EBMT

Cellular Therapy

Data collection handbook for Castor EDC

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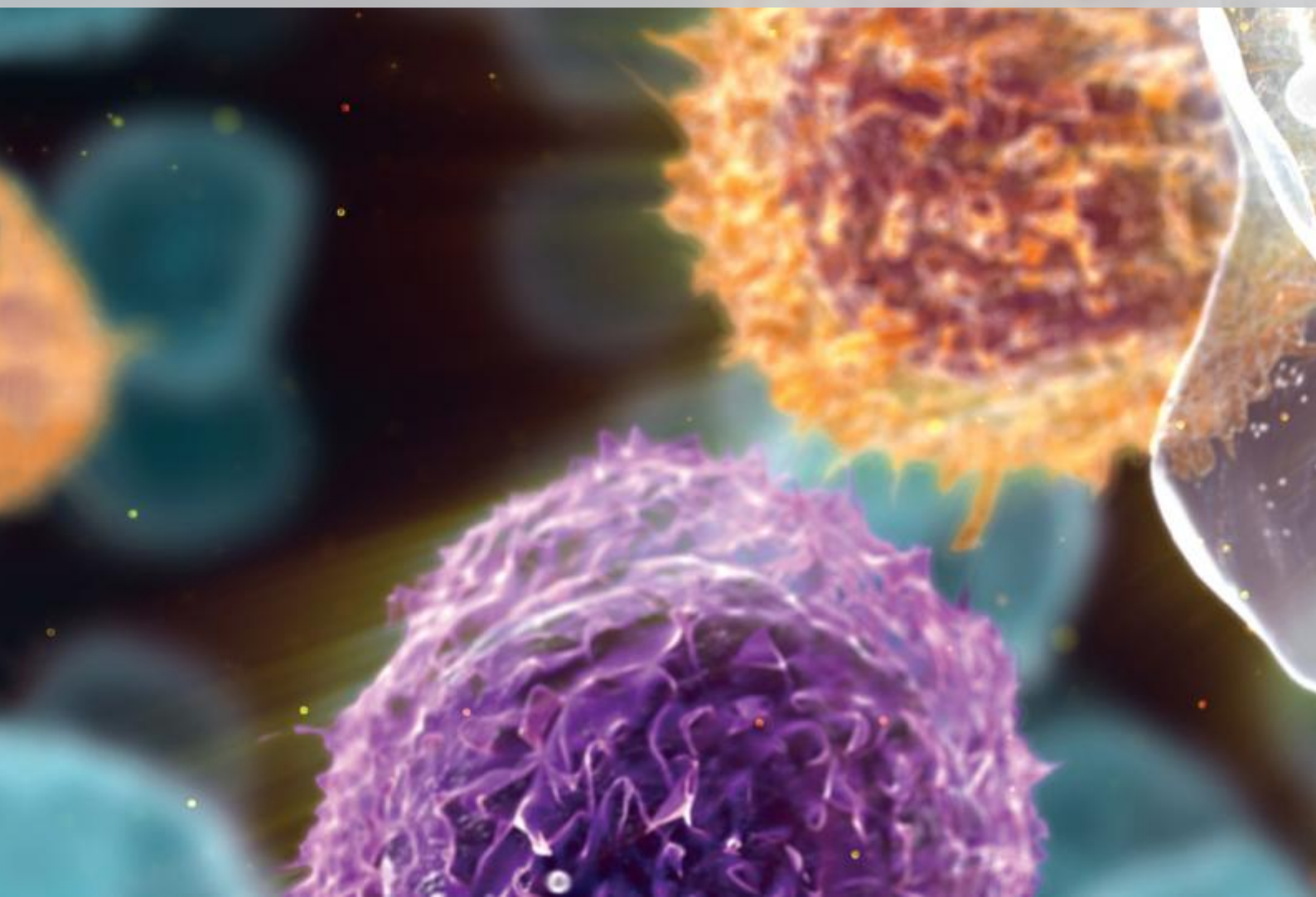

Contents

Contents i

List of Figures iii

List of Tables v

1 Introduction 1

2 Castor EDC 3

3 Data Structure 5

4 Account creation 7
4.1 Two-Factor Authentication 7

5 Account types 11

6 Login 13

7 Record Section 15
7.1 Searching for patients 15

8 Castor Question's 17

9 Mandatory Questions 19

10 Automated Checks 21

11 Audit Trail 23

12 Data Entry Process 25
12.1 Record creation 25
12.2 Filtering 25
12.3 Updating Records 26

13 Query system 31

14 Data Export 33

List of Figures

3.1 Castor structures 5
3.2 Castor Data Structure 5

4.1 Sign up screen 7
4.2 Example of invitation Mail for Castor 8
4.3 Process to activate Two-Factor Authentication 8
4.4 Studies Overview 9

6.1 Castor Log-In screen 13
6.2 Study for Cellular Therapy data collection 14

7.1 Castor Record list view (Default) 15
7.2 Castor Record phase view (With dummy patients and centre) . . . 16
7.3 Castor Record step view (With dummy patients and centre) 16

9.1 Mandatory and Non-Mandatory questions 19
9.2 Record fulfillment tab 20

10.1 Successful check example 21
10.2 Unfinished check example 21
10.3 Unsuccessful check example 22
10.4 Automated validation example 22

11.1 Overview of Castor's Audit Trail 23
11.2 Field History of changes 24
11.3 Field History of reasons for change 24

12.1 Record creation 25
12.2 Record creation confirmation 26
12.3 Data Entry start 26
12.4 Filtering options in the Records tab 26
12.5 Change confirmation 27
12.6 Report table overview 27
12.7 Phases available to fill 28
12.8 Add Annual Report screen 28
12.9 Annual Follow up report in Data Entry screen 29
12.10 Record Section options 29

12.11Report section overview 30

13.1 Query view from Data Entry perspective 31
13.2 Query options 32

14.1 Export selection in Records tab 33
14.2 Different export options 34
14.3 Scope of the export 34
14.4 CSV download file overview 35

List of Tables

5.1 Role capabilities overview 11

CHAPTER 1

Introduction

The EBMT is a collaborative peer network of professionals working in the field of clinical bone marrow transplantation and cellular therapy. EBMT's biggest asset is clinical data, enabling many research possibilities with the goal of saving the lives of patients with blood cancers and other diseases.

Therefore, it is important to ensure adequate data collection and data management processes.

Over the years, data collection and data management tasks were performed through ProMISe. However, the increased complexity of ProMISe negatively affects its ability to cope with the evolving needs of EBMT.

To ensure quality during data collection, Castor is selected as the platform to collect and manage the new Cellular Therapy information.

The purpose of this handbook is to guide the user through Castor, and solve any potential doubts that may arise on the way. The entirety of the system will be explained and when needed, references will be provided for external consultation.

In order to read this document, no previous experience with Castor or Data Entry processes are needed.

CHAPTER 2

Castor EDC

Castor is a cloud-based clinical data collection management platform. Currently, Castor is the most used data capture tool in the market, with more than 85000 users collecting information about more than 2.8 million patients over 90 countries.

In addition to that, the platform is certified by the ISO 27001 and ISO 9001. Furthermore, it is adherent to General Data Protection Regulation (GDPR) and Good Clinical Practices. However, the main reason Castor was chosen to collect and manage the clinical data from Cell Therapy is its user-friendliness. The platform is designed to require minimal training in order to use it.

During the next chapters, the different sections of Castor will be explained as well as the overall procedure of data collection.

CHAPTER 3

Data Structure

Studies in Castor are organised in **phases**, **steps** and **reports** as illustrated in figure 3.1.

Steps are the sections of the form that are related to specific topics, for example *Patient data* or *Comorbid conditions*. Together, the **steps** form a **phase**. Using the previous example, the **steps** *Patient data* and *Comorbid conditions* would be part of **phase Day 0**.

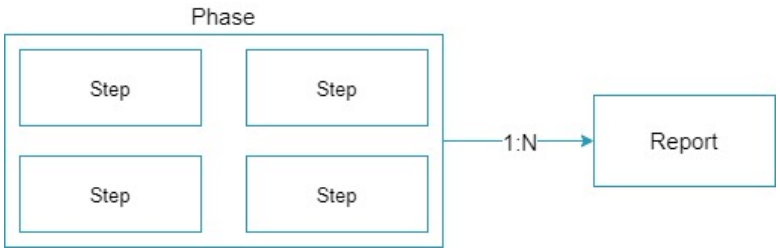

Figure 3.1: Castor structures

The Cellular Therapy study in Castor EDC is composed of the **phases** *Pre-infusion registration*, *Day 0*, *Day 100 - Follow up*, *6 Months - Follow up* and *Annual - Follow up* as seen in figure 3.2.

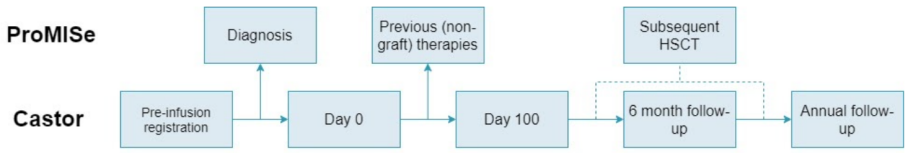

Figure 3.2: Castor Data Structure

On the other hand, as seen in figure 3.2, *Diagnosis*, *Previous treatment* and *Subsequent HSCT* still need to be reported on ProMISe.

Reports are specific sets of questions that can be nested in steps or exist independently and allow iteration. These are associated to a patient directly, or through a **step**. A patient record can have multiple **reports**.

At the moment, the following **reports** are implemented in Castor EDC:

1. Cell Infusion Episode
2. Cell Infusion Unit(s)
3. Cell Therapy Infusion Unit - Manipulation
4. Complications - Infections
5. Other Complications
6. Other Treatment
7. Patient Preparatory Treatment
8. Post Therapy Treatment
9. Radiotherapy
10. Death Report
11. Annual Follow up

The *Annual follow-up* is a **report**, as this needs to be filled in for every year a follow-up assessment with the patient has been performed, iteration is required. The *Death report* in the cellular therapy database is independent of the **phases**, as this can happen any time. Once a *Death report* has been filled, any new data entry is discouraged.

CHAPTER 4

Account creation

An account for Castor can be created at https://data.castoredc.com/ by clicking on **Sign up**. After selecting sign up, the only necessary step is fill the information displayed at figure 4.1.

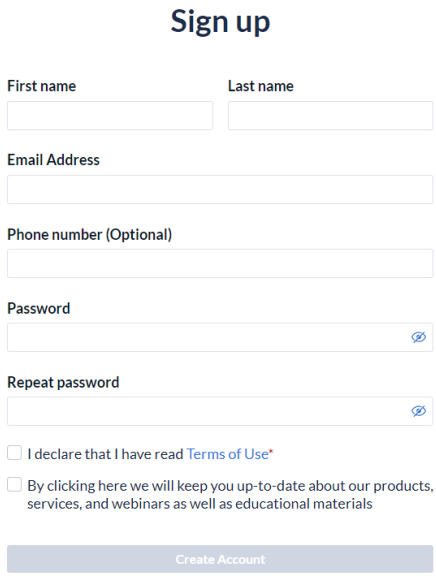

Figure 4.1: Sign up screen

Alternatively, you can also create and account after being invited to a particular study. You are invited to an study after receiving an invitation to do so (see figure 4.2). The email will contain a link, through which an account can be created. After setting up the account, two-factor authentication needs to be activated.

4.1 Two-Factor Authentication

Google authenticator, Authy or Microsoft Authenticator are apps that can be used to set up two-factor authentication for Castor. One of these needs to be

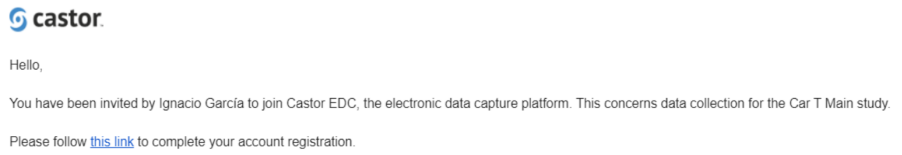

Figure 4.2: Example of invitation Mail for Castor

installed on a tablet or smartphone.

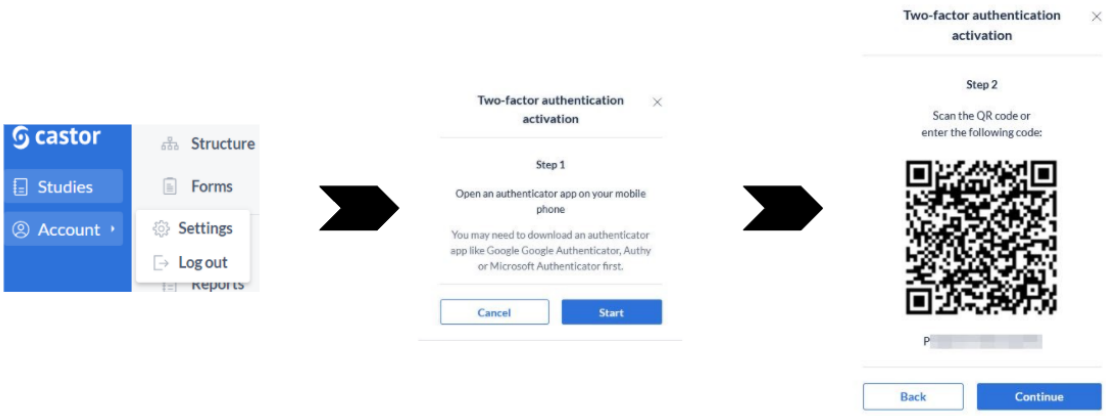

Figure 4.3: Process to activate Two-Factor Authentication

To turn on two-factor authentication, go to **Account** on the left side of the screen and click **Settings**. From the account settings, click **Password Security**. Select the box **Using two-factor authentication with this account** and click the blue button that says **Activate two-factor authentication**. The web page will ask to open the Authenticator app, as previously referred, and scan the QR code or enter the code that is provided (step 2). These steps can be visualized on figure 4.3

The Authenticator app will provide a code, which needs to be entered in the field on the Castor web page. After entering the code, click **configure**. Castor EDC will be added to the list of web pages that the Authenticator app is used for.

For every login to Castor, the newest code in the app needs to be entered after logging in using the login credentials.

After a successful login, the user should be able to see the Cellular Therapy study as per figure 4.4.

Figure 4.4: Studies Overview

CHAPTER 5

Account types

In Castor, different roles for user accounts can be created. Roles can be edited and new ones can be created at any point during the study to suit the needs of potential special users, allowing flexibility. The type of role will depend on the functionalities the user needs to have access to.

1. **Administrator**: The study admin account oversees all other roles and has the possibility to change the study, add new users, and all functionalities other role types have.
2. **Data Manager**: This role can view and edit entered data, sign, lock, query and export.
3. **Data Entry**: Data managers from centers will have data entry accounts, allowing them to add, view, edit, and export data.
4. **Monitor**: Accounts for EBMT or external monitors can be created, which have the functionalities to view data, perform source document verification, and query.

Administrator	Data Manager	Data Entry	Monitor
• Add • View • Edit • Email • Sign • Lock • Verify • Query • Archive • Export • Surveys	• View • Edit • Sign • Lock • Query • Export	• Add • View • Edit • Export	• View • Verify • Query

Table 5.1: Role capabilities overview

CHAPTER 6

Login

To log in to Castor, go to https://data.castoredc.com/. Type in the email address that was used to create the account, and the password. Castor will ask for the authentication code as provided by the authenticator app as described in chapter 4.

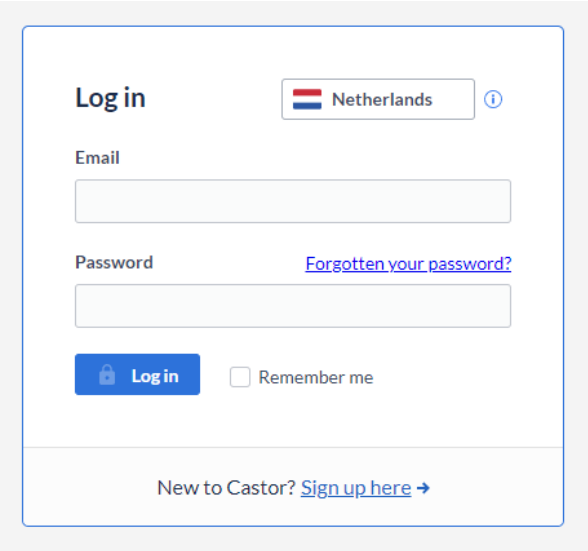

Figure 6.1: Castor Log-In screen

After successful login, the **My Studies** page will become visible, where Cellular Therapy data collection should be selected to enter cellular therapy data (See figure 6.2).

Figure 6.2: Study for Cellular Therapy data collection

CHAPTER 7

Record Section

After selecting the study, the study's record section will become visible. All patients entered for your center are listed in this table. The Records section has different views and functionalities, which will be explained. By default the list view is selected, which is pictured in figure 7.1.

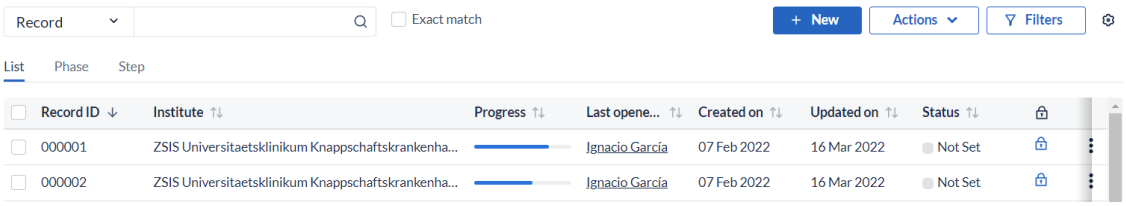

Figure 7.1: Castor Record list view (Default)

In the **List view**, it is possible to sort the cases based on the names in the columns (e.g. *Institute, Progress,* or *Updated on*). It also allows selecting records using the tick boxes, or selecting all records using the tick box in the header of the table, after which records can be downloaded (See chapter 14).

Another view option is by **Phase** (figure 7.2). Here all records are listed with progress bars for completeness, outstanding queries and comments.

A more detailed version of the **Phase** view is **View by step**, available in figure 7.3, where the progress per step of the study can be seen.

Depending on your objectives, different views will be more helpful. For example, when checking for completeness or queries/comments, the **Step** or **Phase** view will be more helpful than the **List** view.

7.1 Searching for patients

Sometimes, finding the appropriate patients is not an easy task. Among other reasons, the Castor id that serves as a unique identification is exclusive to Castor and assigned to each patient created automatically. As a result, it is not

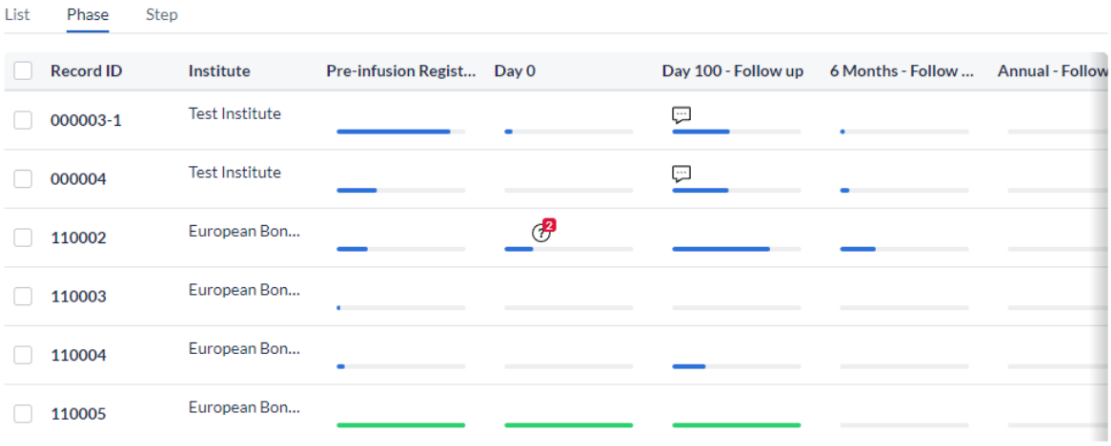

Figure 7.2: Castor Record phase view (With dummy patients and centre)

Figure 7.3: Castor Record step view (With dummy patients and centre)

associated with the information filled in the data collection forms.

In order to find an specific patient, it is possible to filter by centre (*institute*) by selecting the correct option in **Filters**. In addition to that, it is possible to use the search bar located on the top left of the Record section to filter by the answer to any of the study's questions. It is recommended to use the Castor variable *ID_IDAA_PRE* also known as EBMT Unique Identification Code, *DATPATBD_PRE* known as Date of Birth or *UPN_PRE*, Hospital Unique Patient Number or Code.

CHAPTER 8

Castor Question's

Castor allows to add different types of questions. However, not all are used throughout this study. In this section, the used questions are described:

1. **Drop-down**: Used for questions with more than three answer options. The answer options will appear after clicking the field. An option can be selected from the list. If there are more than 25 options available, it is possible to write on the field and obtain suggestions.
2. **Radio buttons**: Used for questions where there is two options available but only one option can be selected. The question can be filled in by clicking the dot before the answer.
3. **Check-boxes**: Used for questions where more than two options are available and more than one option can be selected.
4. **Dates**: All dates in Castor are in DD-MM-YYYY format. When the day of the month is unknown, it is suggested to select the 1st of the month. In cases where the month and day is unknown, it is suggested to select the first of January to report the date. Nonetheless, in the Castor study questions that contain dates, more information will be available.
5. **Text-boxes**: Text boxes in Castor allow both text and numbers. It is important that text boxes to specify *Other* are only used if no alternative from the dropdown or radio buttons is available. It is mandatory to answer in English, as other languages can create codification problems with letters not recognized by the system.
6. **Tables**: Tables are reports associated to steps as repeated measurements. Tables are not standalone questions, but cover different types of questions. The **Add measurement** button will allow the user to fill in the table. Multiple measurements can be added, for example in the case of multiple drugs or cell therapy infusion units. Any of the measurements added in a table can be edited by clicking on the cogwheel that appears on the right side of the measurements.
7. **Calculated Questions**: Calculated questions are used throughout the study to perform calculations such as number of cell infusions, or whether dates or numerical values are within reasonable limits. This particular use of the calculated questions will be explored in Chapter 10.

CHAPTER 9

Mandatory Questions

Questions in Castor can be made mandatory to fill in. The mandatory questions can be recognised by a bold font. Non-mandatory questions appear in a non-bold/normal font. An example of this can be seen in figure 9.1

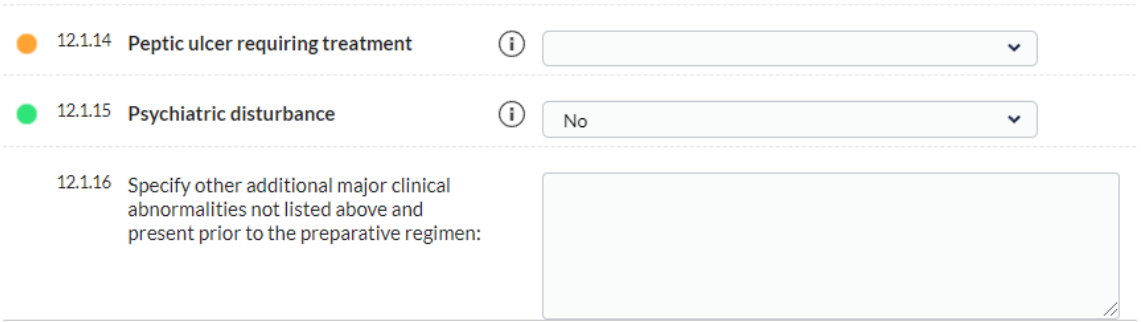

Figure 9.1: Mandatory and Non-Mandatory questions

The percentage in the completion bar visible in the top left corner of the data entry form only counts mandatory questions as seen in figure 9.2.

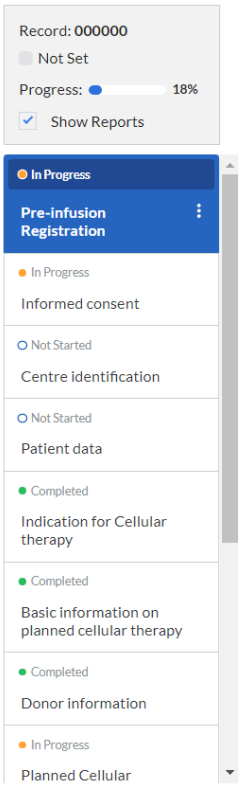

Figure 9.2: Record fulfillment tab

CHAPTER 10

Automated Checks

Answers to questions in Castor can be subject to automated checks. These automations cross-check different fields for correctness to improve data quality and prevent mistakes, or to check if the entered value conforms to the range set for the item.

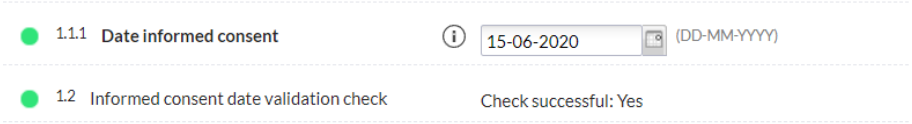

Figure 10.1: Successful check example

Some checks are visible in between questions, as pictured in figures 10.1, 10.2, 10.3. This is the type of automation that cross-checks different fields. If a check appears to be incomplete (showing the text *Not all values for this calculation are available (yet)*), the field that is used for cross-checking has not been filled in yet. This message does not affect data entry and it is aimed to notify data managers and monitors in case information introduced at a later date is in conflict.

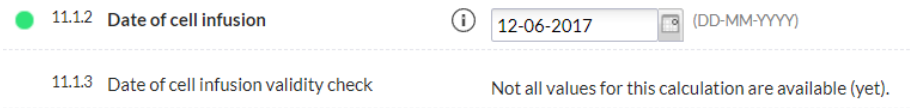

Figure 10.2: Unfinished check example

For values that are expected to fall within set ranges or specific answers, a warning message can be displayed if the entered value does not match the range/expected value, as in figure 10.4. For example, if a value that is entered in percentages is higher than 100, or negative values for weight or height, or the consent is negative. Data entry can be continued after a warning message is displayed. However, a notification will be added to the record, allowing monitors and EBMT data managers to see that an unexpected value

was entered in a field.

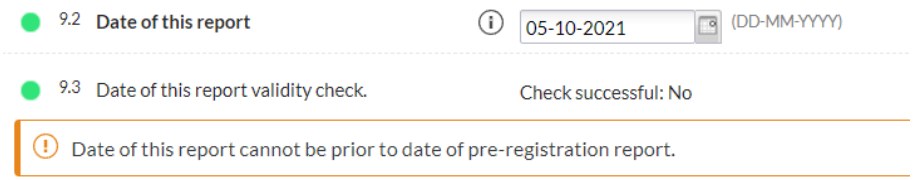

Figure 10.3: Unsuccessful check example

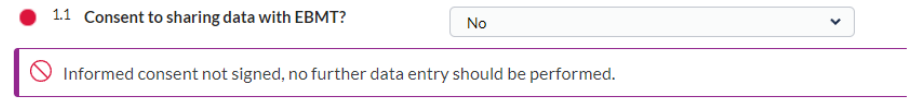

Figure 10.4: Automated validation example

CHAPTER 11

Audit Trail

In Castor, all actions are registered in the audit trail, accompanied by the type of action, the user responsible for it, and the date and record ID. Changes to the system are captured in the audit trail as well. The audit trail is only visible to study administrators. Figure 11.1 shows an overview of the Audit trail.

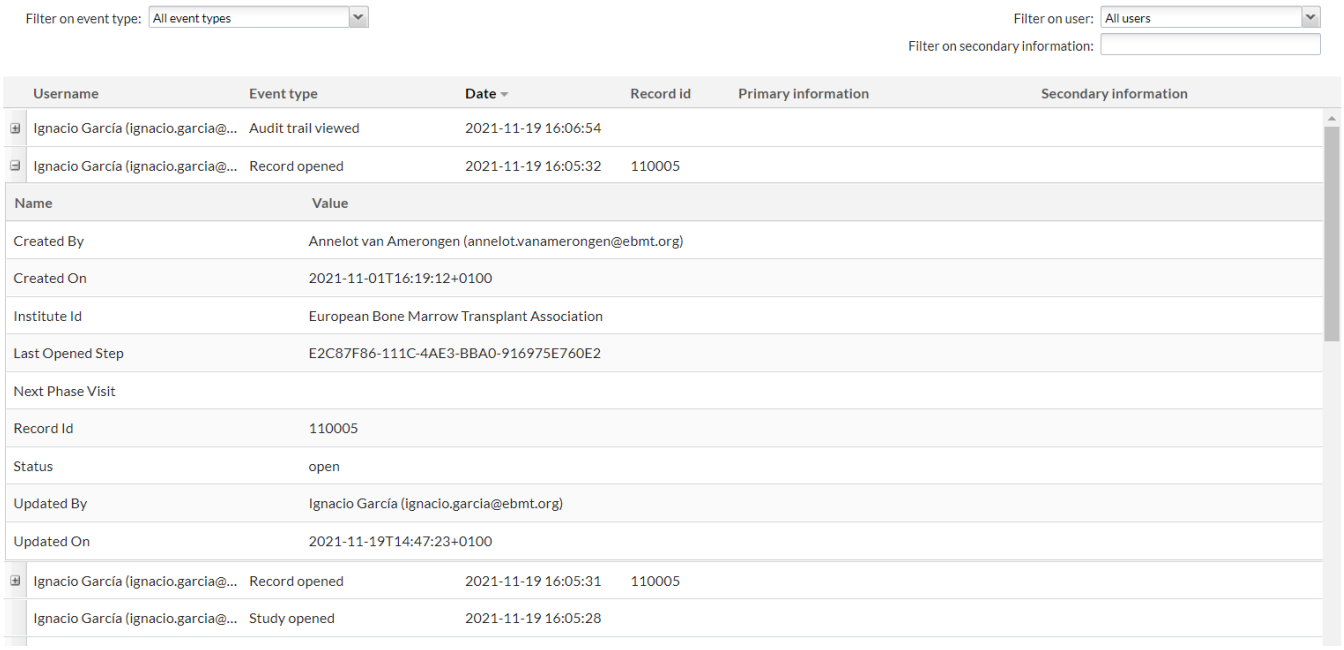

Figure 11.1: Overview of Castor's Audit Trail

Additionally, the history of changes can be seen per item by clicking the cogwheel and selecting **History** as seen in figures 11.2, 11.3. Figure 11.2 shows what is displayed in a field where no comments were added for the changes. Figure 11.3 shows the history of changes on a field where reasons for change were added. This functionality is available for all users. In the Cellular Therapy study, it is mandatory to justify all changes in English.

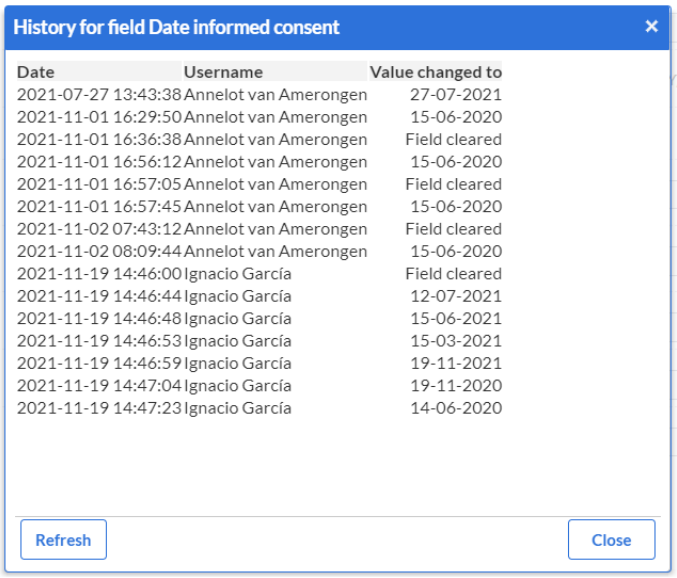

Figure 11.2: Field History of changes

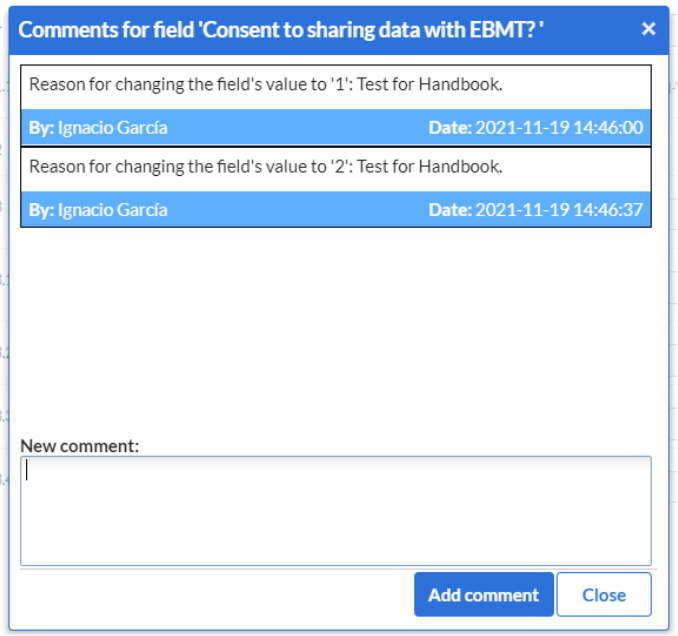

Figure 11.3: Field History of reasons for change

CHAPTER 12

Data Entry Process

The starting point for data entry in Castor is the **Record** section, as described in chapter 7.

12.1 Record creation

A patient should be registered in ProMISe before entering into Castor.

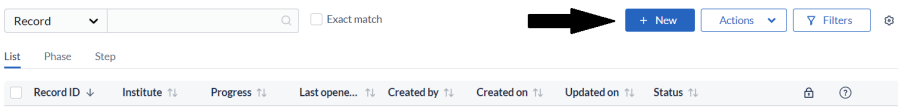

Figure 12.1: Record creation

To create a new patient, click the blue button saying **+ New** that is visible on the right side above the records table, as seen in figure 12.1. A pop-up will open, showing the institute the patient will belong to, the auto-generated record ID, and a field for email address (figure 12.2). The e-mail address must be left empty and nothing should be changed in this popup. Click **Create**.

This will open the data entry fields for the newly created patients, as seen in figure 12.3. The ProMISe center number (CIC) and EBMT (ProMISe) unique identification code need to be entered in the **Patient data** step.

12.2 Filtering

To open an existing patient, select the patient from the **Record** section. This can be done by scrolling through the records or by filtering, using the search bar on the left above the records table (figure 12.4). To search for a patient using the EBMT patient number, select *EBMT Unique Identification Code* from the list. Searching based on the date of birth, hospital unique patient number, or any other variable is possible too.

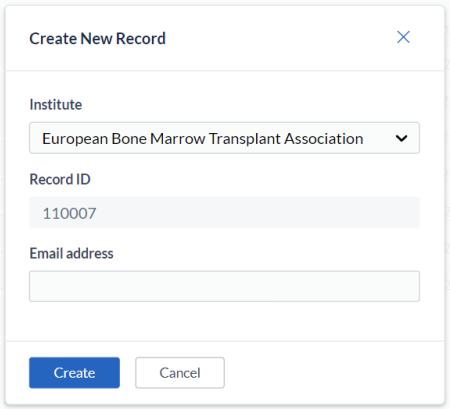

Figure 12.2: Record creation confirmation

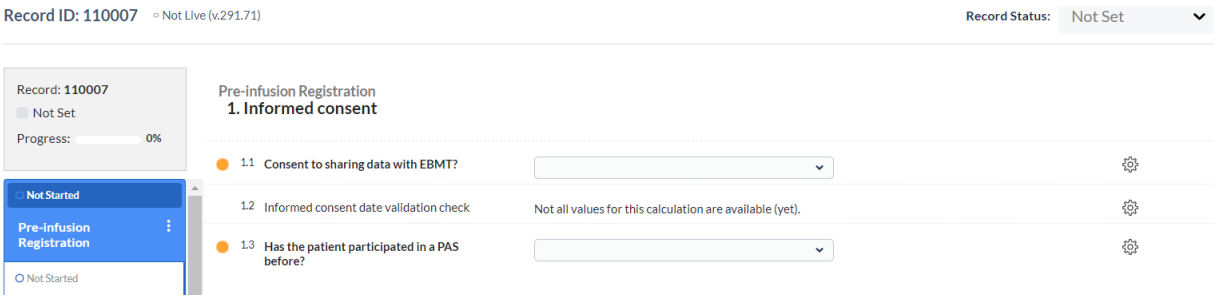

Figure 12.3: Data Entry start

Figure 12.4: Filtering options in the Records tab

12.3 Updating Records

Adding data to existing patients can be done for the following reasons:

- New data was made available to update fields from previous assessments, or needs to be clarified after a query;
- A follow-up assessment was performed and can be added to the patient's record.

Updating Data

Open the patient using the record locator (see section 12.2).

The patient record will open at the last step that was entered. The assessment that needs to be updated can be selected from the blue coloured phases, which open the steps as seen in figure 9.2, chapter 9. Select the step from the

phase to be updated. Change the value of the field of interest, this will trigger a pop-up, asking to confirm that the record should be changed and provide a reason as in figure 12.5.

A reason for changing the data is required before continuing. A logical and valid explanation for changing the data should be entered, for example ‘lab reports from other hospital were sent’ or ‘a mistake was made in entering the data’. Explanations should be written in English.

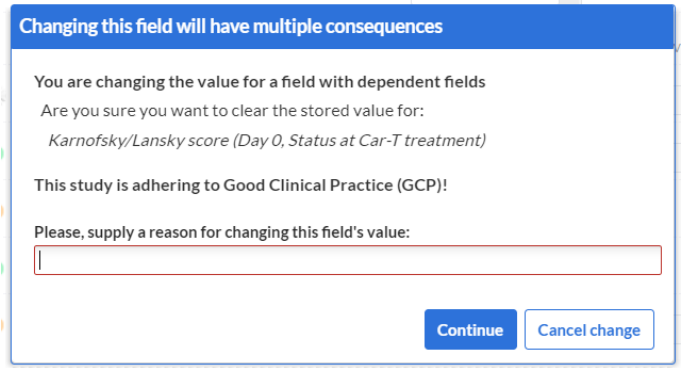

Figure 12.5: Change confirmation

After the change is confirmed and explained, the data can be updated.

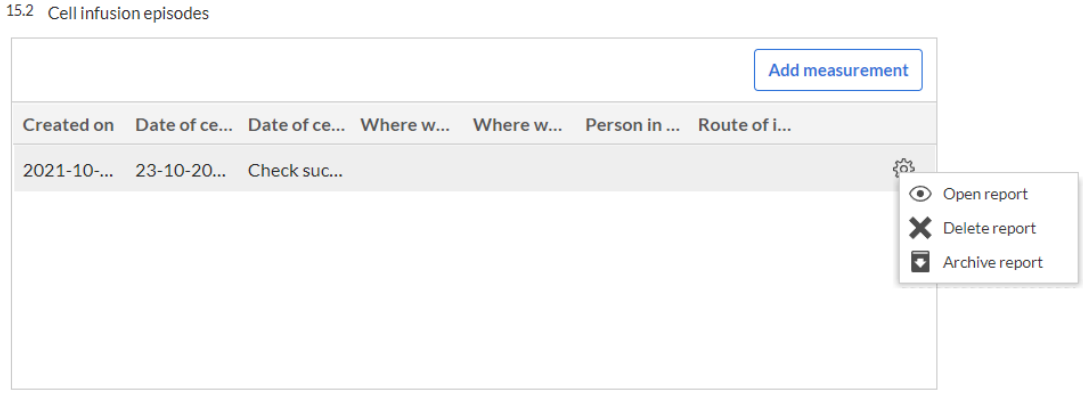

Figure 12.6: Report table overview

If the data that needs to be updated is in a table, the process is the same. After opening the step containing the table, clicking on the cogwheel at the right of the table you need to amend will display the options seen in figure 12.6. Selecting open report, will redirect you to the report where you can perform the necessary changes. On the other hand, adding a new measurement would be as simple as clicking on the **Add measurement** button at the top of the table.

Follow Ups

Open the patient using the record locator (see section 12.2).

The patient record will open at the last step that was entered. In order to enter data for the *Day 100 Follow up* and the *6 Months Follow up*, clicking on the steps associated with those follow ups on the navigation bar to the left of the Data Entry screen is enough as seen in figure 12.7. However, the *Annual Follow up* works differently.

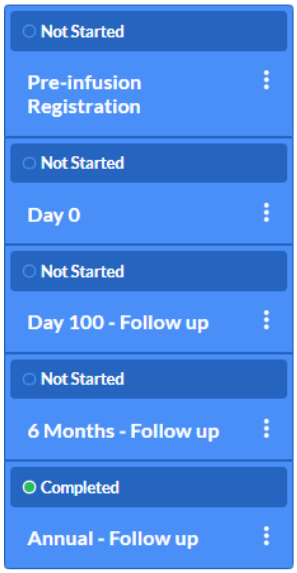

Figure 12.7: Phases available to fill

As *Annual Follow ups* can happen a different number of times based on the patient and the duration of the data collection process, normal phases and steps are not enough. In order to be able to generate as many *Annual Follow ups* as we may need, we use the reports.

In order to create an *Annual Follow up* report, you need to select **Annual - Follow up** from the left tab on the Data Entry screen and click on the button that will appear, **Add annual follow up to the patient** (Figure 12.8).

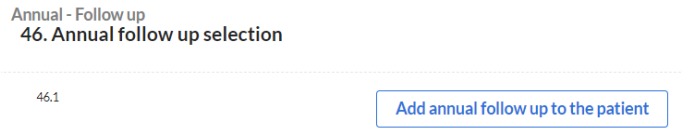

Figure 12.8: Add Annual Report screen

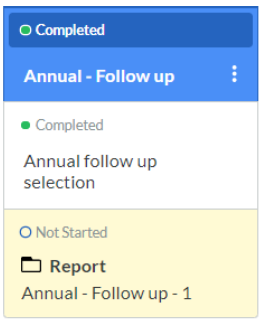

Figure 12.9: Annual Follow up report in Data Entry screen

All the *Annual Follow ups* associated with a patient will appear as in figure 12.9.

Reports

As seen throughout this document, reports are used for different purposes on Castor EDC. In order to have an overview of all the reports (*Annual Follow ups*, *Tables*, and *Death Reports*) associated with a record, you can access the **Report** tab. In the record section (figure 12.10), after selecting a record, we can see different options available on the left menu such as **Study** and **Reports**.

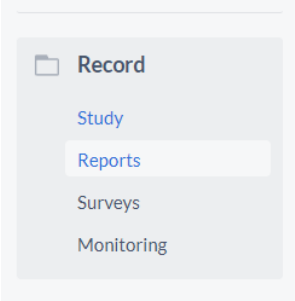

Figure 12.10: Record Section options

By clicking on **Reports**, we will be redirected to the **Report** tab, as seen in figure 12.11. In this tab, filters can be performed as in the **Record** section to find the report you are looking for, such as measurement tables, the *Death Report*, or a particular *Annual Follow-up* associated to that patient.

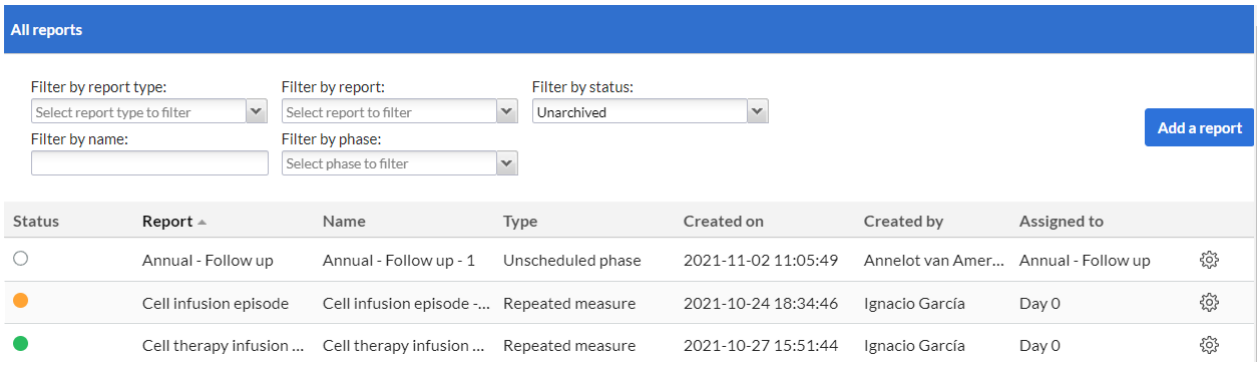

Figure 12.11: Report section overview

CHAPTER 13

Query system

EBMT data managers and monitors will be able to add queries to data entered into Castor. A notification showing there is a query will be visible in the last column of the record section table if it is on list view, or at the applicable phase or step if the record section is set to those views.

If a query is added to an item, a red circle with a question mark will appear next to it. By clicking this, the query will become visible. If the query is added, it will be shown as 'New'. If the query is opened by the center, it will change to 'Open'.

Figure 13.1: Query view from Data Entry perspective

A query can have the following statuses:

1. **New**: the query has been added, but not is not opened yet
2. **Open**: an EBMT data manager or monitor has added a query, and the center opened the query
3. **Unconfirmed**: the center does not agree with the query
4. **Confirmed**: the center agrees with the query and will update the field
5. **Resolved**: the center agreed with the query and updated the field appropriately
6. **Closed**: the EBMT data manager or monitor has seen the updated field and agrees, or accepts the 'unconfirmed' response from the center.

A query status can be updated by selecting the new status from the drop down menu, adding a remark (not mandatory but highly encouraged) and clicking the blue **Update** button (see figure 13.2). Monitors can see the queries and their statuses on the **Monitoring > Queries** page. A separate manual for monitors is available.

Figure 13.2: Query options

CHAPTER 14

Data Export

Data can be exported from the **Record** section. The patients that need to be exported can be selected using the tick boxes before the **Record ID**. After selecting the patients for export, click the **Actions** button on the top right corner above the table, and select **Export selected**, **Export all**, or **Export filtered** depending on the goal.

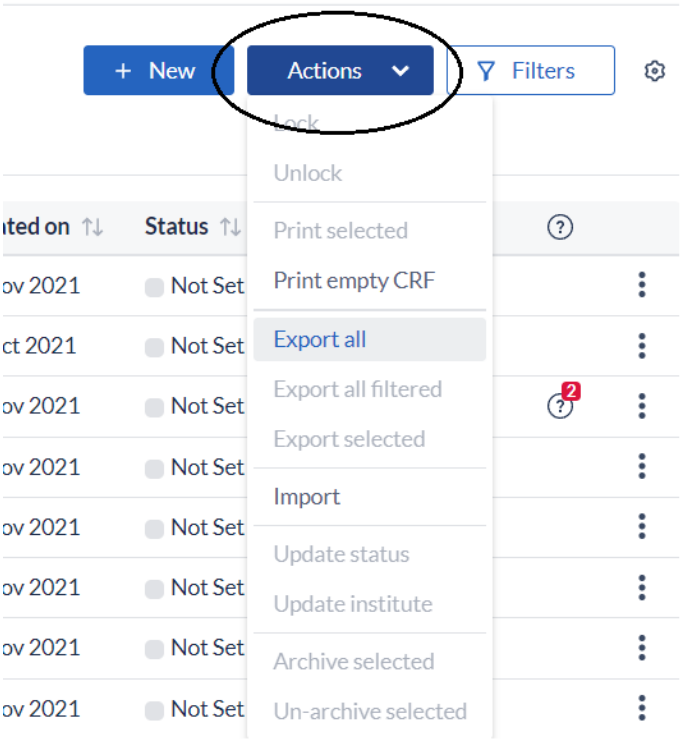

Figure 14.1: Export selection in Records tab

A pop-up window will appear as shown in figure 14.2, where the details of the export can be specified. Exports can be performed in CSV, Excel, or SPSS format. The option *Upload files* is not applicable for this study. Furthermore,

you can select whether the data should be exported using the labels of the fields or the values. In addition to that, you can select the variables you want to export by selecting or by writing its names of the text field.

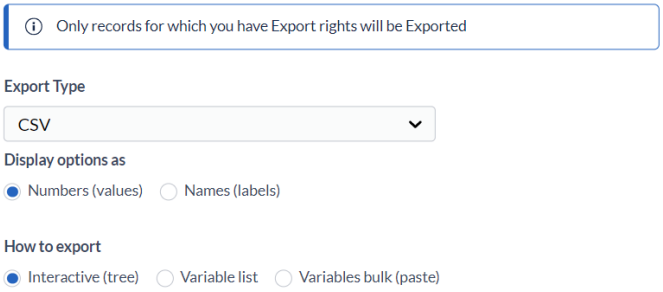

Figure 14.2: Different export options

Once you have selected the desired output and variables from the study, you can select which sections of the study you want to download. You can select up to *Step* level.

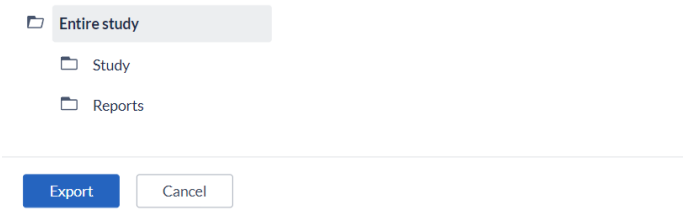

Figure 14.3: Scope of the export

In figure 14.4 you can see an example of CSV download selecting the *Entire Study* option. The default export includes all the reports (tables) available, as well as phases and steps. Moreover, it adds a data dictionary, queries, comments, and verifications.

Figure 14.4: CSV download file overview