eCRF user's guide for clinical sites

EU-SOLIDACT

Version 1.0 20-05-2021

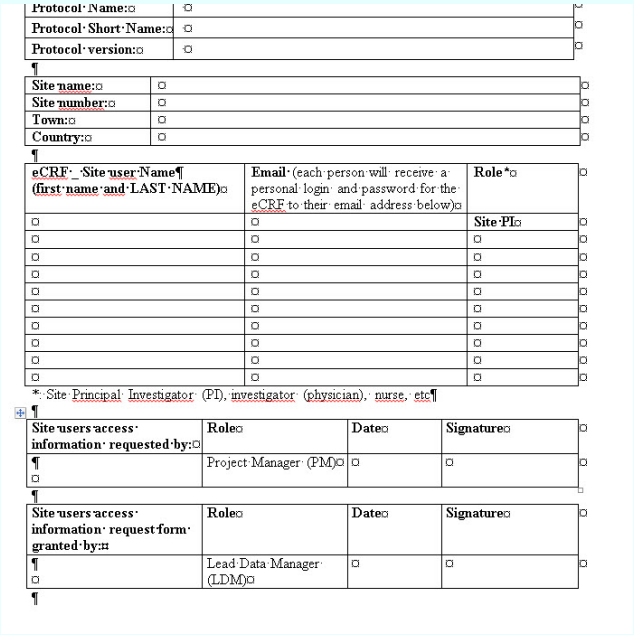
Introduction (1/2)

- CSOnline is a Clinsight solution for online clinical trial management
- It allows investigators to enter the data of their patients directly in the electronic case report form
- All forms should be filled in according to the source document by the investigator or their representatives (representatives should have signed the “list of investigator’s co-worker and their roles in the trial”)
- The principal investigator in each center is responsible for data entry in the eCRF in his/her center

Introduction (2/2)

How to request access to the database?

- A form requesting access to the e-CRF should be sent to the Inserm U1136: solidact.inserm@iplesp.upmc.fr
- The Project Data Manager will send the login and passwords to all the users after receiving the request forms



Protocol Name:	
Protocol Short Name:	
Protocol version:	

Site name:	
Site number:	
Town:	
Country:	

eCRF _ Site user Name (first name and LAST NAME)	Email (each person will receive a personal login and password for the eCRF to their email address below)	Role *
		Site PI

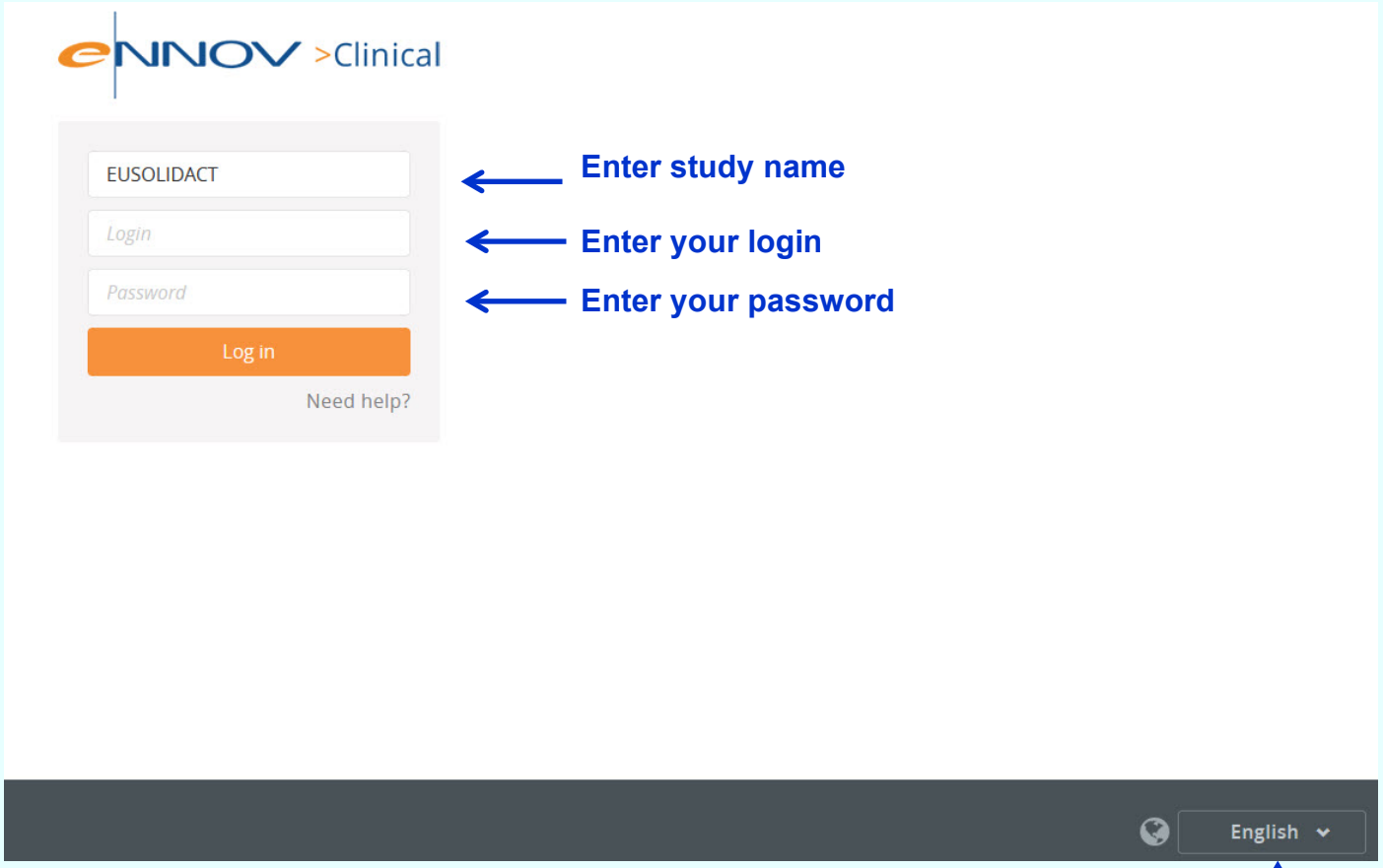
*: Site Principal Investigator (PI), investigator (physician), nurse, etc

Site users access information requested by:	Role	Date	Signature
	Project Manager (PM)		

Site users access information request form granted by:	Role	Date	Signature
	Lead Data Manager (LDM)		

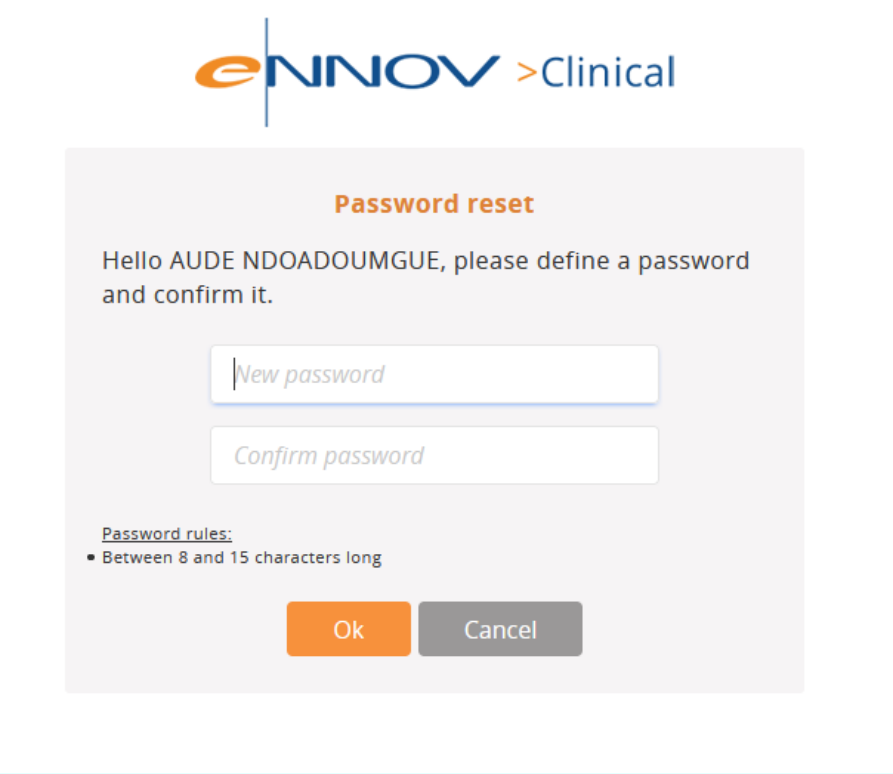
Connection (1/2)

- CSonline has been validated with the following internet browsers:
  - Internet Explorer
  - Mozilla Firefox
  - Nescape Navigator
- Website address: *https://www.ccde-ecrf.com/EnnovClinical/login*



Connection (2/2)

- If you are connected to the study for the first time with the login and password provided by the study manager, you are required to change your password for security reasons:

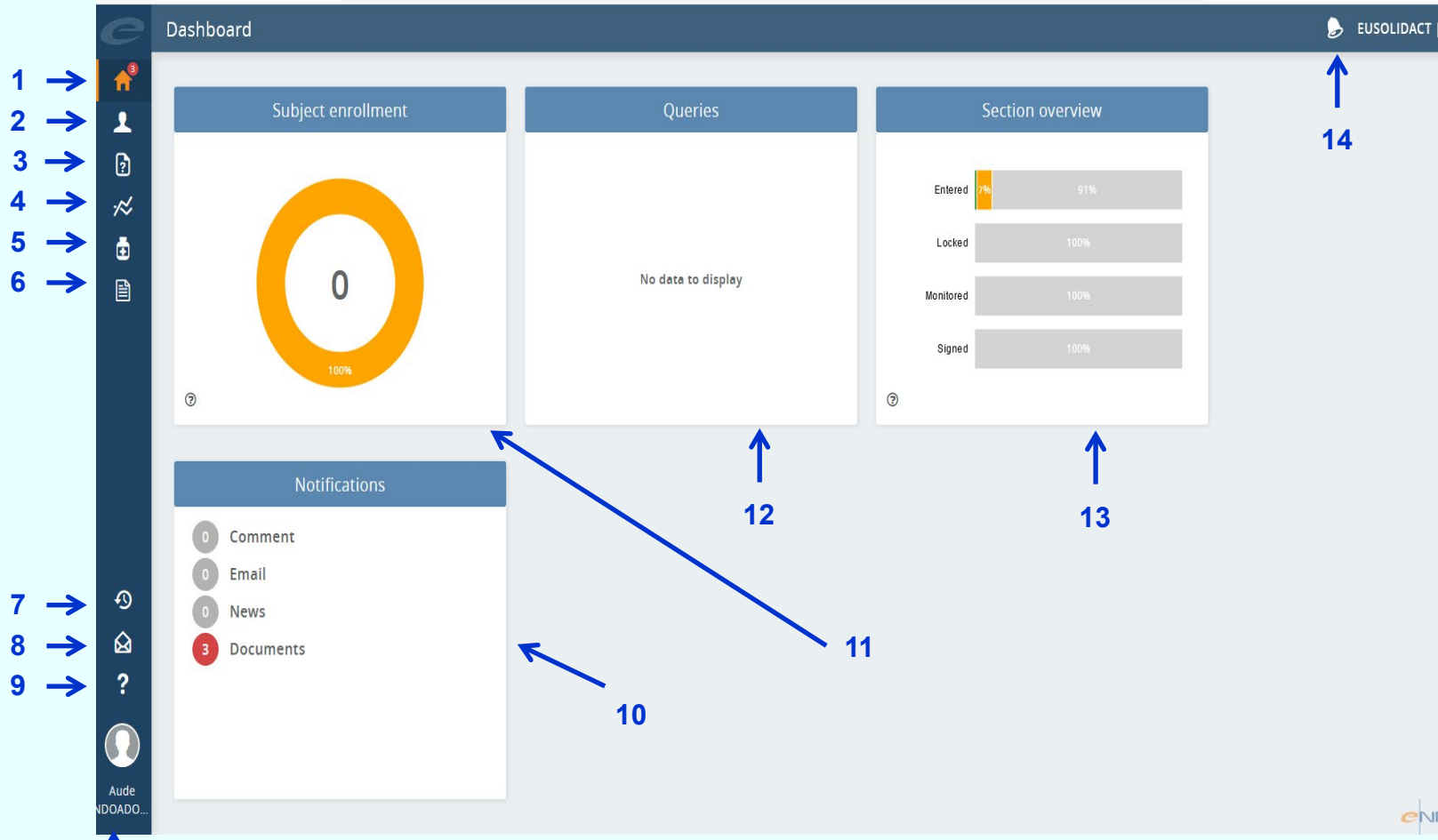


Enter a password containing between 6 and 15 alphanumeric characters without any accents [a-z] [A-Z] [0-9], confirm your password by entering it another time and click "OK".

Now you are the only one to know this new password and connect to the study safely.

Home Page (1/4)

The clinical study home page (Dashboard), accessible once the eCRF user is logged, is presented as follows. It is made up of several widgets providing information on the study



Home Page (2/4)

1: Dashboard : This is the home page of CSOnline. It is made up of several widgets providing information on the study.

2: Patients overview: It displays the progress of the patients and allows you to access the CRF of each patient.

3: Query management: It gives you access to the list of queries

4: Inclusion curve: It displays the total number of patients included into the study based on the expected number. This curve is visible only if it has been configured by the data manager.

5: Therapeutic units: it displays the list of therapeutic units

6: Documents:

News: displays the list of news related to the study
Study documents: displays the documents related to the study (protocol, blank CRF...)
Reports: displays the different reports generated for CSOnline
My documents: stores the CRFs and other documents generated in PDF format

Home Page (3/4)

7: History: History of the navigation through the e-CRF.

8: Internal email box (webmail): To write and read emails.

9: Contact and technical support: Customized page of the structure in charge of the clinical study containing the contact information. In case of technical issues with the CSOnline application, select the technical support menu

10: "Notifications" widget: It displays the number of pending entry comments, emails, news, documents, deviation forms, notes or warning messages.

11: "Subject enrollment" widget : The figure in the middle of the ring displays the number of patients in the study. The colored parts of the ring allow you to view the distribution based on the statuses of the defined patients

Home Page (4/4)

12: "Queries" widget: The figure in the middle of the ring displays the number of pending queries.

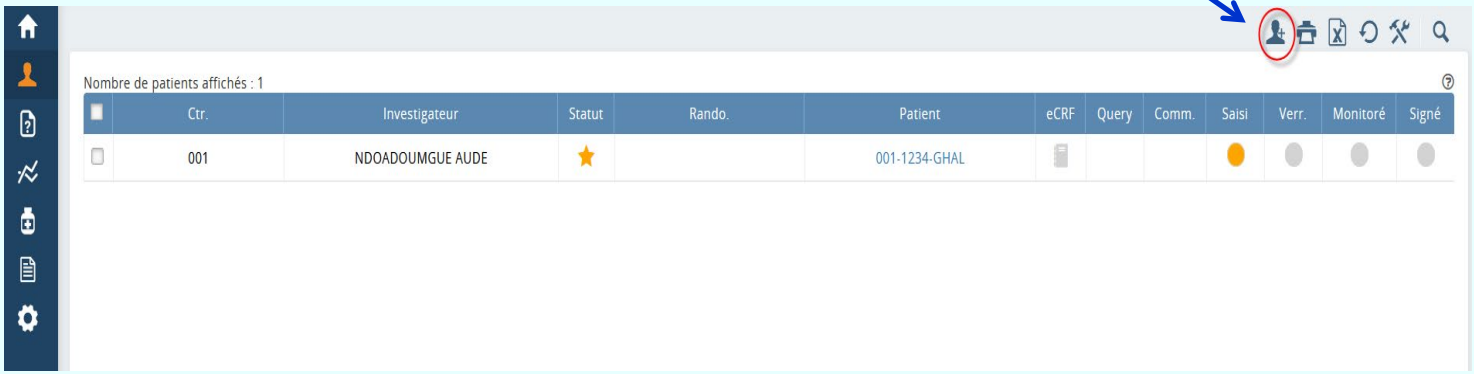
13: "Section overview" widget: The diagrams inform you of the progress of the sections based on the different statuses.

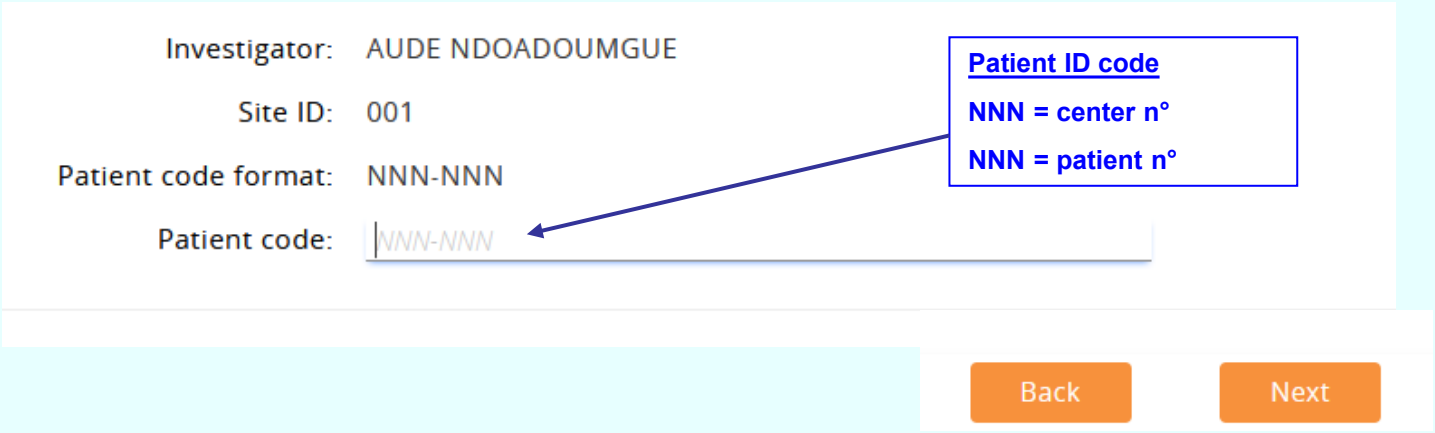
Remarks regarding these 3 widgets: The question mark positioned at the bottom left part of the ring allows you to display or hide the diagram legend. Click the colored parts of the rings (or bars for the section overview) to have direct access to the desired category (e.g.: ongoing included patients, pending queries...). A search zone is available to filter the site (the search availability depends on the logged-in profile). It is also possible to click the widget titles to reach the general menus (e.g.: Patients overview, list of queries and section overview).

14: Document creation: It displays the documents which were generated in PDF after a printing task. The bell informs you when there are pending generated documents.

Creating a patient

Patients are created by clicking the “patient overview” section.
To add a patient to the study, click the "Create new patient" button:

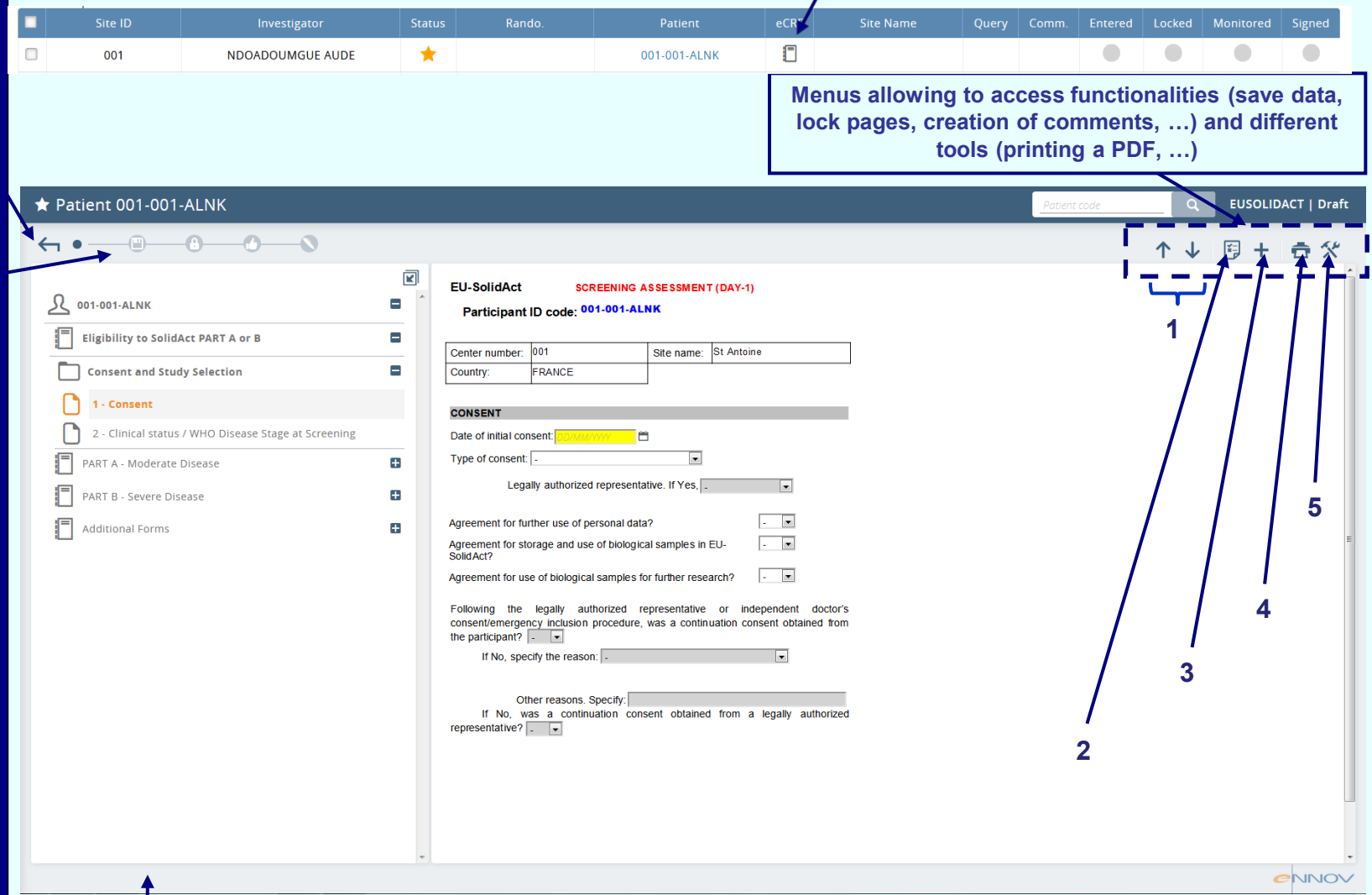




To cancel the creation of the patient, click the "Back" button at the bottom left.
To continue the creation of the patient, click "Next" after filling out the required fields.
If one of the compulsory fields is left blank, an error message is displayed: "Patient code is blank", "Initials not entered"...

Data entry (1/8)

To access the eCRF of each patient and start data entry, investigators should go to the Patient overview and click on eCRF.

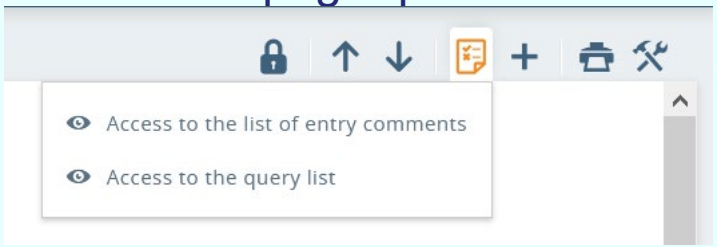


- Introduction
- Connection
- Home page
- Creating a patient
- **Data entry**
- Randomization
- Patient overview
- SAE notification
- DRE notification
- Signatures
- Queries
- Unblinding

Data entry (2/8)

1: These arrows are used to navigate through the pages in the CRF

2: Gives access to page queries and comments



Comments

When entry comments are not replied, a red notification appears containing the number of pending comments on the page. The field concerned has become yellow

When the entry comment is replied, the field becomes green, the red notification disappears and a green checkmark notifies that all the comments of the page are validated.

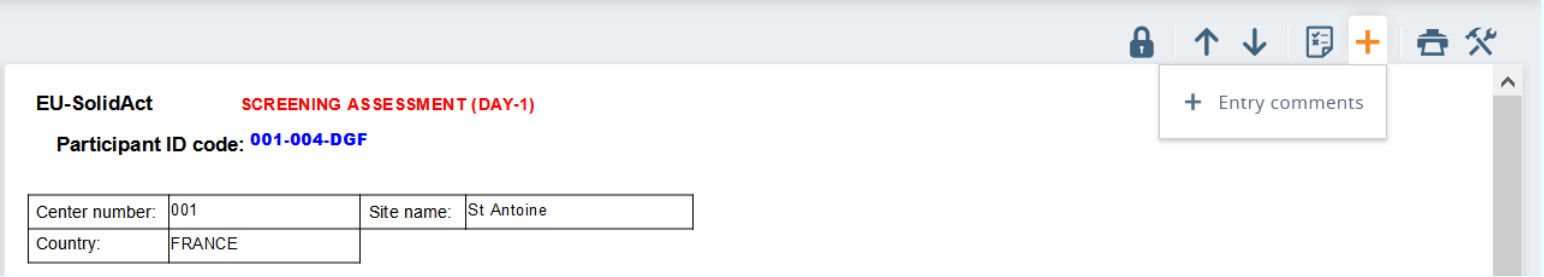
Queries

When queries are not replied, a red notification appears containing the number of pending queries on the page. A red question mark also appears beside the field concerned.

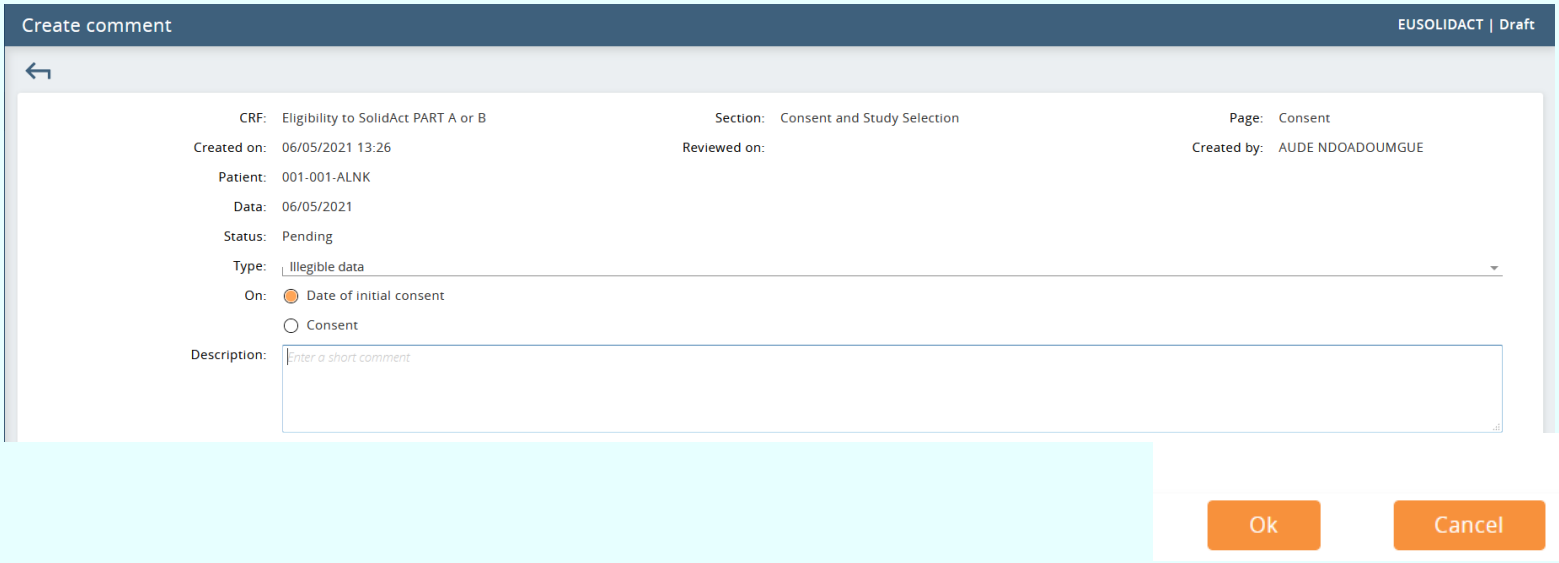
When the query is replied, it becomes green, the red notification disappears and a green checkmark notifies that all the queries of the page are solved

Data entry (3/8)

3: If the investigator or their representatives do not understand a query or he/she cannot enter a value in a field, etc,… he/she can create a comment by placing the cursor in the concerned field and clicking the “**+**”.



The investigator or their representatives will fill in the description box and click “Ok” to save the comment

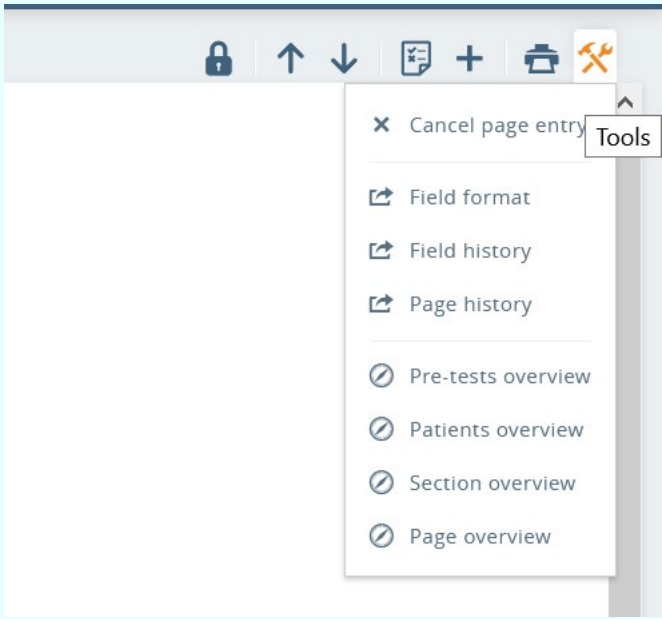


Data entry (4/8)

4: This button allows the CRF to be printed in PDF from the data of the patient. The generated file will be accessible in the "Personal directory“

5: The "Tools" menu is symbolized by the icon and is used to perform the following actions.

-Cancel all actions: enter data, lock, monitor, validate and sign
-Display the field formats (Features of the fields to be entered)
-Display the field history of the selected field
-Display the page history (Audit trail of the page tracking statuses)
-Follow up the pre-tests
-Return to the Patients Overview
-Return to the Section Overview
-Return to the Page Overview



Data entry (5/8)

The EUSOLIDACT e-CRF consists of 4 parts:

- Eligibility to Part A or Part B: this section will determine to which part of the study the participant is eligible and depends on the WHO Disease stage at screening

- Part A- Mild/Moderate disease: from screening visit to D91 visit.

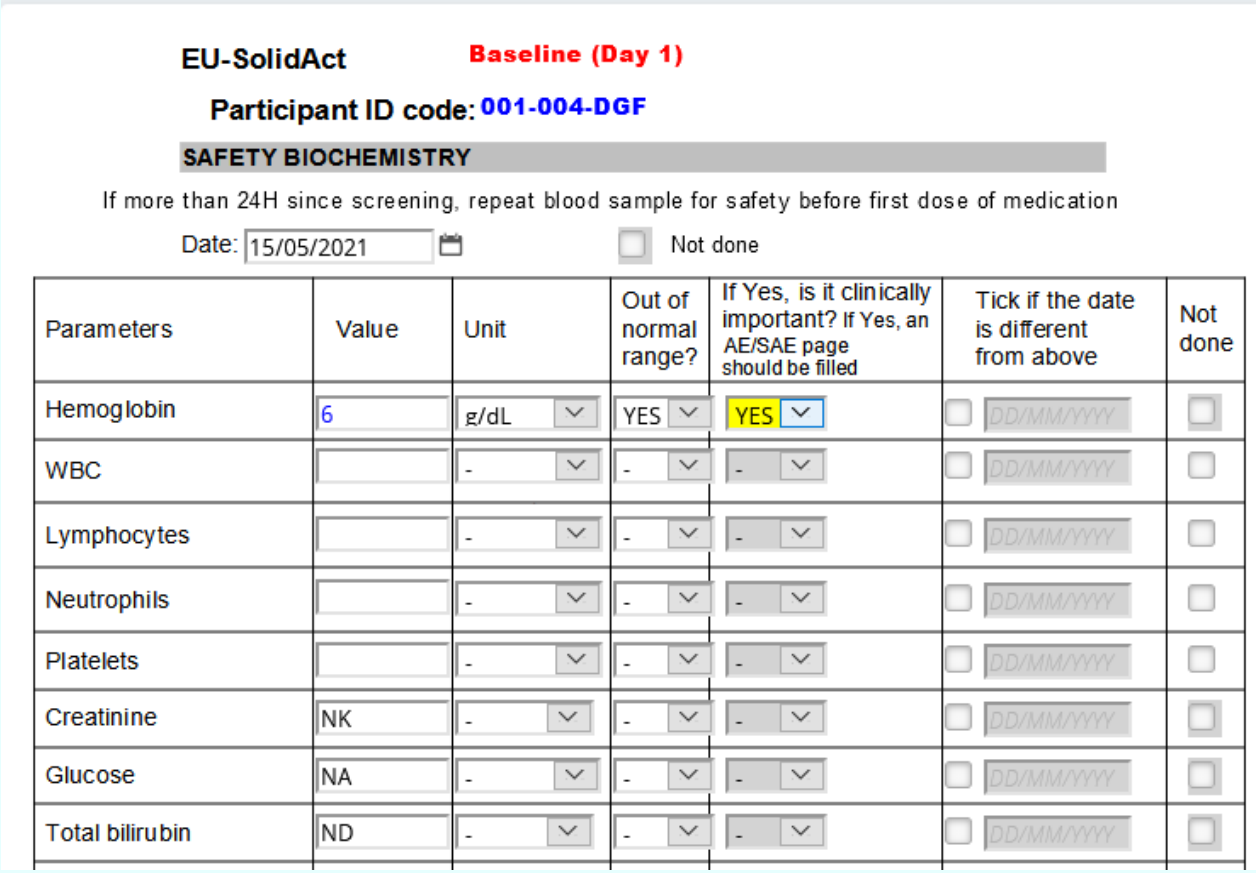
If a participant included in Part A changes from Moderate to Severe Disease, the participant can be included in Part B. “Early stop” pages should be filled in Part A including WHO Disease stage to unlock Part B eCRF.

- Part B- Severe/Critical disease: from screening Visit to D91 visit.

- Additional forms: Adverse Events; Disease Related Events; SAE; Pregnancy

Data entry (6/8)

The following code should be used in the CRF for missing values
NA: Not Applicable
NK: Not Known
ND: Not Done



EU-SolidAct **Baseline (Day 1)**

Participant ID code: 001-004-DGF

SAFETY BIOCHEMISTRY

If more than 24H since screening, repeat blood sample for safety before first dose of medication

Date: 15/05/2021 Not done

Parameters	Value	Unit	Out of normal range?	If Yes, is it clinically important? If Yes, an AE/SAE page should be filled	Tick if the date is different from above	Not done
Hemoglobin	6	g/dL	YES	YES	DD/MM/YYYY	
WBC		-	-	-	DD/MM/YYYY	
Lymphocytes		-	-	-	DD/MM/YYYY	
Neutrophils		-	-	-	DD/MM/YYYY	
Platelets		-	-	-	DD/MM/YYYY	
Creatinine	NK	-	-	-	DD/MM/YYYY	
Glucose	NA	-	-	-	DD/MM/YYYY	
Total bilirubin	ND	-	-	-	DD/MM/YYYY	

Do not forget to fill the AE/SAE page(s) if the biochemistry results are clinically important

Data entry (7/8)

Each icon represents a page status, the statuses are symbolised by two colours:

- Light grey: pending
- Dark blue: completed

Examples of page statuses:

- Page not entered, not locked, not monitored and not signed

- Page entered, not locked, not monitored and not signed

- Page entered, locked, not monitored and not signed

- Page entered, locked, monitored and not signed

- Page entered, locked and to re-monitor

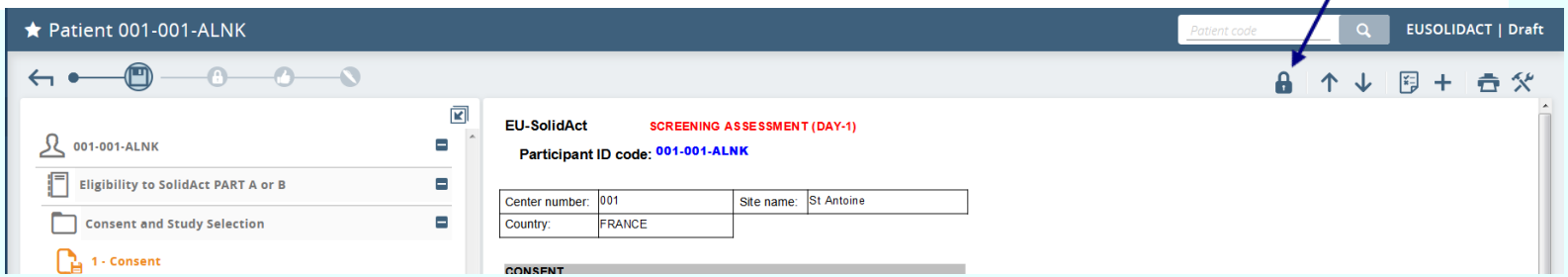
- Page entered, locked, monitored and signed

Data entry (8/8)

Once the pages of the CRF are entered, they must be locked in order to attest that the data entry phase is completed. When the pages are all locked, the job of the monitor can start. There are 2 options:

- Locking the pages one by one, as and when they are entered in the CRF;
- Locking several pages at the same time from the different overviews.

To lock a page, click the "Lock" button (1) located in the CRF menu. Then the page switches to the "Locked" status. The "Unlock" function is accessible via the "Tools" menu and "Cancel "Locked" status" (there is no keyboard shortcut as is the case for the lock function).



Locking a page means that the data can no longer be modified directly from the CRF. Nevertheless, if you want to correct data, you must previously unlock the page, change the data and relock the page in order for the ARC to start monitoring.

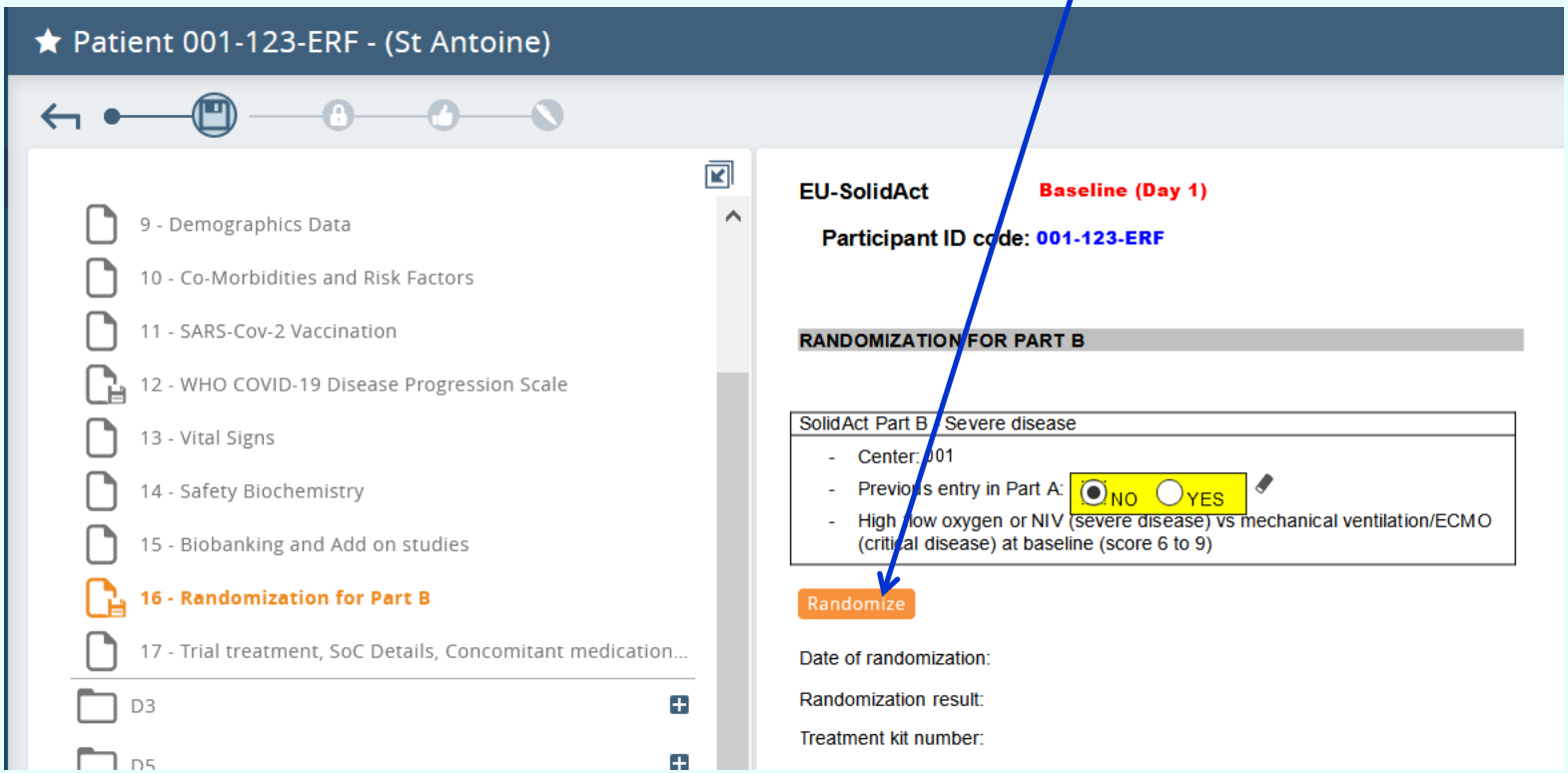
If the page has already been monitored by the CRA, you will not be allowed to cancel the lock status of the page. The only solution is to ask the CRA to unlock the page or create a query on the data to be changed.

Likewise, if the page is already signed or validated, you will not be allowed to cancel the lock status of the page as long as the "signed" and "validated" statuses of the page are not cancelled.

Randomization (1/2)

Randomization of participants to a treatment arm is done at the baseline visit

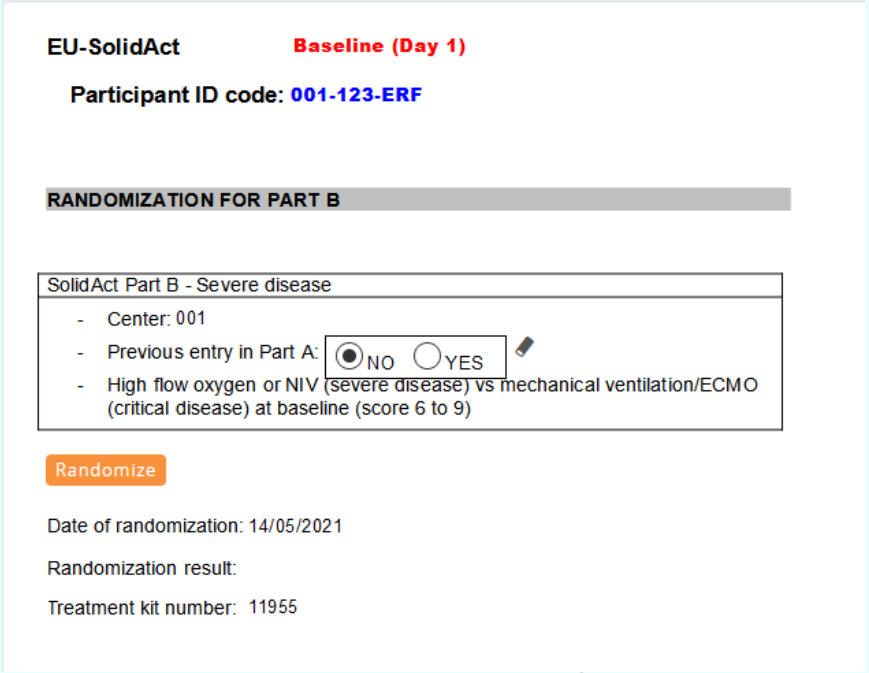
Specify if the participant was previously included in Part A of the study or not and click on the Randomize button



Randomization (2/2)

The date of randomization and treatment kit number is displayed once the randomization is done

Randomization results are hidden for double-blind studies



Should the need for an emergency randomization arise, the fields on the following pages must be filled to enable randomization:

- Consent page
- Clinical status / WHO Disease Stage at screening

Consent and study selection

- Study treatment arm available at the centre (Page 1)
- Inclusion and exclusion criteria (Pages 2-4)
- WHO COVID-19 Disease progression scale at baseline (Page 12)

Patients overview (1/4)

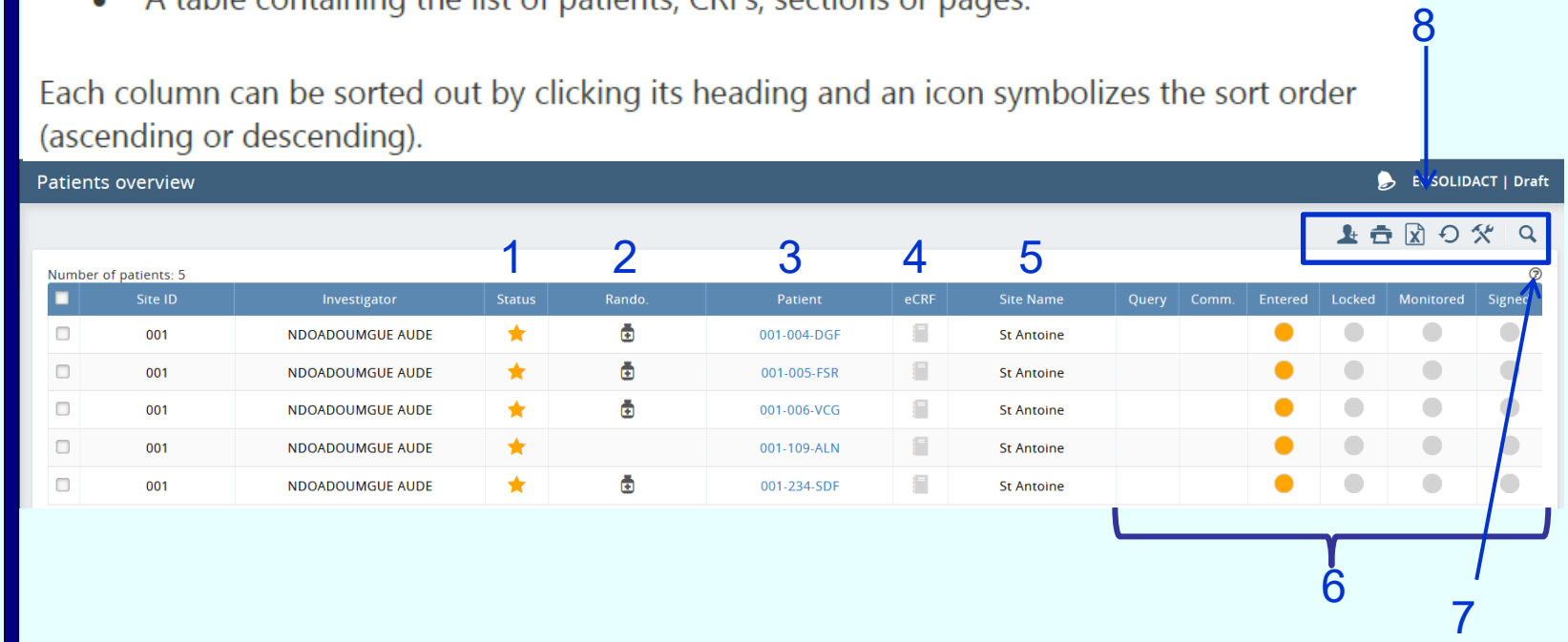
Click on the “Patient overview” in the Home page.

Patients’ overview table displays the CRF progress state for each patient.

Each one of the 4 levels of the overview tables is based on the same appearance:

- A menu bar including all the features of the page based on the level of the overview table (Creation of patient / Printing / Update / Display of the legend and/or filters / Tracking tool).
- A table containing the list of patients, CRFs, sections or pages.

Each column can be sorted out by clicking its heading and an icon symbolizes the sort order (ascending or descending).



Patients overview (2/4)

1: The patent's status (ongoing, selected…)

2: Randomization status: A displayed Randomize icon indicates that the participant has been randomized to a treatment arm

3: The patient code: by clicking the blue link, you have access to the sections overview table for the patient

4: Click the icon in the eCRF column to have access to the first page of the patient's CRF

The CRF icon can have different colour codes based on the actions remaining to be done on the CRF of the patient.


White: No data entered in the CRF yet, data entry must start

Grey: Data has been entered; data entry should continue


Red: Pages are entered but they have not been locked


Green: Pages have to be monitored by the CRA


Blue: Queries awaiting replies


Purple: The CRF has to be signed


Black: All pages are signed

The color of the CRF icon depends on the logged-in user's profile:

- Data entry profile (Investigator, keyboard operator, clinical trial technician): The data entry or locking operations will be privileged over the monitoring.
- CRA or manager-type profile: The monitoring will be privileged over the data entry or locking operations.

Patients overview (3/4)

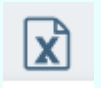
5: Displays the investigator's site

6: These columns indicate the presence of queries, entry comments… and specify the statuses linked to the data entry, lock, monitoring, medical validation and signature

7: Click the "?" to display or hide the legend related to the icon of the eCRF column.

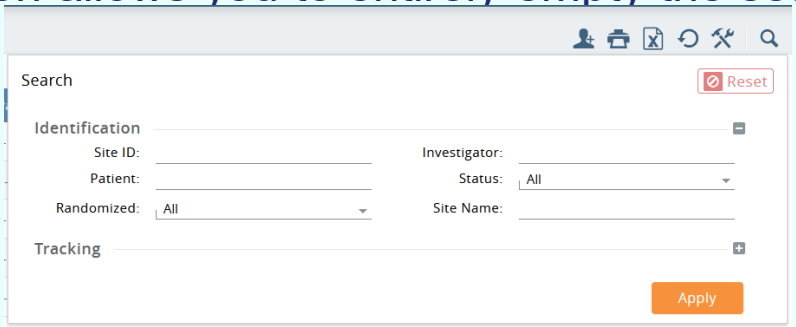
8:

The  icon is used to print the CRF of selected participants

The  icon exports the patients overview in an Excel format

The  refreshes the patients overview page

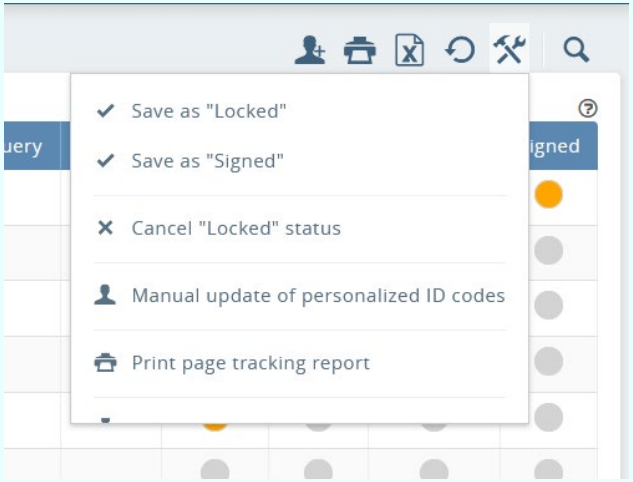
The  icon is used to run searches within the overview tables. The "Reset" button allows you to entirely empty the search zone



Patients overview (4/4)

The icon gives access to patient related functionalities such as:

- Save as “Entered”
- Save as “Locked”
- Save as “Signed”
- Patient code modification
- Patient Deletion
- Treatment unblinding

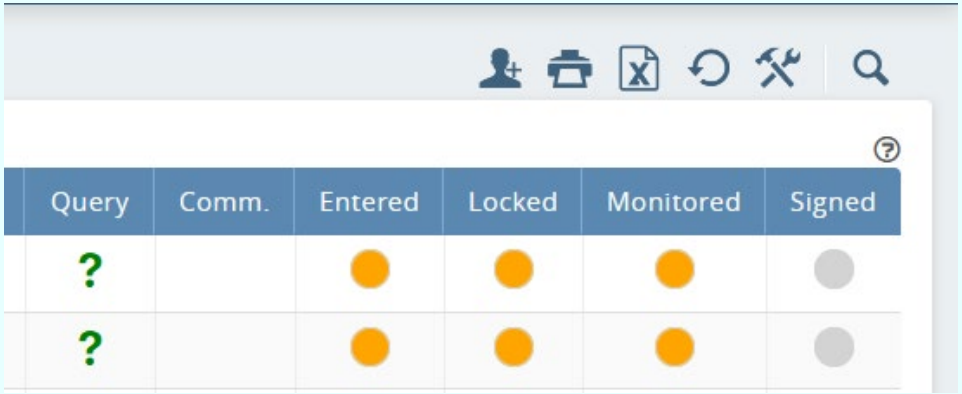


The data entry, lock, monitoring and investigator’s signature statuses are symbolized by colored dots:

Step not done ("Not done" status)

In progress: at least one page of the CRF is entered ("Partial" status)

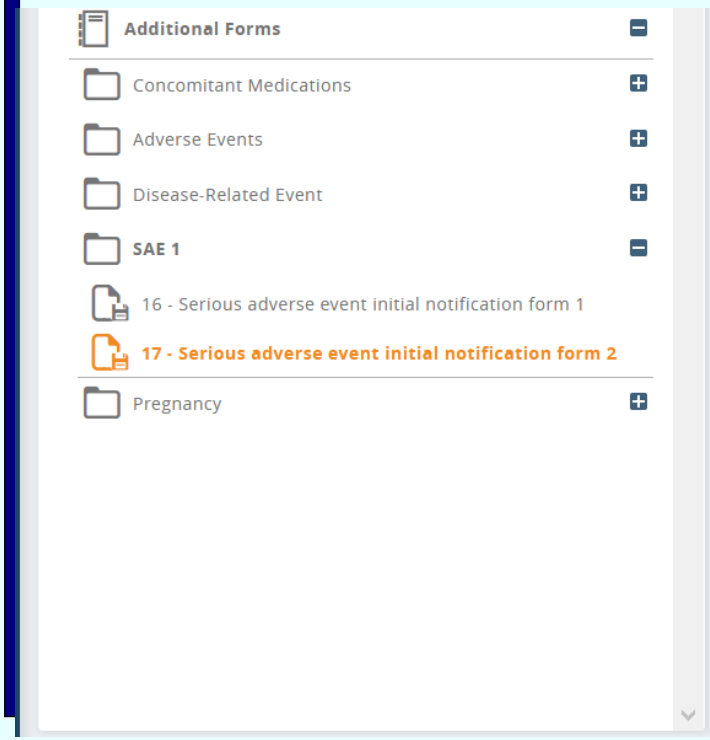
Step completed ("Complete" status)

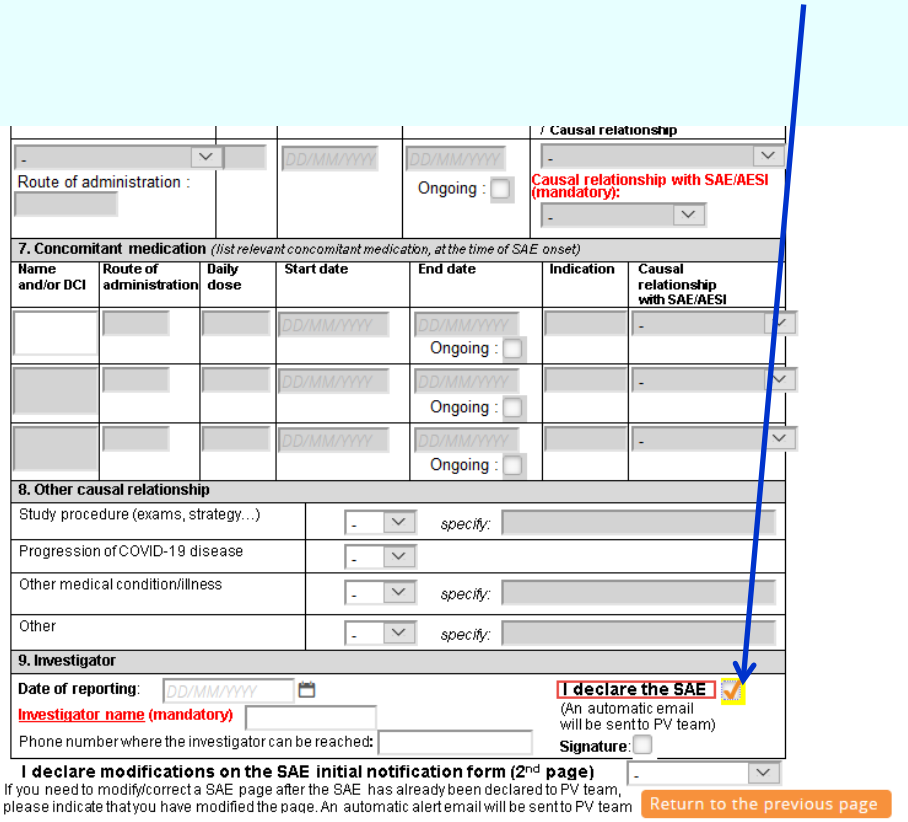


SAE notification (1/2)

-SAE pages are found in the Additional forms section of the eCRF

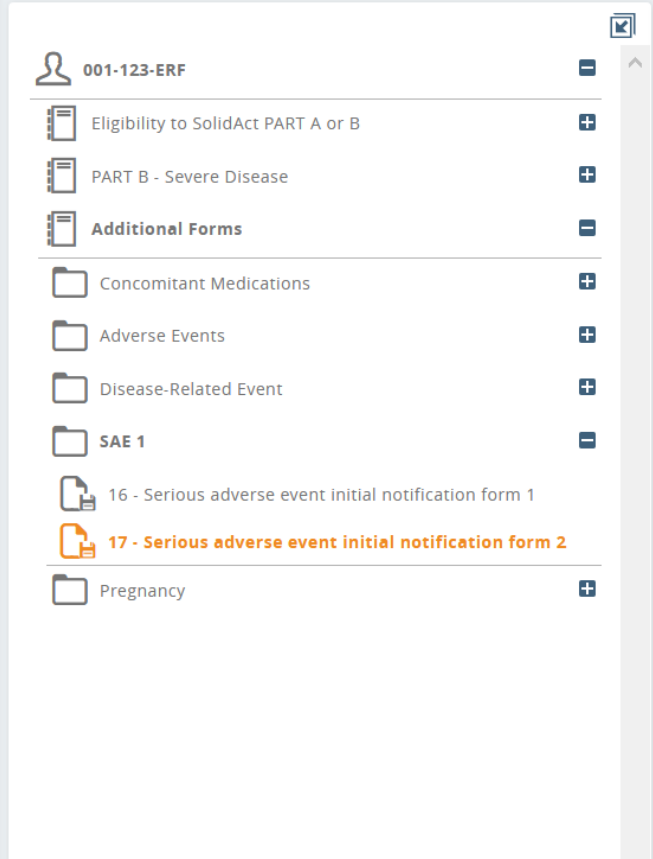
-The two SAE pages need to be completed and the “I declare“ box at the bottom of the second SAE page will have to be ticked for the initial SAE declaration to be made. An e-mail alert will then be sent to the Pharmacovigilance ANRS

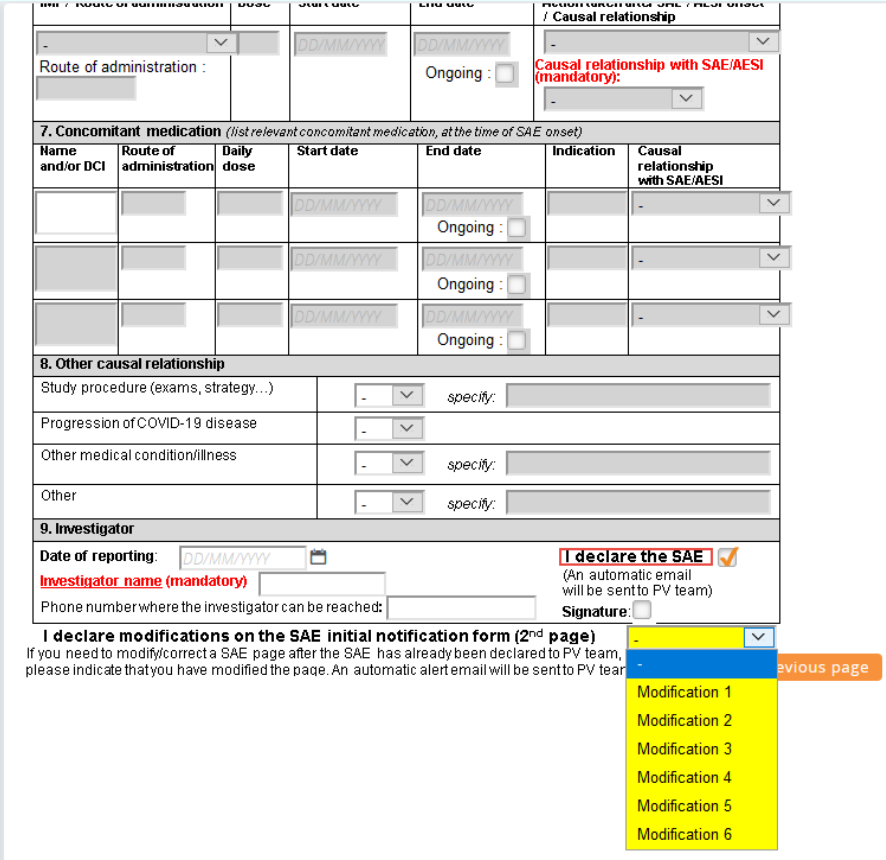




SAE notification (2/2)

If the SAE pages need to be modified/corrected after the initial declaration, you will have to correct the field and choose “Modification 1” in the "I declare modifications on the SAE initial notification form" field at the end of each page so that a new email alert is sent to the Pharmacovigilance team. Modification 2 will be chosen if it is the second time a modification is made on the page and so on.
Once an Initial form is filled, Complementary SAE forms will opened.

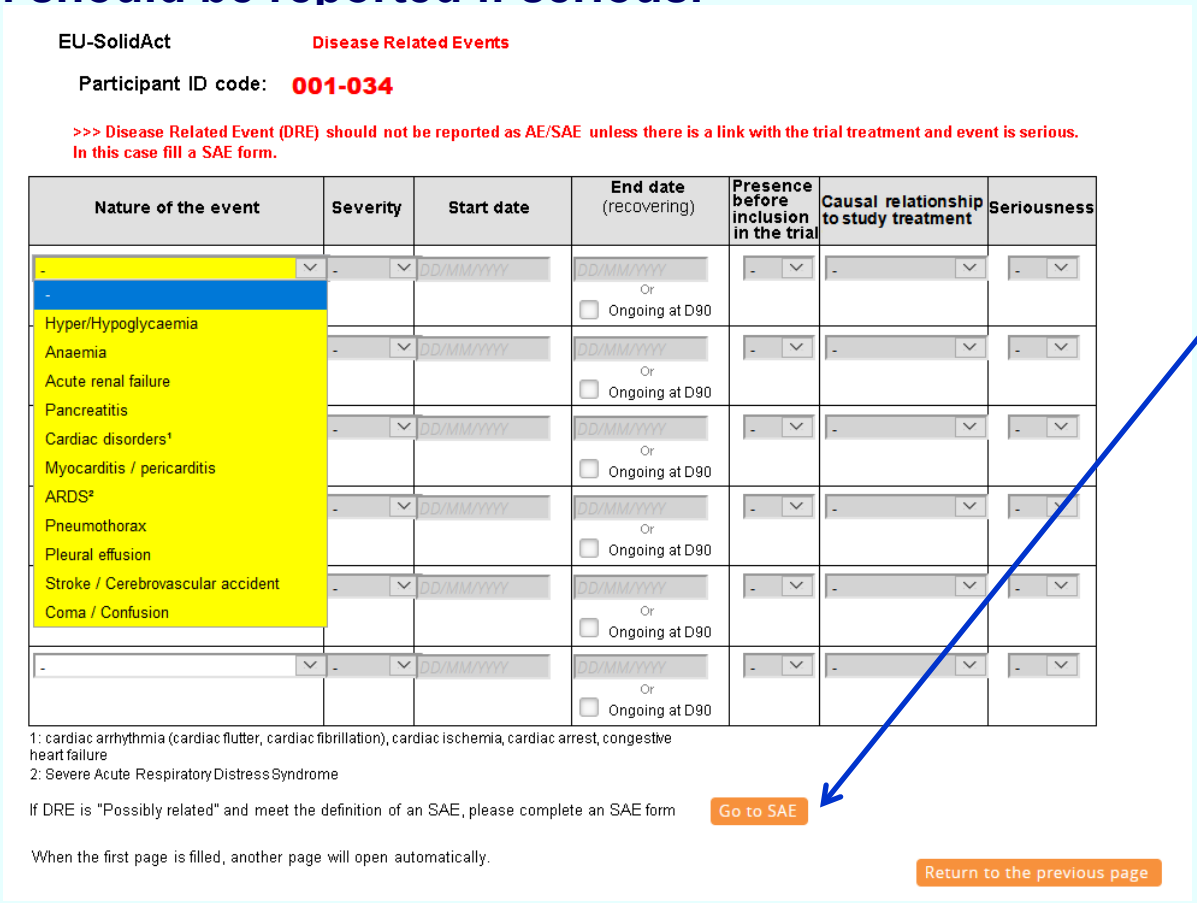




DRE notification

When reporting Adverse Events in the corresponding form, a link allows to access the list of « Disease Related Events » (DRE).

DRE should not be reported as AE but in the DRE page, **unless a causality relationship with IMP is considered: in that case, a SAE form should be reported if serious.**



Signatures (1/2)

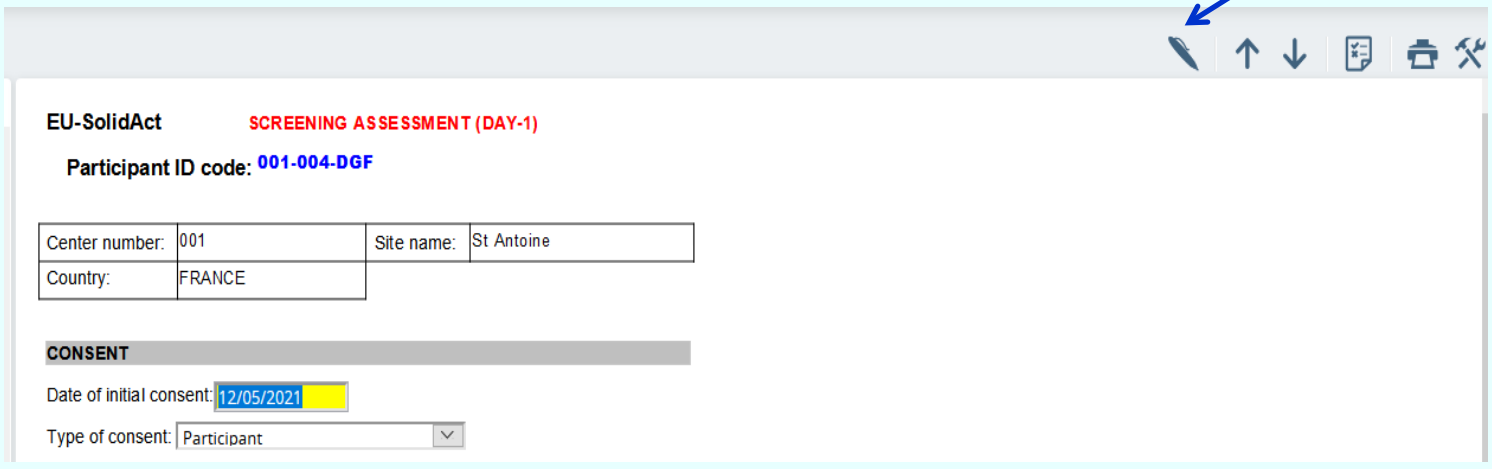
When the pages are entered, locked and monitored by the CRA, the investigator has to sign them which means that s/he is professionally responsible in regards to all the data entered for the patient.

There are two options:

- Sign each page one by one as soon as they are monitored;
- Sign several pages at the same time.

Warning: It is not possible to sign a page that has not previously been entered and locked.

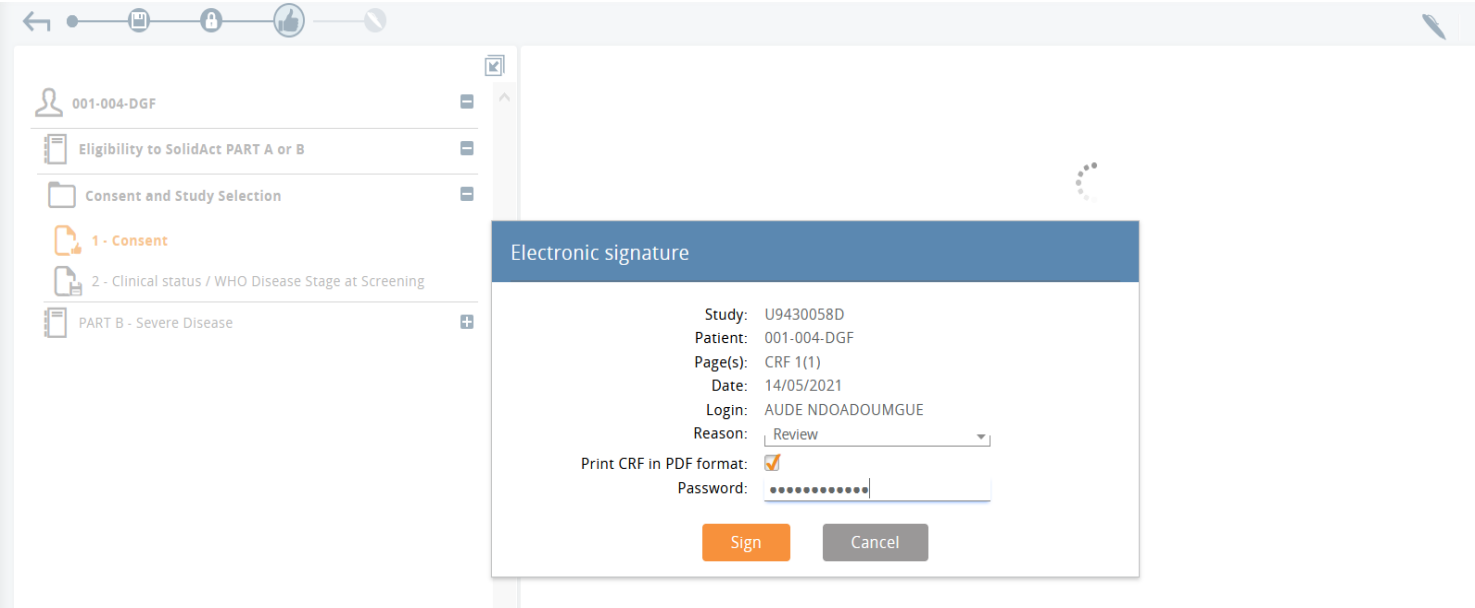
The first option consists in signing the page from the CRF once the CRA has monitored the page. To do so, use the signature button in the CRF menu. The page signature status is symbolized by a colored pen icon located in the upper part of the screen. Grey color: the page is not signed. Blue color: the page is signed.



The second option consists in signing several pages in just a single operation by using the action buttons of the different overviews at the patient, section and page level.

Signatures (2/2)

Your password is required for any operations linked to the page signature.



Monitored and signed data must not be modified. Data modification is not possible when the page is signed since it has to be locked to be signed. Only non-locked pages can be modified.

However, if you want to modify data, first you must unlock the page. Proceed as follows:

- First cancel the signed status of the page;
- Contact the CRA to delete the monitoring of the page, if need be;
- And unlock the page.

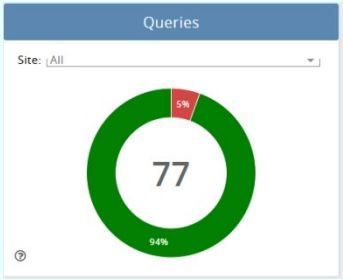
Once the page is unlocked, the data can be modified.

Queries (1/2)

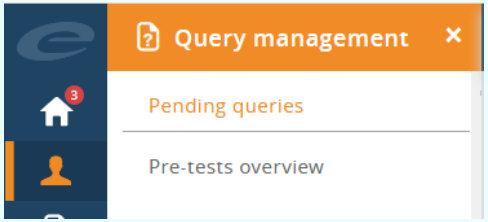
When pages are entered and signed, data is verified by the CRA or the data manager. If inconsistencies are detected, they create manual or automatic queries to which the investigator will have to reply.

Queries can be accessed from:

- The study dashboard by clicking the "Queries" widget title, the list of pending queries is displayed.



- Click the "Query management" menu of CSOnline to have access to the list of "Awaiting reply" queries (modify the search to display the other queries).

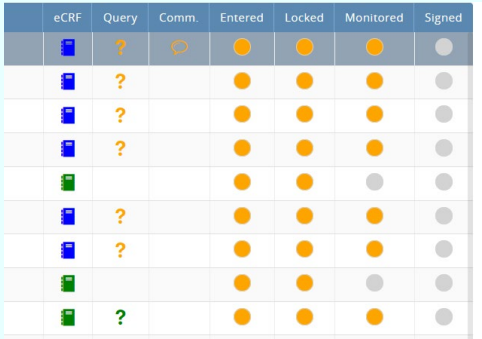


In each overview table (Patients, Section or Page overview), question marks symbolizing the presence of pending queries appear in the "Query" column. The question mark color symbolizes the query status at the patient/section/page level based on the overview table concerned.

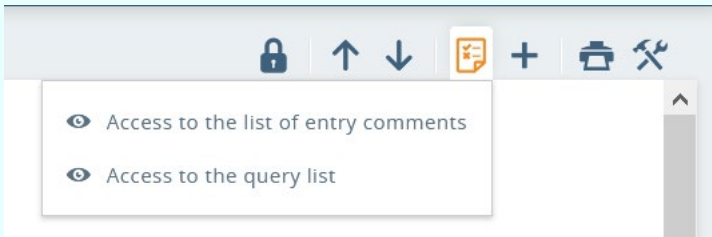
? Orange: at least one pending query

? Green: all queries are processed

Click the question mark to display the queries related to the patient.

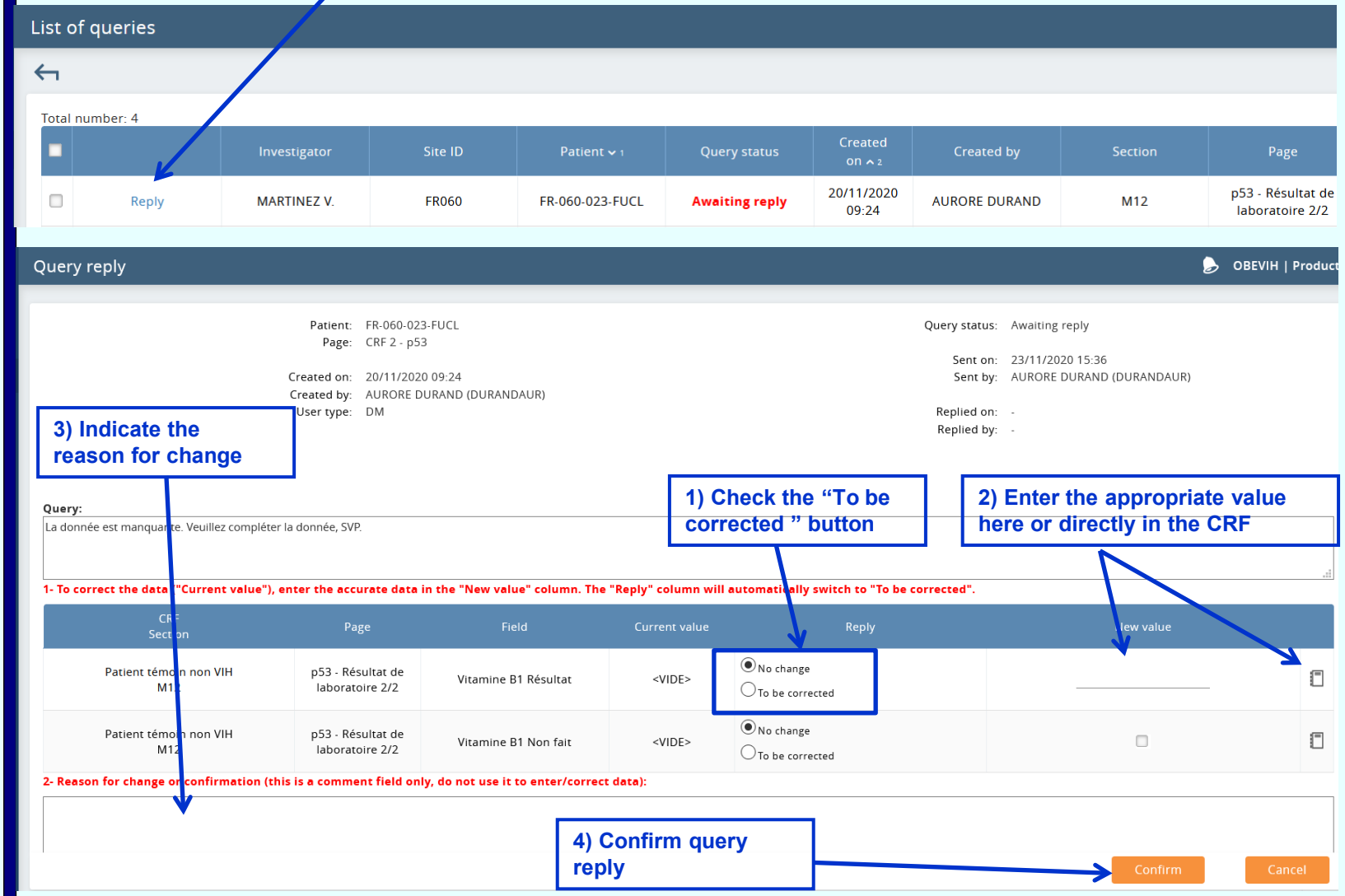


- Through the CRF by clicking on the notification icon



Queries (2/2)

Click the "Reply" link to display the query detail:



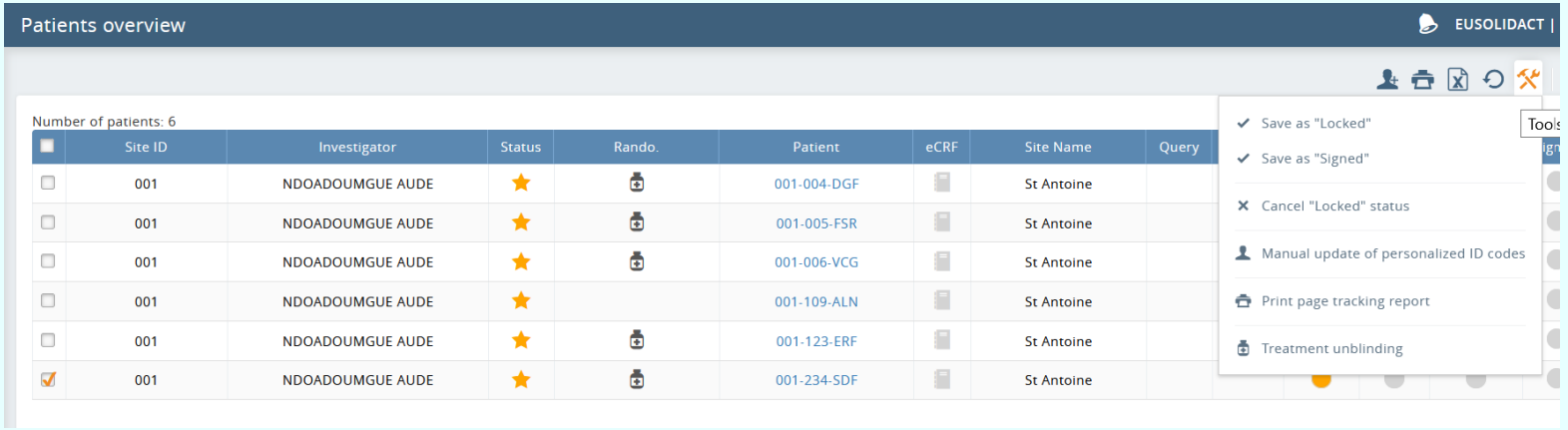
If a correction/modification is done directly in a eCRF page (other than queries), please remember to save the modification.

Unblinding (1/2)

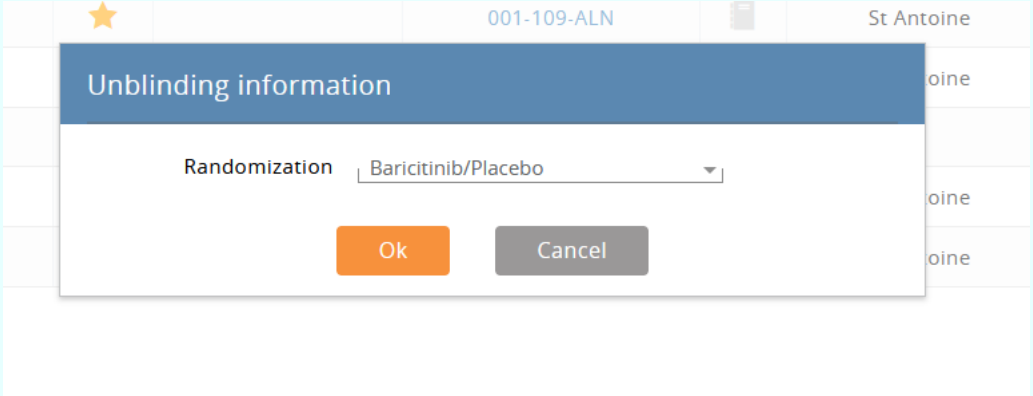
Unblinding should be done only if required for the participant's safety. If possible, contact the sponsor and/or the pharmacovigilance team before proceeding to unblinding.

The unblinding of a randomized patient is done as follows:

- Select the patient to be unblinded and click on the "Tools" icon in the patient overview page

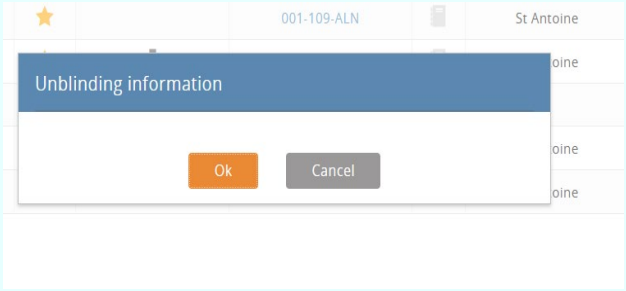


- Select Treatment unblinding and choose the randomization to be unblinded



Unblinding (2/2)

Click on “Ok”



Enter your user password, the patient ID and the reason for Unblinding

Only the site’s principal investigator has access to unblinding with his/her personal login/password

Unblinding results are displayed after you click on “Ok”