PRO-MC Collaboration

EMCG
EUROPEAN
MICROSCOPIC COLITIS
GROUP

in association with
UNITED EUROPEAN
GASTROENTEROLOGY
ueg

INSTRUCTION MANUAL
FOR THE WEB-BASED E-CRF

Dear participant,

In this document you will find a step-by-step explanation on how to use the web-based e-CRF of the PRO-MC Collaboration.

This instruction manual will follow the chronology of the follow-up visits. Explanation of some steps will be supported by print-screens from the registry.

We hope this document will be of use to you when initiating the registry at your centre, or in case you have any questions on how to use the registry.

Nevertheless, if this document does not contain sufficient information to answer your questions, please feel free to contact the PRO-MC Steering Group for help.

In name of the PRO-MC Steering Group

Yours Sincerely,

Andreas Münch, chairman

Bas Verhaegh, project coordinator

Contact: info@pro-mc.eu

Contents

1. Site initiation

To initiate the PRO-MC Collaboration at your site, please read the points below:

- Each center, interested in participation in the PRO-MC Collaboration is requested to download a zip-folder including all essential documentation for initiation and participation. This zip-folder can be retrieved from www.emcg-ibd.eu (tab: 'European Registry PRO-MC')

- Check whether it is necessary to obtain local ethical / IRB approval for study in your centre! All documents which you will require to obtain for approval have been made available to you. Please read the instruction letter first. It will instruct you on how to complete the required documents and which changes you might have to make to these documents before you can submit them.

- Fill out the "Site Initiation Form", which is provided with all other study documents, and send it to info@pro-mc.eu. Please, also add a copy of the letter stating local ethical approval (if applicable).

- Please, study the flow-chart of the study visits and get familiar with the study requirements in advance and consider how to implement these requirements (visits, diary, SHS form, notification emails etc.) in your clinic!

- Please note that we require the participant to involve the local pathologist(s) in this project. We require participating centers to at least inform the pathologist on the PRO-MC Collaboration and to provide them with the PRO-MC Slide kit and the paper on MC diagnosis. All materials can be found in the zip-folder mentioned earlier.

- When everything is ready to start the PRO-MC Collaboration at your site, the contact person for the study will be provided with the login credentials.

- It is the responsibility of the participating center to keep a local file which links the patient's enrolment number in the study to the patient information. Furthermore, the signed informed consent forms should be stored locally as well.

2. General information

The registry is designed as a collection of electronic case record forms (eCRF). These eCRFs form the base of the registry.

The system is developed to be user friendly. Only the information you need will be visible and available, creating a straightforward registry. You can easily check the completeness of the visits of all included patients, which enables maintaining a complete and up-to-date dataset.

The completeness of the individual CRFs is visualized as well. The symbol ! indicates that at least one obligatory item within that part of the visit still has to be filled out. If all obligatory items of the visit are completed, the symbol ✓ will be visualised in the visit menu. This helps you to easily check the completeness of the visit.

When a new patient is added to the registry, you will notice that only a selection of the visits is available. When a patient is registered for a longer time, next follow-up visits will automatically become available.

Note: eCRFs will only be open to record data within a predefined time window around the optimal visit date. Hereafter, the eCRF of the concerning visit will be locked and no data can be added or changed anymore! For the precise time windows of each visit, please see the concerning chapters.

Collection of patient's data

For the baseline visit it is essential that you have a face-to-face contact. For other visits, this might be convenient, but not obligatory. Patient data might *e.g.* also be obtained by telephone contact. With regard to the defaecation diary and a SHS-form: please do provide the patient with these documents in time; *e.g.* on the outpatient clinic or by regular mail.

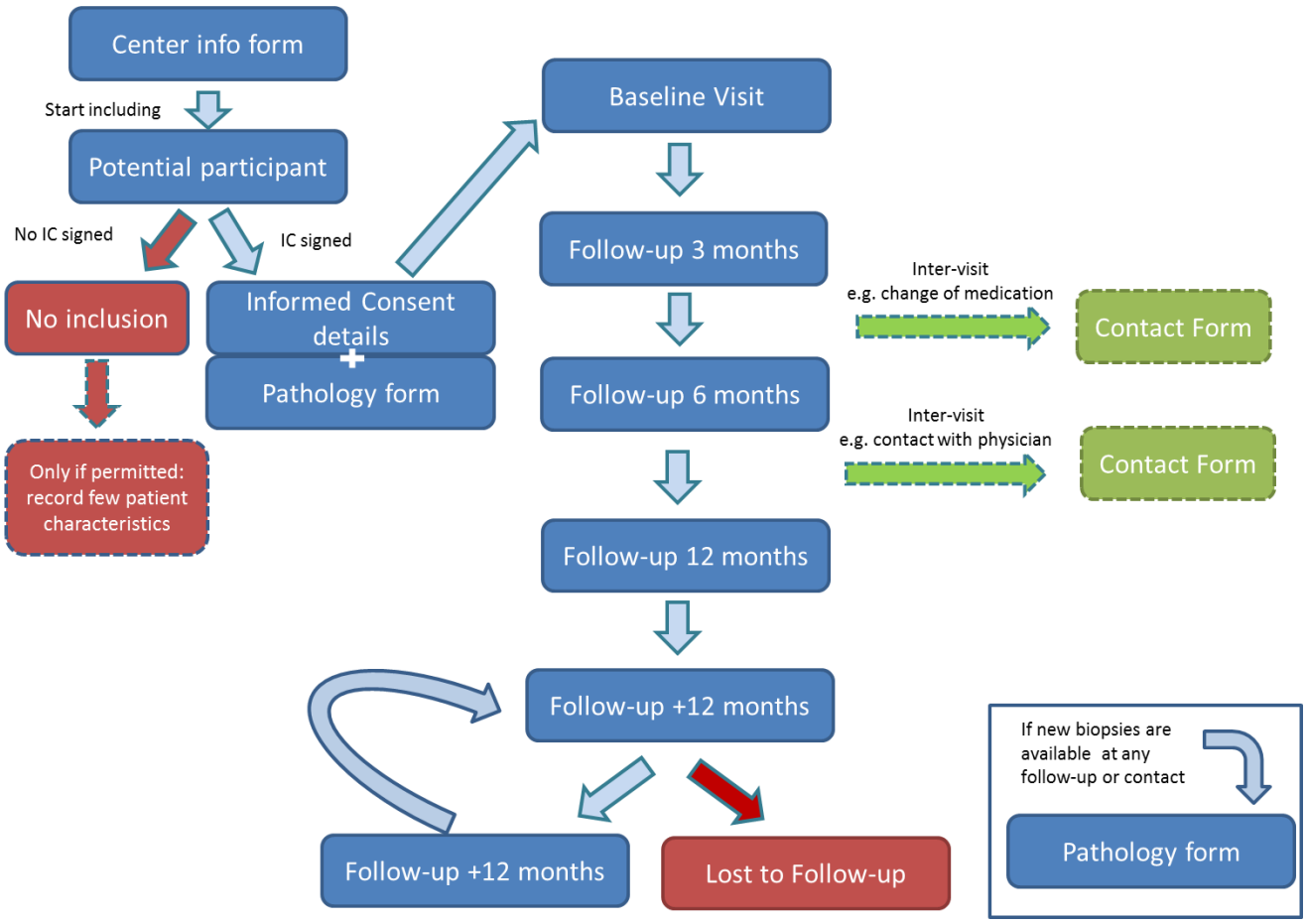
Data safety and data locks

The data in the registry are anonymized. The key to the official patient contact data remains at the participating center. Only data collected at your own center can be visualized.

Please to into account that each visit is open for data input for a restricted period of time! The exact time windows are mentioned in the chapters 7-11. After the time window, data will be locked and cannot be added or changed! Consider this when postponing completion of a visit!

All information visible on the print screen pictures of the registry within this manual, is derived from the test-environment of the registry.

3. Flow-chart of the registry



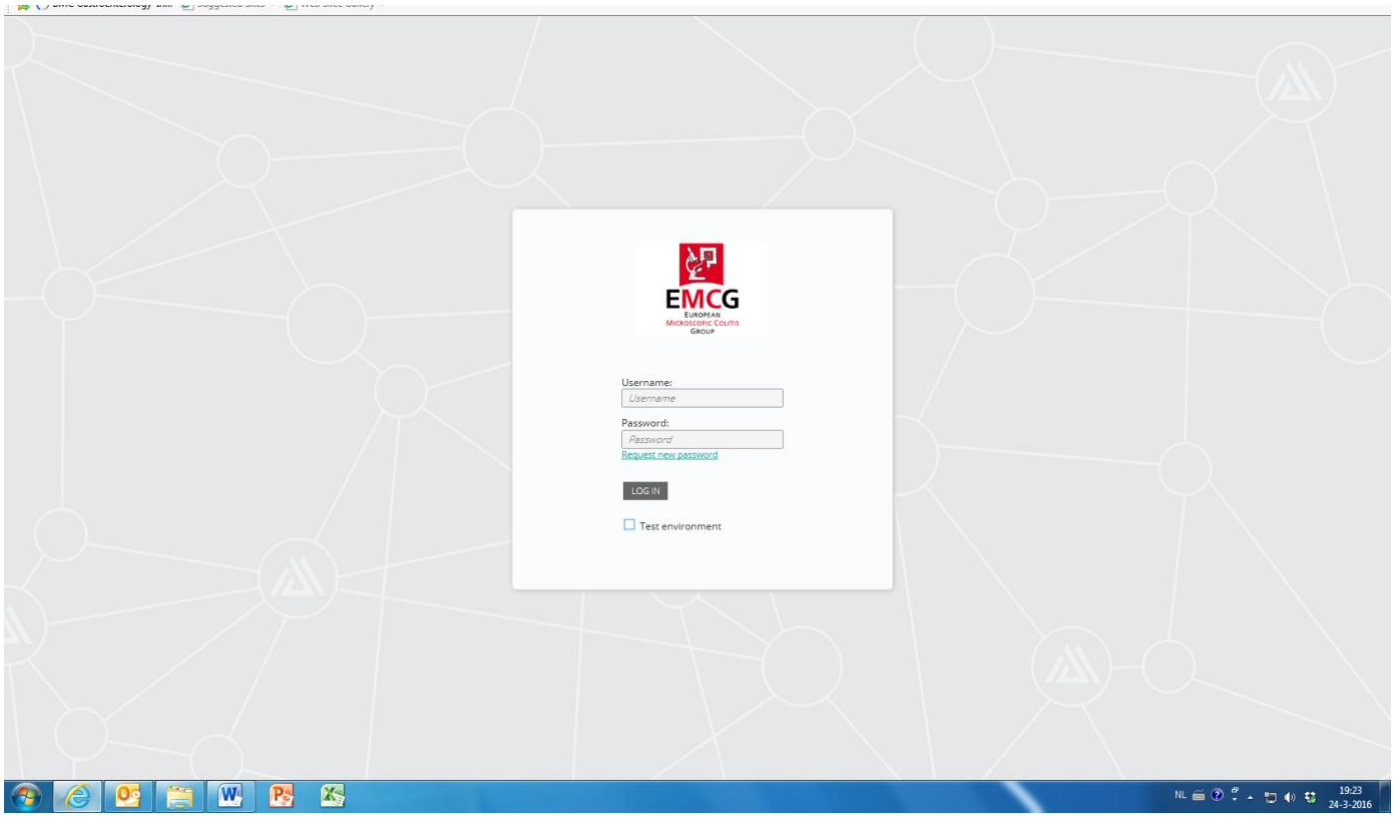
4. Login to the registry

Please use the following hyperlink to open the online registry: www.pro-mc.eu

Use your login credentials to enter the registry. The contact person for this project in your center has been provided with the required login details.

Web browsers

Het registry is developed for Google Chrome and Windows Internet Explorer. The system does not support other web browsers (*e.g.* Safari). Please consider this when the lay-out of the registry appears to be distorted. You might also try to check the settings of your browser (*e.g.* zoom >100%). If the layout still appears distorted to you while using a recommended web browsers and default settings, please contact the PRO-MC Steering Group for help.



5. Patient Overview

The patient overview screen will give you an overview of all patients that are included in the registry in your center.

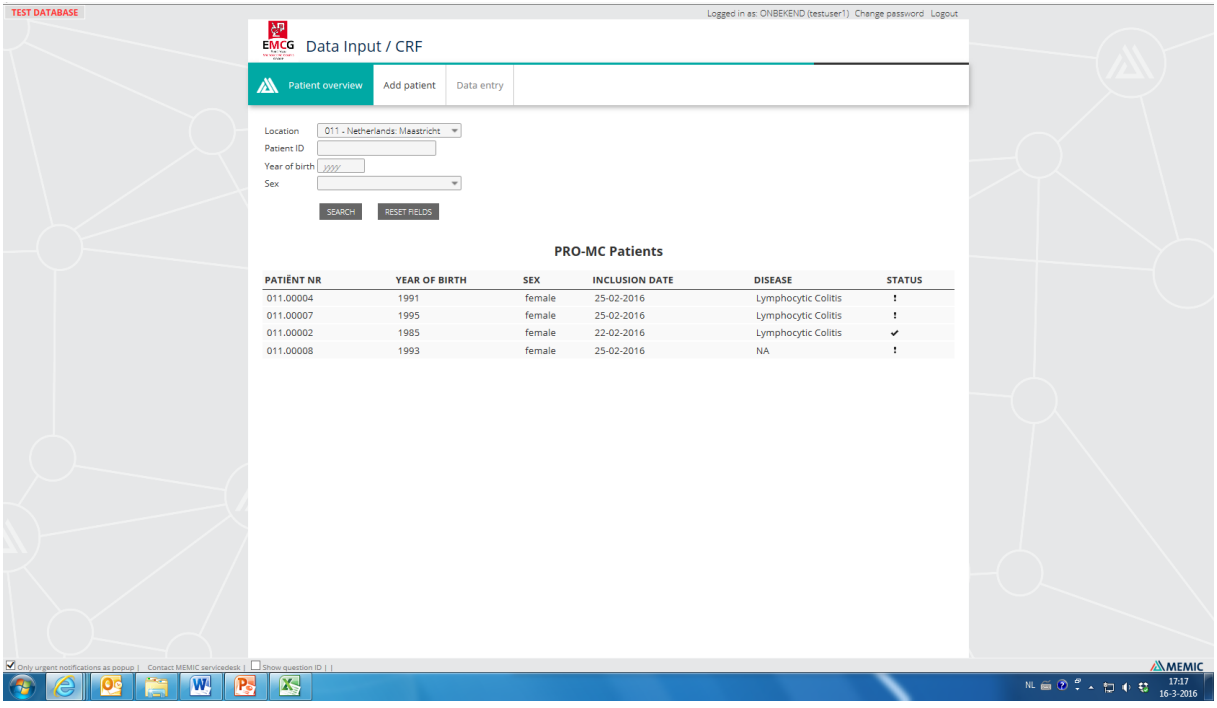
The patient enrolment number is built from the center number (first 3 digits) and a unique sequence number (last 5 digits). The sequence number is project wide, so not center specific! Therefore, each patient in the PRO-MC registry has a unique enrolment number. It is to the center to keep a file which links the enrolment numbers to the patient information.

Beside the year of birth, sex and inclusion date, the type of MC is given. If the type of MC is reported as 'NA', this means that no histologic diagnosis has been entered in the first CRF of the registry.

The last column indicates the completeness status of the CRFs. The symbol ! indicates that obligatory information of at least 1 visit is still missing. If the minimum amount of required data is filled out in all available visits, the symbol is ✔ shown.

Search tool

The search tool in the upper left corner of the screen can be used to search a specific patient in the overview list, by entering one or more variables. This is especially useful when a large number of patients are included in your center.

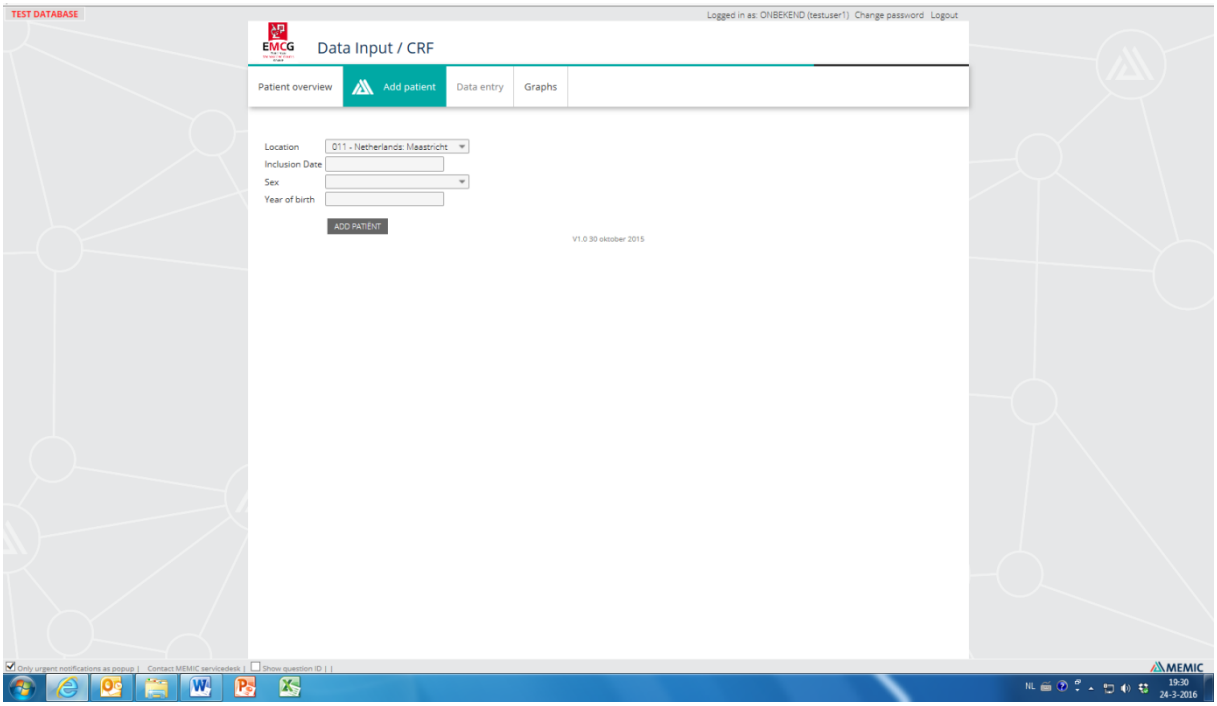


6. Add a patient

To add a new patient to the registry, click the ‘ADD PATIENT’ tab in the top of your screen.

The window to add a patient will appear.

Please fill out all information required to add a patient and click the ‘ADD PATIENT’ button below



7. Inclusion and Informed Consent

Time window:

Not applicable

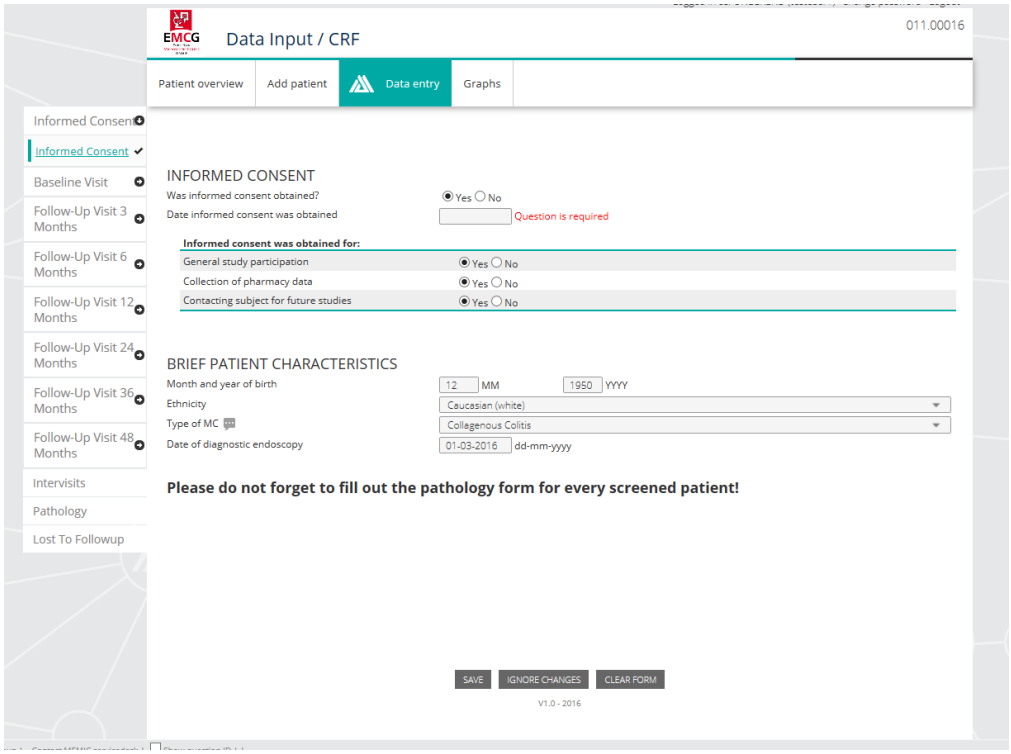
Details

Each patient eligible for inclusion in the PRO-MC Collaboration should be asked for informed consent. In case of participation, written informed consent has to be obtained (use the informed consent forms belonging to the project). Note: only incident (new) cases of MC are to be included in the registry!

Please record all relevant information from the paper informed consent form in the registry!

If no informed consent was obtained, please do fill out this CRF, in order to keep track of the number of screened patients. Please always ask the patient whether he/she agrees that still a few patient characteristics will be documented.

Note: for all screened patients a 'Pathology Form' has to be filled-out. Please see the concerning chapter for further details on this form



8. The baseline visit (BV)

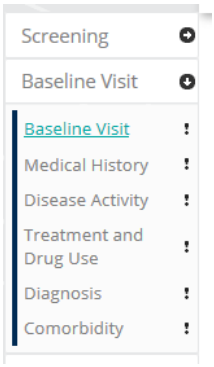
Time window

The BV will be available immediately after informed consent is obtained. The BV form will be permanently locked, 3 weeks after the visit date.

Preparation

The patient should be provided with a "Patient's Diary" and an "SHS form" (if possible, in advance to the visit), in order to be able to fill out the 'Disease activity' CRF

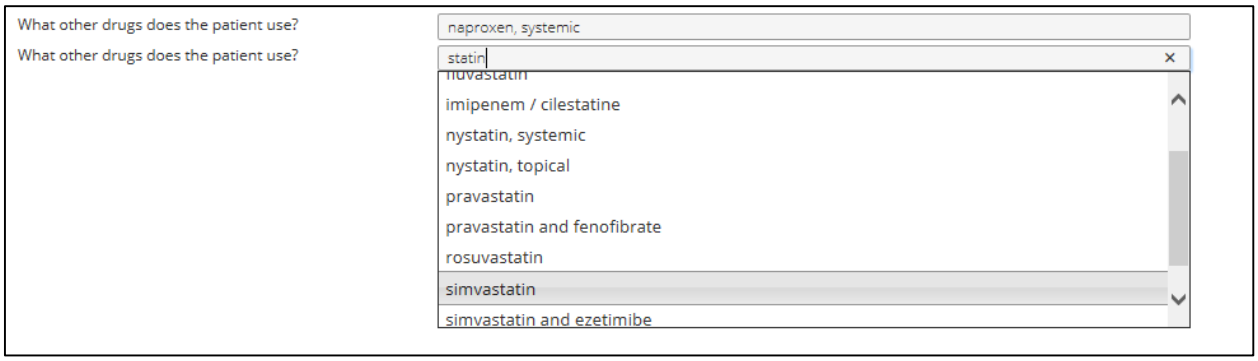
Details



The BV consists of 6 different CRFs. It is convenient to know that for almost all CRFs of this visit (except 'Diagnosis'), **patient contact is required** in order to be able to record all required information!

Provided that you have complete data available regarding any comorbidities and use of medication, the 4th and 6th tab could also be filled-out after a patient's visit.

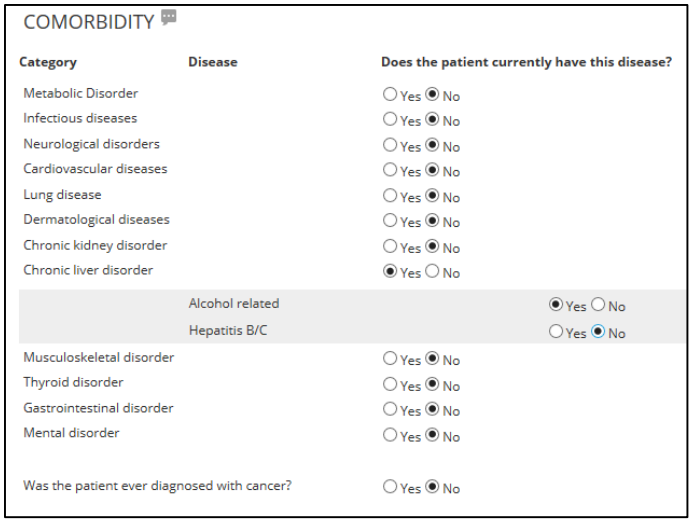
In the 'Treatment and Drug use' CRF, there is a built-in tool to record a patient's full medication overview. Please note that this tool only works on **generic** drug names! In order to add a drug, you need to type at least 3 characters of the substance. Then pick the correct drug form the list. The system will automatically provide you with a next line to add more drugs.



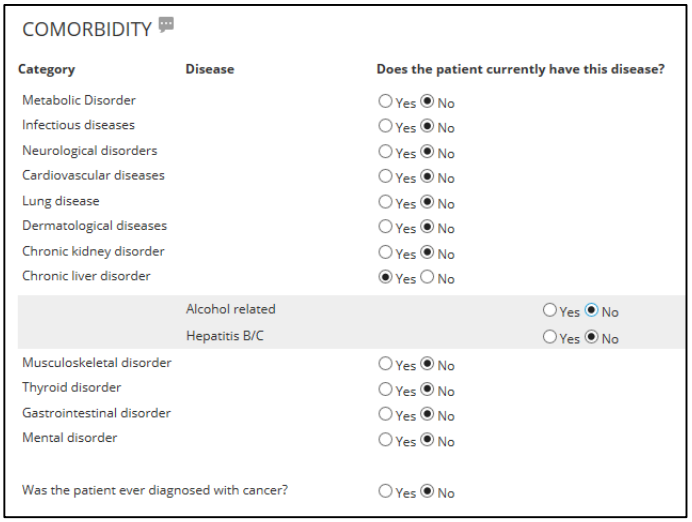
General comorbidities can be recorded in the 'Comorbidity' CRF. This CRF consists of an expandable table. Please, first select the major comorbidity categories that apply. Hereafter, indicate whether the

patient's comorbidity is the same as one of the most frequent diseases within the category. If the specific disease it not mentioned, than select 'no' for all diseases, but keep 'yes' for the category selected.

For example: In the left hand picture you can see that the patient has a chronic liver disorder (category = 'yes'), and the specific disease is an alcohol related liver disorder (disease = 'yes') If the liver disorder would have been hemochromatosis, for instance, than the category chronic liver disorder was still 'yes' but both of the shown diseases 'no' (right hand picture).


COMORBIDITY

Category	Disease	Does the patient currently have this disease?
Metabolic Disorder		○ Yes ◉ No
Infectious diseases		○ Yes ◉ No
Neurological disorders		○ Yes ◉ No
Cardiovascular diseases		○ Yes ◉ No
Lung disease		○ Yes ◉ No
Dermatological diseases		○ Yes ◉ No
Chronic kidney disorder		○ Yes ◉ No
Chronic liver disorder		◉ Yes ○ No
	Alcohol related	◉ Yes ○ No
	Hepatitis B/C	○ Yes ◉ No
Musculoskeletal disorder		○ Yes ◉ No
Thyroid disorder		○ Yes ◉ No
Gastrointestinal disorder		○ Yes ◉ No
Mental disorder		○ Yes ◉ No
Was the patient ever diagnosed with cancer?		○ Yes ◉ No


COMORBIDITY

Category	Disease	Does the patient currently have this disease?
Metabolic Disorder		○ Yes ◉ No
Infectious diseases		○ Yes ◉ No
Neurological disorders		○ Yes ◉ No
Cardiovascular diseases		○ Yes ◉ No
Lung disease		○ Yes ◉ No
Dermatological diseases		○ Yes ◉ No
Chronic kidney disorder		○ Yes ◉ No
Chronic liver disorder		◉ Yes ○ No
	Alcohol related	○ Yes ◉ No
	Hepatitis B/C	○ Yes ◉ No
Musculoskeletal disorder		○ Yes ◉ No
Thyroid disorder		○ Yes ◉ No
Gastrointestinal disorder		○ Yes ◉ No
Mental disorder		○ Yes ◉ No
Was the patient ever diagnosed with cancer?		○ Yes ◉ No

9. The follow-up (FU) visits

Time window

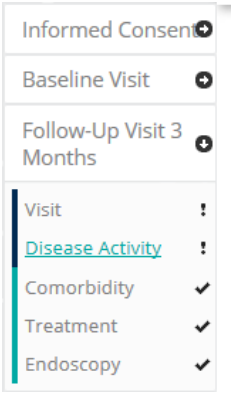
There are several follow-up visits, at 3, 6, 12, and then every 12th month after inclusion.

FU3 and FU6 will be available until 3 weeks after the official follow-up date. Hereafter they will be locked. FU12 and other annual visits are available until 4 weeks after the official follow-up date.

Preparation

Patients should be provided with a "Patient's Diary" and an "SHS form" (preferably in advance to a FU visit), in order to be able to fill out the 'Disease activity' CRF. The other information might be obtained via a face-to-face contact or by *e.g.* a telephone contact.

Details



Basically, the content of the FU-visits is comparable to the CRFs of the baseline visit.

The comorbidity table, will only become available when you indicate that a new comorbidity has occurred since the last visit. If so, the latest comorbidity table will reappear, and can be changed accordingly. This enhances user friendliness.

In the 'Treatment' CRF, you will be asked whether any drugs for MC treatment have been stopped since the last (inter) visit. If so, the 'stop treatment' table will appear. Please indicate all stopped drugs and their dosages on the date of cessation in the table.

Hereafter, you need to record all drugs that are currently used for treatment in the 'current treatment' table below.

10. Inter Visit Contacts (IV)

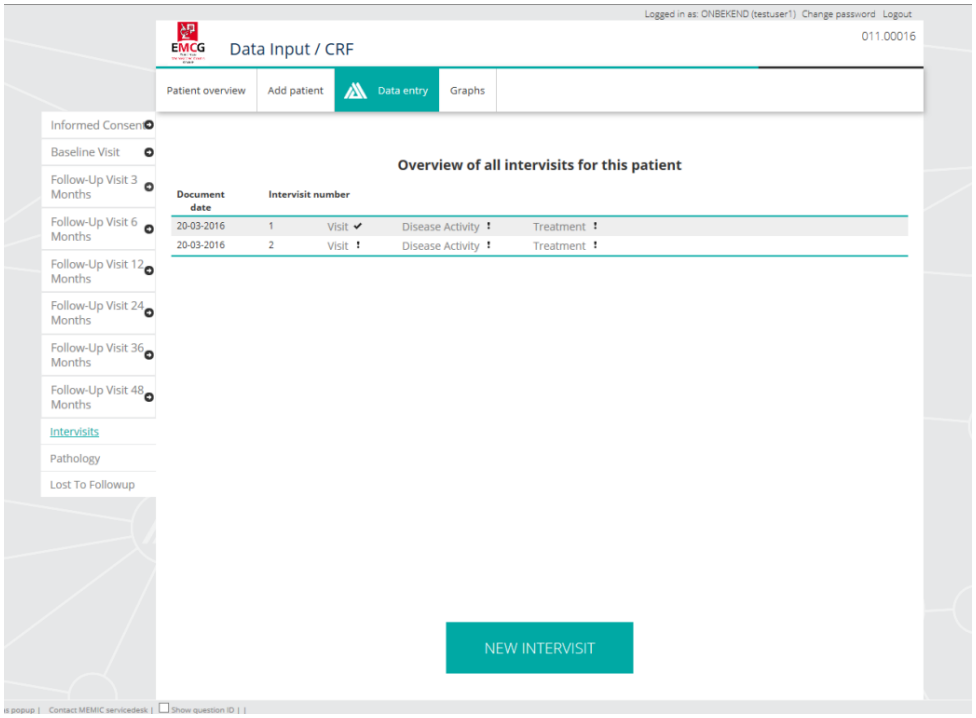
Time window

An inter visit contact can be created at any desired time point *in between* the predefined follow-up visits. For example, when a patient visits your clinic because of a relapse of symptoms, because you want to change medications, or just because an additional visit was scheduled in between the other visits.

Note: The Inver Visit Contact should not be used as an alternative for the predefined visits! But it should be regarded as a possibility to record an in between situation. This CRF will not automatically lock after a certain period of time.

Preparation

If possible, patients should be provided with a "Patient's Diary" and an "SHS form" in advance to an inter visit contact, in order to be able to fill out the 'Disease activity' CRF.

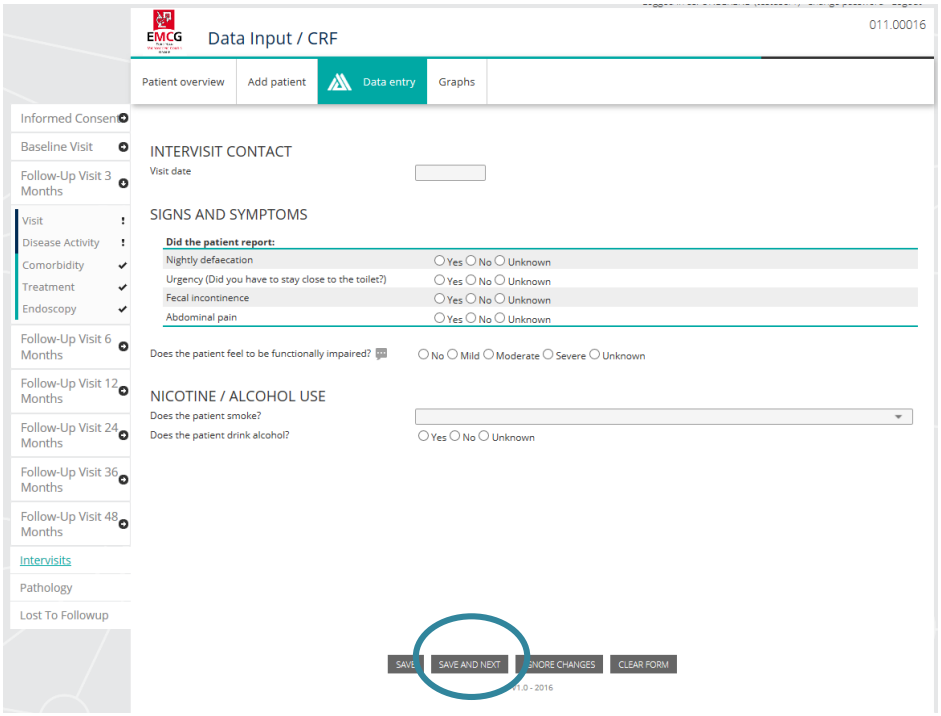


Details

To create a new inter visit, or to see the list of existing inter visits, select 'Intervisit' in the navigation menu. You will then see an overview of all current inter visit contact, listed subsequently. Each visit consists of 3 CRFs, followed by a sign indicating the completeness of each CRF

Click the green button below, to add a new inter visit.

Because the inter visits are not visualized in the navigation menu, a ‘save and next’ button is available (see picture below) to proceed to the second or third CRF of the visit.



11. Pathology Form

Time window

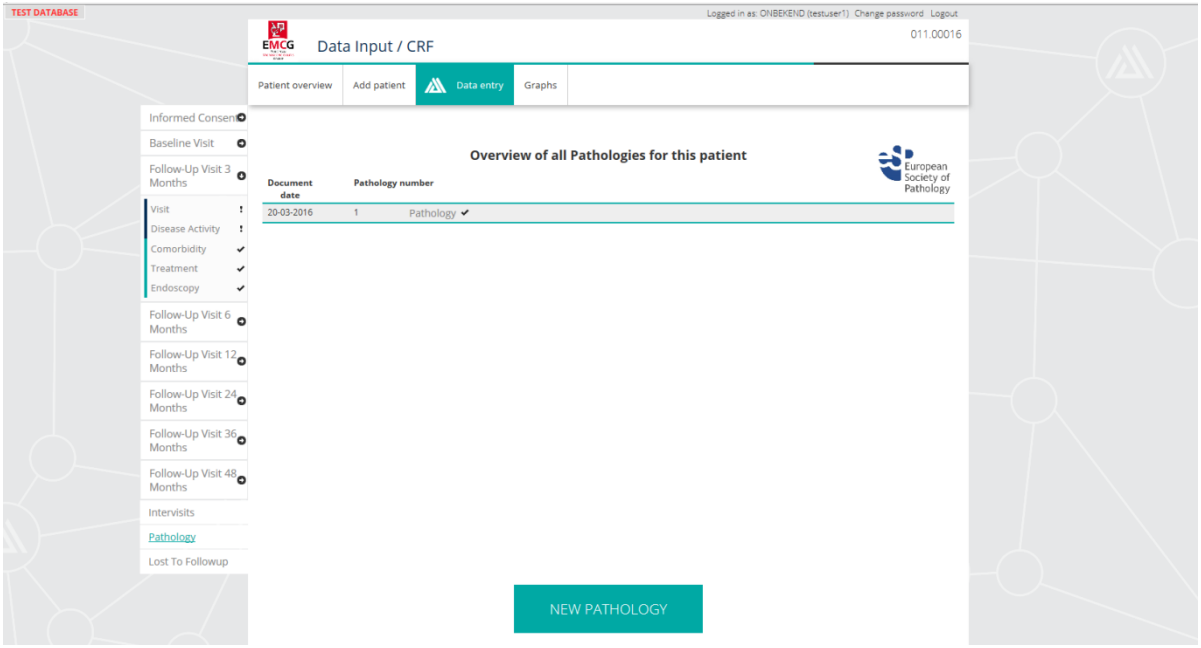
A pathology form can be created at any desired moment, when new colon histology is available for this patient. This CRF will not automatically lock after a certain period of time.

Details

The overview of the pathology forms is comparable to the 'Inter Visit Contacts'. Individual forms are not listed in the navigation menu on the left, but a subsequently listed within the tab 'Pathology'.

To add a new pathology form, click the green button at the bottom of the screen.

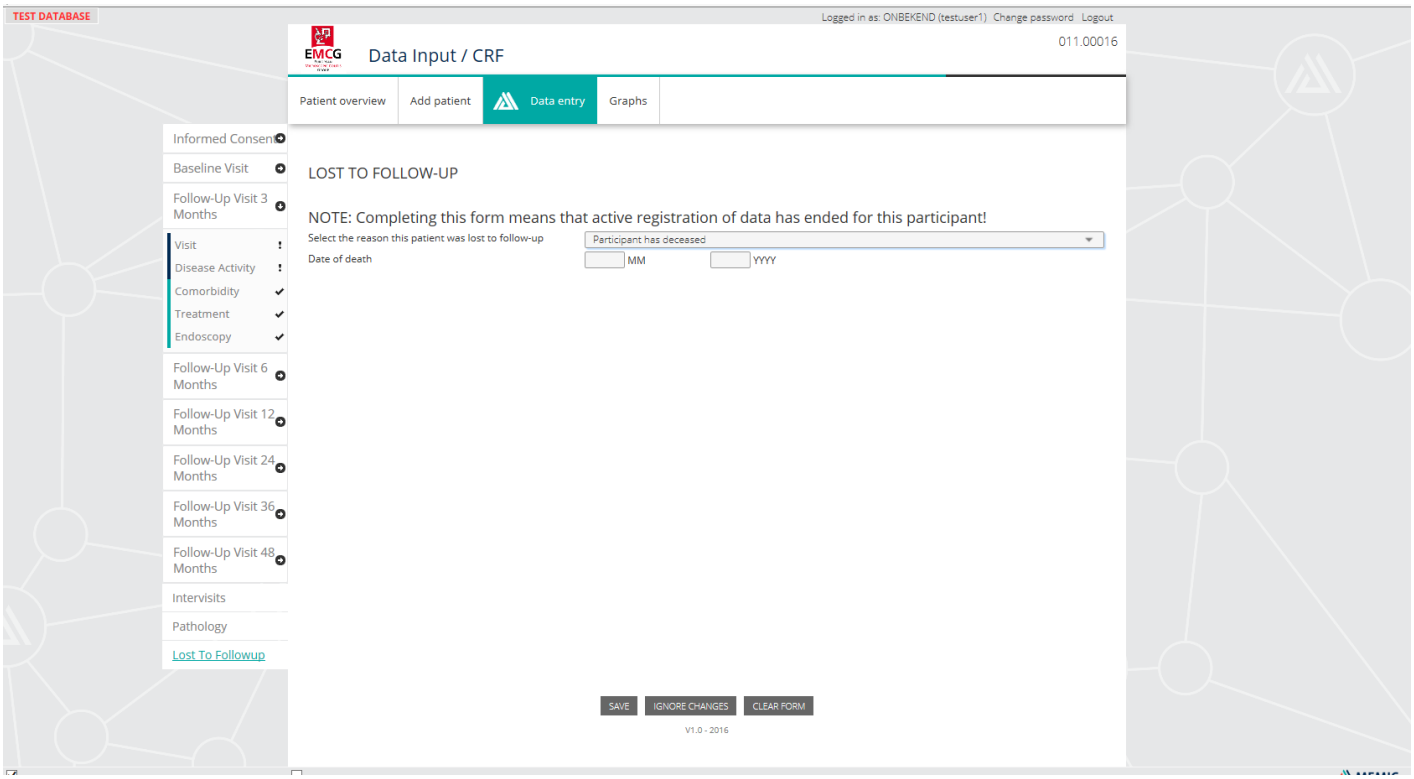
Please report as much detailed information as possible, *e.g.* biopsy location, microscopy details, types of staining used.



12. Lost-to-follow-up

Do only use the “Lost-to-follow-up Form” in case you don’t expect the patient to participate in the PRO-MC Collaboration anymore.

Note: Only when you select death to be the reason for lost-to-follow-up, the complete (!) patient CRF will be locked definitively. In all other cases, the study visits will be locked temporarily. If you want to continue recording data for this patient, you will have to change the ‘lost to follow-up form’ and save it. Then the other visits will become available again.



13. Logistics of the registry

With the logistics of the registry, the sequence of the follow-up visits is meant. The logistics are based upon the flow-chart of Chapter 3 and the time windows mentioned at each visit.

At site initiation, the contact person of the participating center is requested to provide the e-mail addresses to which the notification e-mails have to be sent.

Notification e-mails

Every time a new visit needs to be scheduled for any of the patients included in your center, a notification e-mail will be sent to the designated e-mail addresses. The date of notification is dependent of both the date of inclusion of the patient into the registry and the follow-up visit. The e-mail contains information on both the ideal date for the visit and the allowed time window for the visit. Please see the table below for more information.

Note: only one e-mail will be sent per visit to be scheduled

Visit	**Month no.**	**Notification e-mail**	**Allowed time window around the official date**
Baseline Visit	Month 0	N/A	N/A
Follow-up visit	Month 3	4 weeks before visit	-2 to +2 weeks
Follow-up visit	Month 6	4 weeks before visit	-2 to +2 weeks
Follow-up visit	Month 12	6 weeks before visit	-4 to +4 weeks
.....	Every 12th month	6 weeks before visit	-4 to +4 weeks

Other logistics

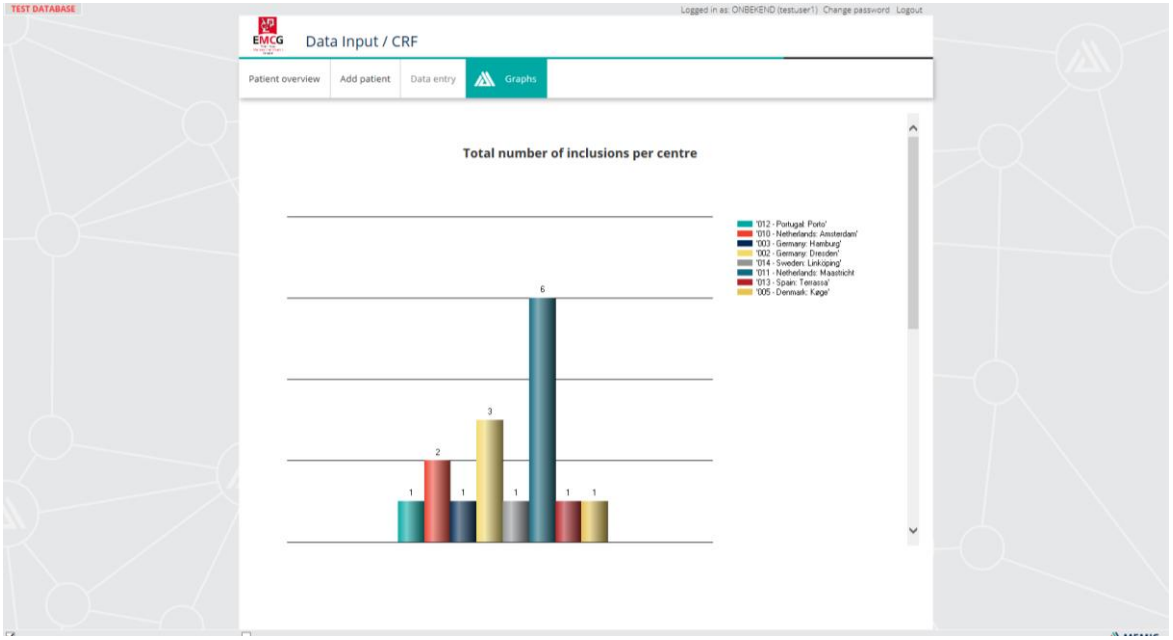
Another logistics that might be necessary is facilitating the patients with the defecation diary and SHS form. These can *e.g.* be provided on the outpatient clinic or via (e-)mail, and also need to be returned. What is the best way to do this will be different form center to center.

14. Overview of the inclusion

The tab ‘Graphs’ in the top of the registry consists of 2 graphs.

The first graph is an overview of the number of included patients per participating center, the second graphs visualizes the number of patients included in your center specifically, split by MC subtype.

Graph 1



Graph 2