

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 -2R² *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 2R² 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:

2R2 SOP20 Website site user's manual_08Sep2020

Higher dose Rifampin for 2 months vs Standard dose Rifampin for Latent TB: a 3-arm randomized trial.

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**)

Forgot your password? / Mot de passe oublié?

Your user name and your password will be sent to the email address you provide in the box below.
 Votre code d'utilisateur et mot de passe vous sera envoyé à l'adresse entrée plus bas.

email address / adresse courriel

Send

[Return to login page / Retour au Log in](#)

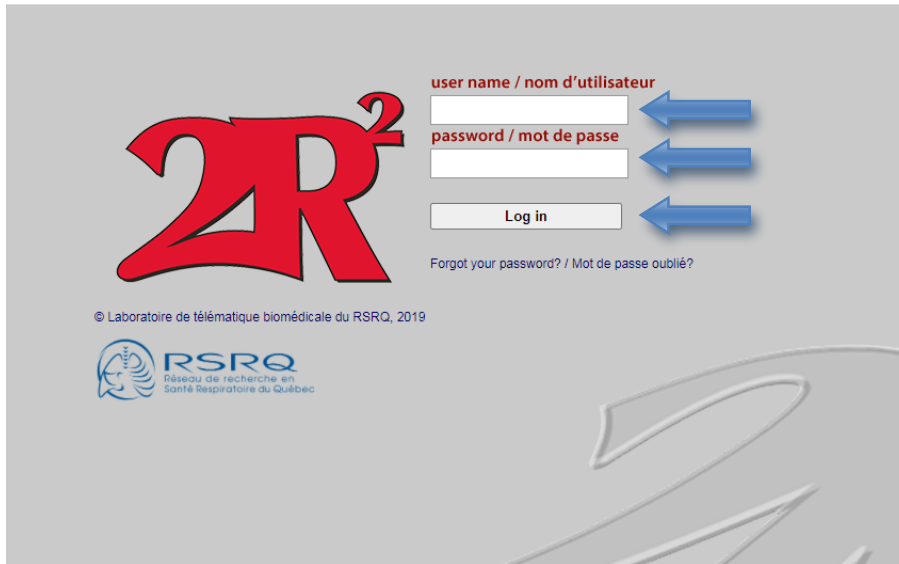
This window will appear,

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

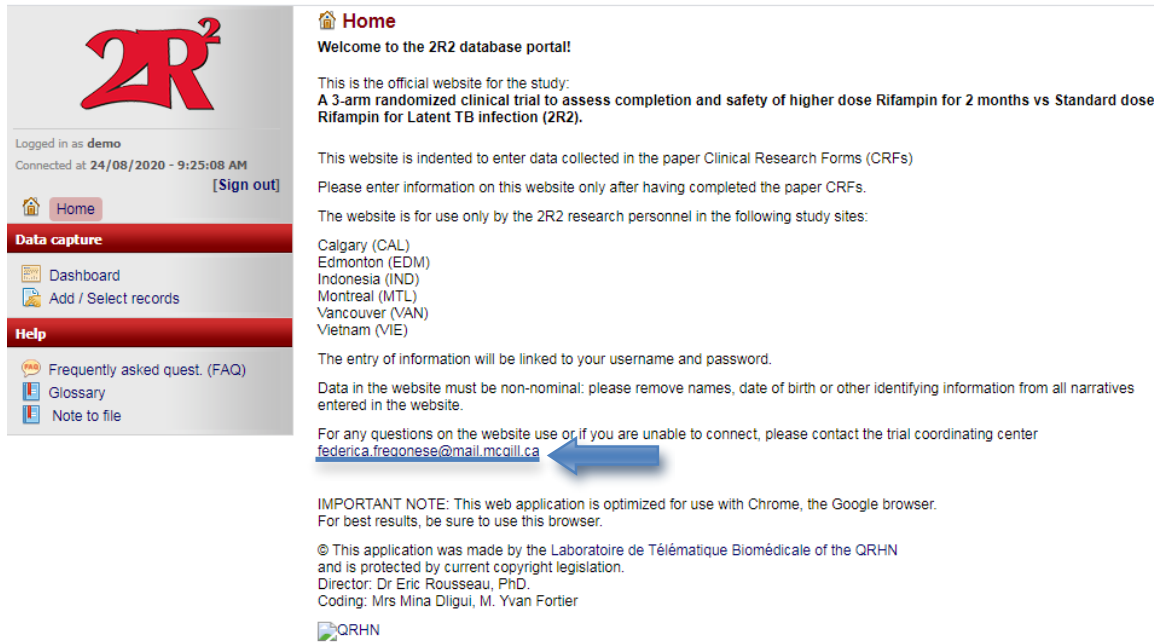


Note: data entered in the 2R2 website are linked to the username of person entering that case report form for the first time. Please do not share your password with anyone.

5.2 General information on the main page

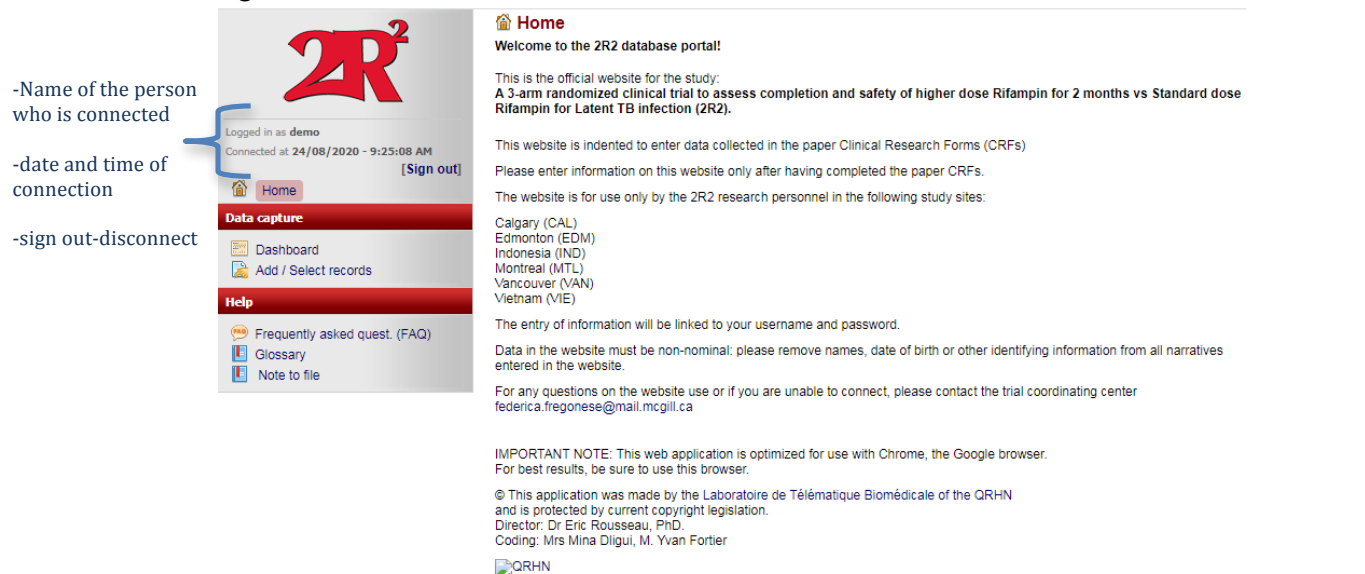
Once you completed the login to the website, you will see the home page (figure 3)
 From that page you can also have access to the contact for the coordinating center.

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



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.

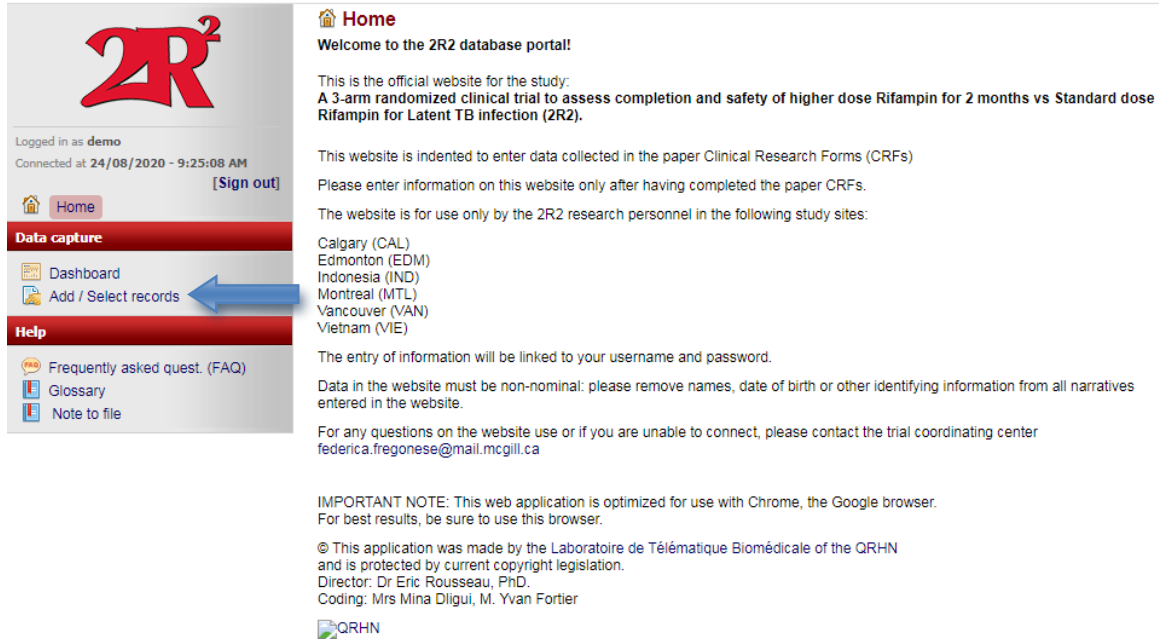
A site user can enter, review and modify only information for participants of that study sites.

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

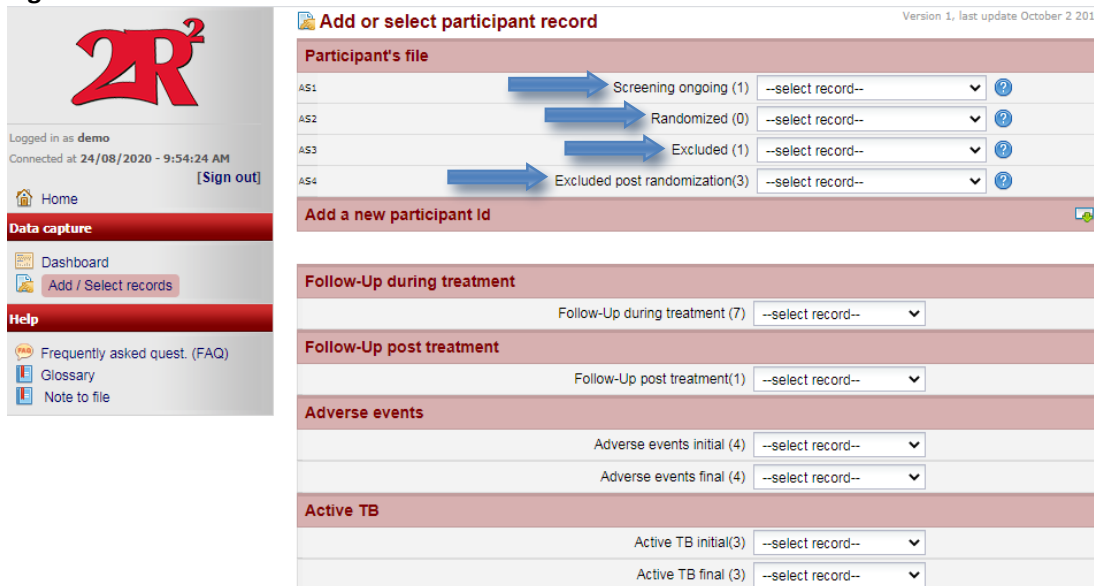
If you want to review a participant's file or if you want to add a new participant, click on "Add/select records" in the left menu (figure 5)

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

The screenshot displays the 2R2 website interface. On the left is a navigation sidebar with the 2R2 logo, user information (logged in as demo, connected at 24/08/2020 - 11:29:15 AM, sign out), and menu items for Home, Data capture (Dashboard, Add / Select records), and Help (Frequently asked quest. (FAQ), Glossary, Note to file). The main content area is titled "Add or select participant record" (Version 1, last update October 2 2019). It features a table under "Participant's file" with columns for ID, status, and a dropdown menu. The table lists AS1 (Screening ongoing (1)), AS2 (Randomized (1)), AS3 (Excluded (2)), and AS4 (Excluded post randomization(5)). Below the table is a section "Add a new participant Id" with a "Show section" button, which is highlighted by a blue arrow. Further down are sections for "Follow-Up during treatment" (7 records), "Follow-Up post treatment" (1 record), "Adverse events" (initial and final, each with 4 records), and "Active TB" (initial and final, each with 3 records).

Participant's file		
AS1	Screening ongoing (1)	--select record--
AS2	Randomized (1)	--select record--
AS3	Excluded (2)	--select record--
AS4	Excluded post randomization(5)	--select record--

Add a new participant Id [Show section](#)

Follow-Up during treatment	
Follow-Up during treatment (7)	--select record--

Follow-Up post treatment	
Follow-Up post treatment(1)	--select record--

Adverse events	
Adverse events initial (4)	--select record--
Adverse events final (4)	--select record--

Active TB	
Active TB initial(3)	--select record--
Active TB final (3)	--select record--

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

Figure 8

The screenshot shows the 'Add or select participant record' interface. On the left is a sidebar with the 2R2 logo, user information (demo), and navigation links. The main area has a header 'Add or select participant record' with a version note. Below are several sections, each with a dropdown menu: 'Participant's file' (AS1-AS4), 'Add a new participant Id' (with a 'Center(s)' dropdown set to 'CAL' and a 'Create a new participant Id' button highlighted by a blue arrow), 'Follow-Up during treatment', 'Follow-Up post treatment', 'Adverse events', and 'Active TB'.

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

The screenshot shows the 'Initial screening form' interface. On the left is a sidebar with the 2R2 logo, user information (ssenechal), and navigation links. The main area has a header 'Initial screening form' with a version note. Below are sections for 'Inclusion criteria' (questions 52-510), 'Exclusion criteria' (questions 513-520), and 'Confirmation of eligibility' (question 521). A 'NOTE' is displayed at the bottom, and there are 'Save/Stay on page' and 'Save/Exit' buttons.

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

Initial screening form Version 1, last update September 18th 2019

Editing participant: **CAL-11 Initial screening form**

50 Research staff completing the form Utilisateur de test

51 Date * 28-08-2020 Today dd-mm-yyyy

Inclusion criteria

52 Treatment of LTBI has been recommended, and the study participant, who is >= 10 years of age, has agreed to meet with the research personnel * Yes

53 Age * 45 years old

54 Sex * Male

55 Was TST testing done? * No

58 Is study participant a TST converter? * No

510 Was QFT testing done? * Yes

511 i.... If Yes, date of test 28-08-2020 Today dd-mm-yyyy

512 Results of QFT Positive

Exclusion criteria

513 Was study participant a contact of a TB patient known to have TB resistant to RIF? * No

514 Does study participant have a history of allergy/hypersensitivity to Rifampin, Rifabutin or Rifapentine? * No

516 Does study participant have Active TB? * No

517 Has study participant already started treatment for LTBI? * No

518 Does the participant take medications that the medical team judge not manageable with rifampin and that participant does not want to change? * No

519 Study participant was already treated for TB disease or LTBI * No

520 Study participant has AST or ALT at least 3 times higher than upper limit of normal OR hematological abnormalities of Grade 3 or 4? * No

Confirmation of eligibility

521 Is the participant eligible according to the 2R2 website? Yes, this patient IS eligible

NOTE: If participants is not eligible according to the website, but you think that study participant should be considered eligible, review and revise information and if still non eligible, contact the coordinating center

Go to next form

Save/Stay on page

Save/Exit

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

Version 1, last update September 18th 2019

Initial screening form

Editing participant's CAL-12 Initial screening form

S0 Research staff completing the form Utilisateur de test

S1 Date * Today dd-mm-yyyy

Inclusion criteria

S2 Treatment of LTBI has been recommended, and the study participant, who is >= 10 years of age, has agreed to meet with the research personnel *

S3 Age * years old

S4 Sex *

S5 Was TST testing done? *

S6 Is study participant a TST converter? *

S10 Was QFT testing done? *

S11 If Yes, date of test Today dd-mm-yyyy

S12 Results of QFT

Exclusion criteria

S13 Was study participant a contact of a TB patient known to have TB resistant to RIF? *

S14 Does study participant have a history of allergy/hypersensitivity to Rifampin, Rifabutin or Rifapentine? *

S16 Does study participant have Active TB? *

S17 Has study participant already started treatment for LTBI? *

S18 Does the participant take medications that the medical team judge not manageable with rifampin and that participant does not want to change? *

S19 Study participant was already treated for TB disease or LTBI *

S20 Study participant has AST or ALT at least 3 times higher than upper limit of normal OR hematological abnormalities of Grade 3 or 4 ? *

Confirmation of eligibility

S21 Is the participant eligible according to the 2R2 website? NOTE: If participants is not eligible according to the website, but you think that study participant should be considered eligible, review and revise information and if still non eligible, contact the coordinating center

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)

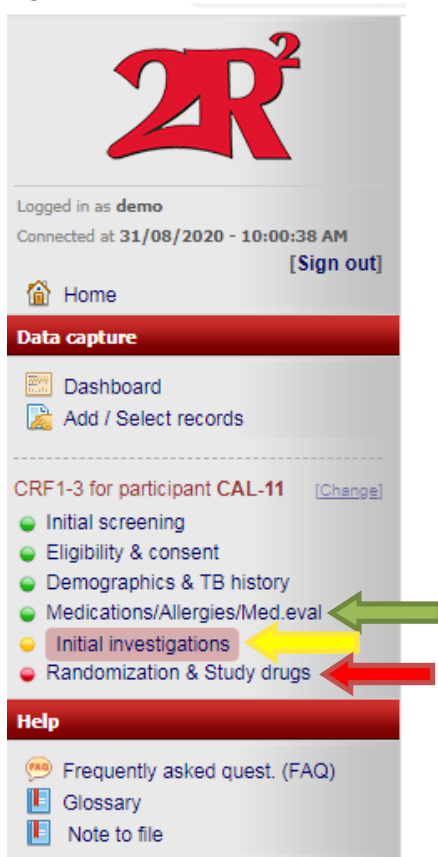
Continue with the Demographics & TB history, Medication/allergies/Med. Eval., Initial investigations and Randomization & Study drugs pages from CRF3 then "save/go to next form" (figure 13).

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

Randomization and study drug Version 1, last update October 2 2019

Editing participant's CAL-5 Randomization and study drug form

Research staff completing the form

Randomization status for this participant

Forms	Status	Randomization criteria
Initial screening	✓	S1 S2 S3 S4 S5 S6 S7 S8 S10 S11 S12 S13 S14 S15 S16 S17 S18 S19 S20
Eligibility & consent	✓	C1 C2 C4 C5 C8
Demographics & TB hist.	! D2	D7 D10 D12 D13 D15 D16 D25 D29 D30 D32 D37 D40
Medications/Allergies	✓	M1 M2.2 M3 M4 M5 M12 M13 M14 M15 M16 M17 M18 M19 M20 M21 M22 M23 M24 M25
Initial investigations	✓	L1 L2 L8 L9 L14 L16 L18 L19 L20 L21 L26.1 L28 L30 L32

Data capture

- Dashboard
- Add / Select records

CRF1-3 for participant CAL-5 [\[Change\]](#)

- Initial screening
- Eligibility & consent
- Demographics & TB history
- Medications/Allergies/Med.eval
- Initial investigations
- Randomization & Study drugs

Help

- Frequently asked quest. (FAQ)
- Glossary
- Note to file

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

Randomization and study drug Version 1, last update October 2 2019

Editing participant's CAL-11 Randomization and study drug form

Research staff completing the form

Randomization status for this participant

Forms	Status	Randomization criteria
Initial screening	✓ S1 S2 S3 S4 S5 S6 S7 S8 S10 S11 S12 S13 S14 S15 S16 S17 S18 S19 S20	
Eligibility & consent	✓ C1 C2 C4 C5 C8	
Demographics & TB hist.	✓ D2 D7 D10 D12 D13 D15 D16 D25 D29 D30 D32 D37 D40	
Medications/Allergies	✓ M1 M2.2 M3 M4 M5 M12 M13 M14 M15 M16 M17 M18 M19 M20 M21 M22 M23 M24 M25	
Initial investigations	✓ L1 L2 L8 L9 L14 L16 L18 L19 L20 L21 L26.1 L28 L30 L32	

Randomization and study drugs

R1 Are you ready to randomize this participant?



★ **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

Initial investigations form Version 1, last update September 18th 2019

Editing participant's CAL-11 Initial investigations form

Research staff completing the form Utilisateur de test

Chest X Ray

L1 Date of chest-x ray * dd-mm-yyyy

L2 Chest-x ray results *

CXR uploaded file:

L4 Other radiological tests

Microbiology

L8 Microbiology *

Laboratory

L19 Date test was performed * dd-mm-yyyy

L20 Alanine transaminase (ALT) U/L

L20.1 Upper Normal value for ALT

L21 Aspartate aminotransferase (AST) U/L

L21.1 Upper Normal value for AST

Please fill at least one of the two between L20 and L21

L22 Total bilirubin umol/L

L22.1 Upper normal limit (total bilirubin) umol/L

L23 Hemoglobin g/L

L24 Hematocrit L/L

L25 White blood cells 10⁹/L

L26 Platelets 10⁹/L

L26.1 Is there any hematological abnormality of grade 3 or 4?

L27 If participant is HIV+, viral load copies/ml

HIV testing

L28 Has treating team offered HIV testing to study participant? *

L32 Pregnancy test



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

The screenshot shows the 2R2 website interface. On the left is a navigation sidebar with a red '2R²' logo at the top. Below the logo, it says 'Logged in as demo' and 'Connected at 31/08/2020 - 12:37:03 PM'. There are links for 'Home', 'Data capture', 'Dashboard', and 'Add / Select records'. Under 'CRF1-3 for participant CAL-11', there are several items with colored dots: Initial screening (green), Eligibility & consent (green), Demographics & TB history (green), Medications/Allergies/Med. eval (green), Initial investigations (yellow), and Randomization & Study drugs (yellow). A blue arrow points to the 'Randomization & Study drugs' item. Below this is a 'Help' section with links for 'Frequently asked quest. (FAQ)', 'Glossary', and 'Note to file'. The main content area is titled 'Randomization and study drug' and 'Editing participant's CAL-11 Randomization and study drug form'. It shows a table of randomization criteria with columns for 'Forms', 'Status', and 'Randomization criteria'. The criteria include 'Initial screening', 'Eligibility & consent', 'Demographics & TB hist.', 'Medications/Allergies', and 'Initial investigations'. The 'Initial investigations' row has yellow highlights on L20, L21, and L26.1. Below the table is a section 'Randomization and study drugs' with a question 'Are you ready to randomize this participant?' and a 'Yes, please randomize this participant' button. There are also 'Save/Exit', 'Save/Stay on page', and 'Save/Go to next form' buttons.

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

The screenshot shows the 2R2 website interface after randomization. The left sidebar menu is similar to Figure 18, but the 'Randomization & Study drugs' item now has a red dot. The main content area is titled 'Randomization and study drug' and 'Editing participant's CAL-11 Randomization and study drug form'. It shows a table of randomization criteria with columns for 'Forms', 'Status', and 'Randomization criteria'. The criteria include 'Initial screening', 'Eligibility & consent', 'Demographics & TB hist.', 'Medications/Allergies', and 'Initial investigations'. The 'Initial investigations' row has yellow highlights on L20, L21, and L26.1. Below the table is a section 'Randomization and study drugs' with questions R1 through R9. R1 is 'Are you ready to randomize this participant?' with a 'Yes, please randomize this participant' button. R2 is 'Study participant is randomized to' with a dropdown menu showing '4 months of Rifampin standard dose'. R3 is 'Dose should be' with a dropdown menu showing '600 mg/day'. R7 is 'Number of daily doses of study medication dispensed today' with a dropdown menu showing 'doses'. R8 is 'How many days will these pills be for?' with a dropdown menu showing 'days'. R9 is 'Suggested date of next visit is' with a dropdown menu showing '25-09-2020'. There are also 'Save/Exit', 'Save/Stay on page', and 'Save/Go to next form' buttons.

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:

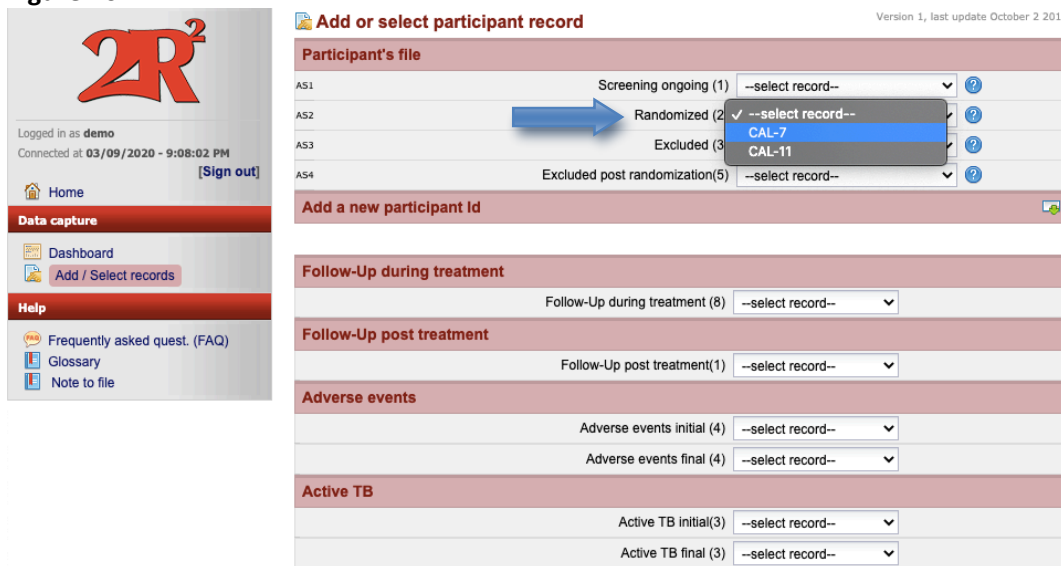
1. In the website, CRF5 has been divided in 4 pages: "General Information", "Symptoms and physical exam", "Investigations during follow-up" and "Treatment Plan".

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.

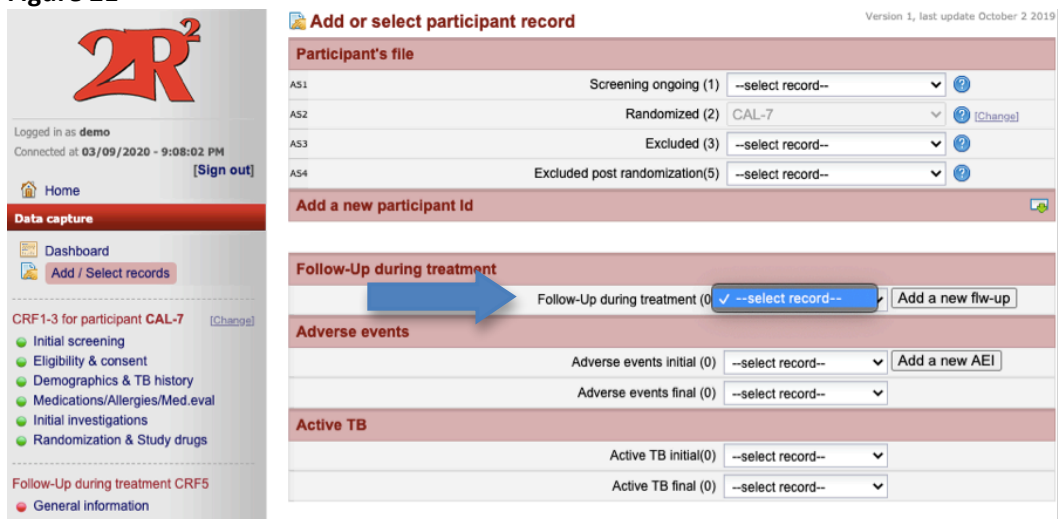
Click on a participant who has been already randomized (by opening the scroll down list at "Randomized") and for whom you want to enter the follow-up form (figure 20)

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

Current symptoms and Physical exam Version 1 - Last update October 3 2019

Editing participant's CAL-7 Current symptoms and Physical exam form

Y0 Research staff completing the form Utilisateur de test

Current symptoms and Physical exam

Does the study participant have any of the following symptoms TODAY?

Y1	Fever/Night sweats?	No
Y3	Weight loss without dieting?	No
Y5	Cough?	No
Y7	Sputum production?	No
Y9	Skin problems? ?	No
Y11	Gastrointestinal problems? ?	No
Y13	Neurological problems? ?	No
Y15	Other? ?	No
Y17	Physical exam is ?	Not necessary

Save/Go to next form
Save/Stay on page
Save/Exit

Figure 25

Investigations during follow-up Version 1 - Last update October 3 2019

Editing participant's CAL-7 Investigations during follow-up form

F0 Research staff completing the form Utilisateur de test

Investigations

Note: at the 4 weeks FOLLOW-UP VISIT, the following ARE REQUIRED, otherwise as clinically indicated

F1	Date tests were performed	01-09-2020	Today	dd-mm-yyyy
F2	Alanine transaminase (ALT)	20		U/L
F3	Aspartate aminotransferase (AST)	30		U/L
F4	Total bilirubin			umol/L
F5	Creatinine			mg/dL
F6	BUN (blood urea nitrogen)			mg/dL
F7	Hemoglobin			g/L
F8	Hematocrit			L/L
F9	White blood cells			10 ⁹ /L
F10	Platelets			10 ⁹ /L
F11	Other investigations			
F12	Does study participant require monitoring of other medications being taken?	No		
F16	If this is the 4 weeks FOLLOW-UP VISIT: were samples for PK taken?	-		

Save/Go to next form

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

CRF5 form status

Please indicate in N8 if CRF 5 is now completed.

N8 CRF5 form status is :

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

2R2

Logged in as demo
Connected at 04/09/2020 - 10:32:01 AM [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

Adverse event

- AE initial evaluation-CRF9

Active TB

- ATB initial-CRF11

Treatment plan Version 1 - Last update October 3 2019

Editing participant's CAL-7 Treatment plan form

N0 Research staff completing the form: Research staff / Utilisateur de test

Other medications

N1 Is the study participant taking any NEW medications prescribed by a doctor? No

Action regarding study medication

N5 Plan Study medication continued as per protocol at same dose

N5.1 Pills of study medication that were dispensed today for participant who is in 2 months high dose arm 72 pills

N5.3 How many days will the pills dispensed today be for? 18 days

N6 Suggested date for next visit

Suggested date for Follow-Up during treatment 1: 07-09-2020

Suggested date for Follow-Up during treatment 2: 21-09-2020

Suggested date for Follow-Up during treatment 3: 19-10-2020

N7 General comments

CRF5 form status

CRF5 status will be confirmed by 2R2 coordinator.

N8 CRF5 form status is :

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

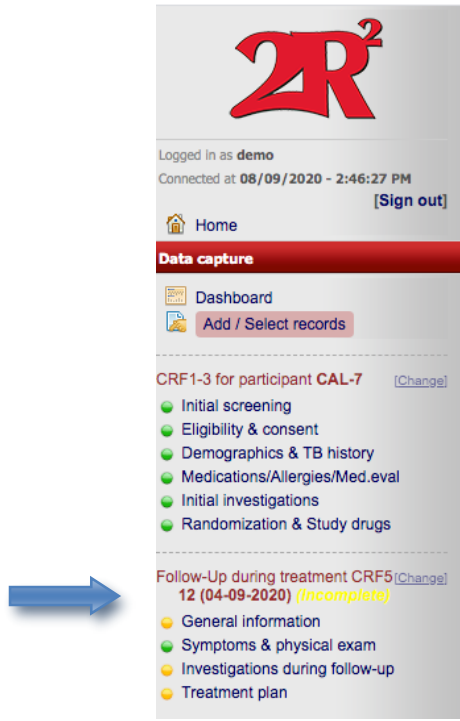


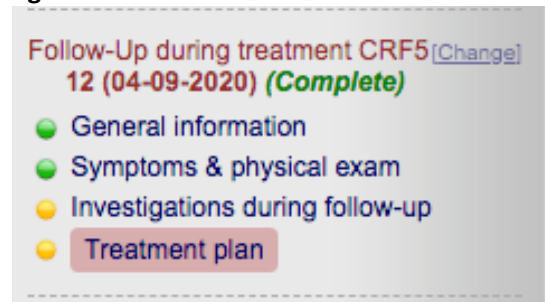
Figure 28

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 is 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 word 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

End of treatment Version 1 - Last update October 3 2019

Editing participant's CAL-11 End of treatment form

T0 Research staff completing the form

End of treatment

T1 Reason for stopping *

T5 General comments

Study participant is now in post treatment follow-up

T6 Suggested date of 1st FOLLOW-UP CALL/VISIT for this participant is

Save/Go to next form

Save/Stay on page

Save/Exit



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

End of treatment Version 1 - Last update October 3 2019

Editing participant's CAL-11 End of treatment form

T0 Research staff completing the form

End of treatment

T1 Reason for stopping *

Study medication stopped due to an adverse event

REPORT Adverse Event Initial CRF 9, if not already done

T4 Date of the last dose taken by participant ? 04-09-2020 Today dd-mm-yyyy

T5 General comments

Study participant is now in post treatment follow-up

T6 Suggested date of 1st FOLLOW-UP CALL/VISIT for this participant is

Save/Go to next form

Save/Stay on page

Save/Exit

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 screenshot displays the 'Add or select participant record' page. On the left, a sidebar menu lists various CRF sections. Under 'Follow-Up post treatment', 'Post treatment follow-up-CRF7' is highlighted with a blue arrow. The main content area is titled 'Add or select participant record' and includes a table of participant records:

Participant's file		
AS1	Screening ongoing (1)	--select record--
AS2	Randomized (2)	CAL-11
AS3	Excluded (3)	--select record--
AS4	Excluded post randomization(5)	--select record--

Below the table, there are sections for adding new records:

- Follow-Up during treatment:** Follow-Up during treatment (1) --select record-- Add a new flw-up
- Follow-Up post treatment:** Follow-Up post treatment(0) --select record-- Add a new pst (highlighted with a blue arrow)
- Adverse events:** Adverse events initial (0) --select record-- Add a new AEI; Adverse events final (0) --select record--
- Active TB:** Active TB initial(0) --select record--; Active TB final (0) --select record--

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

The screenshot displays the 'Post treatment follow-up' form for participant CAL-7. The sidebar on the left provides navigation through various data capture and follow-up stages. The main form area is divided into several sections:

- Post treatment follow-up:** Contains fields for date of call/visit (P1), contact status (P2, P5, P6), and a comments box (P7).
- Changes in health status since last call:** Includes questions about changes in health status (P8), hospitalization (P9), new diagnoses (P10), and new medications (P11). A narrative box (P12) is provided for detailed notes.
- Current symptoms:** A section titled 'Does the study participant have any of the following symptoms TODAY?' with checkboxes for fever/night sweats (P13), weight loss (P15), cough (P17), sputum (P19), other (P21), and physical exam (P23).
- Follow-up:** A final question (P25) asking if this is the last follow-up call, with 'Save/Go to next form', 'Save/Stay on page', and 'Save/Exit' buttons.

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 screenshot displays the 2R2 website interface. On the left is a sidebar menu with a red '2R' logo at the top. Below the logo, it shows the user is logged in as 'demo' and connected at '04/09/2020 - 2:03:52 PM'. The sidebar is divided into sections: 'Data capture' (with 'Dashboard' and 'Add / Select records' options), 'CRF1-3 for participant CAL-11' (with a 'Change' link and a list of CRFs: Initial screening, Eligibility & consent, Demographics & TB history, Medications/Allergies/Med.eval, Initial investigations, Randomization & Study drugs), 'Follow-Up during treatment CRF5' (with 'General information' and 'End of treatment-CRF6'), 'Follow-Up post treatment' (with 'Post treatment follow-up-CRF7', 'End of post treat. follow-up-CRF8', and 'Death during post treat.-CRF14'), 'Adverse event' (with 'AE initial evaluation-CRF9'), and 'Active TB' (with 'ATB initial-CRF11'). A blue arrow points to 'AE initial evaluation-CRF9'.

The main content area is titled 'Add or select participant record' (Version 1, last update October 2 2019). It contains several sections:

- Participant's file:** A table with columns for participant ID, status, and a dropdown menu.

AS1	Screening ongoing (1)	--select record--	?
AS2	Randomized (2)	CAL-11	Change
AS3	Excluded (3)	--select record--	?
AS4	Excluded post randomization(5)	--select record--	?
- Add a new participant Id:** A button with a plus icon.
- Follow-Up during treatment:** A dropdown menu for 'Follow-Up during treatment (1)' with an 'Add a new flw-up' button.
- Follow-Up post treatment:** A dropdown menu for 'Follow-Up post treatment(0)' with an 'Add a new pst flw-up' button.
- Adverse events:** Two dropdown menus for 'Adverse events initial (0)' and 'Adverse events final (0)'. The 'Add a new AEI' button is highlighted with a blue arrow.
- Active TB:** Two dropdown menus for 'Active TB initial(0)' and 'Active TB final (0)'.

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

The screenshot shows the 'Adverse event initial evaluation' form. The left sidebar contains navigation options like 'Data capture', 'Dashboard', and 'Add / Select records'. The main content area is titled 'Adverse event initial evaluation' and includes the following sections:

- Editing participant's CAL-11 Adverse event initial evaluation form**
- Adverse event initial evaluation**
 - A10 Research staff completing the form
 - A11 Event number
 - A12 Date of event * (calendar icon, Today, dd-mm-yyyy)
 - Regarding study medication status, please select one (dropdown menu)
- Description of adverse event and investigations done**
 - Which was the most important reason for stopping study medication?** (choose one or more, as applies)
 - A15 Death
 - A18 Hepatotoxicity
 - A117 Hematologic
 - A120 Drug interaction
 - A122 Gastrointestinal intolerance
 - A129 Pregnancy
 - A132 Rash
 - A135 Possible active TB
 - A136 Other reason for stopping
 - Which of the following MANDATORY TESTS were undertaken for this event?** (choose all that applies except if differently specified)
 - A139 Was any other investigation done (a part from the one already listed in A15-A137)? (dropdown menu)
 - A141 Was the participant referred to other specialist? (dropdown menu)
 - A142 Was the participant hospitalized? (dropdown menu)
- History of adverse event**
 - A143 Date of onset of symptoms (calendar icon, Today, dd-mm-yyyy)
 - A144 Date in which study participant took the last dose of study medication (calendar icon, Today, dd-mm-yyyy)
 - A145 Describe the symptoms and the current history of the event using as much detail as possible. Make sure that all the points below are mentioned in the narrative. If any of these points are not known, please write "NOT DONE/NOT KNOWN".
 - 1. Time at which medication is usually taken
 - 2. Number of hours between ingestion of medication and onset of symptoms
 - 7. If participant had any recent exposure to allergens or food
 - 8. If participant had any past history of disease

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

The screenshot shows the bottom of the form with two buttons: "Save/Stay on page" and "SAVE & CLOSE".

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

Adverse event initial evaluation Version 1 - Last update September 24th 2019

Editing participant's CAL-7 Adverse event initial evaluation form

A10 Research staff completing the form Utilisateur de test

Adverse event initial evaluation

A11 Event number 1

A12 Date of event * 04-09-2020 TS Today dd-mm-yyyy

Regarding study medication status, please select one

A13 ▼
Study medication was stopped before the study participant completed the full course

Why was study medication stopped?

A14 ▼
Treating team stopped medication due to potential adverse event

Description of adverse event and investigations done

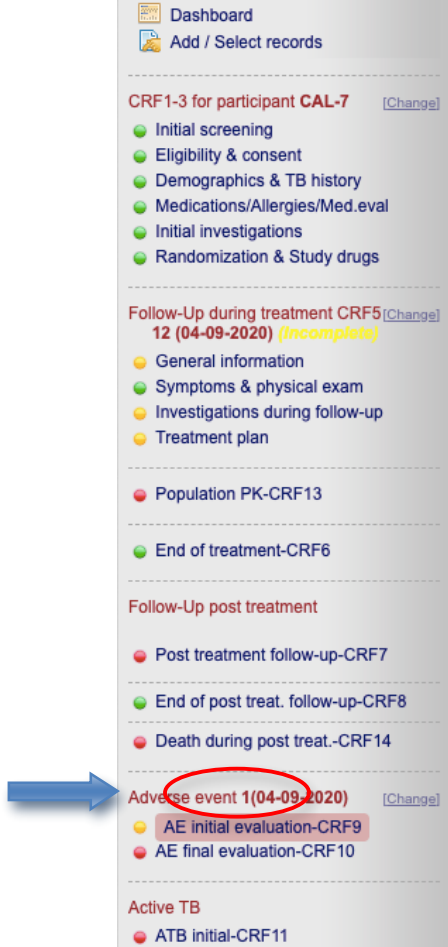
Which was the most important reason for stopping study medication? (choose one or more, as applies)	Which of the following MANDATORY TESTS were undertaken for this event? (choose all that applies except if differently specified)	
A15 <input type="checkbox"/> Death		
A18 <input type="checkbox"/> Hepatotoxicity		
A117 <input type="checkbox"/> Hematologic		
A120 <input type="checkbox"/> Drug interaction		
A122 <input checked="" type="checkbox"/> Gastrointestinal intolerance		
A123 <input type="checkbox"/> Specify	<input checked="" type="checkbox"/> Liver function test	<input checked="" type="checkbox"/> Complete blood count
A124 <input type="checkbox"/> Specify	<input type="checkbox"/> Amylase	<input type="checkbox"/> Pregnancy test
A125 <input type="checkbox"/> Specify	<input type="checkbox"/> Date of last menstrual period was asked	
A126 <input type="checkbox"/> Specify	<input type="checkbox"/> Abdominal/liver ultrasound (not mandatory)	
A127 <input type="checkbox"/> Specify		
A128 <input type="checkbox"/> Specify		
A129 <input type="checkbox"/> Pregnancy		
A132 <input type="checkbox"/> Rash		
A135 <input type="checkbox"/> Possible active TB		

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

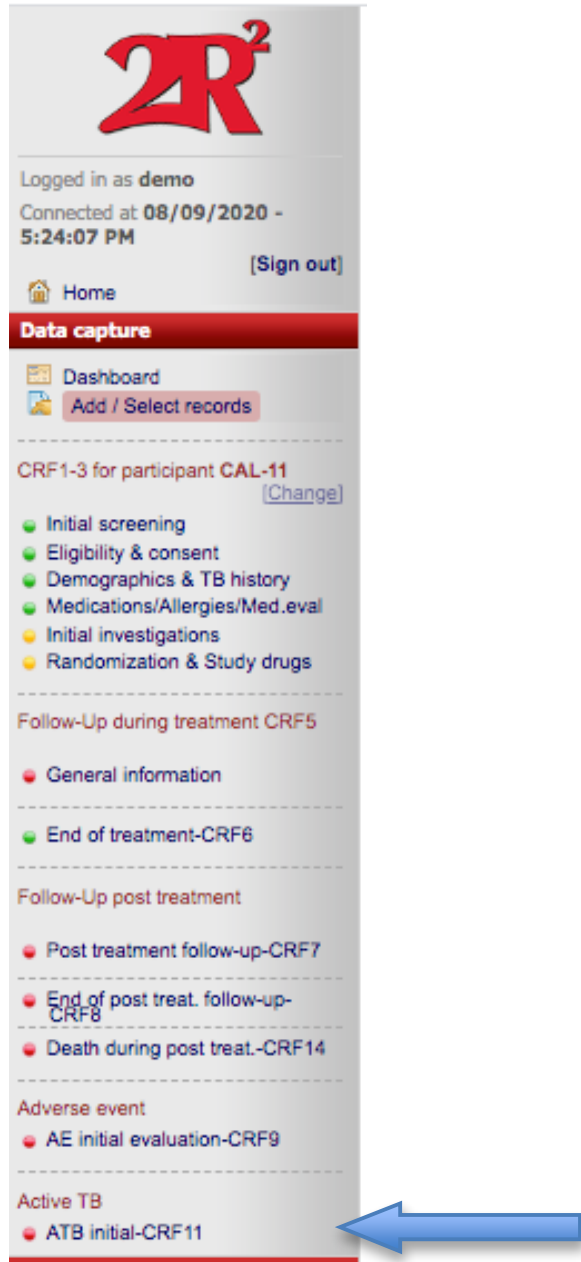
2R2 SOP20 Website site user's manual_ 08Sep2020

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

Active TB initial evaluation Version 1 - Last update November 8th 2019

Editing participant's CAL-11 Active TB initial evaluation form

TB0 Research staff completing the form

Active TB initial evaluation

TB1 Date * Today dd-mm-yyyy

TB2 Is the study participant suspected to have active TB? -

Potential symptoms of active TB

Does the study participant have any of the following symptoms?

TB3 Night sweats/Fever -

TB5 Cough -

TB7 Sputum production -

TB9 Other -

TB11 Physical exam -

Description

TB15 Describe the symptoms and other relevant details of the suspected active TB in as much detail as possible

Treatment

TB16 Treatment started -

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

REMINDER

Chest x-rays are needed at 3 time points (see below), send results for all 3 to the coordinating center

- 1 - Randomization
- 2 - Time of TB diagnosis (now)
- 3 - End of the TB treatment

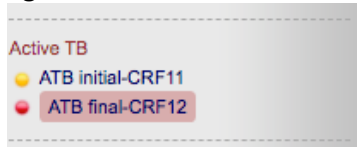
Culture at the time of the diagnosis is mandatory - at least 2 sputum samples for AFB smear and TB culture must be done

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**".

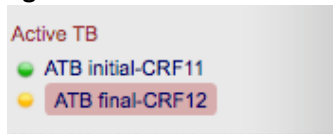
Once you clicked on "**SAVE&CLOSE**" the dot beside **ATB initial-CRF11**, on the left menu, will become yellow, and **ATB Final-CRF12** will appear (figure 45).

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** will 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

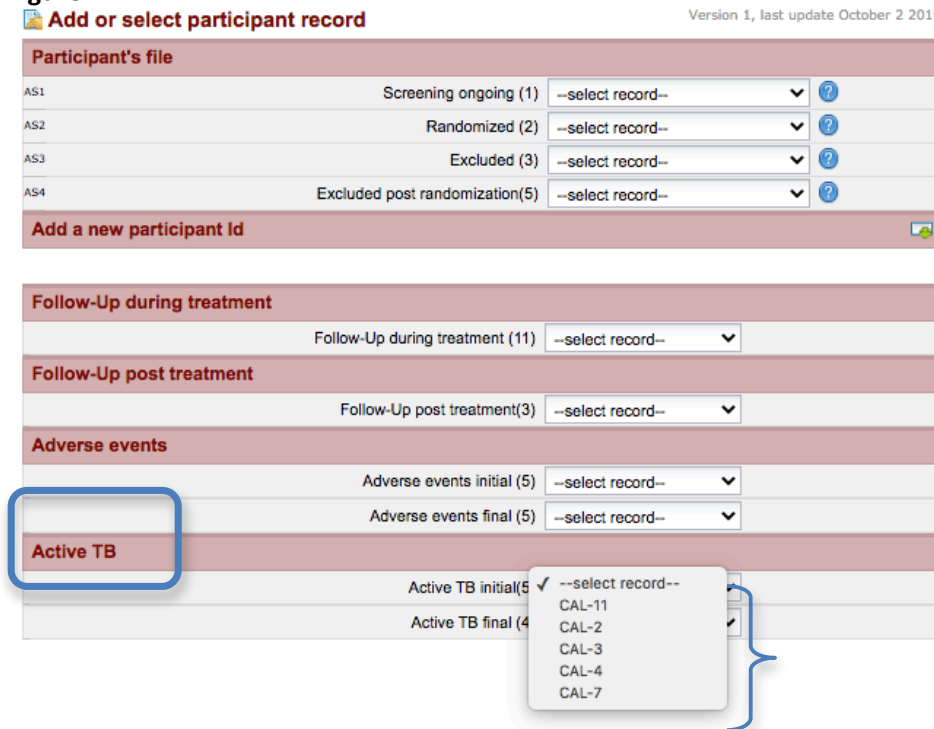


You need to complete a **CRF12** (ATB Final evaluation report) for each **CRF11** you have entered.

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

TF6	Other radiological tests	Yes	▼
TF7	Date radiological test done	04-03-2020	Today dd-mm-yyyy
TF8	Name of the test	<input type="text"/>	
Send copy of film to the coordinating center by 2R2 website			
File uploaded:			
Choose File		No file chosen	
Upload & save			

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

Figure 52

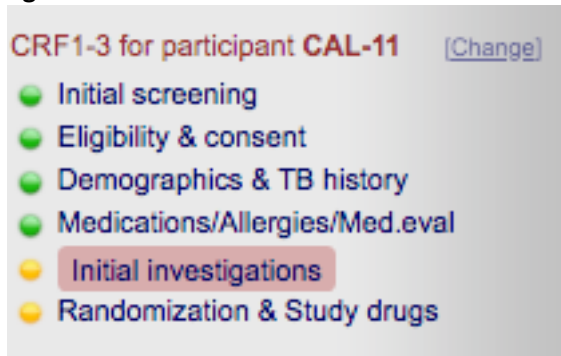
Response to treatment			
TF41	Symptoms resolved	Yes	▼
TF42	Tolerability of the therapy	<input type="text" value="good"/>	
TF43	Estimated adherence	<input type="text" value="good"/>	
TF44	Completed therapy	Yes	▼
TF45	Date completed	10-09-2020	Today dd-mm-yyyy
TF46	Treatment outcome	Cured	▼
TF48	Sputum for AFB and culture during treatment	Yes	▼
TF49	AFB smear done	Yes	▼
TF50	Number done	<input type="text" value="2"/>	
TF51	Results	All negative	▼
TF52	Cultures done	Yes	▼
TF53	Number done	<input type="text" value="2"/>	
TF54	Results	All negative	▼
TF56	Chest x-ray or other imaging at the end of treatment for active TB	Yes	▼
TF57	Date done	10-09-2020	Today dd-mm-yyyy
Send film to the coordinating center by 2R2 website			
File uploaded:			
Choose File		No file chosen	
Upload & save			

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**).

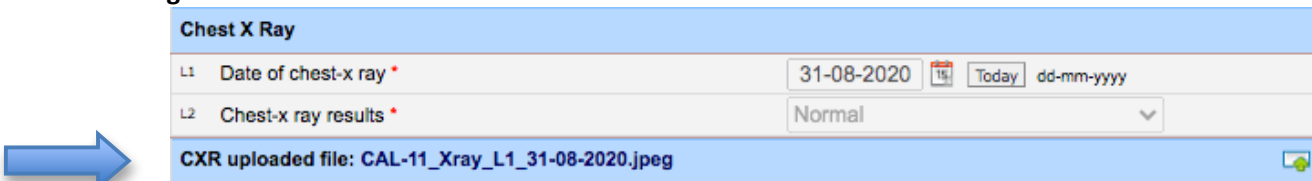
Figure 53



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

Add or select participant record Version 1, last update October 2 2019

Participant's file

AS1	Screening ongoing (1)	--select record--	[?]
AS2	Randomized (2)	CAL-7	[?] [Change]
AS3	Excluded (3)	--select record--	[?]
AS4	Excluded post randomization(5)	--select record--	[?]

Add a new participant Id

Follow-Up during treatment

Follow-Up during treatment (2) ✓ --select record-- Add a new fiw-up

Follow-Up post treatment

Follow-Up post treatment(2) CAL-7-2020-09-04 [Change]

Adverse events

Adverse events initial (0) --select record-- Add a new AEI

Adverse events final (0) --select record--

Active TB

Active TB initial(0) --select record--

Active TB final (0) --select record--

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

Figure 56

Add or select participant record Version 1, last update October 2 2019

Participant's file

AS1	Screening ongoing (1)	--select record--	[?]
AS2	Randomized (2)	CAL-7	[?] [Change]
AS3	Excluded (3)	--select record--	[?]
AS4	Excluded post randomization(5)	--select record--	[?]

Add a new participant Id

Follow-Up during treatment

Follow-Up during treatment (2) CAL-7-2020-09-03 [Change]

Follow-Up post treatment

Follow-Up post treatment(2) CAL-7-2020-09-04 [Change]

Adverse events

Adverse events initial (0) --select record-- Add a new AEI

Adverse events final (0) --select record--

Active TB

Active TB initial(0) --select record--

Active TB final (0) --select record--

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

Figure 57

Version 1 - Last update September 25th 2015

Editing participant's CAL-7 Population PK form

K0 Research staff completing the form

Data on PK sampling

K1 Date of sampling 15 Today dd-mm-yyyy

K2 When was the study drug taken at home? hh:mm (24 hour clock)

K3 Did the participant had anything to eat since midnight?

K4 Is the participant taking other drugs?

Name of other drugs taken

K5-K9	Name	Date and time of last dose	dd-mm-yyyy - hh:mm	Daily dose	Unit
Click on the green "+" sign to add another medication					

Blood sampling

	Time point	Scheduled time	Actual time sampling	Operator	Centrifuge time	Done by	Storage time	Done by
K10-K16	H2	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
K17-K23	H4	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>

K24 Comments

Save/Stay on page

Save/Exit

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

The screenshot displays the 'Death during post-treatment' form in the 2R2 website. On the left, a navigation menu lists various CRFs, with 'Death during post treat.-CRF14' highlighted by a blue arrow. The main form area is titled 'Death during post-treatment' and includes a sub-header 'Editing participant's CAL-7 Death during post-treatment form'. It contains several data entry fields: 'Date form is completed', 'Date of death of the participant', 'Was the participant hospitalized before dying?', and 'Was Active TB likely the cause/contributor of death?'. Below these is a 'Narrative' section with a list of nine points to document, such as 'Hospitals where participant has been hospitalized' and 'Relevant images done and results'. A large text box is provided for the narrative, and the form concludes with 'Save/Go to next form', 'Save/Stay on page', and 'Save/Exit' buttons.

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

Death during post-treatment Version 1 - Last update September 23rd 2019

Editing participant's CAL-7 Death during post-treatment form

H0 Research staff completing the form

Death during post-treatment information

H1 Date form is completed 04-09-2020 Today dd-mm-yyyy

H2 Date of death of the participant * 04-09-2020 Today dd-mm-yyyy

H3 Was the participant hospitalized before dying? Yes

H4 Was Active TB likely the cause/contributor of death? Yes

If Yes, please complete ACTIVE TB report CRF11 form

Narrative

H6 Narrative that describes the circumstance of death

Make sure that all the points below are mentioned in the narrative.
If any of the points below are not known, please specify that there were "NOT DONE" or "NOT KNOWN"

- 1- Hospitals where participant has been hospitalized
- 2- Treating physicians and dates of hospitalization
- 3- List of symptoms and duration
- 4- Laboratory done and results
- 5- Relevant images done and results
- 6- Names of disease diagnosed
- 7- Treatment received by participant
- 8- Autopsy results
- 9- Any other relevant information

Get and document permission to obtain clinical, laboratory, treatment information, and copies of relevant X-rays from participant's treating physician.

Save/Go to next form

Save/Stay on page

Save/Exit

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:

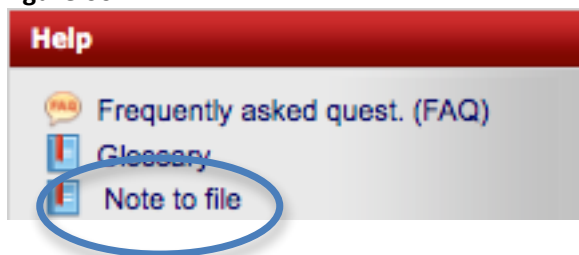
1. A manual randomization was done, and you need to inform the coordinating center so that the website can be updated to match the randomization received by the envelope used for the manual randomization;
2. A participant who has been randomized, meets one of the criteria for exclusion post randomization (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.

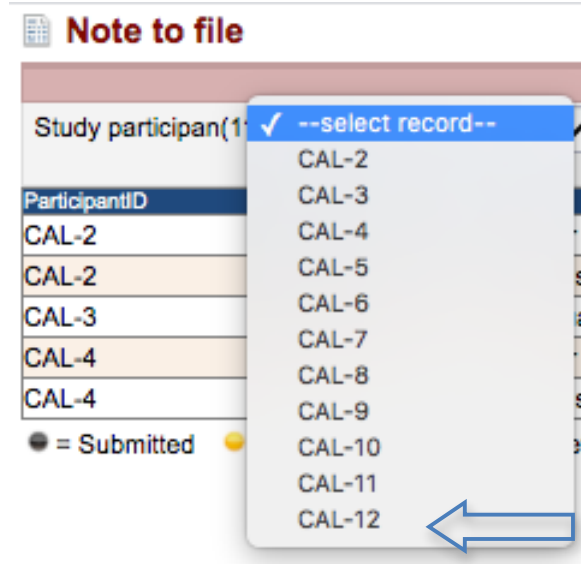
The “Note to file” can be found at the bottom of the left menu, in the “Help” section (**figure 60**)

Figure 60



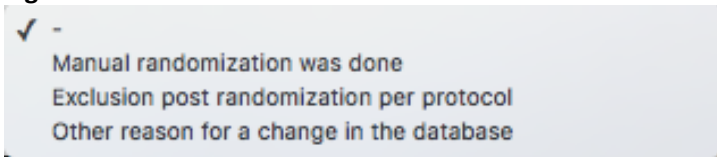
After clicking on “**Note to file**”, select the participant for whom you would like to do the changes (**figure 61**).

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

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

NF3 If manual randomization was done, 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

NF6 If 2 months, please write the code given

Figure 64

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

NF7 Please state the reason why the participant should be excluded

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.

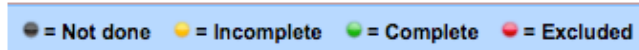
Participant	Scr	Elig	Dem	Med	Invest	Rand	End Flup	End pst Flup	Death	ATB	Flw-up	Pst Flw-up	AE
CAL-5	●	●	●	●	●	●	●	●	●	●	0	0	0
CAL-7	●	●	●	●	●	●	●	●	●	●	3	2	1
CAL-11	●	●	●	●	●	●	●	●	●	●	1	0	0

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:

Record status dashboard



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)

2R2 website: site user's manual

2R2 SOP20_08Sep2020

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	<input type="checkbox"/>		
CRF2	<input type="checkbox"/>		
CRF3	<input type="checkbox"/>		
CRF5	<input type="checkbox"/>		
date			
CRF5	<input type="checkbox"/>		
date			
CRF5	<input type="checkbox"/>		
date			
CRF5	<input type="checkbox"/>		
date			
CRF6	<input type="checkbox"/>		
CRF7	<input type="checkbox"/>		
CRF8	<input type="checkbox"/>		
CRF9	<input type="checkbox"/>		
CRF10	<input type="checkbox"/>		
CRF11	<input type="checkbox"/>		
CRF12	<input type="checkbox"/>		
CRF13	<input type="checkbox"/>		
CRF14	<input type="checkbox"/>		

7.0. SOP Revision history

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