRF11 Active TB Initial

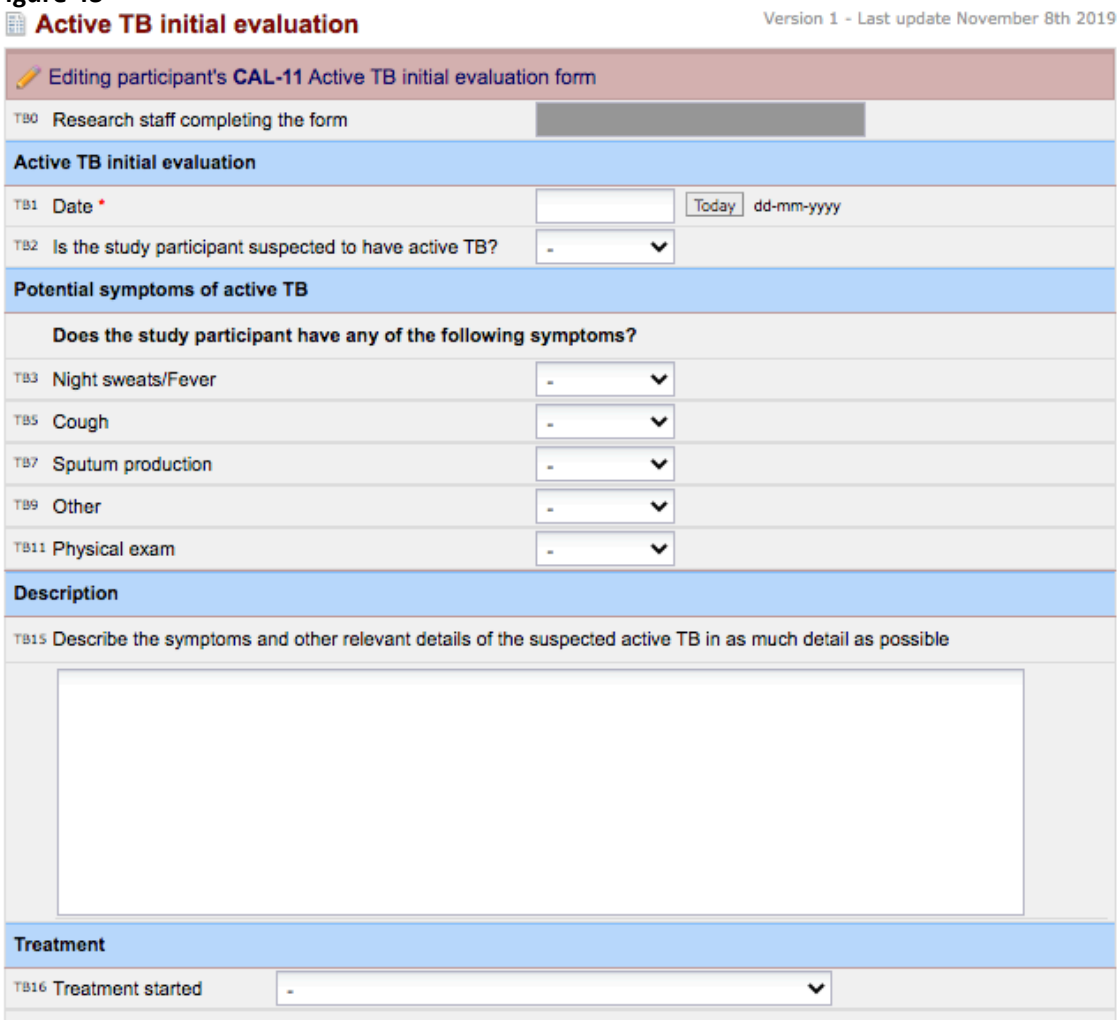
To enter **CRF11**: select, from the "**Add/select participant record page**, the randomized participant for whom you want to enter an "Active TB Initial evaluation" form; find the form at the bottom of the left menu.(**figure 42**)

Figure 42



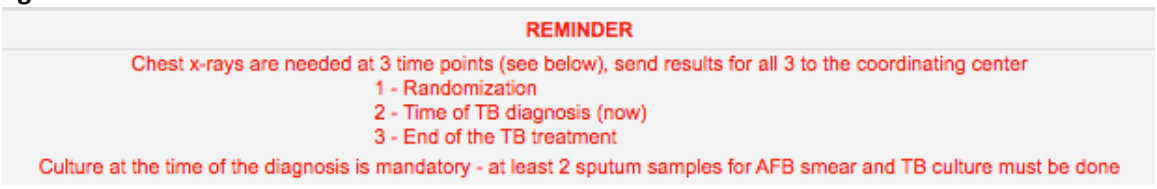
Complete the form **CRF11** that will appear (**figure 43**)

Figure 43



Note: at the bottom of the page you have a reminder of what needs to be collected when one participant is suspected to have active TB (**figure 44**)

Figure 44



Make sure you have the CXR done for the diagnosis of this suspected TB event and that you have the file of the CXR done at randomization for this participant. Both these two CXR (i.e. the one done at randomization and the one done now, at diagnosis) will be submitted, together with the final CXR (at end of treatment) to coordinating center via the 2R2 website, at the moment in which you will complete **CRF12** (ATB final evaluation report).

Once you are done with entering **CRF11**, you can click on **"SAVE&CLOSE"** at the bottom of the page. At this point the form cannot be modified any longer. **Note** : if you just want to save the page, and come back to work on it later, click on "**Save**".
Once you clicked on **"SAVE&CLOSE"** the dot beside **ATB initial-CRF11**, on the left menu, will become yellow, and **ATB Final-CRF12** will appear (**figure 45**).

Figure 45

An automatic message is also sent by the website to the coordinating center informing that there is a new ATB initial report to review. The coordinating center will review the **CRF11** and either ask you for more information (in that case the **CRF11** we be "reopen" and you will be able to modify it), or confirm it is complete. In this case the dot beside **CRF11** will become green (**figure 46**)

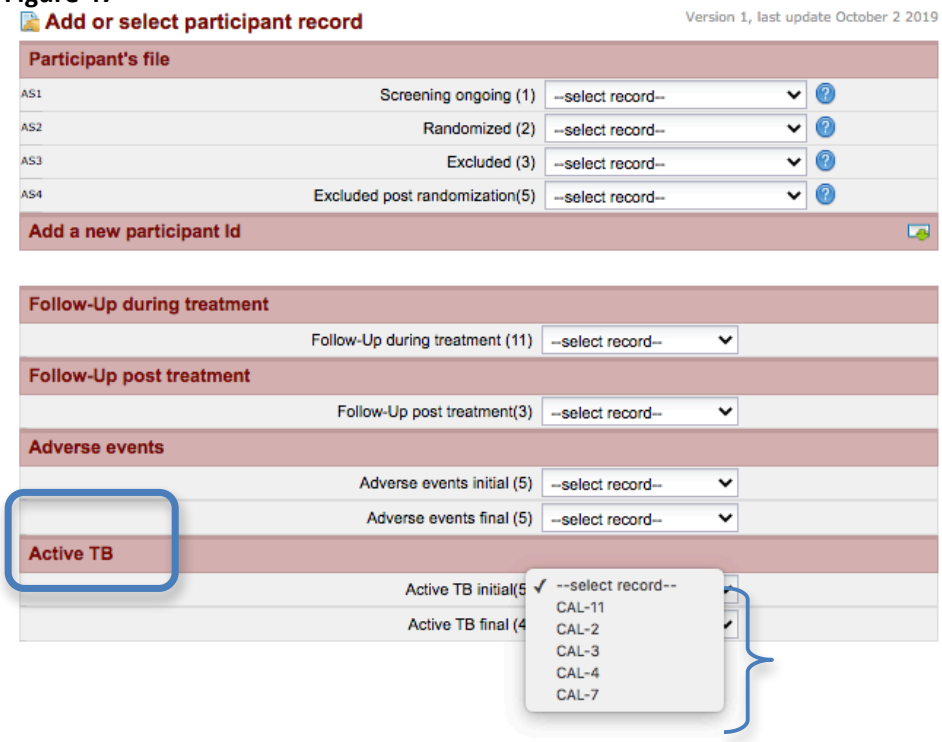
Figure 46

You need to complete a **CRF12** (ATB Final evaluation report) for each **CFR11** you have entered.

5.3.11 CRF12 Active TB Final evaluation

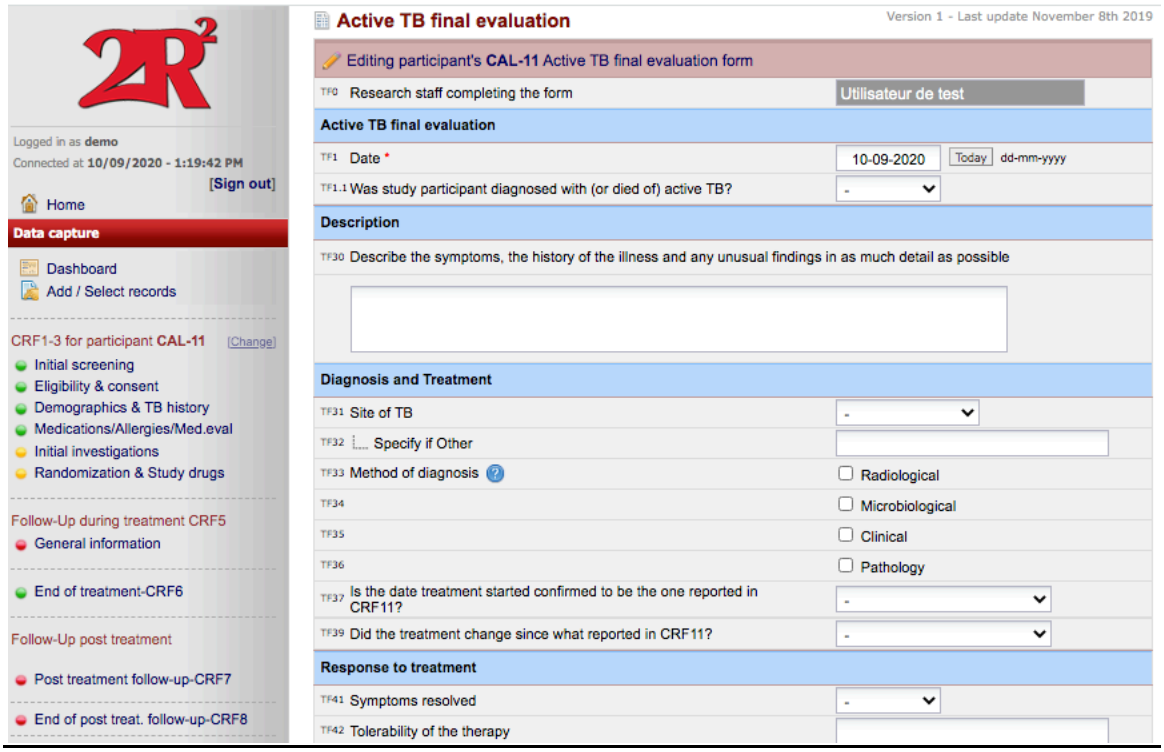
Once you are ready to enter information for **CRF12**, select the participant you want to enter **CRF12** for from the **"Add/Select participant records"** page, at the section "Active TB" (**figure 47**).

Figure 47



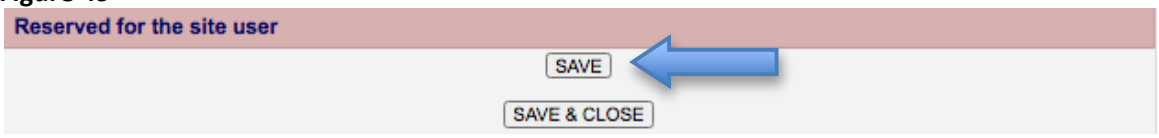
Once you have selected the participant in the dropdown list of **"Active TB Initial",** you can click on **CRF12** on the bottom of the left menu and **CRF12** will open (**figure 48**).

Figure 48



Complete the form with all the available information, then click on **"Save"** at the bottom of the page (**figure 49**).

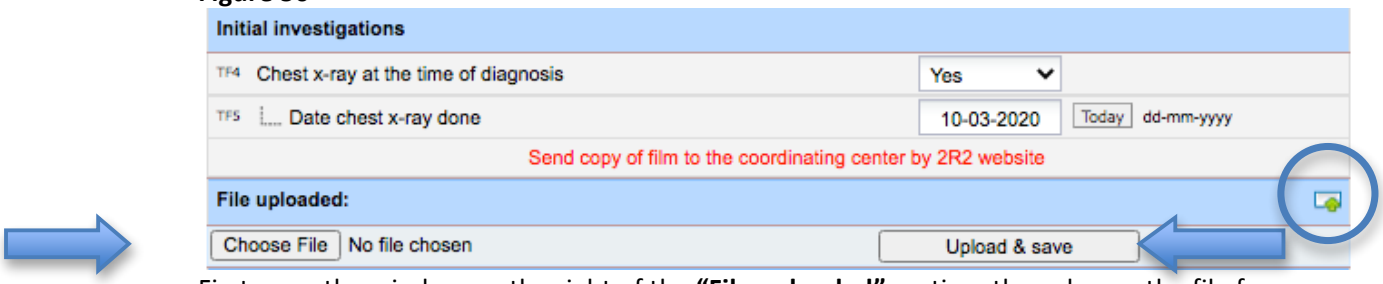
Figure 49



At this point, after having save all information, you will be able to upload the CXR pictures for this ATB report.

Upload the chest x-ray done at diagnosis of this Active TB event in the section **"File uploaded"** after variable TF5 (**figure 50**).

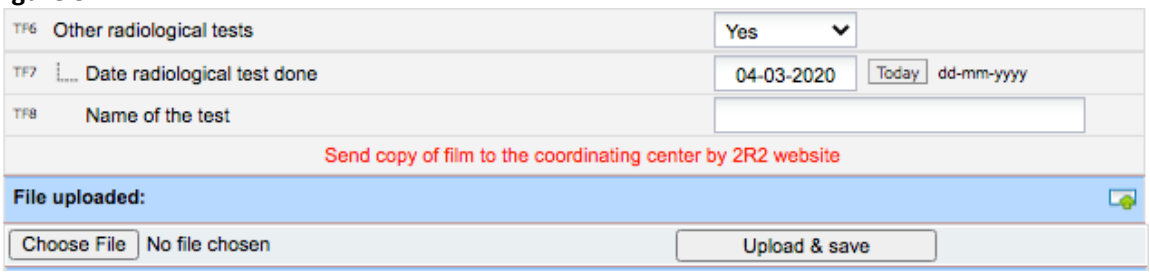
Figure 50



First open the window on the right of the **"File uploaded"** section, then choose the file from your computer (Note: file must be an .jpeg format) then, click on **"Upload & save".**

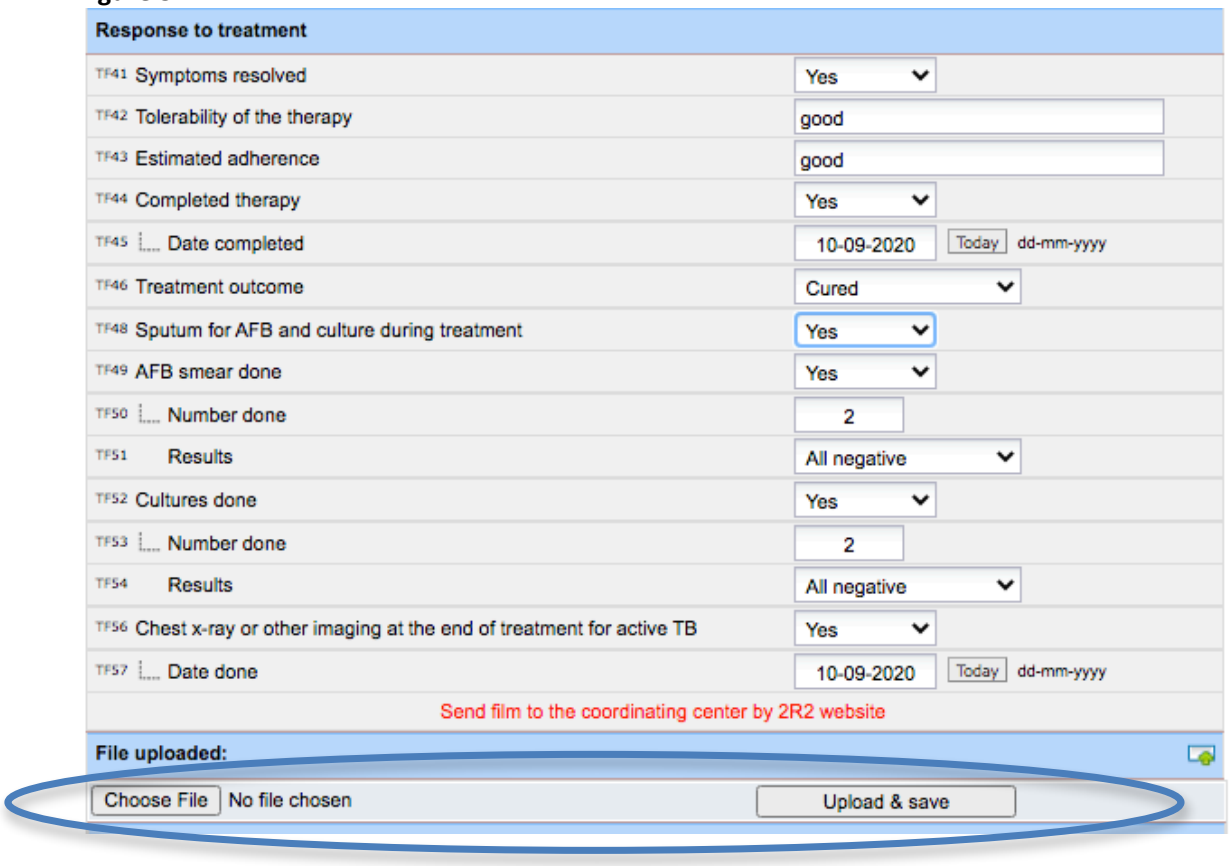
Upload in the same way other radiological test (if any), in the section **"File uploaded"** after variable TF8 (**figure 51).**

Figure 51



Upload the CXR done at the end of treatment (for all participants with ATB), after variable TF57 (**figure 52**).

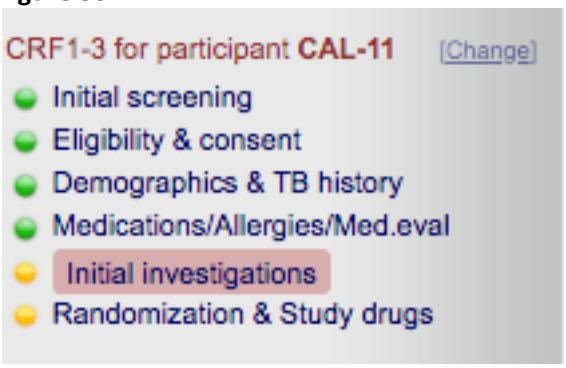
Figure 52



Once you are done with entering **CRF12**, you can click on **"SAVE&CLOSE"** at the bottom of the page. At this point the form cannot be modified any longer. **Note** : if you just want to save the page, and come back to work on it later, click on "**Save**".
Once you clicked on **"SAVE&CLOSE"** the dot beside **ATB initial CRF12**, on the left menu, will become yellow. An automatic message is also sent by the website to the coordinating center informing that there is a ATB final evaluation report to review. The coordinating center will review the **CRF12** and either ask you for more information (in that case the **CRF12** we be "reopen" and you will be able to modify it), or confirm it is complete. In this case the dot beside **CRF12** will become green. The ATB panel members will independently review the **CRF11** and **CRF12** for this ATB report and evaluate. If there is agreement the report is consider final. If there is no agreement and more information are needed, the coordinating center will contact you for more information, **CRF12** will be reopened and you will be able to modify it.

For participants who have an ATB report, please upload also the CXR done before randomization. To upload the CXR done before randomization, please go to **"Initial investigations" (in CRF3)**, choosing the page from the left menu for the participant for whom you just completed **CRF12 (figure 53)**.

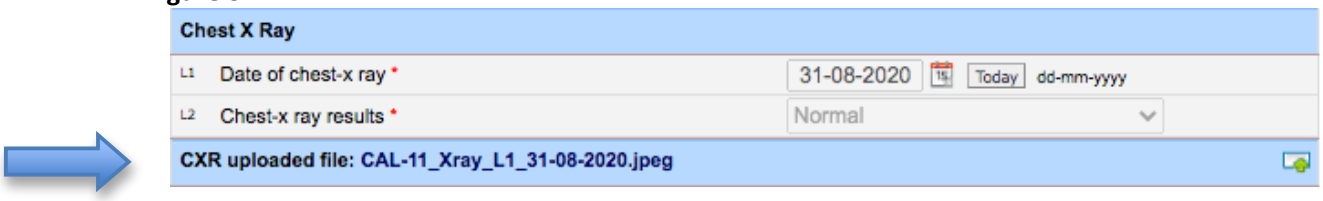
Figure 53



The CXR done at randomization can be uploaded after variable L2 (Chest-x ray results).

Please note that, for all the CXR uploaded, a unique name, without nominal information, is automatically given by the website (see example in **figure 54**)

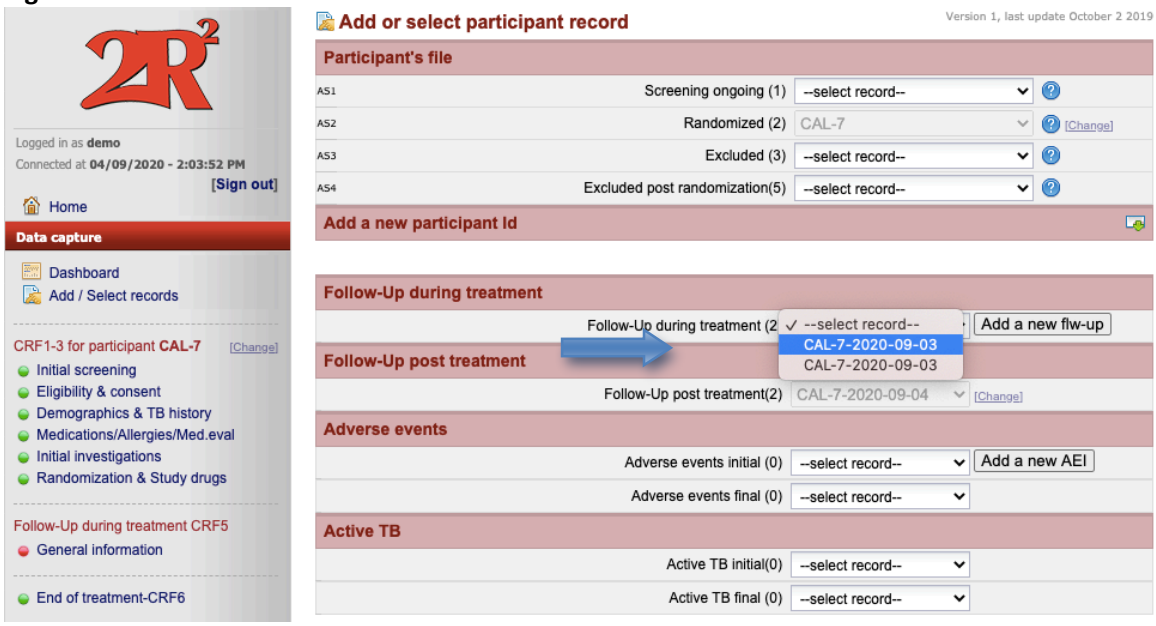
Figure 54



5.3.12 CRF13 Population PK

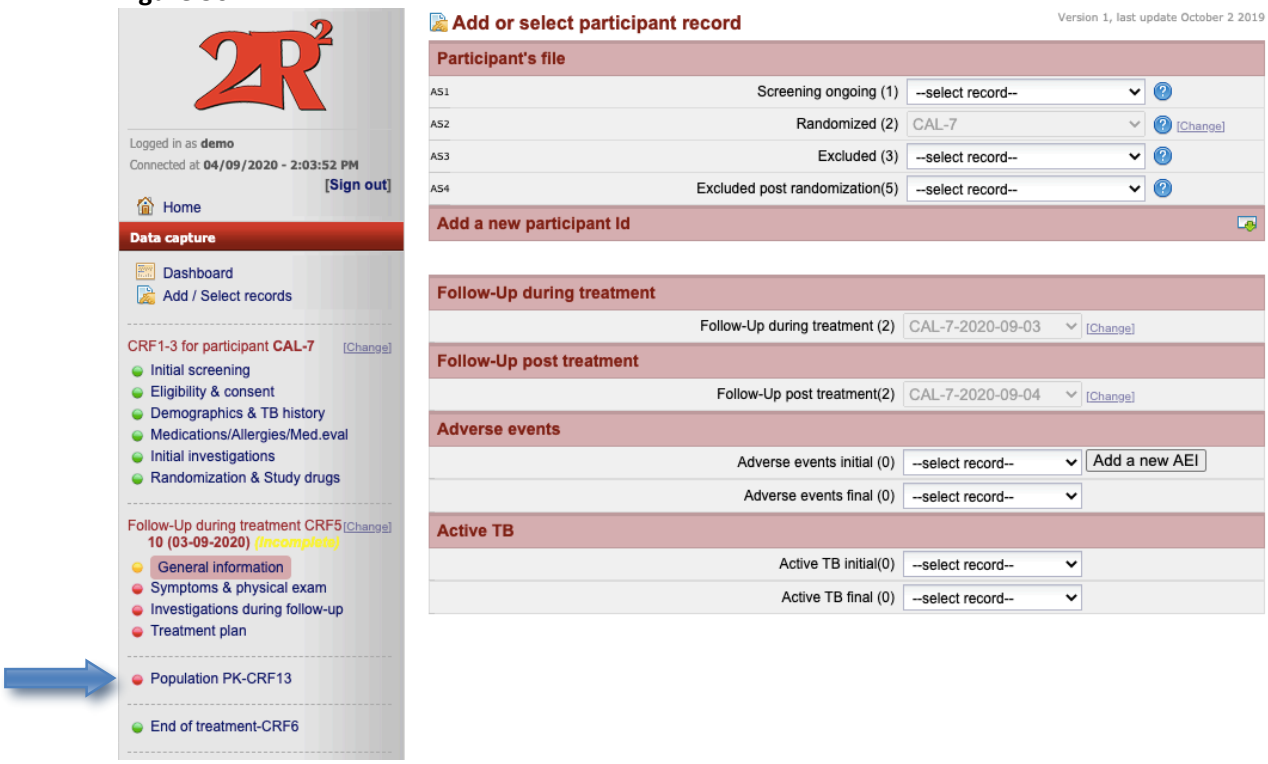
When you are ready to enter data from the Population PK form **CRF13**, select the "Follow-up during treatment" visit in which the PK was done for that participant, from the **"Add/select participant record"** (**figure 55**)

Figure 55



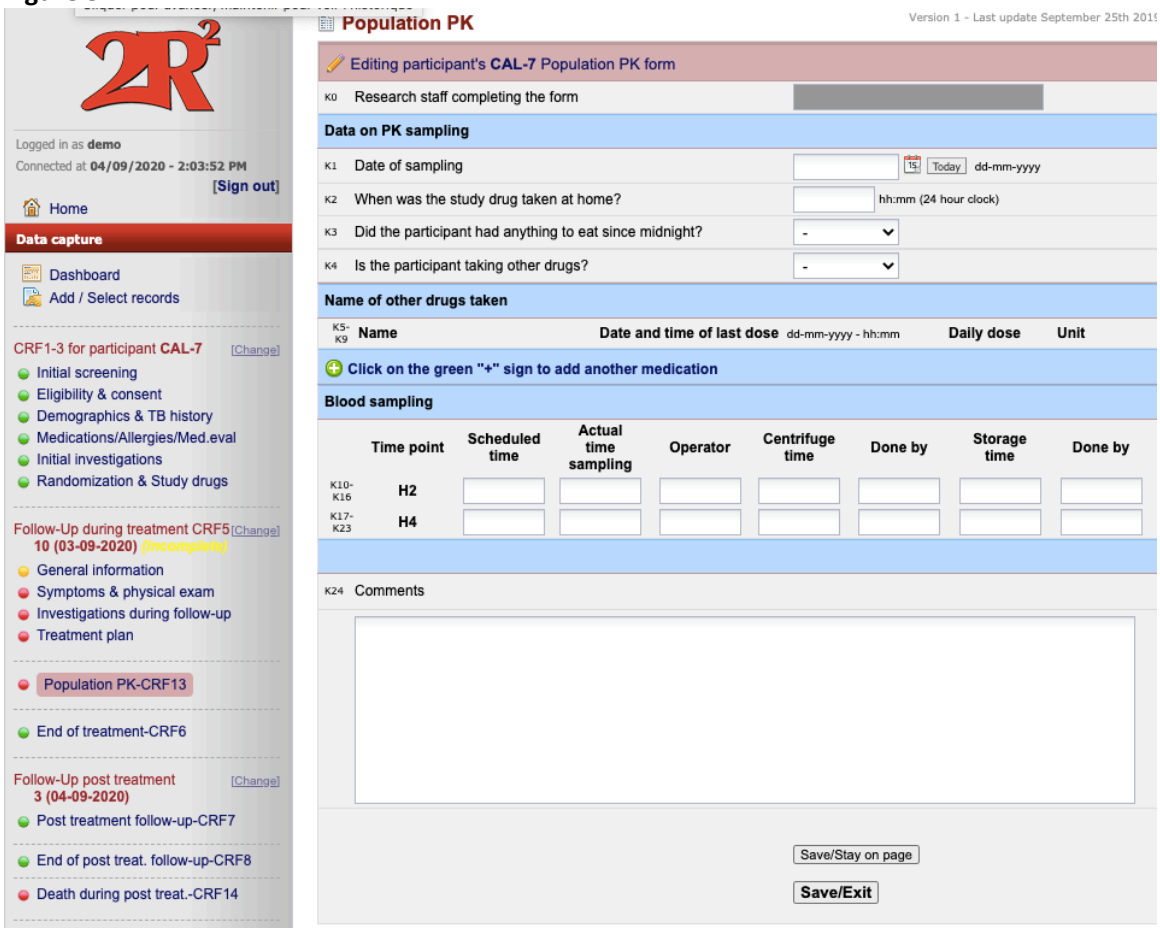
The population PK form **CRF13** will appear on the left menu, after the Follow-up form (**figure 56**)

Figure 56



Click on it, and the **CRF13** will appear. Once the form is completed, click on "**Save/Exit**" (**figure 57**).

Figure 57

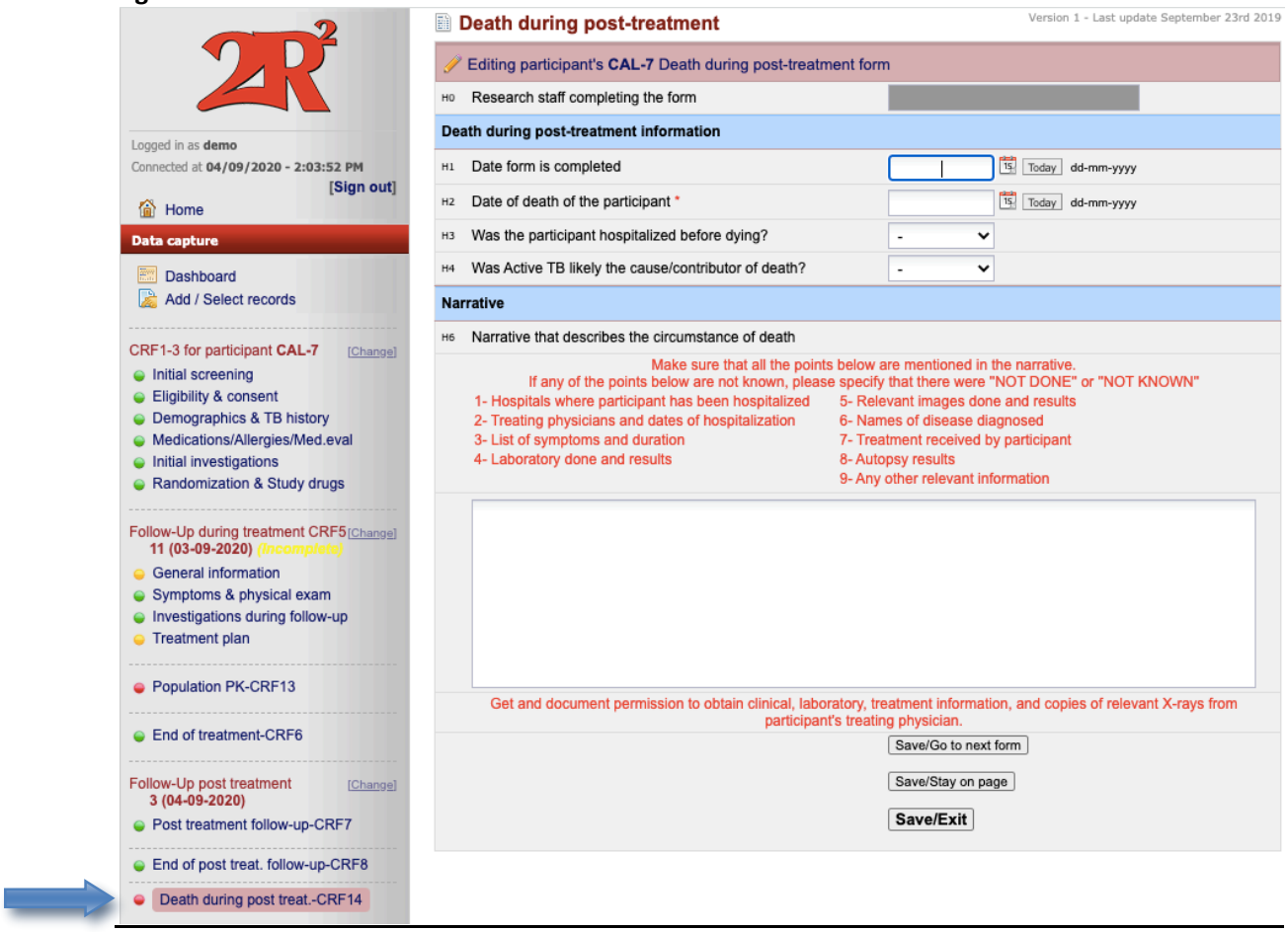


Note: if the participant has not done the PK sampling at a follow-up visit in which he/she was supposed to (i.e. the 4 weeks visit), remember to write it in variable F16 of **CRF5**. In that case, no **CRF13** needs to be completed.

5.3.13 CRF14 Death in post treatment follow-up

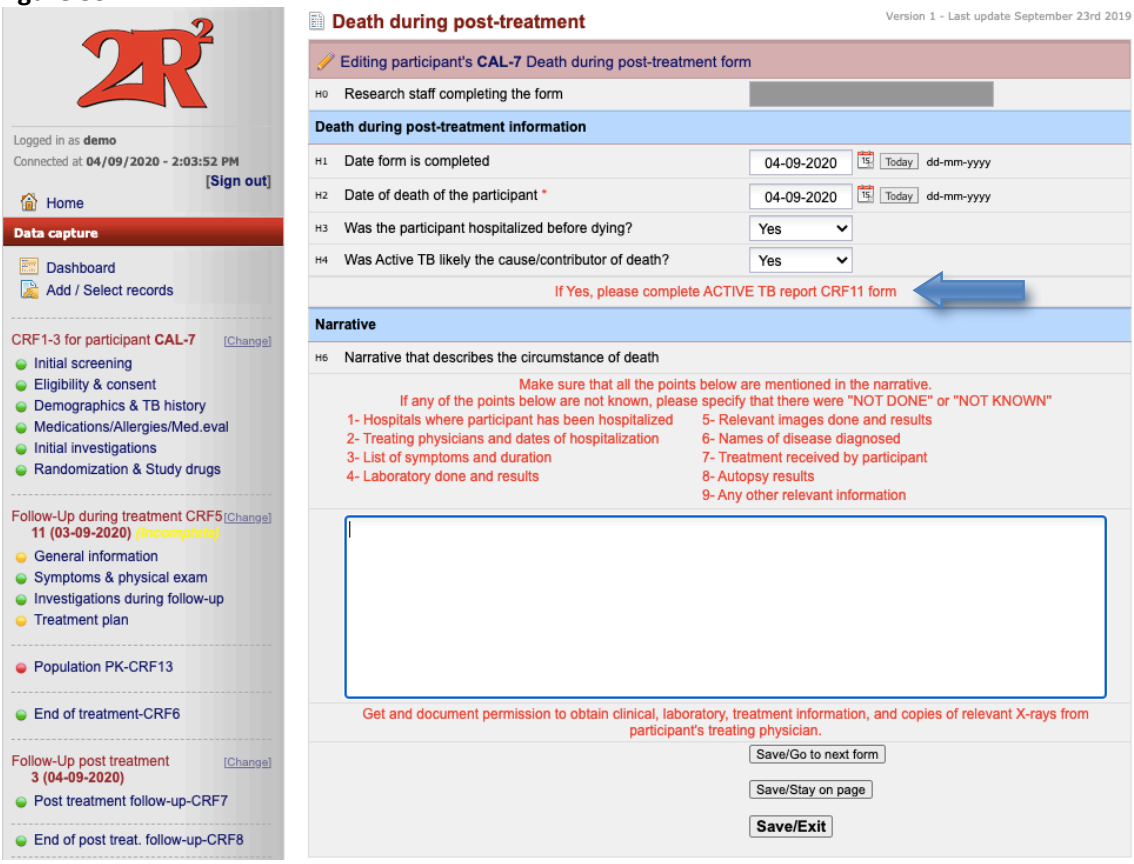
The form **"Death during post treatment follow-up"** becomes visible in the left menu when you already completed a form **"End of treatment CRF6"** for the same participant. If you need to enter a **CRF14**, select the participant from **"Add/Select records";** then click on "**Death in post treatment CRF14"** in the left menu and fill out the form. Click on **"Save/Exit"** when it's complete (**figure 58**).

Figure 58



Note: if a sentence in RED appears when you select a Yes on the question H4, **pay attention!** This means that you must fill out the ACTIVE TB report form **CRF11** before or after completing the Death during post treatment form (**figure 59**).

Figure 59



5.3.14 "Note to file" form site

If a change needs to be made to a completed and saved CRF you need to fill a " 2R2 Note to file" (see **Appendix 1).** Please complete first a paper "Note to file" (see SOP folder in 2R2 drop-box), then enter the "Note to file" in the 2R2 website. **Note**: if you prefer, you can complete a "Note to file" directly in the 2R2 website, but then you need to print it out and add it to the participant's folder (in order to have a copy of the "Note to file" both in the participant's folder and in the website).

The "Note to file" form is the official and standardized way to communicate between sites and coordinating center when there are modifications needed in CRFs. In this way, all the changes made are stored in the website, with a record of why and when they were made.

Changes could be done for the following reasons:

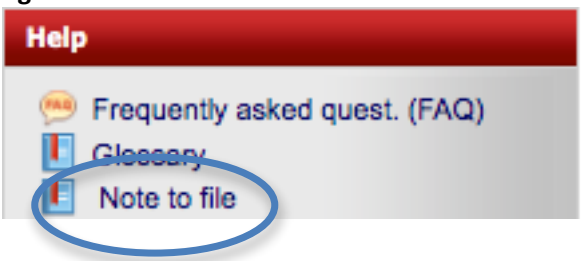
1. A manual randomization was done, and you need to inform the coordinating center so that the website can be updated to match the randomization received by the envelope used for the manual randomization;
2. A participant who has been randomized, meets one of the criteria for exclusion post randomization (see protocol, "Exclusion criteria post-randomization");
3. An error has been made in any CRF that needs to be corrected.

In all these cases you need to describe briefly what made the changes necessary.

Note: all changes done in e-CRFs must reflect the changes done in the paper CRFs. In paper CRFs changes will be dated and signed by the person doing them.

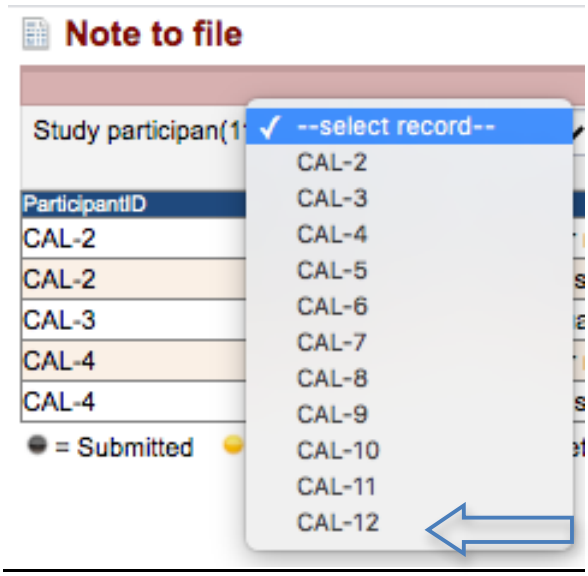
The "Note to file" can be found at the bottom of the left menu, in the "Help" section (**figure 60**)

Figure 60



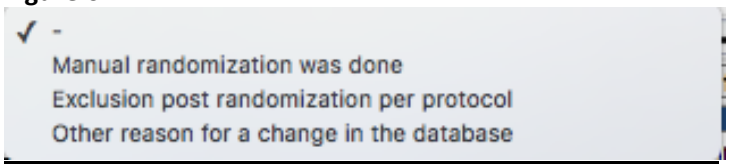
After clicking on **"Note to file",** select the participant for whom you would like to do the changes **(figure 61).**

Figure 61



Choose the reason why you need to make the change(s) for that participant among three choices given at variable NF1 (**figure 62**).

Figure 62



Fill in the required information for the option you have chosen **(figures 63-65)** and click on "**Add note to file**" at the bottom of the form.

Figure 63

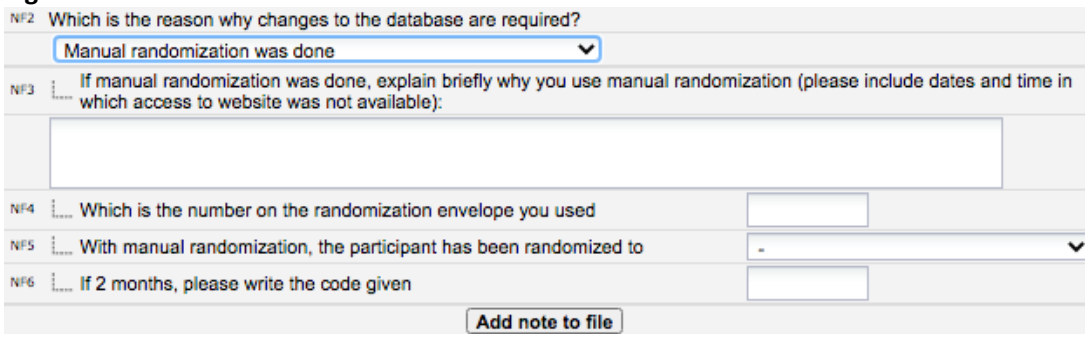
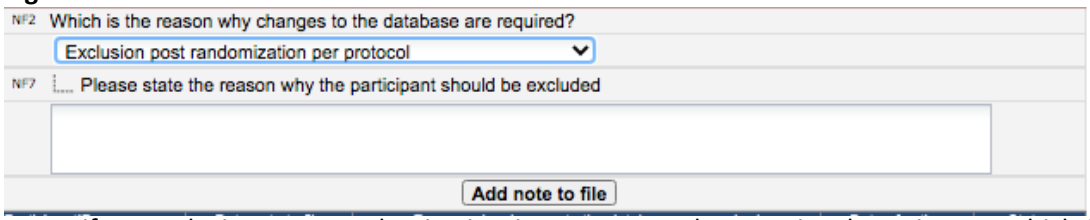
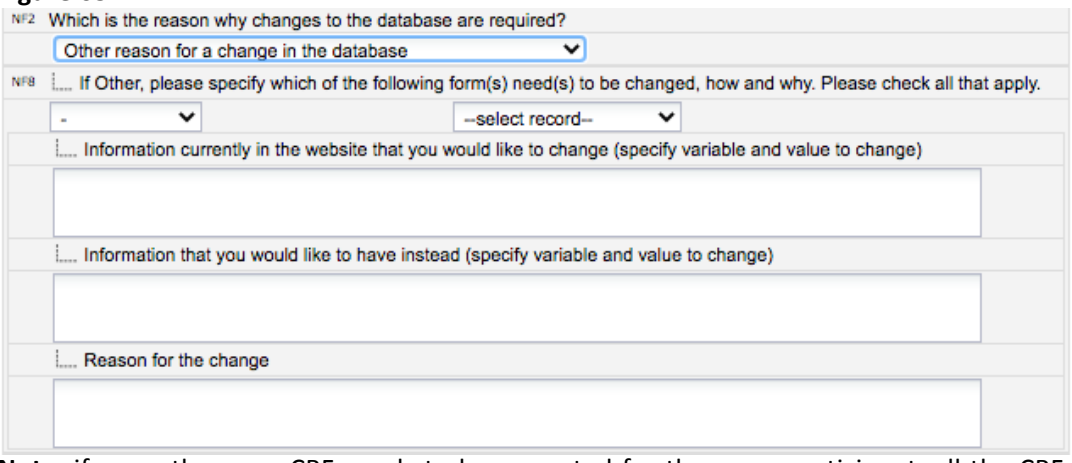


Figure 64



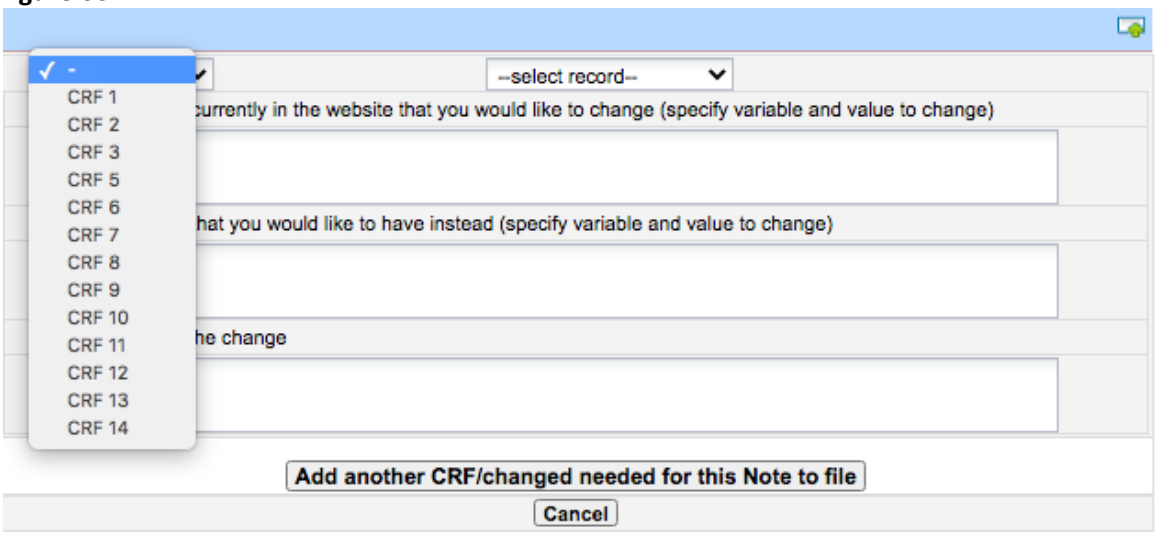
Note: if an exclusion post-randomization is necessary, please write down in NF7 which is the reason why that participant should be excluded. For example, write which are the result of the baseline lab test which are abnormal and which are the normal limit, etc.

Figure 65



Note: if more than one CRF needs to be corrected for the same participant, all the CRFs to be modified can be communicated in the same **"Note to file".** Once you have completed the information required for the first change, click on "**Add note to file**", then select another CRF from the scroll down menu. Click on "**Add another CRF/changed needed for this Note to file**" when you have entered the required information for the second change you want to make (**figure 66**).

Figure 66



When **"Add Note to File"** is clicked, an automatic message will be sent to the coordinating center who will process the required change. You will be contacted if more information is needed. Otherwise the note to file will be addressed, the required modifications will be made in the eCRF(s) and this **"note to file"** will be archived by the coordinating center. You can check the status of your notes on the **"Note to file page"** by clicking on **"Note to file"** in the left menu. You will see a summary table (**figure 67**)

Figure 67

ParticipantID	Date note to file	Reason why changes to the database are required	Date of action	Status
CAL-2	20-08-2020	Other reason for a change in the database	20-08-2020	
CAL-2	20-08-2020	Exclusion post randomization per protocol		

The notes that have been taken care of have a green dot in the "Status" column, the ones which are still on treatment at the coordinating center have a black dot. In this example, for participant CAL-2 the note to change CRF for other reasons has been processed on August 20th, the note on exclusion post randomization is still under process.

5.3.15 Checking your site's participants status

To check the list of your participants and the forms you have completed for your site, you can go to Dashboard (on the left menu) and then click on **Show section** in the Participants forms status (**figure 68**).

Figure 68

For each participant screened at your site (either randomized or not randomized yet), you will be able to see the status of each form.

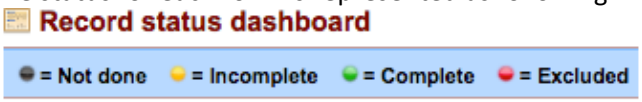
Participants forms status

Participant	Scr	Elig	Dem	Med	Invest	Rand	End Flup	End pst Flup	Death	ATB	Flw-up	Pst Flw-up	AE
CAL-5											0	0	0
CAL-7											3	2	1
CAL-11											1	0	0

Abbreviations used in this table:

Scr: CRF1
Elig: CRF2
Dem: CRF3-Demographic
Med: CRF3-Medical evaluation
Invest: CRF3-Initial investigations
Rand: CRF3-Randomization
End Flup: CRF6
End post Flup: CRF8
Death: CRF14
ATB: CRF11
Flw-up: Number of CRF5 entered
Post Flw up: Number of CRF7 entered
AE: Number of CRF9 entered

The status for each form is represented as following:



6.0. References

To practice you can access the demonstration site 2R2 demo at:
http://2r2-demo.crc.chus.qc.ca/index.aspx?uc=0
username: demo; password: demo

Appendix 1: 2R² Note to file
Note this paper form can be found in the 2R2 drop-box

A1.Participant's Study ID number ☐☐☐-☐☐☐ **A2. Center _____**

NF0. Research Staff completing the form _____

NF1. Date ☐☐☐☐☐☐☐☐
D D M M M Y Y Y Y

NF2. Which is the reason why changes to the database are required?

☐ **Manual randomization was done. If manual randomization was done:**

NF3: Explain briefly why you use manual randomization (please include dates and time in which access to website was not available):

_____

_____

_____

NF4: Which is the number on the randomization envelope you used: _____

NF5: With manual randomization, the participant has been randomized to :

☐ **4 months of Rifampin 10mg/kg/day**

☐ **2 months of Rifampin high dose, if 2 months, please write the code given (NF6)** ☐☐

☐ **Exclusion post randomization per protocol,**

NF7. Please state the reason why the participant should be excluded:

_____

☐ **Other reason for a change in the database**

(see next page)

NF8: If Other, please specify which of the following form(s) need(s) to be changed, how and why. Please check all that apply.

Form(s) to change	Information currently in the website that you would like to change (specify variable and value to change)	Information that you would like to have instead (specify variable and value to change)	Reason for the change
CRF1 ☐			
CRF2 ☐			
CRF3 ☐			
CRF5 ☐ date_____			
CRF5 ☐ date_____			
CRF5 ☐ date_____			
CRF5 ☐ date_____			
CRF6 ☐			
CRF7 ☐			
CRF8 ☐			
CRF9 ☐			
CRF10 ☐			
CRF11 ☐			
CRF12 ☐			
CRF13 ☐			
CRF14 ☐			

7.0. SOP Revision history

SOP code	Effective date	Summary of changes
SOP20_08Sep2020	15 September 2020	NA (original version)