PreVent-ACaLL

REDCap Guide

Version 3.0

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1 Introduction

REDCap is a secure web platform for building and managing online databases. In the PreVent-ACaLL study, each site must use REDCap to enter study data and report serious adverse events and protocol deviations to sponsor. The two projects available in REDCap are:

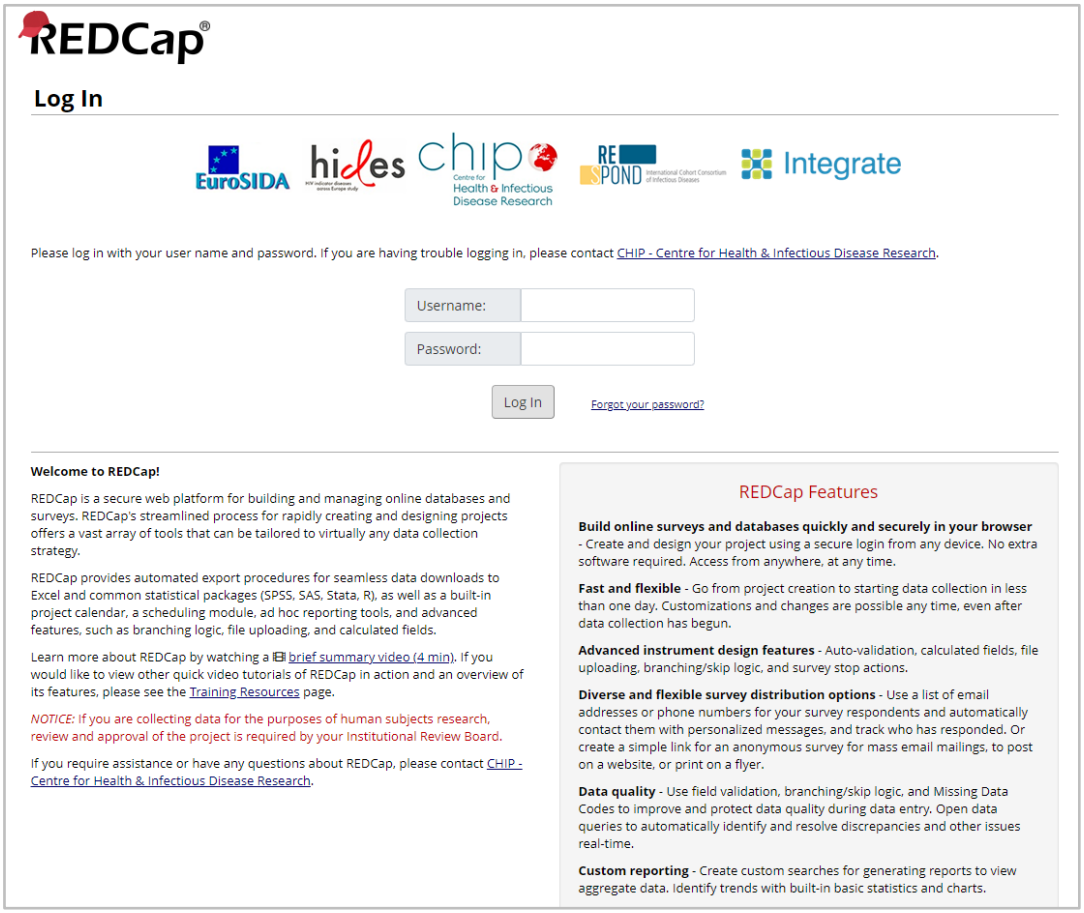
1. PreVent-ACaLL – pre-screening
2. PreVent-ACaLL – low risk/observation/treatment

In the first project, pre-screening data must be entered for each participant who has signed the pre-screening informed consent. It is also in this project the CLL-TIM algorithm is run and the participants are randomized if screening result is high risk/high confidence and the patient has signed the informed consent to the main part of the study. The second project is developed to report study data for the enrolled participants incl. those in the low risk category (screen failures).

2 REDCap Access

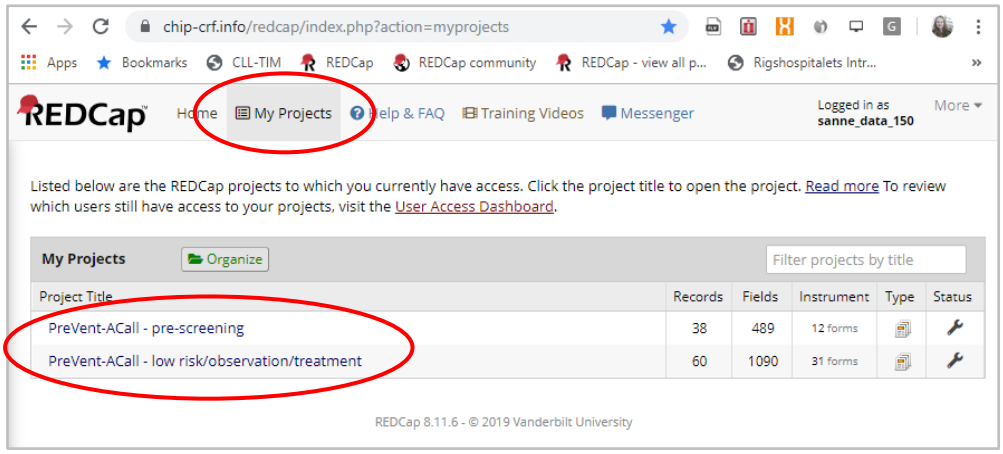
To request REDCap access, you must write to: chip-prevent.rigshospitalet@regionh.dk. Remember to include name, role in the study, email address and site of the person who requires access. Once access has been granted the user will receive an email with username and a link to set password. The login details for REDCap are personal and must not be shared. Below you find the study specific REDCap link.

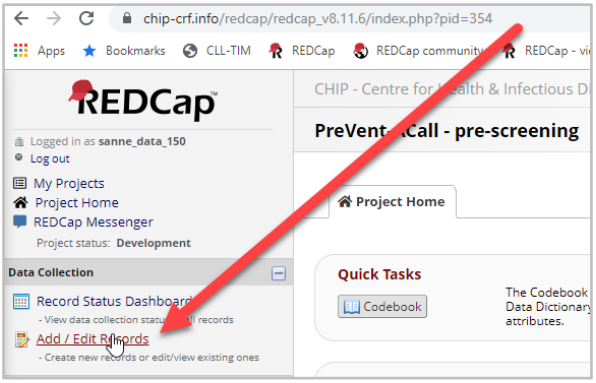
REDCap Log In webpage: https://www.chip-crf.info/redcap/index.php

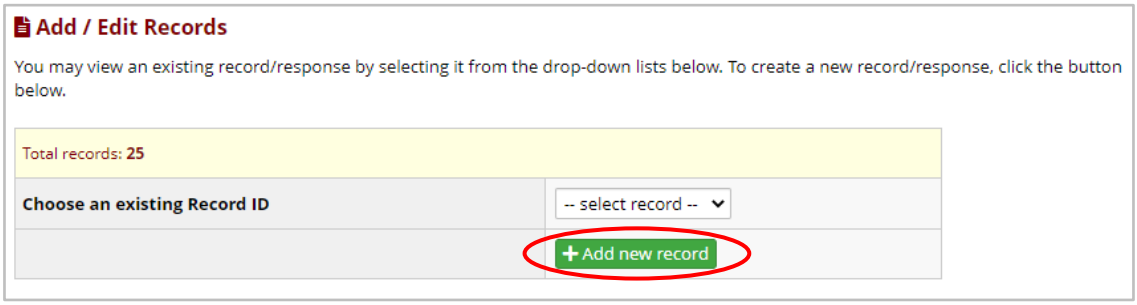


3 How to create a new participant/retrieve PID number

When logged in, the two PreVent-ACaLL projects can be found under *My projects*. All participants **must** be created in the "PreVent-ACaLL – pre-screening" project. NEVER create a new participant in the "PreVent-ACaLL – low risk/observation/treatment" project.





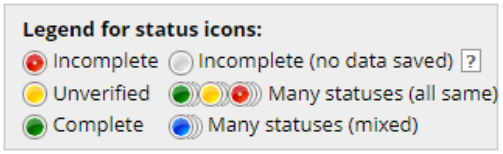


1. Click on the "PreVent-ACaLL – pre-screening" project
2. Click *Add / Edit Records* in the left-hand menu
3. Click on the green button *+ Add new record*

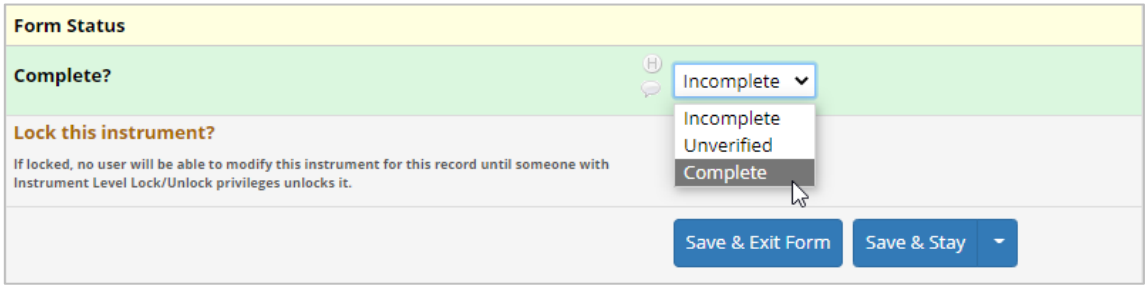
A new record will automatically be assigned to the patient with a unique record identification (ID) number. This record ID is the patient's participant ID (PID) during the entire trial.

4 Data reporting in general

Each record ID/PID will have a data collection instrument that consists of different electronic case report forms (eCRFs). To open one of these forms, click on the status icon. The status icon is grey if no data is saved yet and turns red if some data is saved in the form.



Data does not have to be reported into the forms chronologically. Once all data have been entered, the form status must be changed to *Complete* and the form must be saved. The status icon will now change to green.



4.1 Estimated date and time

Specific dates and timepoints should always be written if REDCap requires, however sometimes these can be unknow and in these cases, following estimates must be done:

Unknown date for medical history
In case date is unknown when reporting medical history for the participant (in the eCRF named medical history), an estimated date of 01 January the year before enrollment should be entered as the date.
Unknown time point
In case a time point is unknown 00:00 must be written.

4.2 How to use barcode scanner in REDCap

Barcode scanner model: GryphonTM GD4500

1. Plug in the barcode scanner in your computer (via USB).
   The scanner will hereafter make a “bip” sound and a red scanning light will appear.
2. Open REDCap and log in to your account.
   It does not matter if you plug in the barcode scanner before or after you have logged into REDCap.
3. Open the eCRF you want to scan the barcode data into.
4. Place the computer marker in the barcode field.
5. Scan the barcode by pointing the red lighted scanning arena at the barcode and press on the scanner’s button. The scanner will make another “bip” sound.
6. The barcode/sample ID should now be registered into the field.
7. Remember to save the eCRF when done with entering/scanning the data.

If the barcode/sample ID is not registered correctly in REDCap (exactly as written on the barcode), please inform sponsor via email: chip-prevent.rigshospitalet@regionh.dk

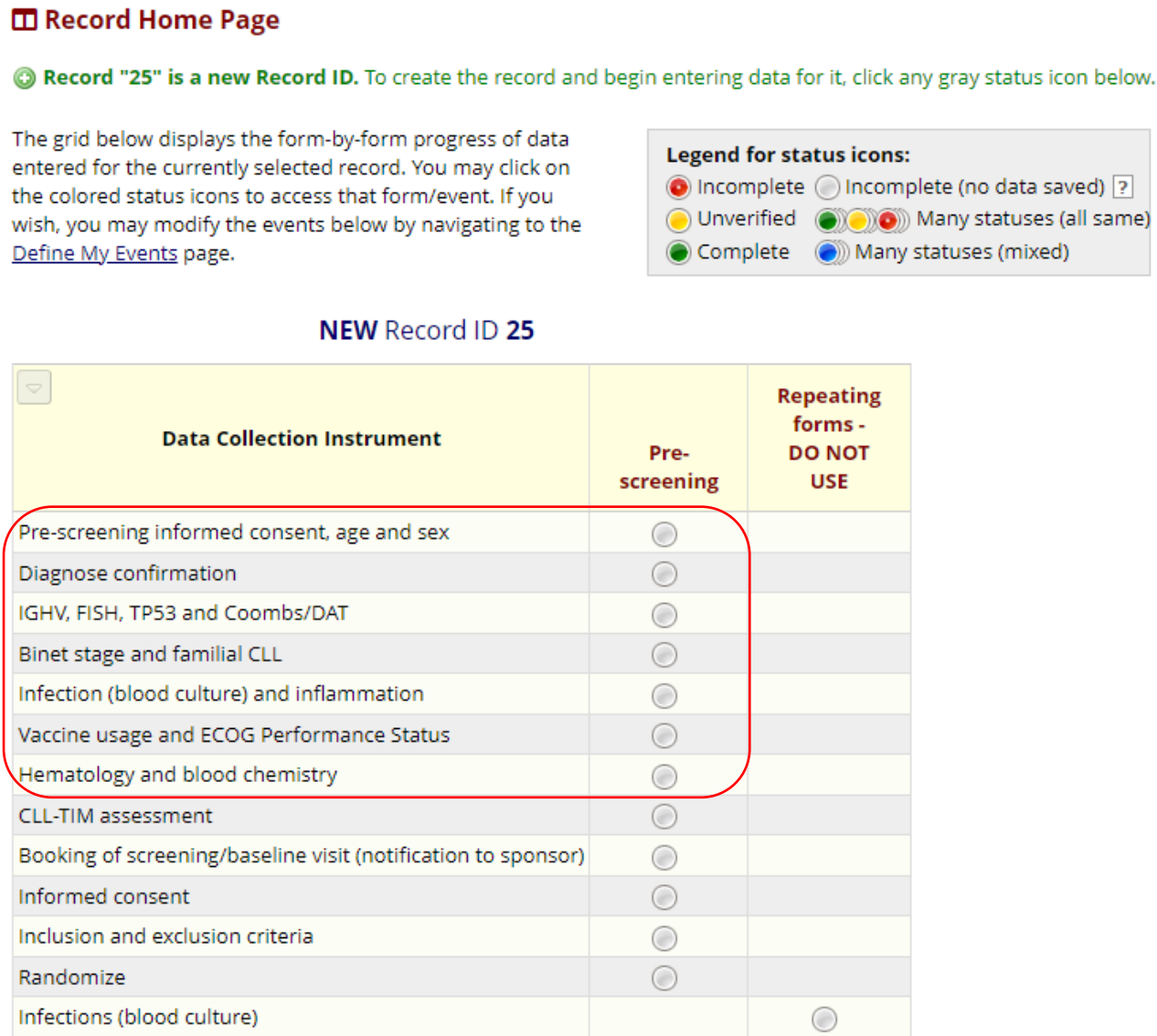
5 Queries

Queries will be created in REDCap in case data resolution is needed. This can be done by sponsor or by monitor. Queries will be assigned to a specific person in REDCap when the query is created. This person will be notified about the query through a REDCap message or by email. Make sure to check spam/unwanted email folder.

To avoid unnecessary queries, please delete incorrectly entered data in branched fields before changing the response to the data field.

6 The Pre-screening project

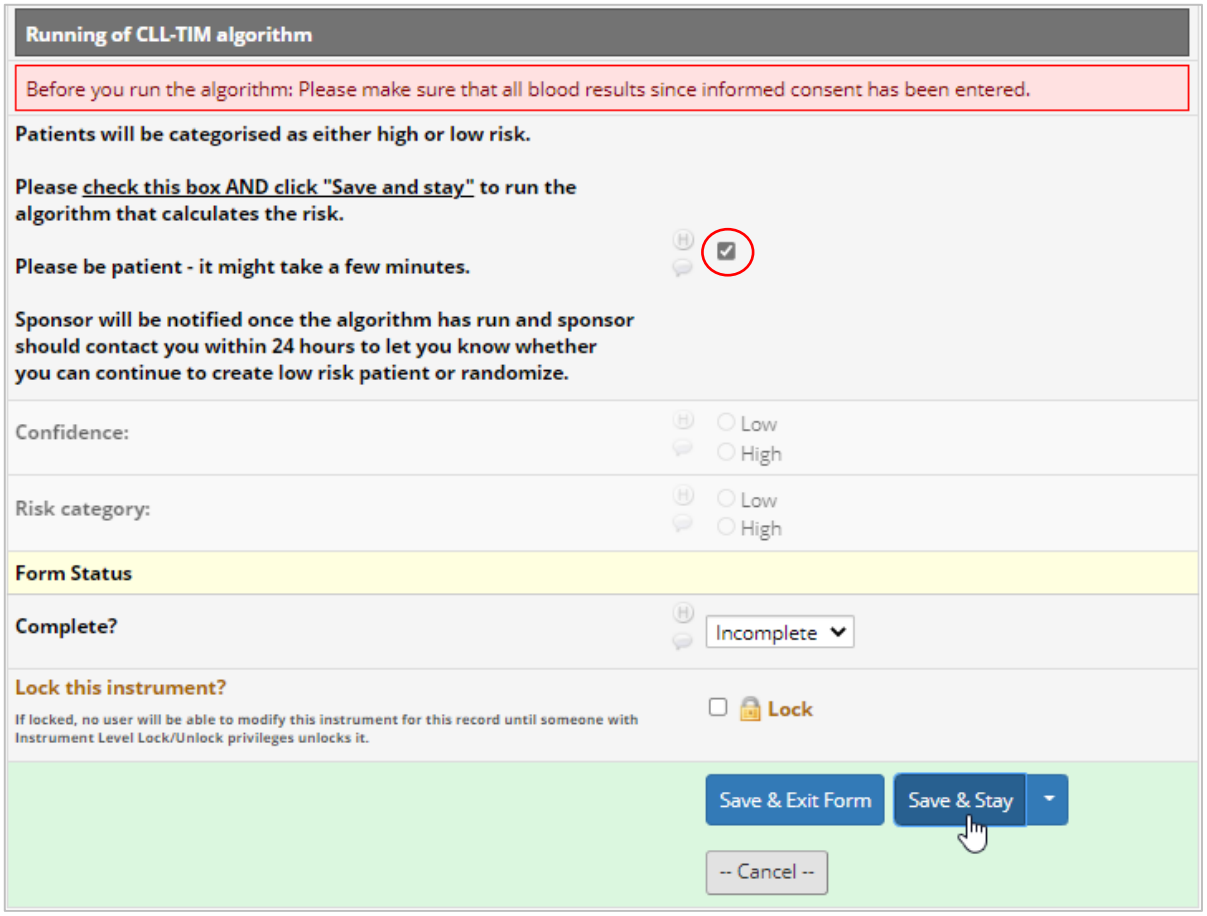
In the pre-screening project, all the pre-screening data needed to run the CLL-TIM algorithm must be entered. In the picture below, you can see all the eCRF's for the pre-screening project. The eCRFs within the red square below are the eCRFs containing pre-screening data (data that are used in the CLL-TIM algorithm). When all pre-screening data has been entered, the CLL-TIM algorithm can be run in the eCRF "CLL-TIM assessment". Rest of the eCRFs are used after the participant has been pre-screened and only if the result from the pre-screening is high risk/high confidence.



6.1 CLL-TIM assessment eCRF

The CLL-TIM algorithm is built into the form “CLL-TIM assessment”. For all patients, please answer the field asking if the algorithm will be run.

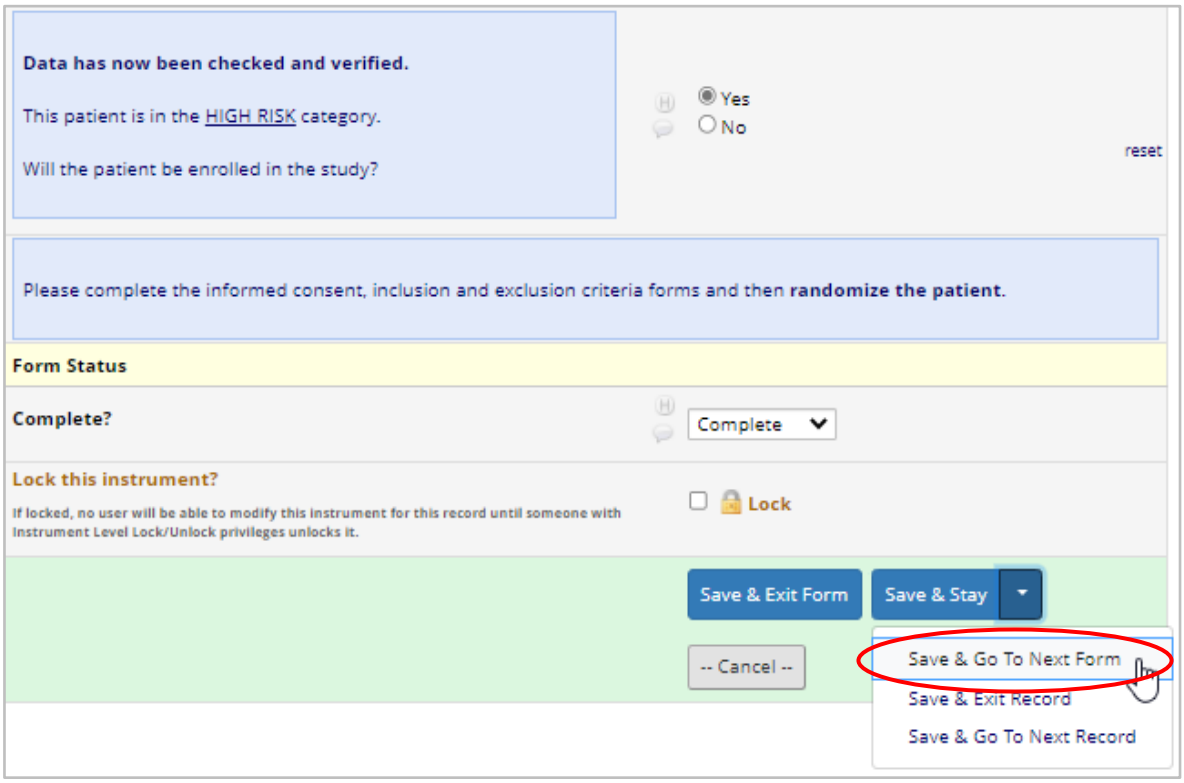
To run the algorithm, you must tick off the marked box (see picture below) and click “Save & stay”. When clicking “Save & stay” the algorithm will be run. It might take a few minutes to run the algorithm - please make sure to stay on the page until the algorithm has been run. When finished, the result will be shown and indicate whether the patient’s risk is low or high risk and if the confidence is low or high.



The entered data must be verified by sponsor after the algorithm has been run. The data verification will be done within 24 hours. When data has been verified, sponsor will let you know whether you can continue to create the patient in the low risk category or randomize in case patient is in high risk. You can also see if data has been verified by the tick off as the box below.

6.1.1 CLL-TIM result: High risk/high confidence

If the patient's CLL-TIM result is high risk/high confidence, the patient is eligible for study participation and must be contacted to sign the informed consent for the main part of the study (see the instruction



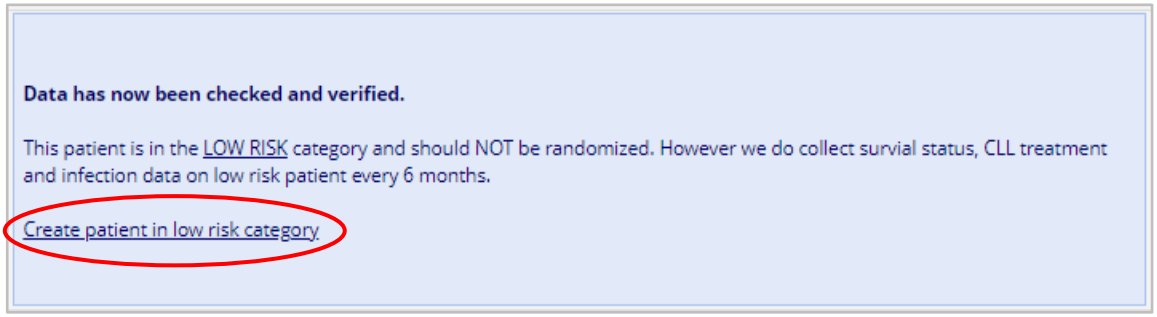
"Enrollment procedure"). Hereafter, the instructions in the eCRF in REDCap must be followed. If the patient is not being enrolled, the patient must be created in the low risk category. If the patient is being enrolled, the eCRFs "informed consent", "inclusion and exclusion criteria" and "randomize" must be completed.

6.1.2 CLL-TIM result: Low risk category

If the patient's CLL-TIM result is either:

- low risk/low confidence
- low risk/high confidence
- high risk/low confidence

the patient must be created in the low risk category, which is done through the eCRF in REDCap.

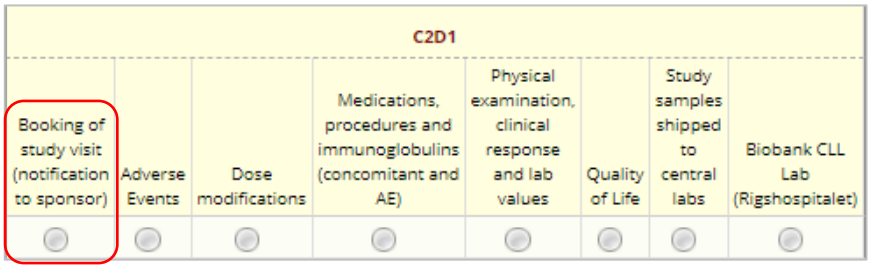


7 Notification of study visit date to sponsor

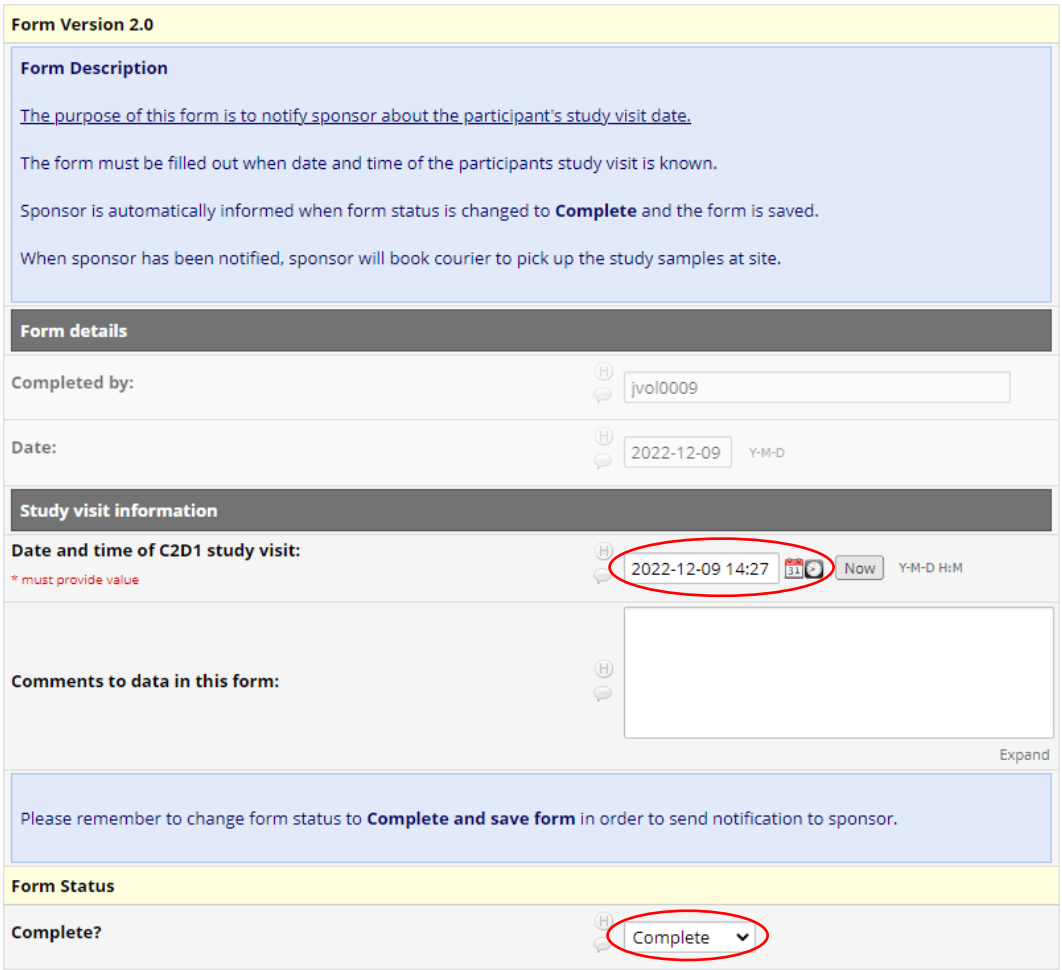
Electronic CRF: Booking of study visit (notification to sponsor)

For those study visits where study specific samples are collected from the participant, sponsor must be notified about date and time for when the specific study visit takes place. Study visits where study specific samples are collected are:

- Screening/baseline
- C1D8 (treatment arm only)
- C1D15 (treatment arm only)
- C2D1
- C3D1
- 12 weeks after C1D1 / End of treatment
- 24 weeks after C1D1
- 1 year after C1D1
- 2 years after C1D1
- Progressive Disease



When date and time has been entered into the form and the form status is changed to *Complete* and saved, sponsor will automatically be notified about the study visit date and time. Sponsor will hereafter book courier to pick-up the study samples at site for the same date as the study visit.



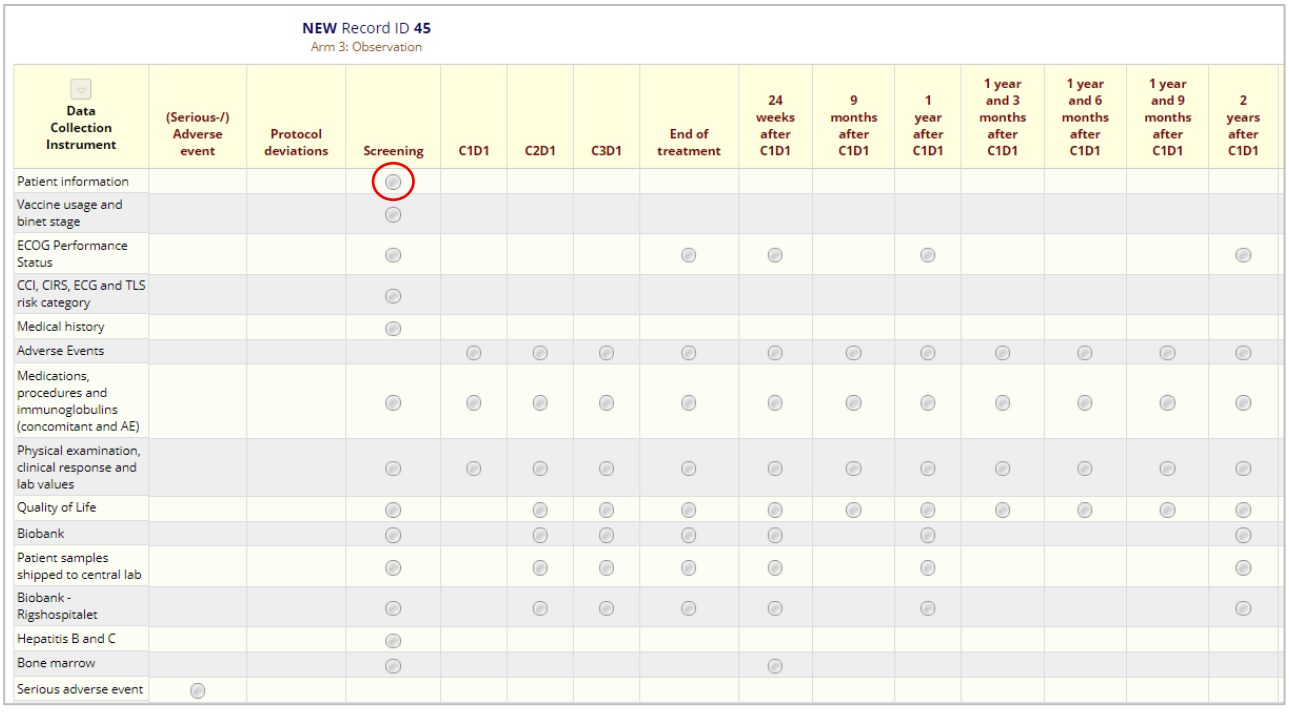
8 The Low risk/observation/treatment project

Important: Patients must NEVER be created in the "PreVent-ACaLL – low risk/observation/treatment" project using the *Add new record* button. The auto-number functionality is enabled, and the patient will therefore not get the same participant/record ID as in pre-screening project. Patients should therefore always be added via links in the CLL-TIM assessment eCRF or randomization eCRF in the pre-screening REDCap project.

Low risk: To create a patient in the low-risk category, you should open the form "CLL-TIM assessment" and create the patient in the low-risk category after data has been verified by sponsor (see previous page).

Observation/treatment: To create a patient in the high-risk category, you should fill out the forms "Informed consent" and "Inclusion and exclusion criteria". In case patient is eligible for enrollment and have signed the informed consent to the main study, the patient should be randomized in the form "Randomize". After randomization, you can create the patient in the arm the patient has been randomized to: observation or treatment.

After clicking on one of the two links, a screen as the picture below will appear. Click on the eCRF's status icon to report data in the form. **Important**: Even though you are not ready to enter data, you should always access one of the forms and click save – otherwise the data collection instrument will not be created in the project.



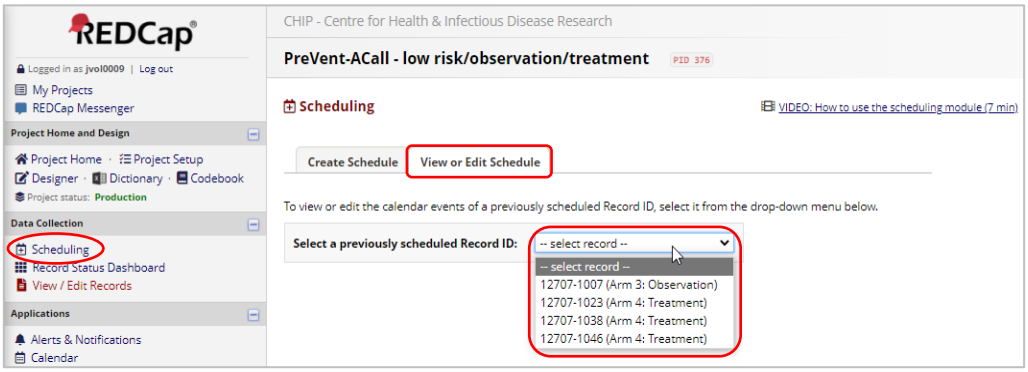
8.1 How to automatically create visit schedule

In the "PreVent-ACaLL – low risk/observation/treatment" project, study visits can automatically be scheduled for each participant once the C1D1 date has been entered in the "Physical examination and clinical response" form. **Important**: Do NOT use the create schedule function since the schedule will be automatically created as soon as you have entered the C1D1 date.

8.1.1 How to view or edit visit schedule for a participant

To get an overview of all scheduled study visits for one participant:

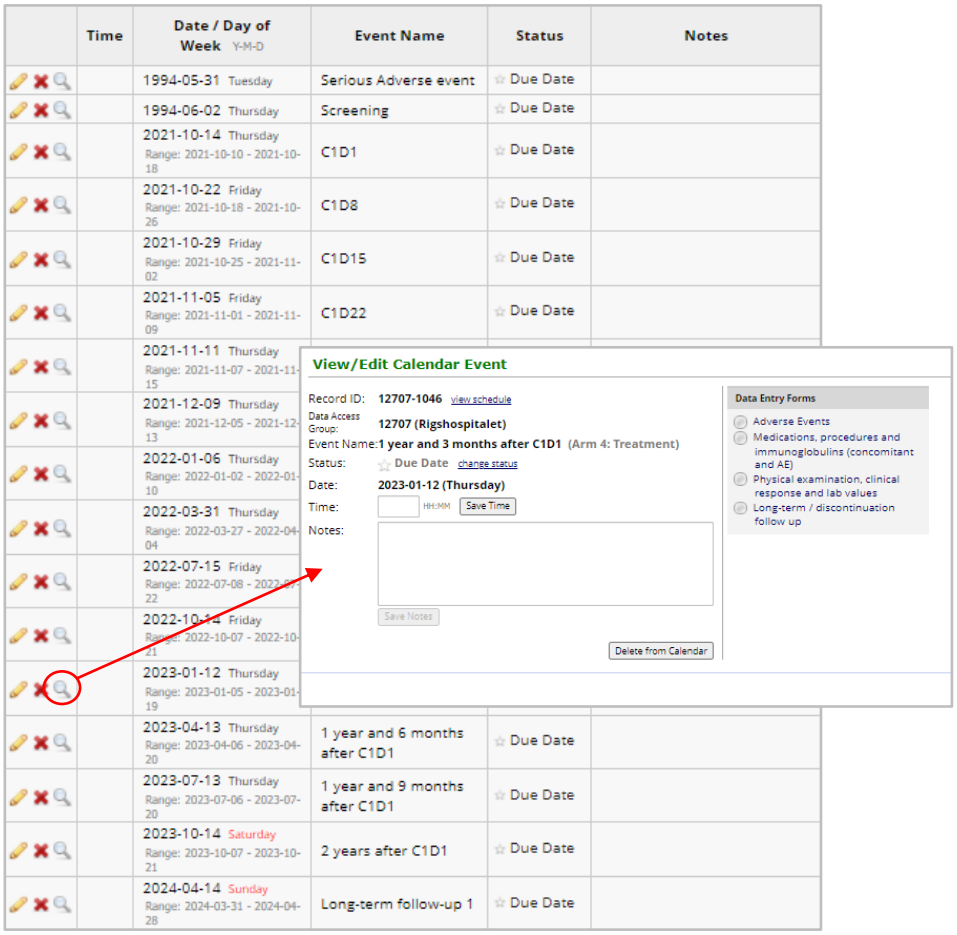
1. Click **Scheduling** in the left-hand menu
2. Click on **View or Edit Schedule** and select the participants record ID



Study visit schedule

The scheduled study visit can be changed by clicking on the small pen to the left.

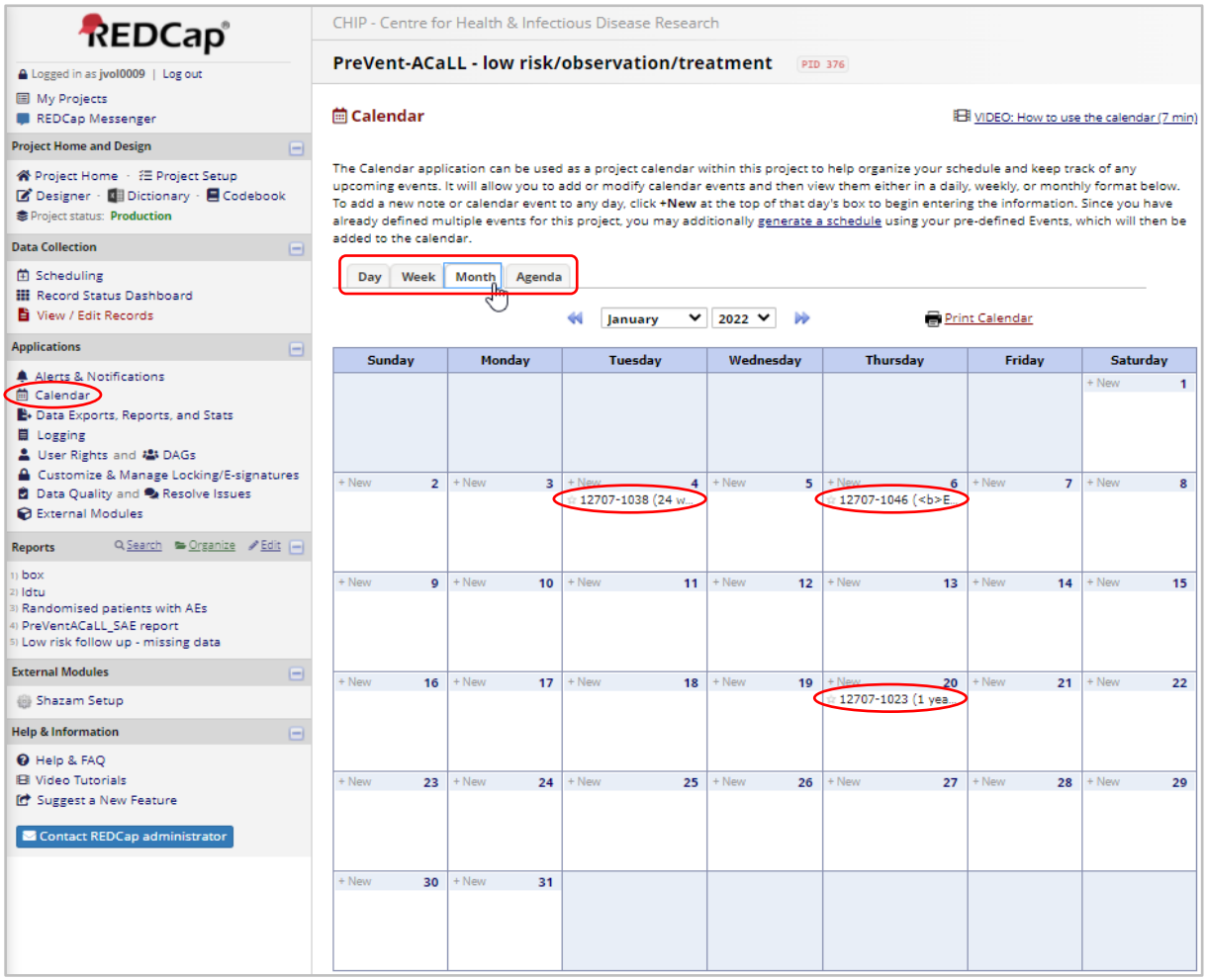
By clicking on the small loop, a new window will pop-up, which shows more details on the visit, e.g. data entry forms to be reported and notes to the study can be written if necessary.



8.1.2 How to view scheduled study visits for all participants

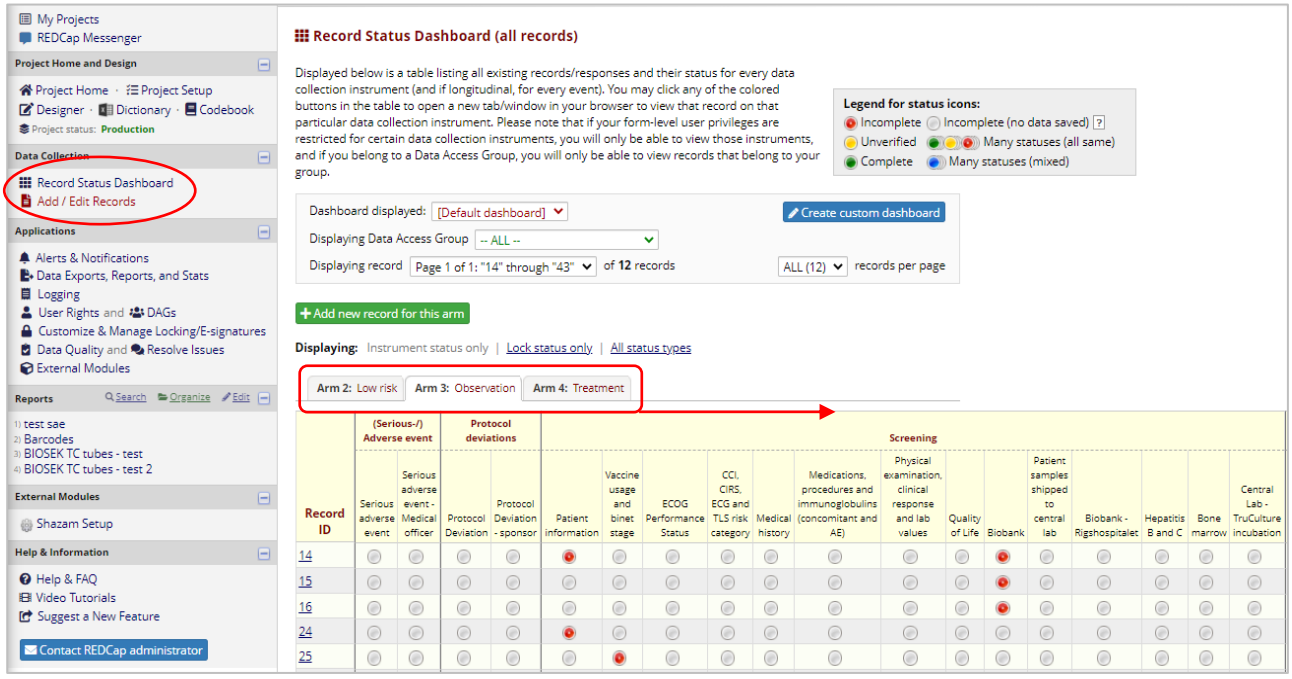
To get an overview of all scheduled study visits for all participants:

1. Click **Calendar** in the left-hand menu
2. As needed, browse the Day, Week, Month or Agenda tabs

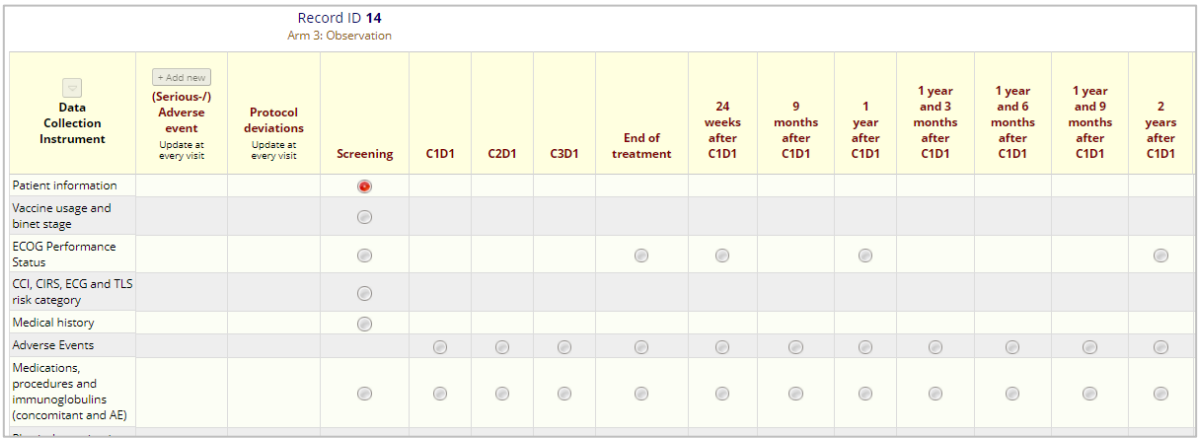


8.2 Data reporting in the low risk/observation/treatment project

When you need to report data in an existing record, go to either the *Record Status Dashboard* or click on *Add / Edit Records* in the left-hand menu. In the *Record Status Dashboard*, all transferred pre-screening participants can be seen for all three arms: low risk, observation and treatment. The participants will be listed in rows, while the forms will be listed in columns under each associated study visit.



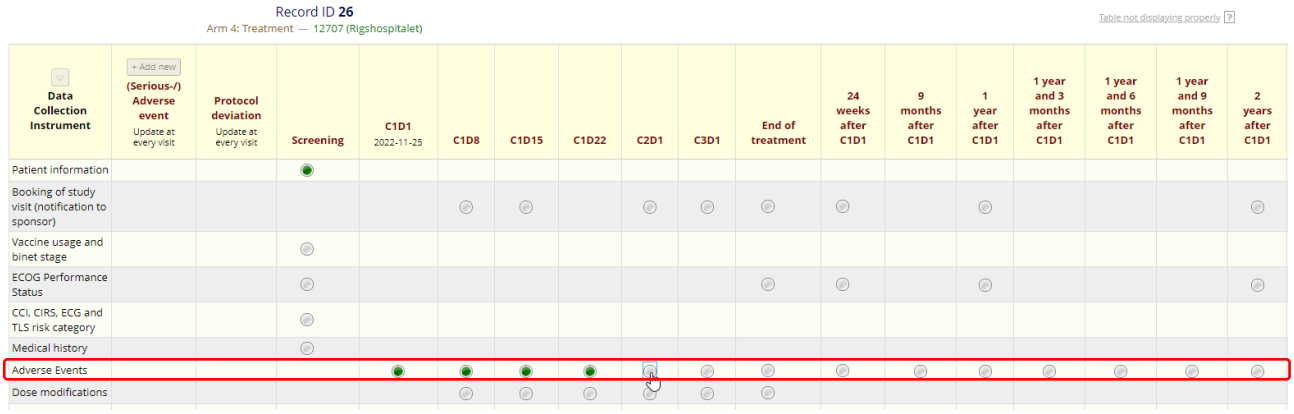
When clicking *Add / Edit Records*, record ID must be chosen. When done, the Data Collection Instrument for this chosen participant will be shown as picture below. Here the study visits are listed in columns and the eCRFs are listed in rows.



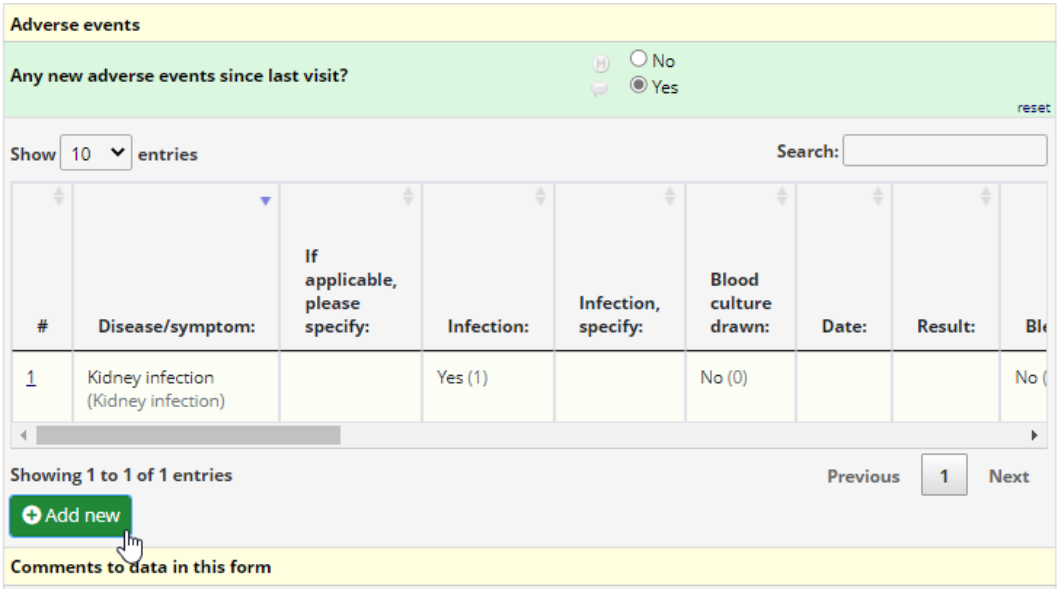
Make sure to change the form status to *Complete* when all data has been reported in the form.

8.3 Specific data reporting: Adverse Events

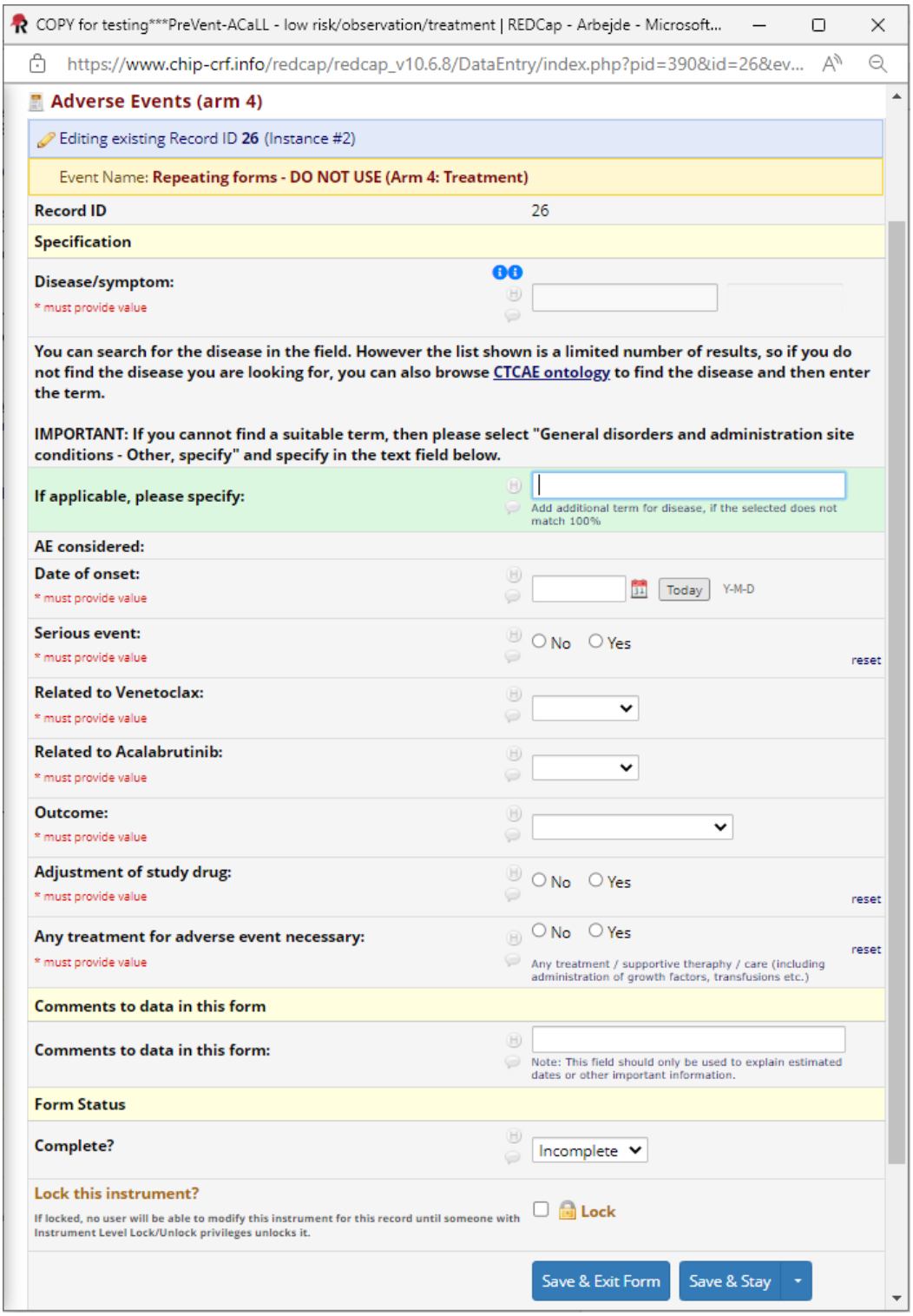
The eCRF "Adverse Events" must be filled out at every study visit. In the instruction "How to handle AE and SAEs", the AE definition is stated and it is described when an AE must be reported. The "Adverse Events" eCRF is listed for all study visits.



In the form, all AEs reported so far for this participant will be listed. When reporting a new AE, you must answer "Yes" to the question Any new adverse events since last visit? and click on *+ Add new*.

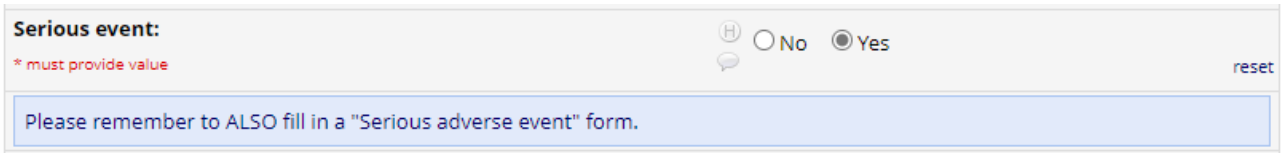


Hereafter a pop-up window will open, which must be completed with data regarding the AE:

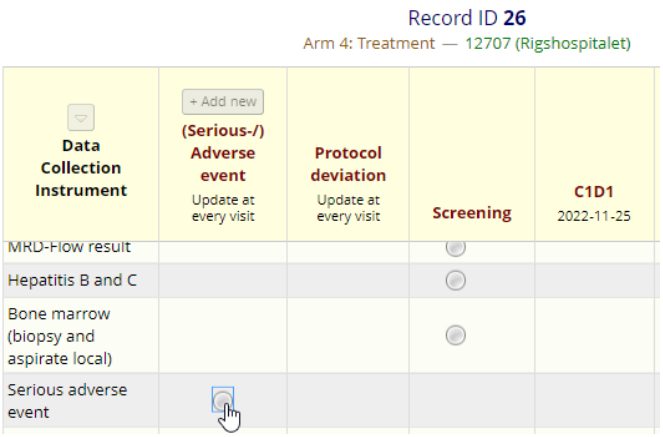

COPY for testing***PreVent-ACaLL - low risk/observation/treatment | REDCap - Arbejde - Microsoft...
https://www.chip-crf.info/redcap/redcap_v10.6.8/DataEntry/index.php?pid=390&id=26&ev...
Adverse Events (arm 4)
Editing existing Record ID 26 (Instance #2)
Event Name: Repeating forms - DO NOT USE (Arm 4: Treatment)
Record ID
26
Specification
Disease/symptom:
* must provide value
You can search for the disease in the field. However the list shown is a limited number of results, so if you do not find the disease you are looking for, you can also browse CTCAE ontology to find the disease and then enter the term.
IMPORTANT: If you cannot find a suitable term, then please select "General disorders and administration site conditions - Other, specify" and specify in the text field below.
If applicable, please specify:
Add additional term for disease, if the selected does not match 100%
AE considered:
Date of onset:
* must provide value
Today
Y-M-D
Serious event:
* must provide value
No
Yes
reset
Related to Venetoclax:
* must provide value
Related to Acalabrutinib:
* must provide value
Outcome:
* must provide value
Adjustment of study drug:
* must provide value
No
Yes
reset
Any treatment for adverse event necessary:
* must provide value
No
Yes
reset
Any treatment / supportive theraphy / care (including administration of growth factors, transfusions etc.)
Comments to data in this form
Comments to data in this form:
Note: This field should only be used to explain estimated dates or other important information.
Form Status
Complete?
Incomplete
Lock this instrument?
If locked, no user will be able to modify this instrument for this record until someone with Instrument Level Lock/Unlock privileges unlocks it.
Lock
Save & Exit Form
Save & Stay

8.4 Specific data reporting: Serious Adverse Events

When reporting an AE you will be asked if the evet is serious. In case of a serious event you must ALSO fill out an Serious Adverse Event form.



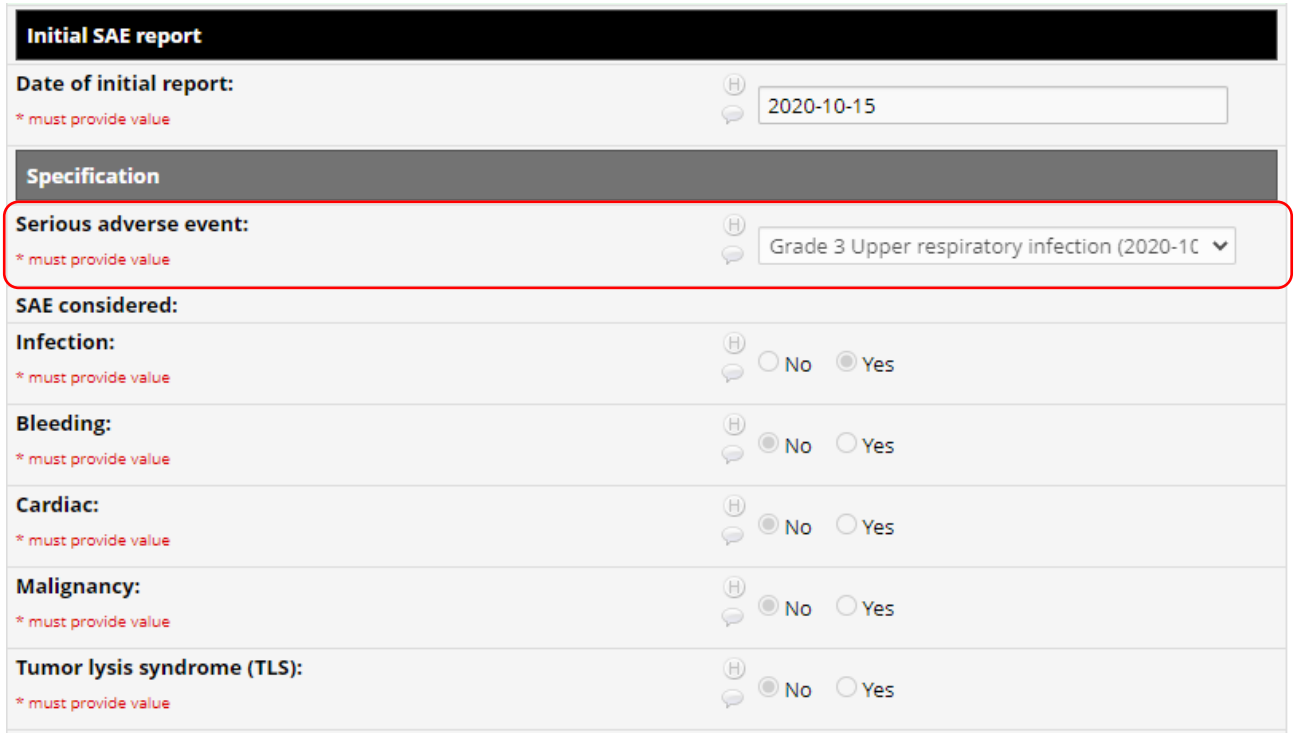
The eCRF "Serious adverse event" must be filled out if a participant develops a serious adverse event (SAE). All SAEs should also have an AE eCRF. The SAE definition is stated in the instruction "How to handle AE and SAEs".



<u>All SAEs must be reported in the eCRF within 24 hours from awareness.</u>

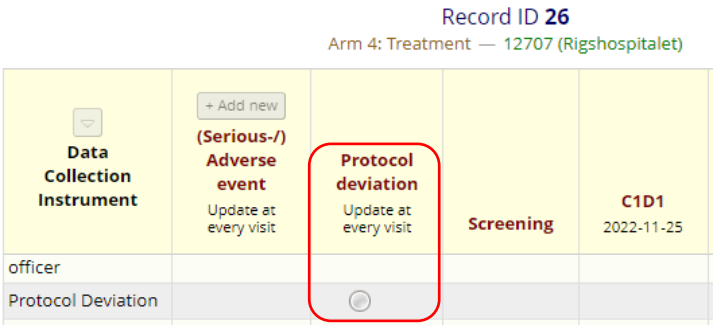
The "Serious adverse event" eCRF can be found in the beginning of the data collection instrument. For each new SAE, a new eCRF must be created. When one SAE has been reported, a new eCRF can be created by clicking *+ Add new* in the participants Data Collection Instrument.

In this form, data on the SAE must be reported and linked to the related AE (indicated below).



8.5 Specific data reporting: Protocol Deviation

The eCRF "Protocol Deviation" must be filled out if a protocol deviation occurs. The eCRF and the instruction 'Reporting of protocol deviations' lists which protocol deviations that must be reported for this trial, however these are also listed in the CRF as shown below.



Example on Protocol Deviation form (version 1.0) can be seen below.

Reporting

Protocol deviation to report

In all clinical trials, there can be deviations from the protocol. Some deviations are important for the patient's safety or the quality of the trial data. It is your responsibillity as a study nurse/PI to report protocol deviations to sponsor. Below you can see which protocol deviations that should be reported to sponsor.

IMPORTANT: Only one protocol deviation per form!
If more than one protocol deviation occurs per participant a new Protocol Deviation form must be created.

Date protocol deviation occured: 2023-03-13 Today Y-M-D

Please tick off which protocol deviation has occured

- ○ Patient enrolled into the study even though its been more than 1 year from CLL diagnosis to randomization
- ○ Patient enrolled into the study even though its been more than 42 days from signed informed consent (main study) to randomization
- ○ Patient enrolled into the study even though its been more than 14 days from randomization to start of study treatment
- ○ No pregnancy test result were collected before start of study treatment
- ○ Collected pregnancy test were older than 7 days before start of study treatment
- ○ Incorrect dose of study treatment prescribed or dispensed to the participant
- ○ Participant did not ingest the fully assigned study treatment
- ○ Participant wants to end study treatment before planned
- ◉ Visit window was not kept within timeframe
- ○ Study data were collected from the patient before informed consent were signed

reset

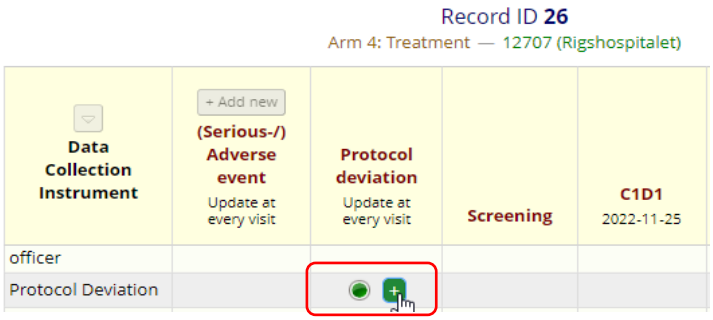
Please elaborate:

If deviation revolves around study treatment, then please also note exact dose prescribed/dispensed to participant.

The participant had the 24 weeks study visit within a five day visit window instead of a four day visit window.

Expand

For every new protocol deviation that occurs, a new eCRF must be created. When first deviation has been completed, a new eCRF can be created by clicking on the + button as shown below.



8.6 Specific data reporting: Progressive Disease

If a participant's disease progresses, the eCRFs listed under "Progressive disease" (see below) must be filled out. These can be found after all the long-term follow-up visit forms in the Data Collection Instrument.

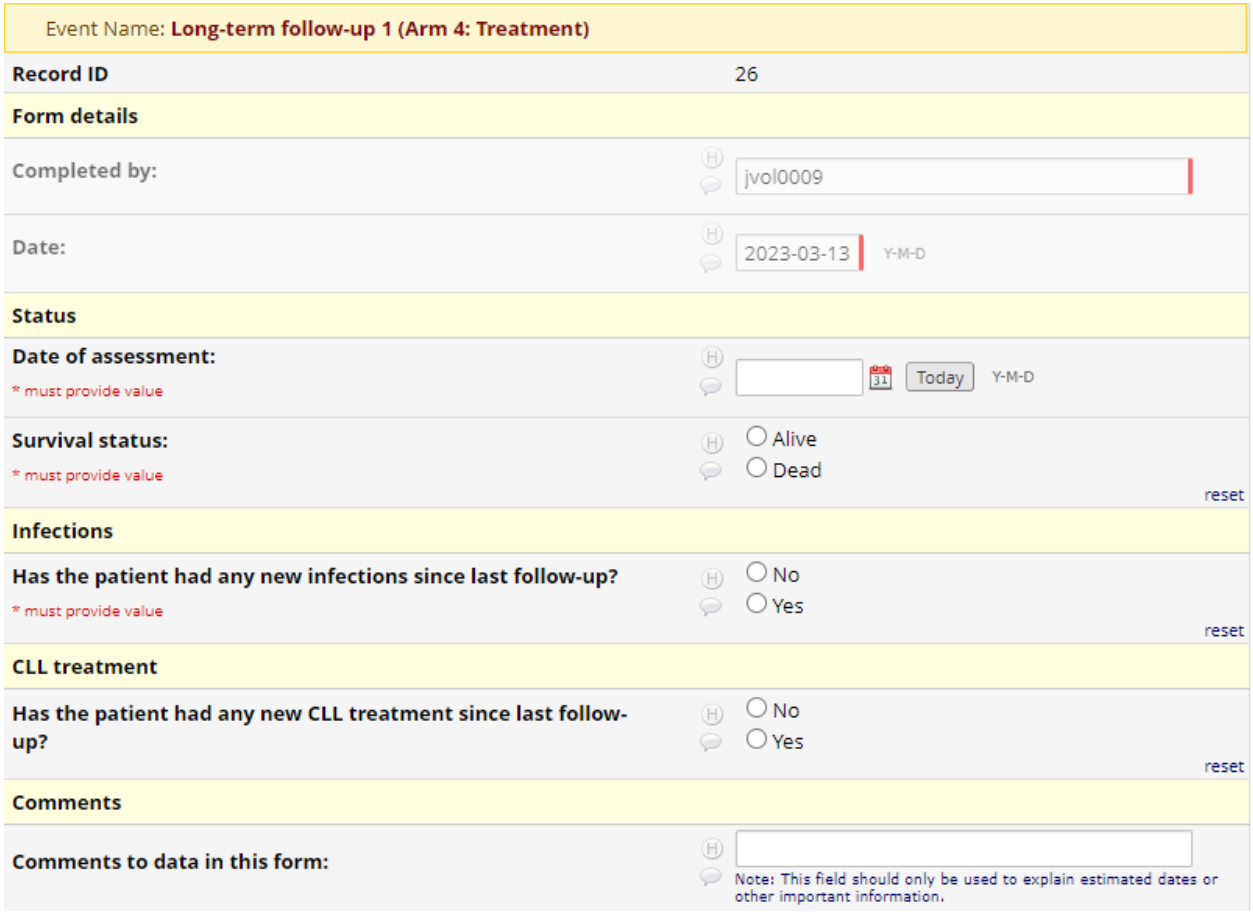
Progressive disease									
Booking of study visit (notification to sponsor)	Adverse Events	Medications, procedures and immunoglobulins (concomitant and AE)	Physical examination, clinical response and lab values	Study samples shipped to central labs	MRD-Flow results	Hepatitis B and C	Bone marrow	IGHV, FISH and TP53	New CLL treatment

8.7 Specific data reporting: Long term / Discontinuation follow-up

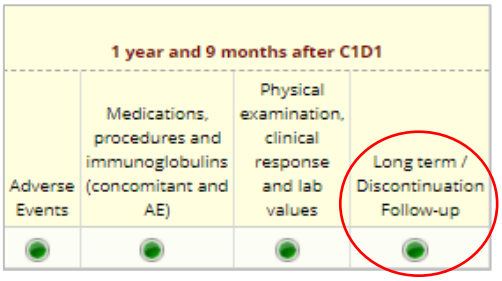
When the participant has had the last physical study visit (2 years after C1D1), the participant must still be followed with long term study visit every 6 months for additional five years (the participants will be followed for a total of 7 years). These eCRFs are listed in REDCap as shown here:

Long-term follow-up 1	Long-term follow-up 2	Long-term follow-up 3	Long-term follow-up 4	Long-term follow-up 5	Long-term follow-up 6	Long-term follow-up 7	Long-term follow-up 8	Long-term follow-up 9	Long-term follow-up 10
Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up	Long term / Discontinuation Follow-up

The data that must be collected at these study visits are survival status, use of alternative CLL therapy and infections (see screenshot below).



If the participant's disease progresses before the last physical study visit: 2 years after C1D1, the participant must still be followed with all remaining study visits – however, only "Long-term / discontinuation follow-up" form should be filled out. These eCRFs can be found in REDCap as the last form underneath all study visit post study visit 12 weeks after C1D1/End of treatment:



Following message will be shown in all other forms:

You have entered a date for progression before 2 years after C1D1. Please follow the normal visits, but only fill in the Long-term/discontinuation follow-up form.

For all the other eCRFs listed underneath the study vist, please go into the form and change form status to *Complete* and save the form. Hereafter fill out the "Long term / Discontinuation follow-up" eCRF.

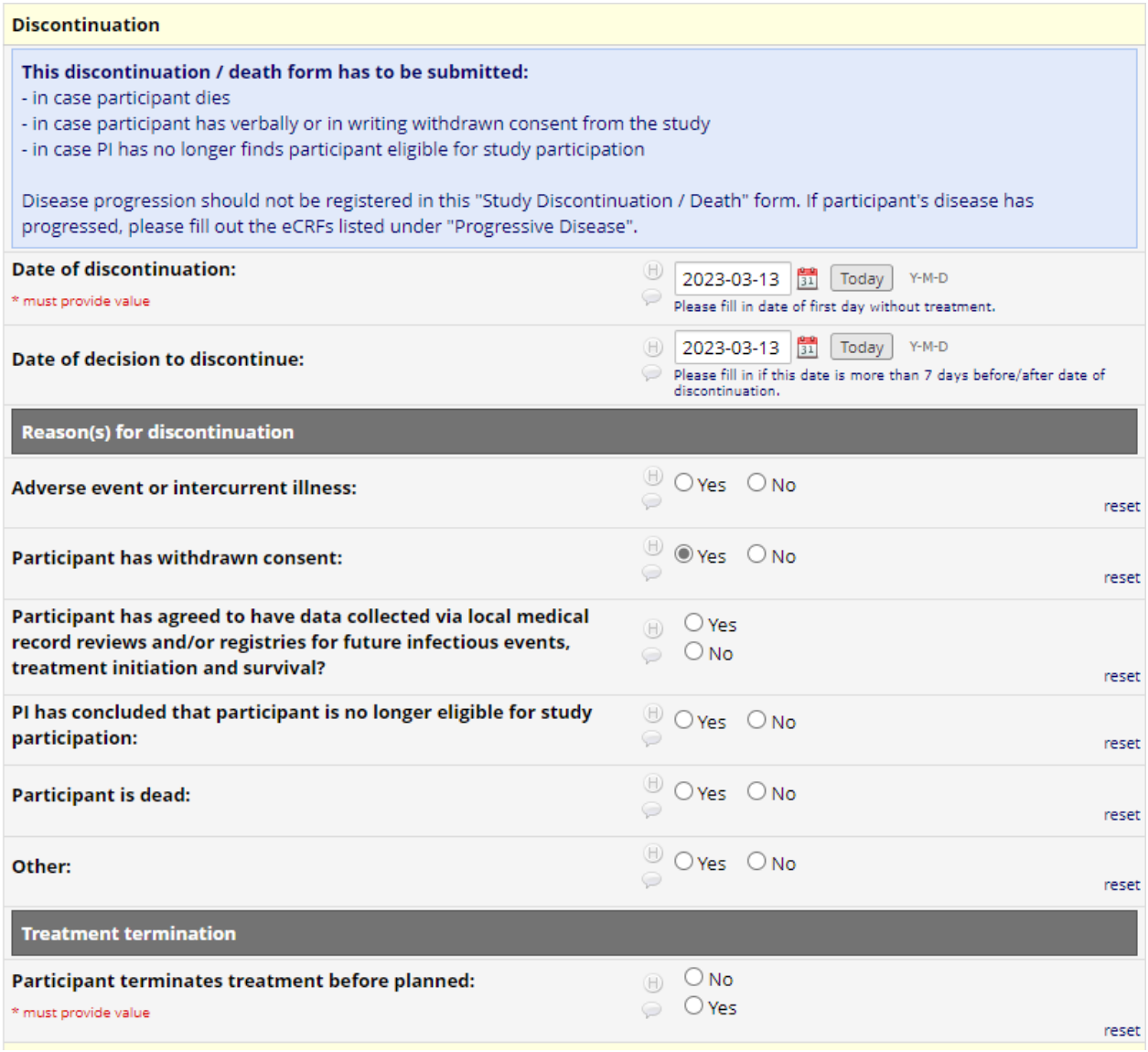
8.8 Specific data reporting: Discontinuation / Death

The eCRF “Discontinuation / Death” must be filled out if:

- participant dies
- participant has withdrawn informed consent for the trial verbally or in writing
- PI no longer finds the participant eligible for study participation

It must also be listed in this form whether or not the participant terminated treatment before planned (only relevant for the treatment arm).

Example on a Discontinuation / Death form (version 2.0) can be seen below.



Discontinuation

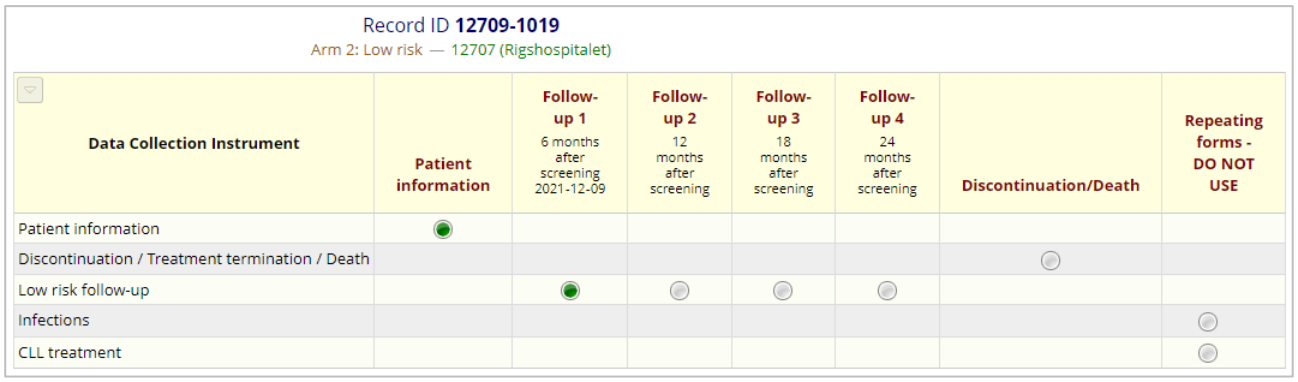
This discontinuation / death form has to be submitted:
- in case participant dies
- in case participant has verbally or in writing withdrawn consent from the study
- in case PI has no longer finds participant eligible for study participation

Disease progression should not be registered in this "Study Discontinuation / Death" form. If participant's disease has progressed, please fill out the eCRFs listed under "Progressive Disease".

Date of discontinuation: * must provide value	2023-03-13 Today Y-M-D Please fill in date of first day without treatment.
Date of decision to discontinue:	2023-03-13 Today Y-M-D Please fill in if this date is more than 7 days before/after date of discontinuation.
Reason(s) for discontinuation	
Adverse event or intercurrent illness:	○ Yes ○ No reset
Participant has withdrawn consent:	◉ Yes ○ No reset
Participant has agreed to have data collected via local medical record reviews and/or registries for future infectious events, treatment initiation and survival?	○ Yes ○ No reset
PI has concluded that participant is no longer eligible for study participation:	○ Yes ○ No reset
Participant is dead:	○ Yes ○ No reset
Other:	○ Yes ○ No reset
Treatment termination	
Participant terminates treatment before planned: * must provide value	○ No ○ Yes reset

8.9 Specific data reporting: Low risk participants (arm 2)

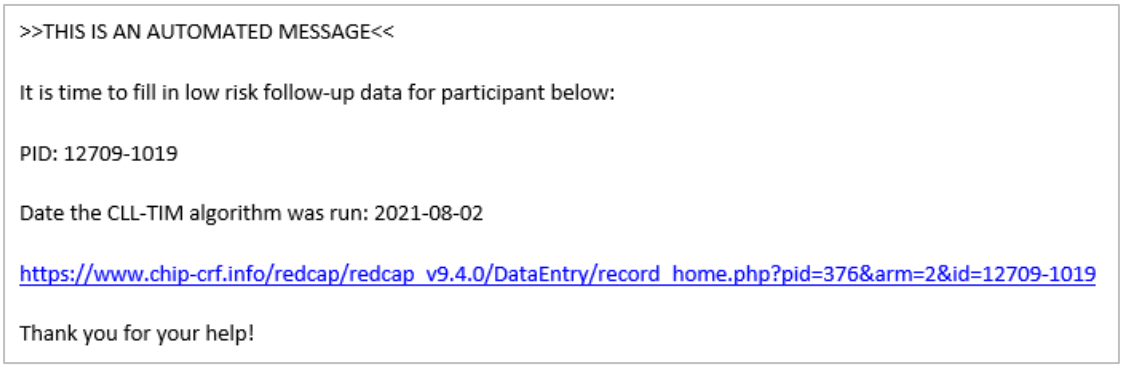
All participants pre-screened with a low-risk result will be listed in the Low risk arm (arm 2) when created in the low-risk category. Each participant's Data Collection Instrument will appear as the picture below.



Record ID **12709-1019**
Arm 2: Low risk — 12707 (Rigshospitalet)

Data Collection Instrument	Patient information	Follow-up 1 6 months after screening 2021-12-09	Follow-up 2 12 months after screening	Follow-up 3 18 months after screening	Follow-up 4 24 months after screening	Discontinuation/Death	Repeating forms - DO NOT USE
Patient information	●						
Discontinuation / Treatment termination / Death						○	
Low risk follow-up		●	○	○	○		
Infections							○
CLL treatment							○

Low risk data must be reported every 6 months from the participant's pre-screening date. An automatic email notification will be forwarded to the data collector(s) approximately two weeks before data must be entered. The email notification will look like the one below. The link can be used to enter the participant's Data Collection Instrument in REDCap.



>>THIS IS AN AUTOMATED MESSAGE<<

It is time to fill in low risk follow-up data for participant below:

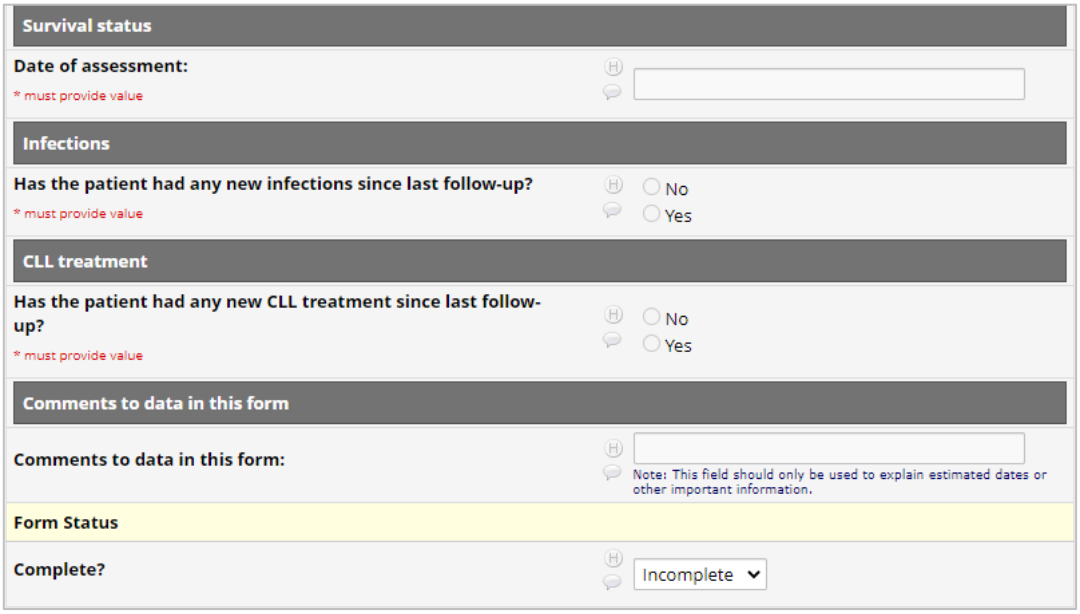
PID: 12709-1019

Date the CLL-TIM algorithm was run: 2021-08-02

https://www.chip-crf.info/redcap/redcap_v9.4.0/DataEntry/record_home.php?pid=376&arm=2&id=12709-1019

Thank you for your help!

Data that must be collected as low-risk data is survival status, infections and use of alternative CLL therapy.



Survival status

Date of assessment:
* must provide value

Infections

Has the patient had any new infections since last follow-up?
* must provide value
○ No
○ Yes

CLL treatment

Has the patient had any new CLL treatment since last follow-up?
* must provide value
○ No
○ Yes

Comments to data in this form

Comments to data in this form:
Note: This field should only be used to explain estimated dates or other important information.

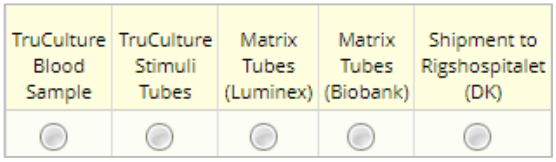
Form Status

Complete?
Incomplete

8.10 Specific data reporting: TruCulture (local central labs)

TruCulture data reporting in REDCap is only relevant for those sites that are incubating, harvesting and freezing the TruCulture blood sample themselves. For site 12707 and 12708, this is done by Kvalitetskontrollab at Rigshospitalet, hence this section is not relevant for these sites.

All the TruCulture sample data must be reported in REDCap. Following eCRFs must be completed for each TruCulture blood sample tube received:

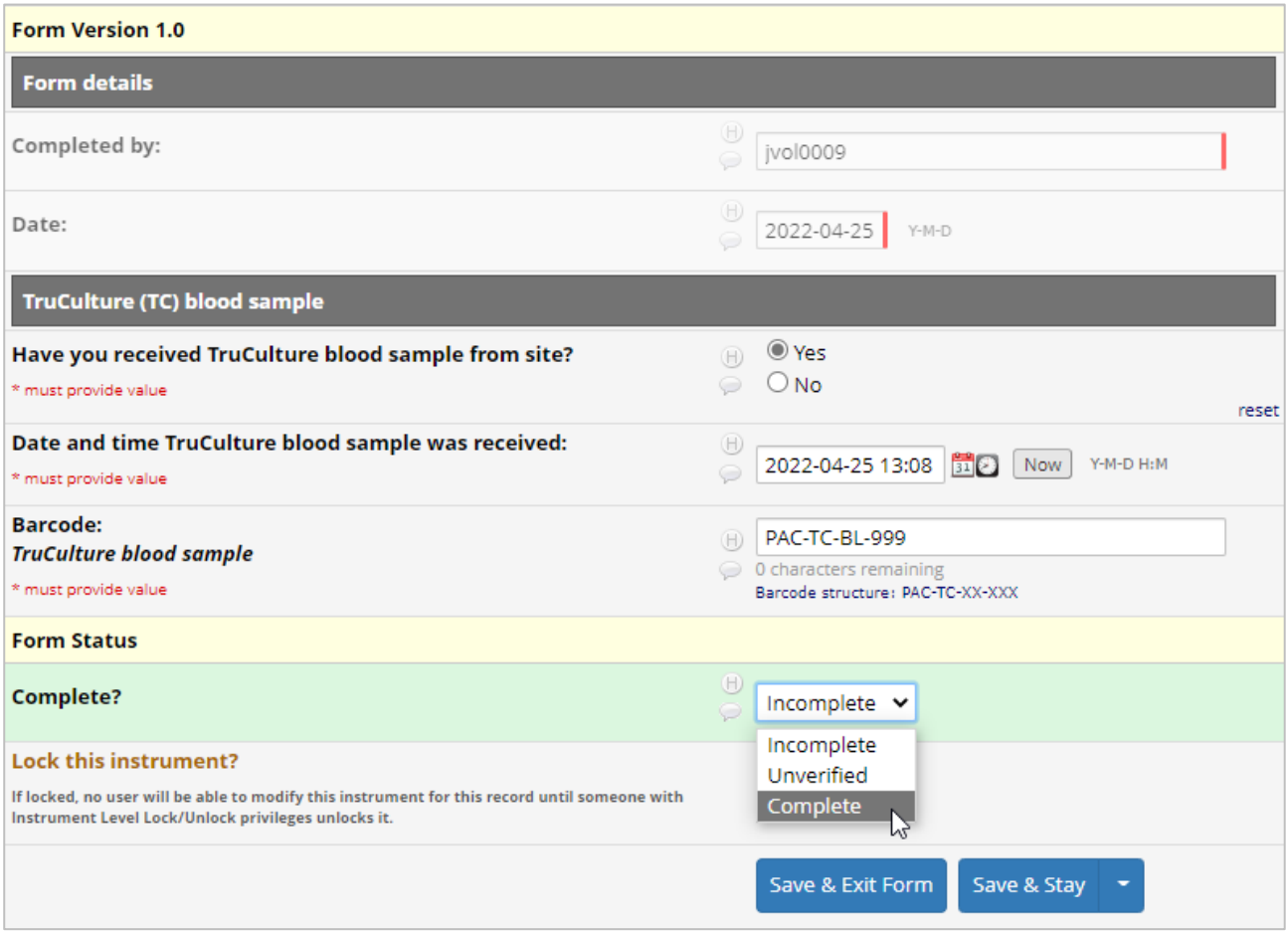


For all eCRFs: Once all data have been entered, the form status must be changed to *Complete* and the form must be saved. The status icon will then change to green.

It is described in sections below how and what to report for all five TruCulture eCRFs. The data that must be reported is the same data as on the Specimen & Shipping Log for local central lab. It is recommended to enter the data into REDCap a long the way as stated in the TruCulture instruction since barcodes must be scanned into REDCap.

8.10.1 eCRF: TruCulture Blood Sample

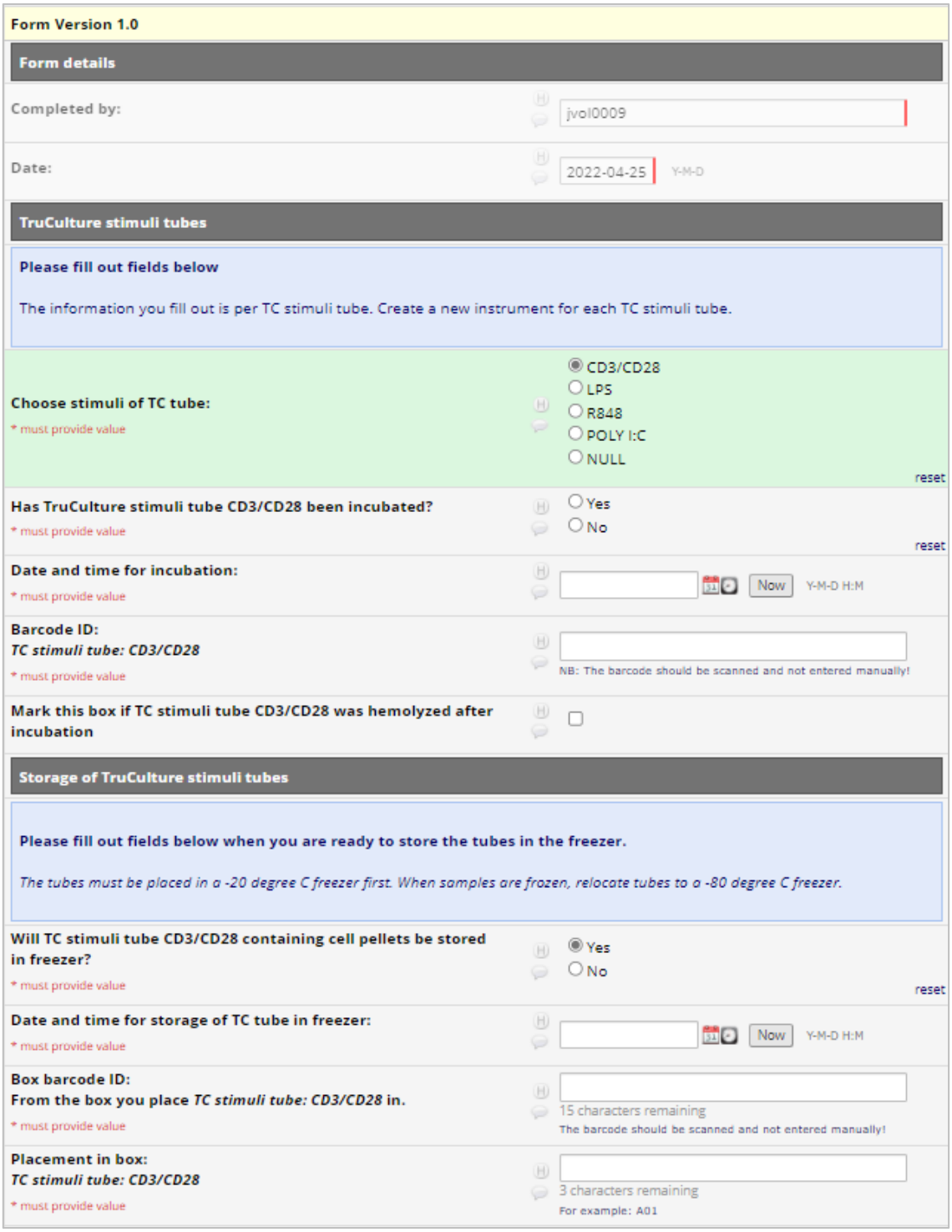
In the eCRF "TruCulture Blood Sample", information about the TruCulture blood sample received from site must be reported.



8.10.2 eCRF: TruCulture Stimuli Tubes

In the eCRF "TruCulture Stimuli Tubes", information about the five TruCulture stimuli tubes that are incubated with whole blood must be entered – including storage information about the cell pellets that remains in the TruCulture stimuli tubes after harvest of the supernatant. On the screenshot below you can see how this eCRF looks like.

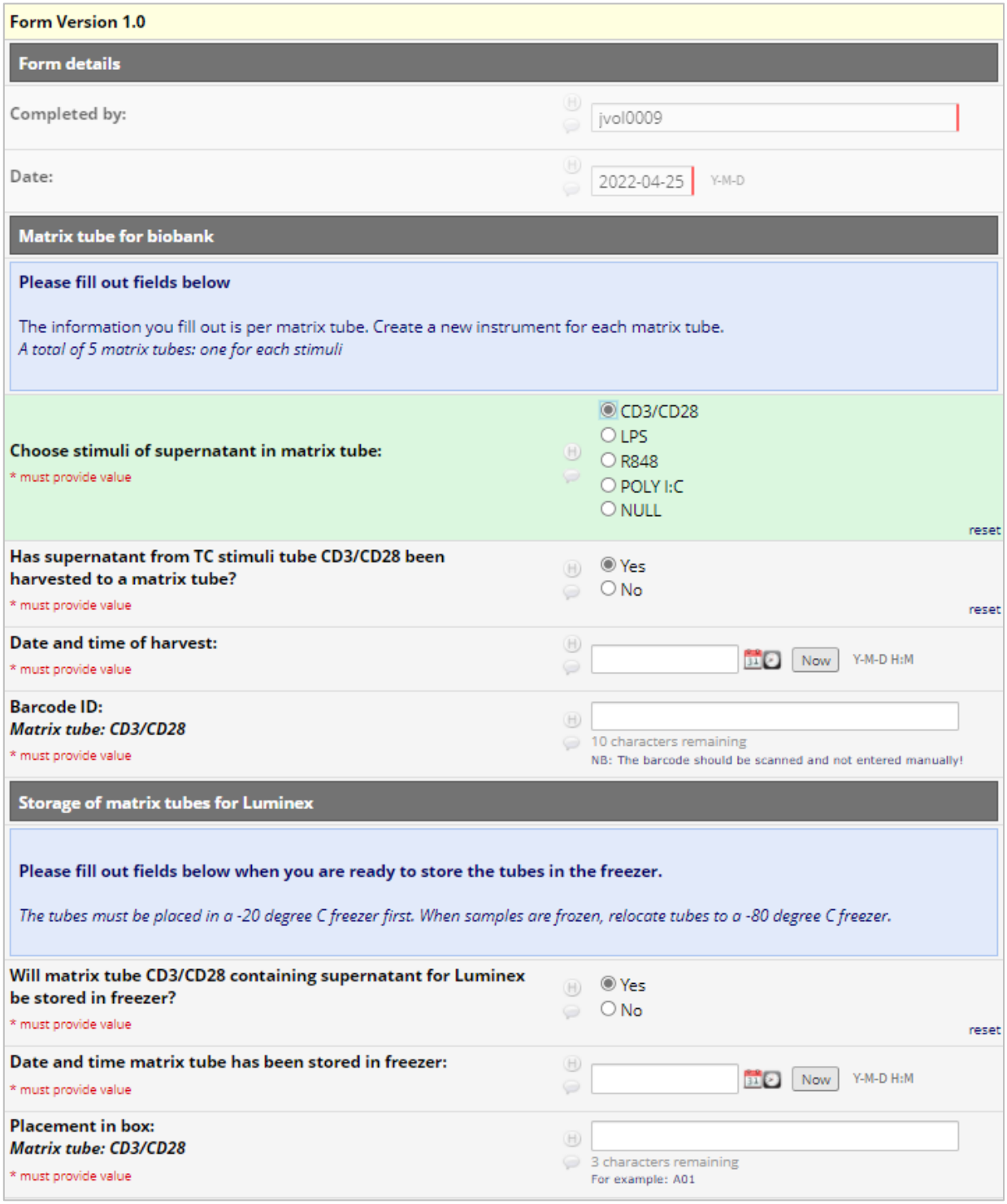
One form must be completed per stimuli. When first form has been saved, a new form is created by clicking *+ Add new* in the 'Current instance' drop down on top of the page or by clicking on the plus button in the Record Status Dashboard or the participant's Data Collection Instrument.



8.10.3 eCRF: Matrix Tubes (Luminex)

In the eCRF "Matrix Tubes (Luminex)", information about the five matrix tubes containing supernatant for Luminex analysis must be entered – including storage information about when the tubes are being stored in freezer. On the screenshot below you can see how this eCRF looks like.

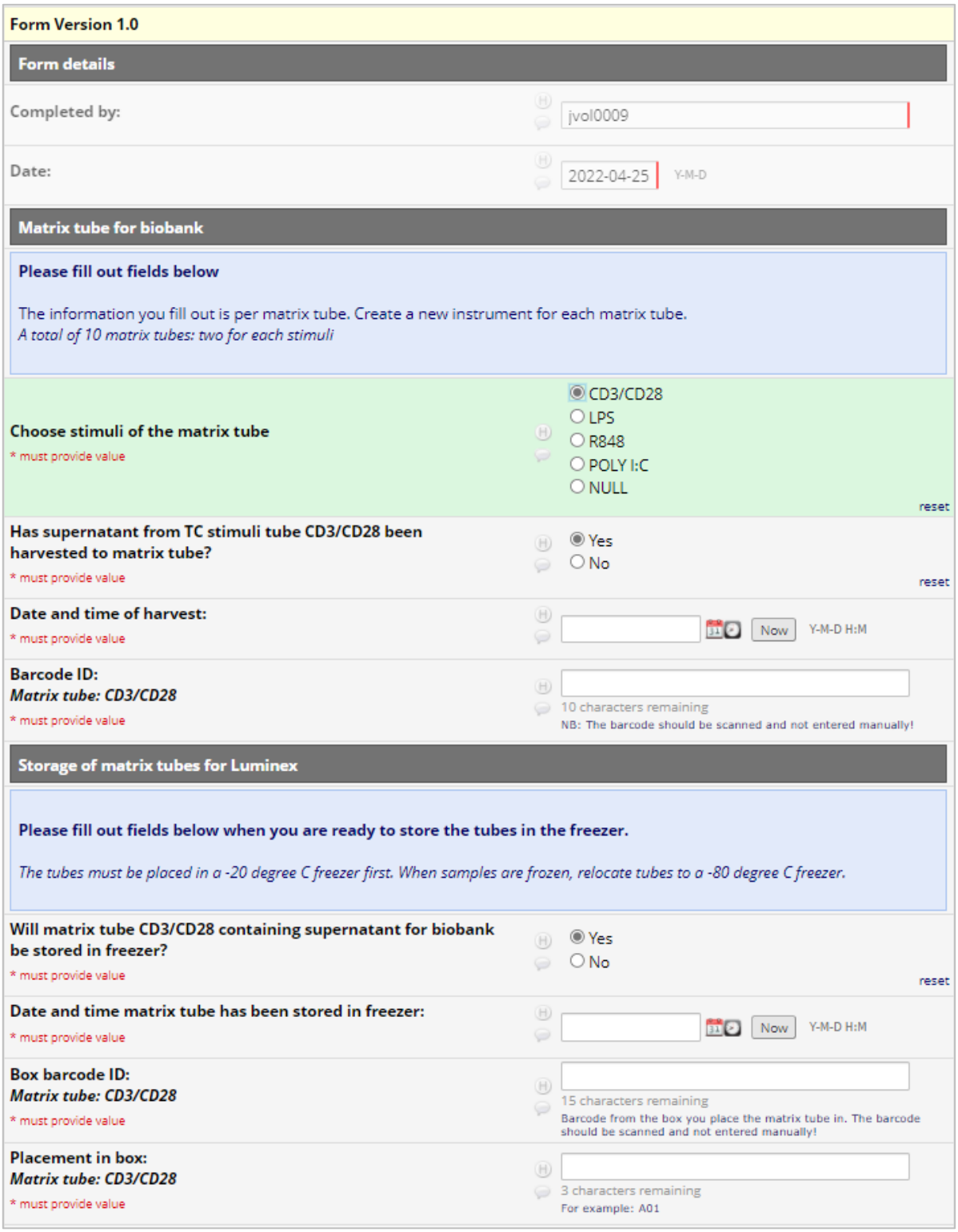
One form must be completed per matrix tube. When first form has been saved, a new form is created by clicking *+ Add new* in the 'Current instance' drop down on top of the page or by clicking on the plus button in the Record Status Dashboard or the participant's Data Collection Instrument.



8.10.4 eCRF: Matrix Tubes (Biobank)

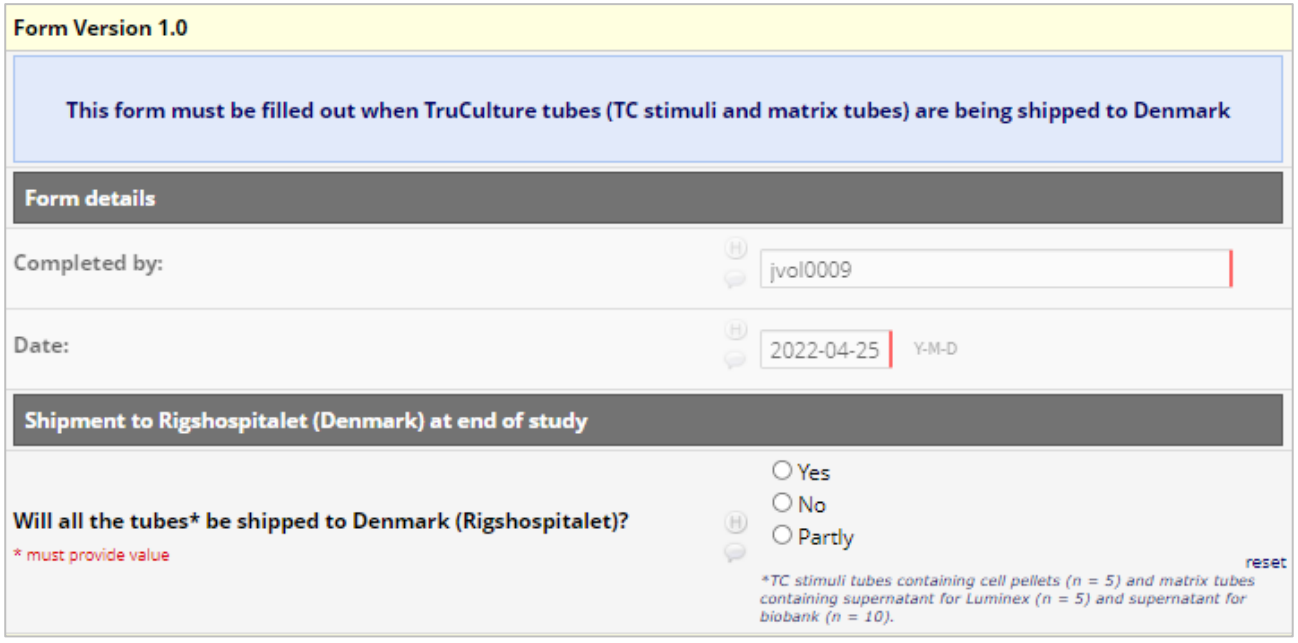
In the eCRF "Matrix Tubes (Biobank)", information about the 10 matrix tubes containing supernatant for biobank storage must be entered – including storage information about when the tubes are being stored in freezer. On the screenshot below you can see how this eCRF looks like.

One form must be completed per matrix tube. When first form has been saved, a new form is created by clicking *+ Add new* in the 'Current instance' drop down on top of the page or by clicking on the plus button in the Record Status Dashboard or the participant's Data Collection Instrument.

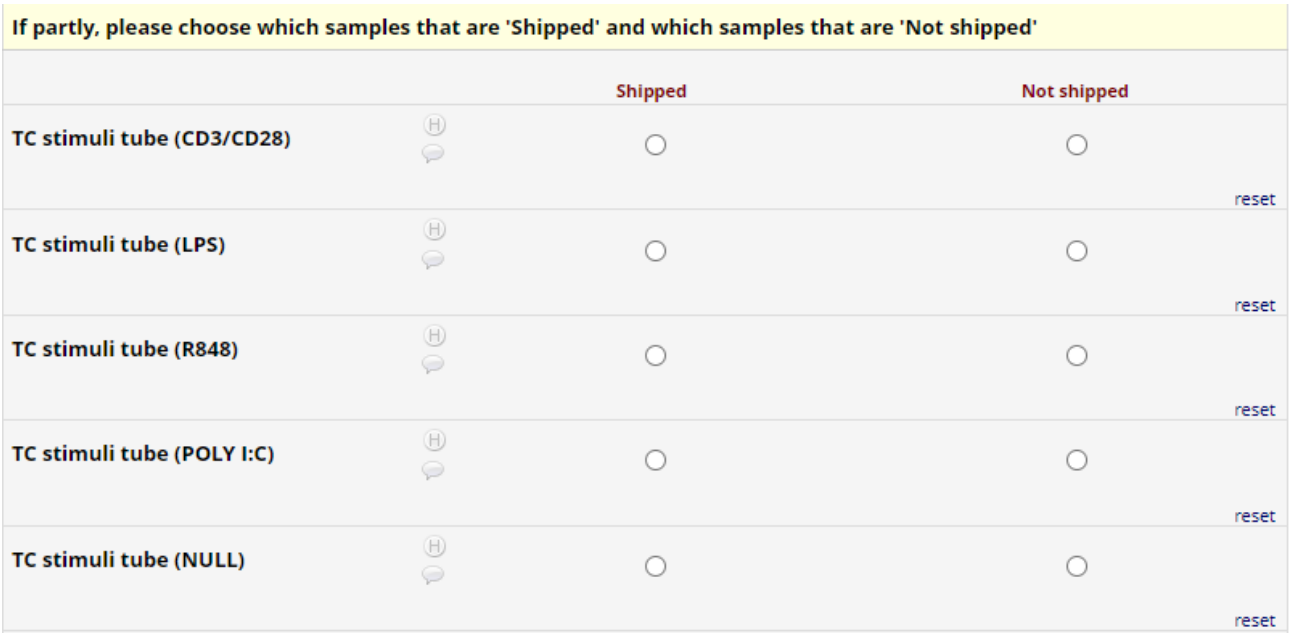


8.10.5 eCRF: Shipment to Rigshospitalet (DK)

In the eCRF "Shipment to Rigshospitalet (DK)", information about shipment of the tubes (TruCulture stimuli tubes and matrix tubes) must be entered. This eCRF must be completed prior to the shipment.



In case not all tubes are being shipped, it must be reported whether or not the specific tube is being shipped or not (example shown below):



9 Resolve issues

The resolve issues function can be accessed from the left-hand menu and provides an easy way for e.g. the monitor or sponsor to communicate regarding problems with specific values/data for a specific patient. Here it is also possible to view all queries created in the project.

You are also more than welcome to write to the project email: chip-prevent.rigshospitalet@regionh.dk