SYNTAX®
FOR SCIENCE

OpenClinica Investigator's Manual

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1. INTRODUCTION

This manual provides an introduction to OpenClinica particularly designed for the Investigator user, including key terminology and concepts, as well as basic skills such as navigation. The software is web based and users can access it with a standard web browser and internet connection.

2. LOGIN INTO OPENCLINICA

2.1 Login

To access OpenClinica login page use the URL provided by Syntax for Science for the current Study (Figure 1).

Figure 1

Provide your authorized *User Name* and *Password*, and then click *Login*. Remember both your User Name and Password are case sensitive.

Note: You should take into account to use recommended web browsers: Firefox or Internet Explorer. If you use other web browsers OpenClinica will advise you with the following message: *"OpenClinica recommends using Firefox 25 and Internet Explorer 11. While OpenClinica is designed to work on all standards-compliant browsers, we have not verified that the application functions correctly on other browsers or browser versions. If you do not have one of the above browsers installed you may need to contact your IT support group for assistance."*

2.2 Reset Password

For security purposes, OpenClinica might be configured so that under certain conditions (e.g. first login) you must reset your password when you try to login. When the Reset password page displays, complete the fields in the page:

1. Specify the original password provided by Syntax for Science
2. Enter the desired new password (your new password must be at least eight characters long)
3. Re-enter the desired new password

4. Choose a password challenge question
5. Specify the answer to the password challenge question
6. Then click Change Password

You can also change your password anytime you need from Change User Profile page by clicking your User Name (on the top right).

If you forget the password, click on *Forgot Password?* link next to the Login button (Figure 1) and the Request Password page opens. For further help, please contact with Syntax for Science.

2.3 Homepage

After login into OpenClinica, the homepage will be displayed providing tools and links to different features. The body of the homepage shows to the Investigator the *Subject Matrix* of the current Study/Site (Figure 2).

We will see Subject Matrix in more detail in section Subject Matrix.

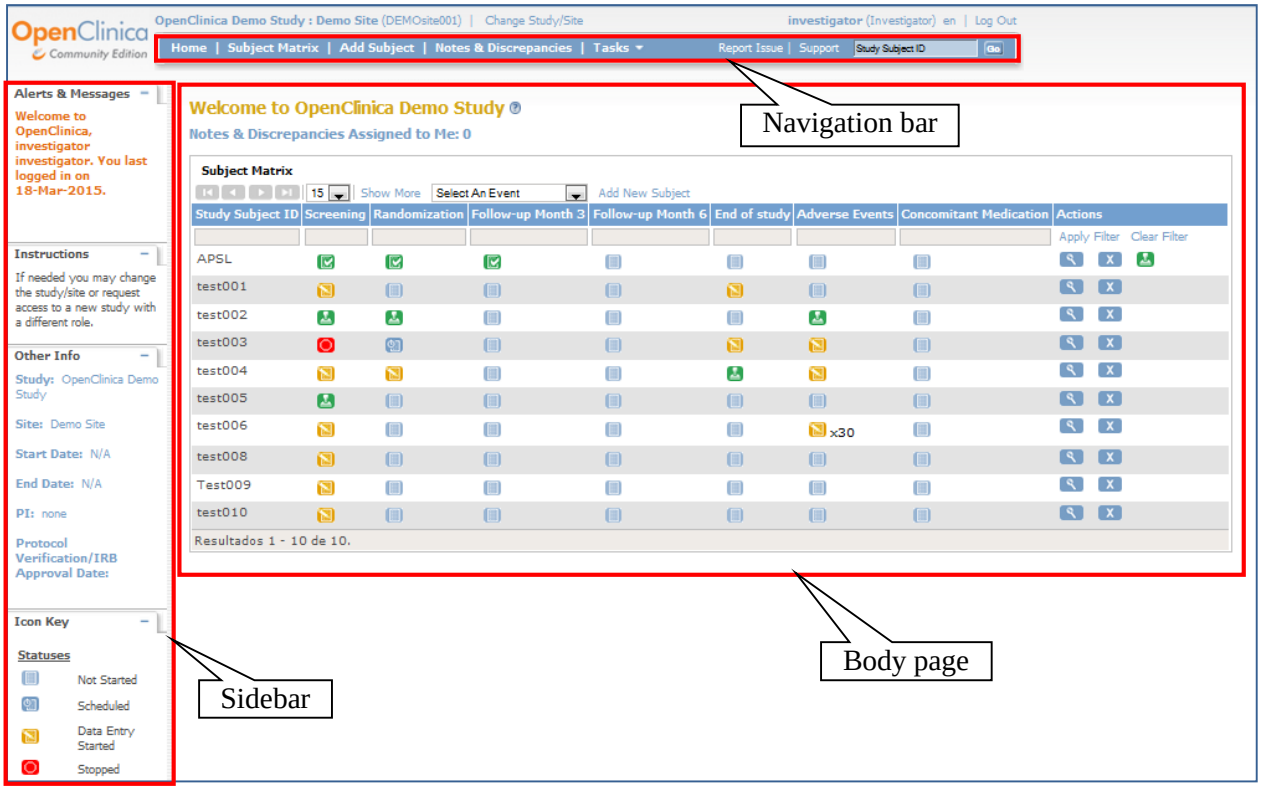


Figure 2

2.4 Change Study or Site

When working in OpenClinica, you are always working in reference to a specific Study/Site. You will only be able to view those which you have been given access to.

Most Investigators will only have access to one Study/Site, therefore they **will not need to use the '*Change Study/Site*' link**.

If you have access to more than one Study/Site, as shown in Figure 3, you must select the right Study/Site before proceeding:

1. Click the *Change Study/Site* link
2. Select the Study/Site you want to change (studies are indicated in bold and sites in regular font)
3. Click *Change Study* button to confirm

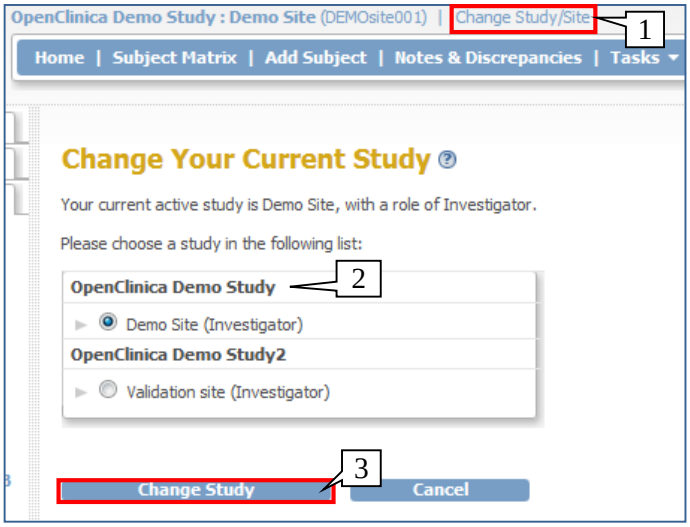


Figure 3

3. MODULES AND TASKS AVAILABLE

Modules (groups of Tasks, Figure 4) available for the Investigator are:

- Submit Data
- Extract Data
- Other

Some Tasks Investigators can perform are:

- View all subjects (Subject Matrix)
- Add Subjects
- View and manage Notes & Discrepancies
- Add new study events (Schedule Event)
- View Events
- Sign Subject Data
- View Datasets
- Create Datasets

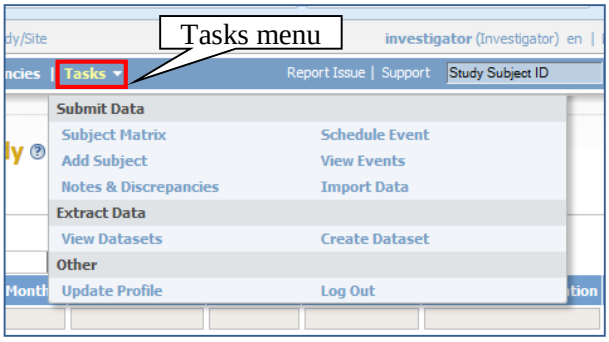


Figure 4

3.1 Submit Data

OpenClinica's *Submit Data* module allows Investigators to track subjects in the current study, add new subjects to the study, view and schedule events, enter and change information about subjects and events, create notes and discrepancies, and import data.

To access features in the *Submit Data* module, click *Tasks* button from the navigation bar and select the feature you want.

In the following sections the most important features are explained. If you need any further information, please contact with Syntax for Science.

3.1.1 Subject Matrix

The Subject Matrix can be acceded from the Navigation bar, is a table with information of all subjects included in a Study/Site.

There is one Subject per row and one column for each Event Definition in the Study (Figure 5).

Each cell in the matrix contains an icon that identifies the Event status (check the *Icon Key* in the sidebar Figure 6).

Subject's information and events can be managed in two different ways:

- Clicking any Event icons, or
- Clicking *View Subject Record* icon

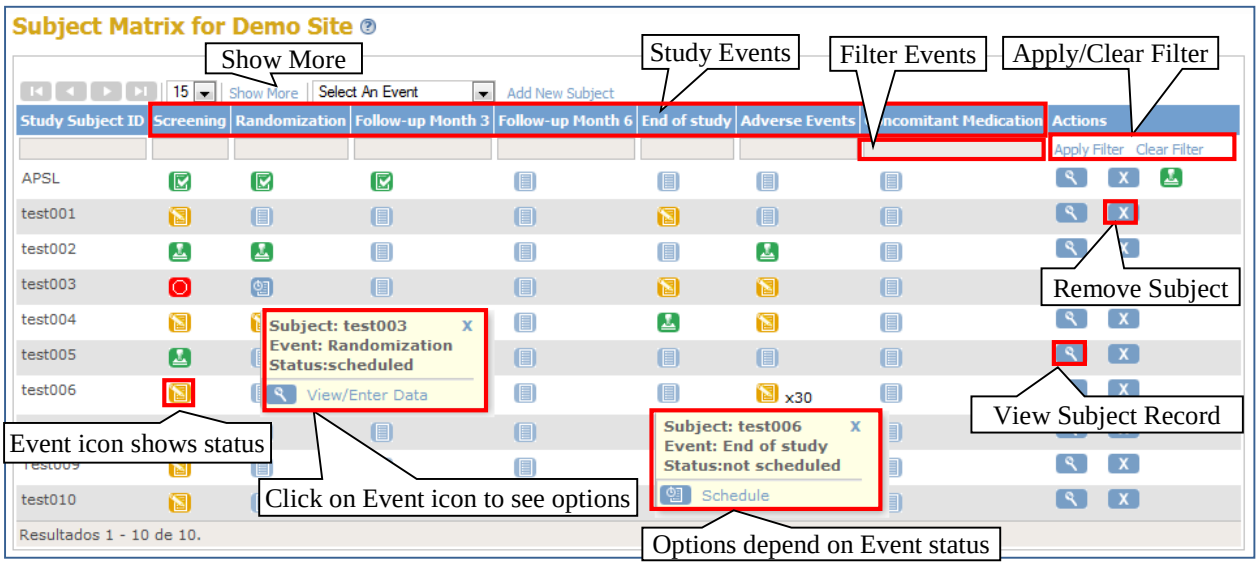


Figure 5

To see or enter data for a Subject in a specific Event, click over the icon and select the action you want to perform. Depending on the status of the Event, the actions could be:

- Schedule
- View
- Enter Data
- Edit
- Remove
- Add Another Occurrence

Clicking the *Show More* link widens the matrix giving you more information about the subjects:

- Subject Status
- Site ID
- Sex
- Secondary ID
- Group Information

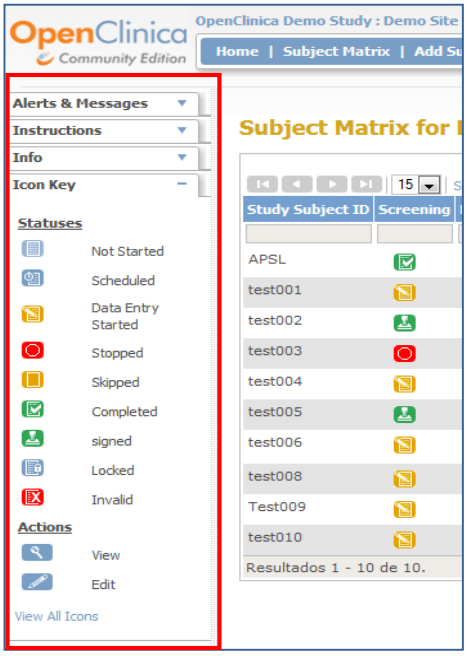


Figure 6

Stop showing this additional information by clicking the *Hide* link.
To view details for an event select it from Select Event drop-down list (Figure 7). In the *Subject Matrix* the columns show the different Case Report Forms (CRFs) for the related Study Event.

Icons in the columns show the CRFs status for each subject. Put the cursor over an icon to see more information in a pop-up window. To perform actions in a specific subject's CRF, click the icon, and select the action you want to perform.

Figure 7

To see all study information for a subject, click the *View* icon in the *Actions* column (Figure 5, Figure 7).

The *View Subject* page will be opened showing the different sections. Click the plus or minus sign next to each section to show or hide the information. By default the *Events* section will be shown (Figure 8).

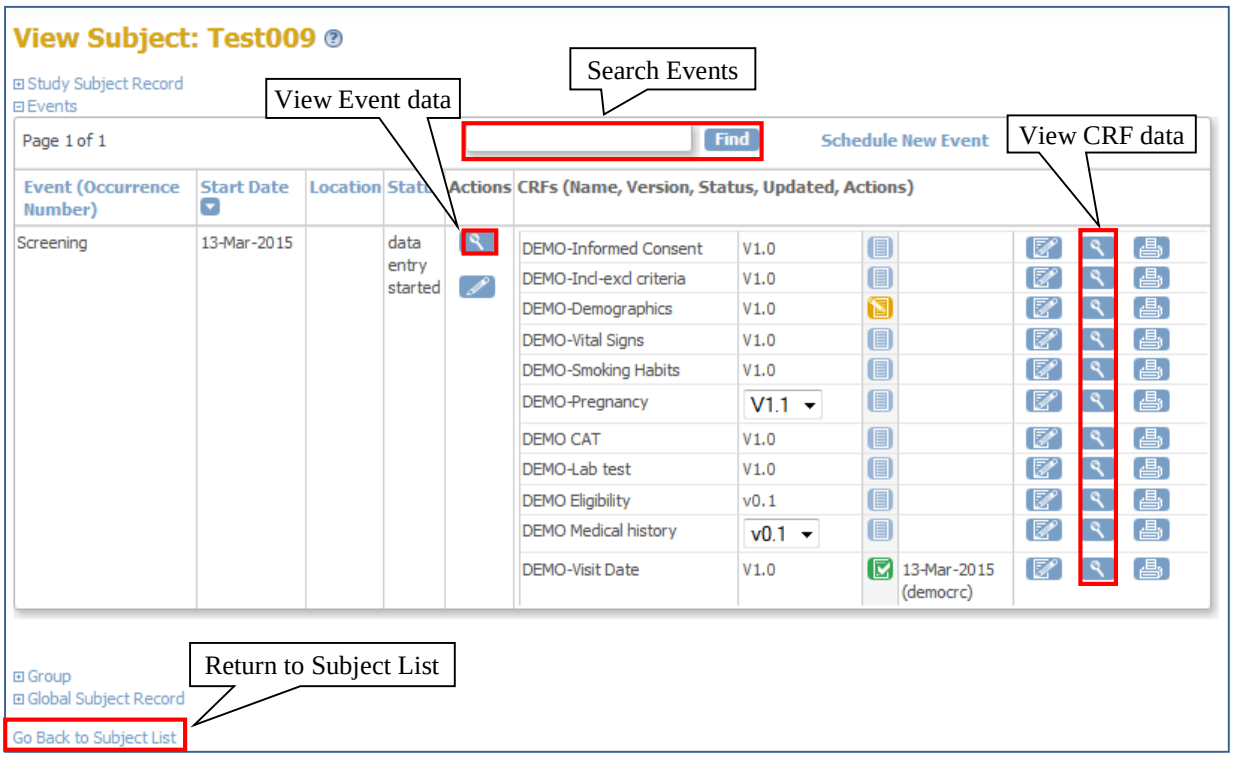


Figure 8

3.1.2 Add Subject

Investigators can create a new Subject in three different ways:

1. Using the *Add Subject* link on the navigation bar
2. Selecting the *Add Subject* option under the Submit Data section on the *Tasks* menu (navigation bar)
3. Clicking on the *Add New Subject* link in *Subject Matrix*

When you create a new subject through the third option (Subject Matrix) the *Add New Subject* window opens (Figure 9) and allows you to schedule the **first** event for that subject. Complete the information asked as follows:

1. Study Subject ID: code to identify the subject
2. Enrolment Date: select the date throughout the calendar
3. Sex: select the gender
4. Study Event: select the **first** event from the drop-down list
5. Start Date: select the date throughout the calendar
6. Click *Add* to confirm and create the subject

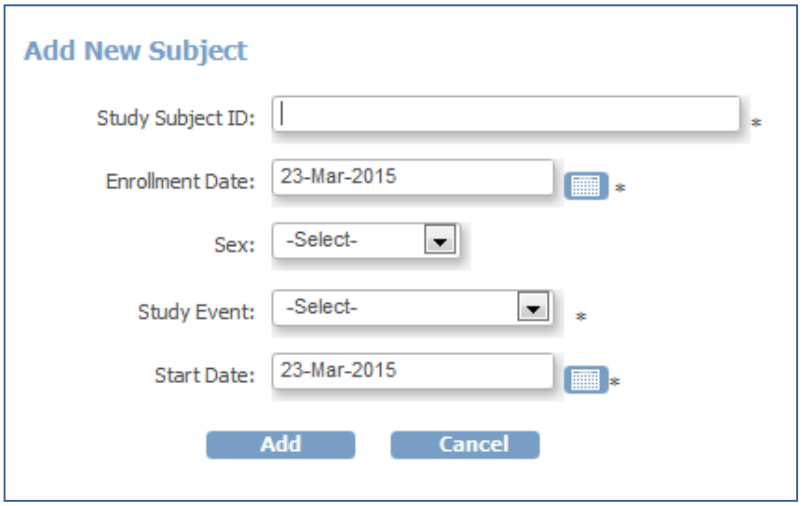


Figure 9

Notice: fields marked with an asterisk (*) are mandatory.

Once the subject has been created, the *View Subject* page opens (Figure 8) showing the first Study Event. If you want to enter data into a CRF see Enter data into a CRF or if you want to schedule a new event see next section.

3.1.3 Schedule Event

The *Schedule Study Event* page (Figure 10) can be accessed through the *Subject Matrix*, click the icon in the event column you want to schedule.

The actions allowed will depend on the type and status of the event:

- For a Non-repeating event, click the *Not Started* icon and then click *Schedule* in the pop-up window (Figure 5).
- For a repeating event, the cell will show the number of occurrences of the event that have already been scheduled or completed. Select the icon in the cell and click *Add Another Occurrence* in the pop-up window.
- For a new Subject, see Add Subject.

Once in the *Schedule Study Event* page (Figure 10), data can be entered in order to schedule the event. Remember that fields marked with an asterisk (*) are mandatory.

After completing the requested information, you can select *Proceed to Enter Data*.

Notice: You can also access to the *Schedule Study Event* page from the navigation bar, select *Tasks* and then *Schedule Event* (the study subject ID will be required).

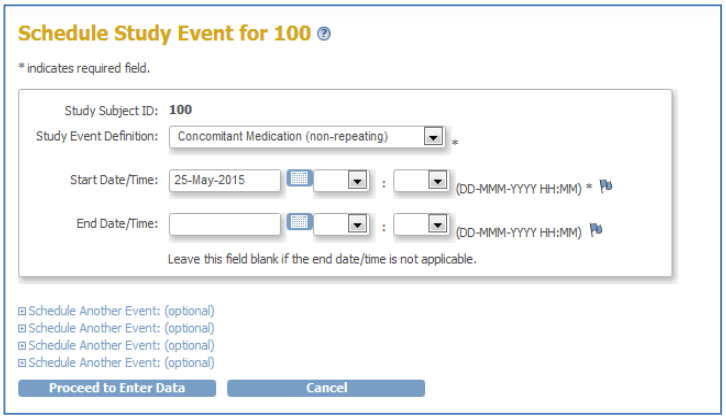


Figure 10

3.1.4 Enter data into a CRF

After the first event has been scheduled, the *View Subject* page shows all CRFs for each Event (Figure 11). The CRFs are listed in the order they are meant to be completed. When data are entered to CRFs these are reordered. Thereby the "next" CRF to be completed will always appear at the top of the list.

If there is more than one version of the CRF for the current site or study, make sure to select the right version from the drop-down list.

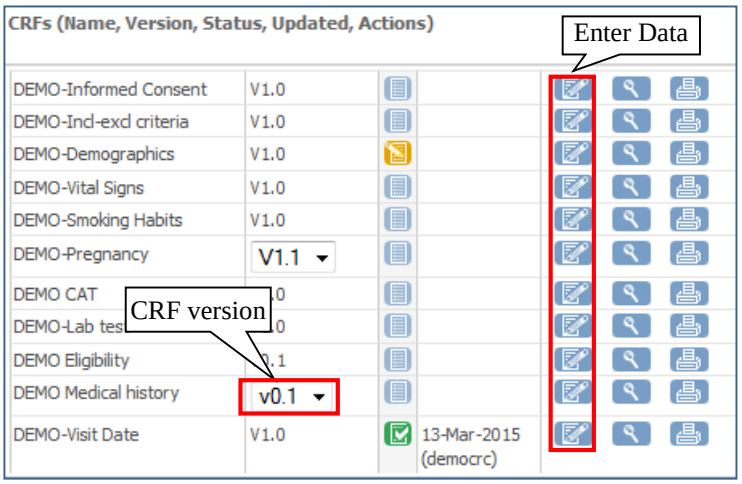


Figure 11

To enter data for a CRF, click the *Enter Data* icon for that CRF.

Notice: There are other ways to open a specific CRF in order to enter data:

- In the *Subject Matrix* page choose the subject and event you want to enter data for, click the icon, and select *View/Enter Data*. (Figure 5, Figure 7).

- When scheduling an event, once you have completed the *Schedule Study Event* page, click *Proceed to Enter Data*. After that the *Enter or Validate Data for CRFs* page will open. This page works like *View Subject* page (Figure 8).

Once the CRF is open (Figure 12), the page shows *the Study Subje*ct ID at the top right, and the CRF name with the CRF's status icon at the top left.

The *CRF Header Info* is a box which summarizes information about the CRF. It is hidden by default so click the plus (+) or minus sign (-) to show or hide it.

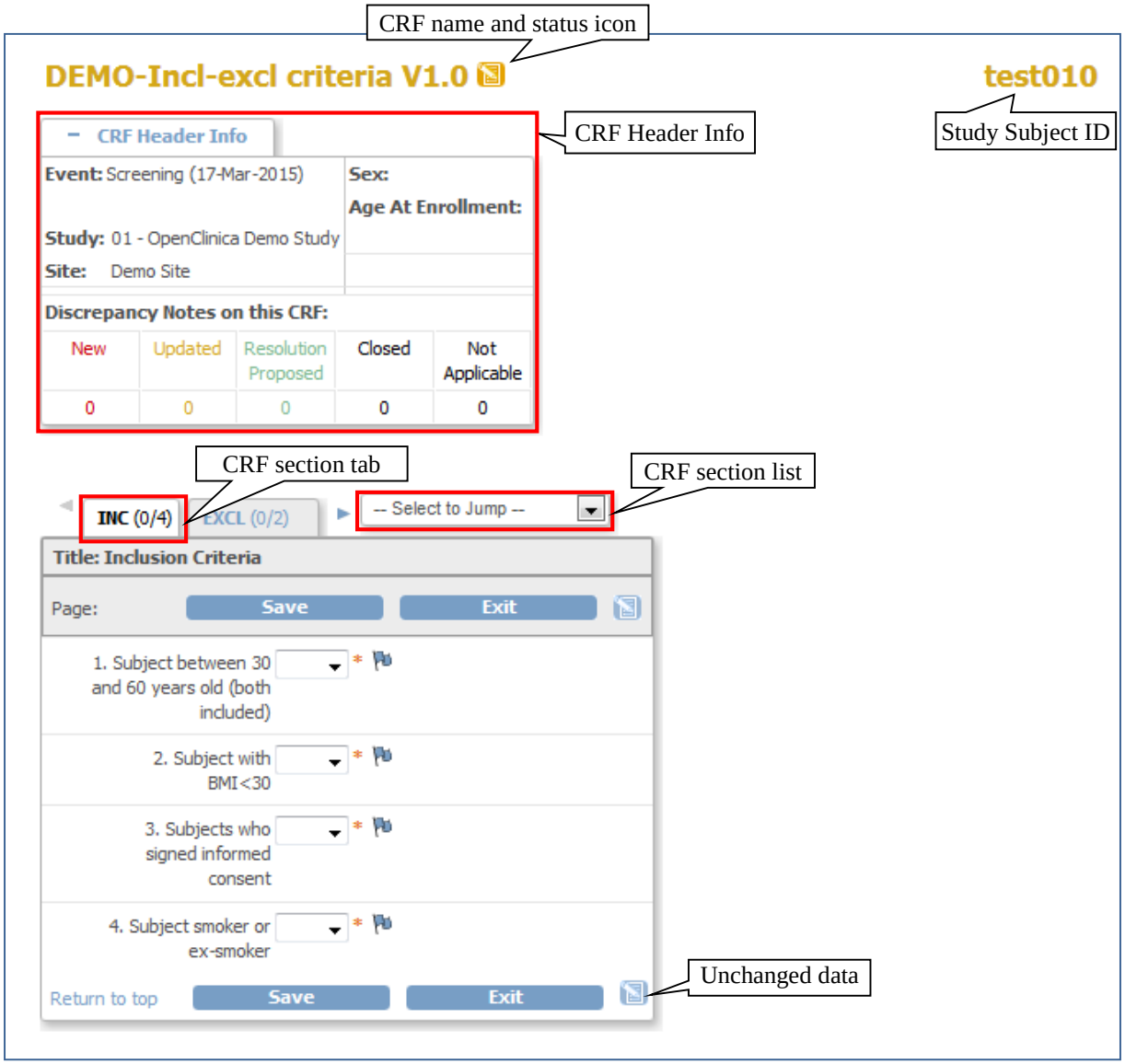


Figure 12

The CRF sections' tab will show the number of items completed within the total, for example 0/4 indicates 4 items in the section and 0 completed. If there are more than one section, select the CRF's section by clicking the related tab, or select it from the drop-down list.

Instructions for completing items will be shown at the top of the page or in each item if it was defined previously.

Once the required information has been entered the icon will change from to indicating the page contains unsaved data. Also, fields with unsaved data turn yellow - so it's easy to see if you've missed a field due to it will not be yellow (Figure 13).

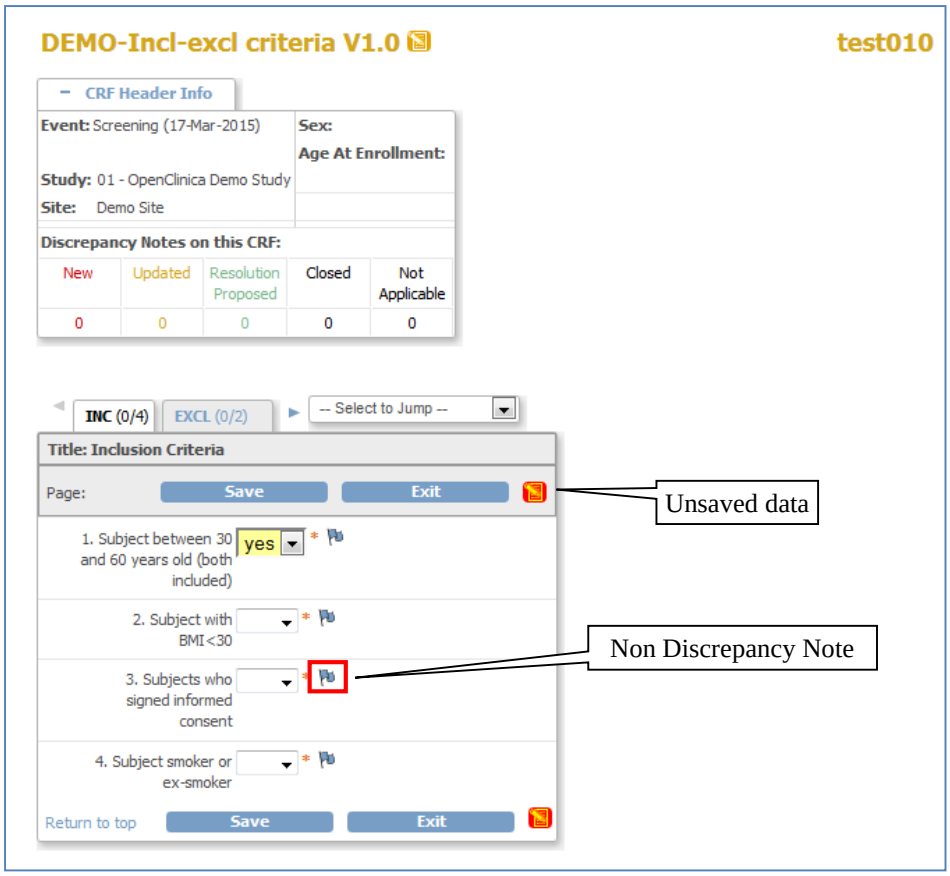


Figure 13

If you need to enter a value that differs from what is indicated, have a question, or want to make a note, add a discrepancy note by clicking the *Add Discrepancy Note* icon in the item and complete the pop-up note. For further details, see Notes and Discrepancies.

3.1.5 Mark a CRF as complete

When all CRF data have been filled the box *Mark CRF Complete* must be selected. Remember to click *Save* to store the data entered (next section).

Data can later be edited even after marking *CRF Complete* (Figure 14). In that case, a clarification will be required to explain the reason for change. For further information, see Discrepancy Note creation.

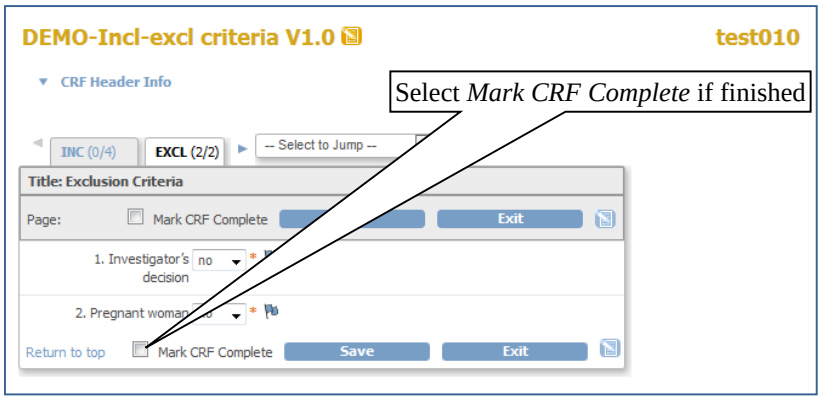


Figure 14

3.1.6 Save data

After completing a CRF's:

- If you don't want to save the information you have entered click *Exit* to end data entry. A message box will pop-up asking if you want to proceed without saving the data.
- If you want to keep the information you have entered click *Save*. After saving OpenClinica displays the CRF list or next CRF's section. If the CRF has more than one section you have to save each section.

If there are problems with the data entered OpenClinica will not save the data and will display failure messages (Figure 16).

These messages can be due to different reasons:

- Data types (as an integer, a real number or a date) or expressions for an item definition (as a time format hh:mm).

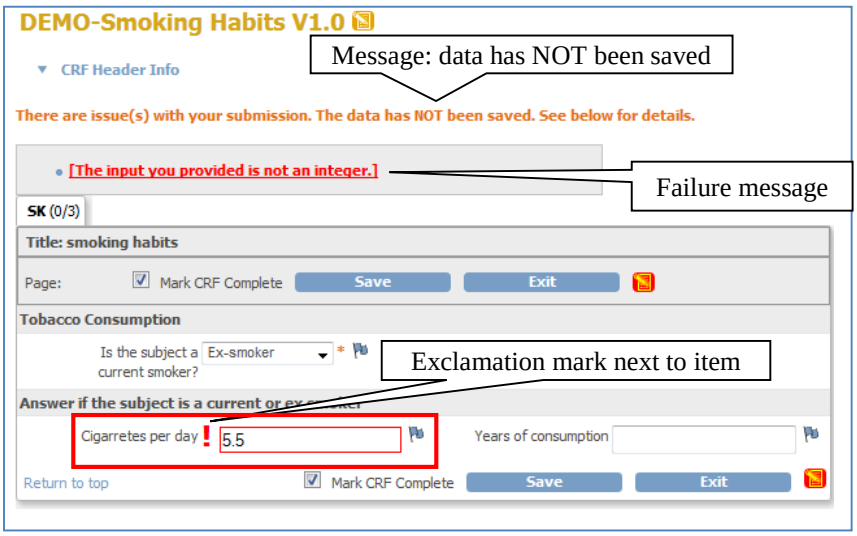


Figure 15

In this case you should provide the correct data type or expression because OpenClinica will not accept any other possibility. You can also provide a Discrepancy Note for that item, but it is optional. For further information about how to provide discrepancy notes see Notes and Discrepancies.

- Validation checks requested by the Sponsor (Figure 16). These failure messages advise you about some data error but OpenClinica will save the data (even if it wrong) clicking *Save* twice.

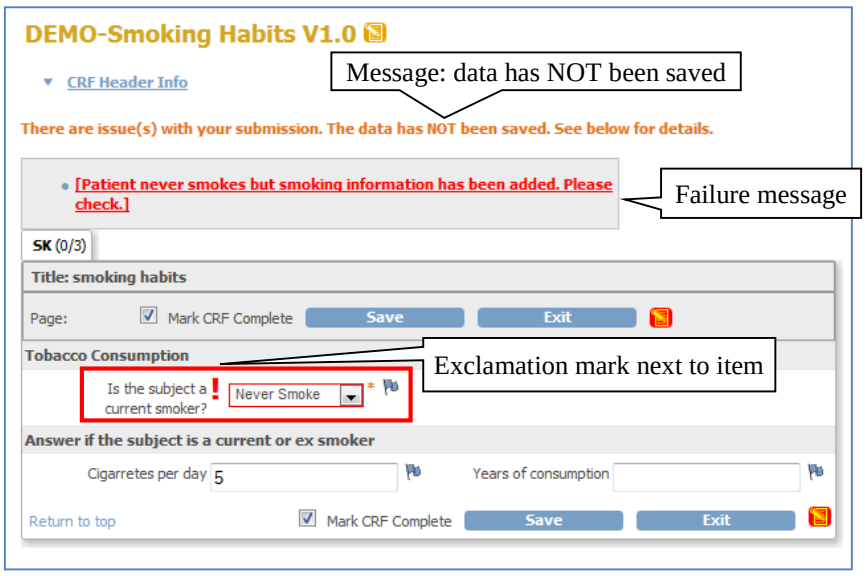


Figure 16

After correcting those mistakes or provide a discrepancy note, remember to click *Save* again. For further information about how to provide discrepancy notes see Notes and Discrepancies.

Notice: A checking of the required values and their compliance can be done automatically through validation checks if it has been previously defined for the CRF.

3.1.7 Sign a casebook (entire subject record)

The subject's casebook should be signed only when all CRFs in all study events have been marked as complete.

When you sign a casebook, you are approving all CRF data for all study events for the subject. Any changes, including queries answered after signing the subject casebook, will invalidate the signature and require re-signing.

To sign the casebook, the *Sign* icon should appear in the *Actions* column (Figure 17), if not it means that at least an event remains incomplete.

After clicking the *Sign* icon, your user name and password will be asked before allowing you to click *Submit.* To confirm the signing is compulsory to click the *Submit* button.

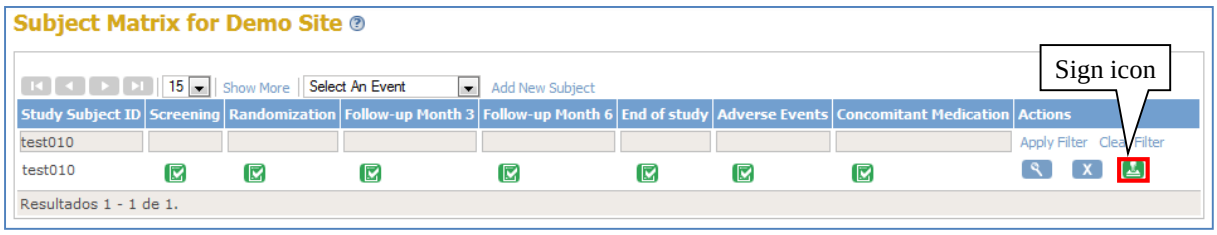


Figure 17

After submitting the signature, the *Subject Matrix* will open showing all signed events (Figure 18).

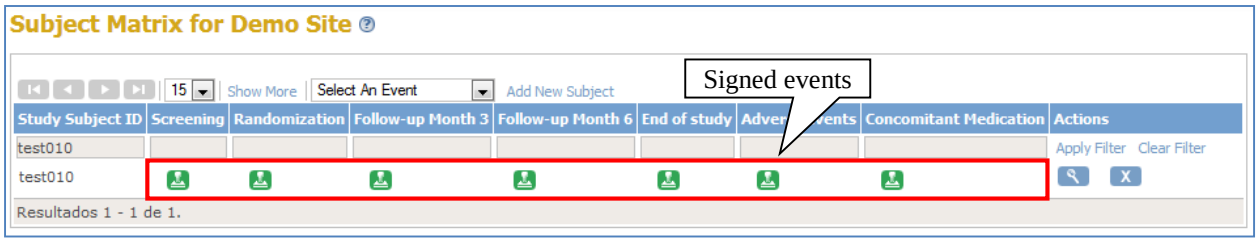


Figure 18

3.1.8 Notes and Discrepancies

The feature *Notes and Discrepancies* allows users to document, communicate, and manage issues about data in clinical trials to facilitate the accuracy and completeness of the data.

There are various situations where you might use *Discrepancies Notes*, for example:

- To explain why a required item has been left empty.
- To flag an item as incomplete or when it has an unexpected value.
- If validation checks are requested by the Sponsor, automatic Discrepancy Notes will be created when CRFs with data errors are saved.

After creating a Discrepancy Note another user, like a Monitor, will review and reply it to help to resolve the issue.

The original note is referred to as the 'parent note'. Responses to the original note are referred to as 'child notes'. The thread of a single parent note with child notes under it is referred to as one Discrepancy Note.

Once a Discrepancy Note has been created, it cannot be deleted. If it has been created by mistake, a common practice is to add a new child note with *Closed* status, explaining that it was a mistake.

Discrepancy Notes allow you many possibilities. In following sections you will find a review and explanation about their basics features. You will also find a specific section: Working with individual Discrepancy Notes, with Syntax for Science's recommendations to manage properly the most important Discrepancy Notes.

3.1.8.1 Discrepancy Notes types and status

Depending on the purpose, OpenClinica has different Discrepancy Note types as follows:

- **Failed Validation Check**: is used for data that does not comply with expected values. When validation checks have been created, OpenClinica will automatically generate it. Nevertheless, *Failed Validation Checks* can be also created by the Investigator.
- **Query**: is used to request further information about data provided for an item. Only the Monitor can create and assign the *Query* to a specific user, and also send a notification email. Investigator cannot create a *Query* but should review and reply it.
- **Reason for Change**: is used to explain the reason for changing a data item after a CRF has been marked complete. It can only be created by an Investigator.
- **Annotation**: is used to make comments or provide further information about the data to the Monitor. It can only be created by an Investigator.

The status of a Discrepancy Note indicates what has been done and what should be done next. The different statuses are:

- **New** : A new discrepancy note has been created and requires a response.
- **Updated** : Information has been added to the note thread, but it requires further follow up or additional information.
- **Resolution Proposed** : Investigator answers a Discrepancy Note (fixing a data or explaining why the existing data is correct) in a child note and the response is awaiting to be reviewed by a Monitor.
- **Closed** : The final action. A Monitor has reviewed the proposed resolution to the discrepancy note, and has found that the response is satisfactory.

  Only a Monitor can mark a Discrepancy Note as Closed. When a note has a status of Closed, it cannot be changed in any way.
- **Not Applicable** : No action or resolution is required.

The Discrepancy Note type determines what statuses are allowed:

	Use	Status
Failed Validation Check	Used for data that does not comply with expected values.	New, Updated, Resolution Proposed, Closed
Query	Used to request further information about data provided for an item.	New, Updated, Resolution Proposed, Closed
Reason for Change	Used to explain the reason for changing a data item after a CRF has been marked complete.	Not Applicable
Annotation	Used to make comments or provide information about the data to the monitor.	Not Applicable

Table 1

Notice: When there is more than one Discrepancy Note associated with a CRF item, only the most urgent status is shown.

3.1.8.2 Discrepancy Note creation

Discrepancy Notes can be created manually by an Investigator or automatically by OpenClinica:

- **Manually-Created Discrepancy Notes** (during data entry or when reviewing a CRF)

When entering data or reviewing a CRF item, click the *Add Discrepancy Note* icon next to the item. The *Add Discrepancy Note* window opens for that item and you can proceed to complete the fields.

Some available options are based on the circumstances under which the Discrepancy Note has been created. The most common Manually-Created Discrepancy Notes for an Investigator are Annotations, which are used to make comments or provide further information to the Monitor.

Once a manually Discrepancy Note has been added, follow the next steps:

1. Complete the Description and Detailed Note fields.
2. Select the Type from the drop-down list. The list includes only the appropriate options.
3. Select the Status for the Discrepancy Note from the drop-down list. The list includes only the appropriate options.

Finally, click *Submit*. A message will replace the contents of the window, indicating the note was created. In the CRF page, the flag icon for the item will change to a color reflecting the status of the Discrepancy Note.

Notice: When there are multiple Notes associated with an item and you want to create new one for that item, click the flag icon of the existing Note and then click *Begin New Thread*. Complete the process as a *Manually-Created Discrepancy Note*.

- **Automatically-Created Discrepancy Notes** (as part of data validation)

When entering data into a CRF, if you do not provide a value for a required field or you provide a wrong value and click *Save*, OpenClinica first prompts you to provide or correct it (Figure 16). If you do not provide or correct a value after that prompt and click *Save* again, OpenClinica will save the CRF and automatically will create a Failed Validation Check Discrepancy Note for you to complete or correct (Figure 19). For further information go to section Working with individual Discrepancy Notes.

If you try to change an item in a CRF which does not have any previous Discrepancy Note and which have been marked as complete, OpenClinica first prompts you to provide a Reason for Change Discrepancy Note. By clicking the icon *Add Discrepancy Note* next to the item, OpenClinica automatically creates a Reason for Change Discrepancy Note for you to fill out.

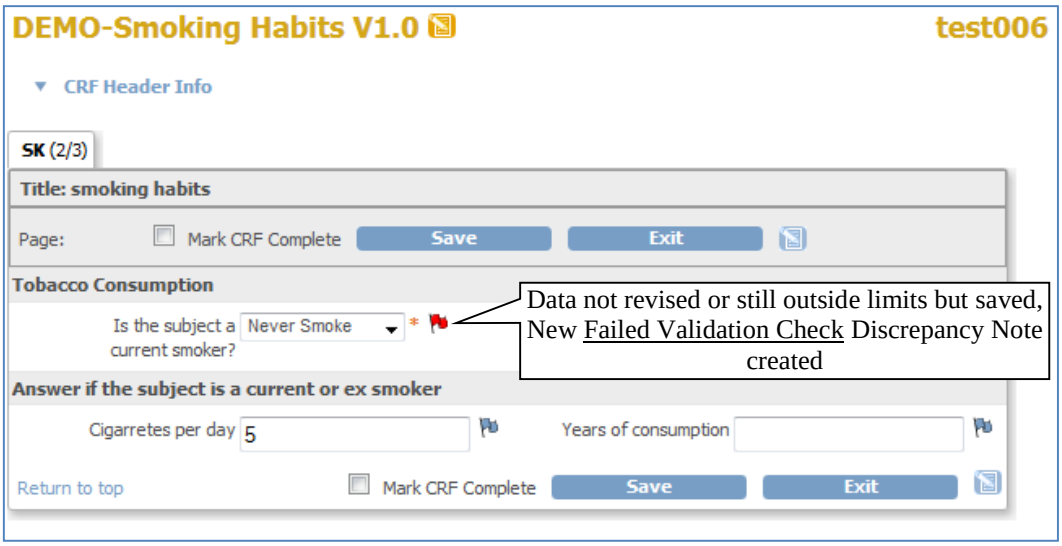


Figure 19

3.1.8.3 View, update and manage a Discrepancy Note

There are different ways to view a Discrepancy Note:

1. Click *Notes & Discrepancies* in the navigation bar to view the table of all Notes and Discrepancies.
2. In the Homepage click the blue link *"Notes & Discrepancies Assigned to Me"* to see only the Notes and Discrepancies assigned to you.
3. Go to the CRF page that contains the Discrepancy Note and click over the related flag icon.

We recommend using the first option where a table summarizes all Notes and Discrepancies for the current study or site (Figure 20) containing among others:

- Entity Name: refers to the CRF item that is associated with the Note
- Entity Value: is the value recorded in the CRF for the item
- Description: is the definition provided in the Discrepancy Note
- Assigned User: to whom the Discrepancy Note is assigned (if anyone)

From the Notes and Discrepancies table you can:

- **View Details for a Note:** To view all details of a single Discrepancy Note, click the *View* icon in the *Actions column* (Figure 20).
- **View CRF and Note Details:** In the *Actions column*, click the *View within Record* icon. OpenClinica opens the Discrepancy Note window (Figure 21) as well as the CRF page.

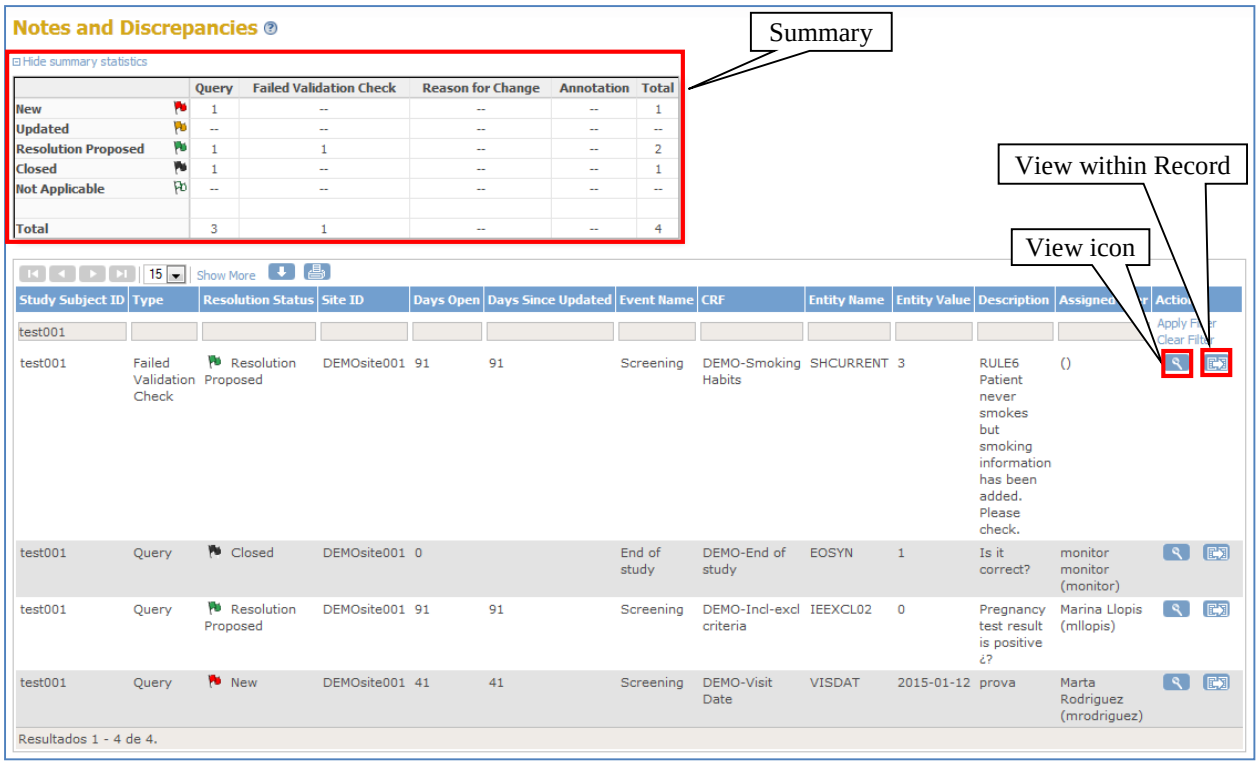


Figure 20

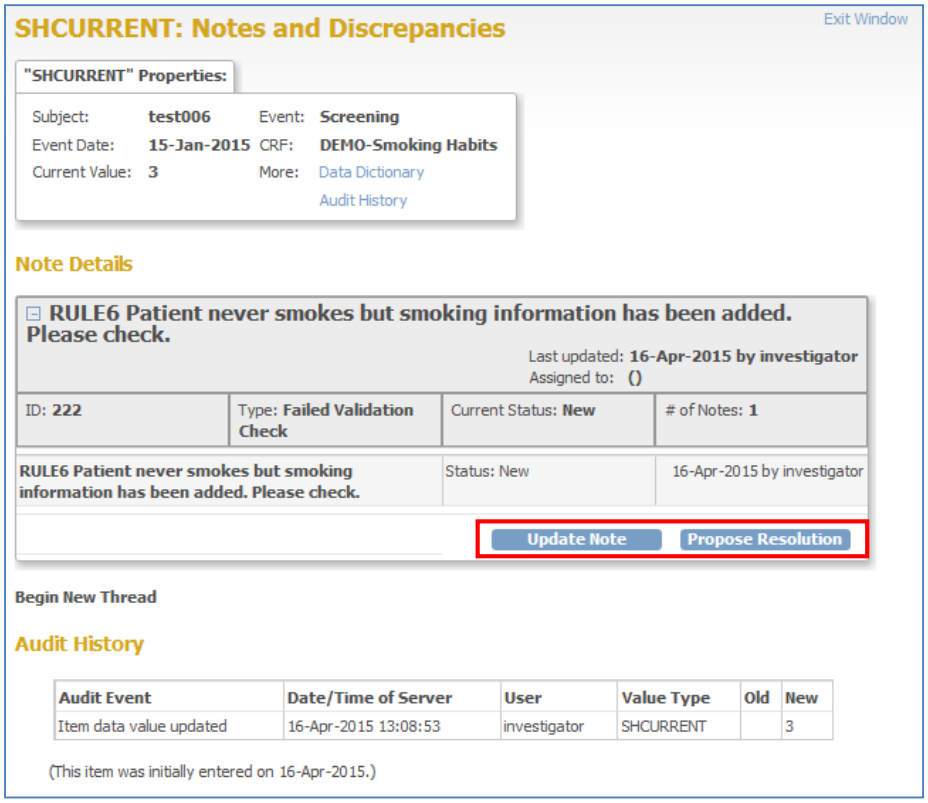


Figure 21

To update any Discrepancy Note:

- Click *Update Note* (Figure 21): to add information that needs to be reviewed.
- Click *Propose Resolution*: to add information that allows the Note to be closed.

In both cases, the Discrepancy Note will include the information you have added as a new child Note in the thread (Figure 22). In the CRF and in the Notes and Discrepancies table, the color of the flag icon will change to reflect the new status (Figure 23).

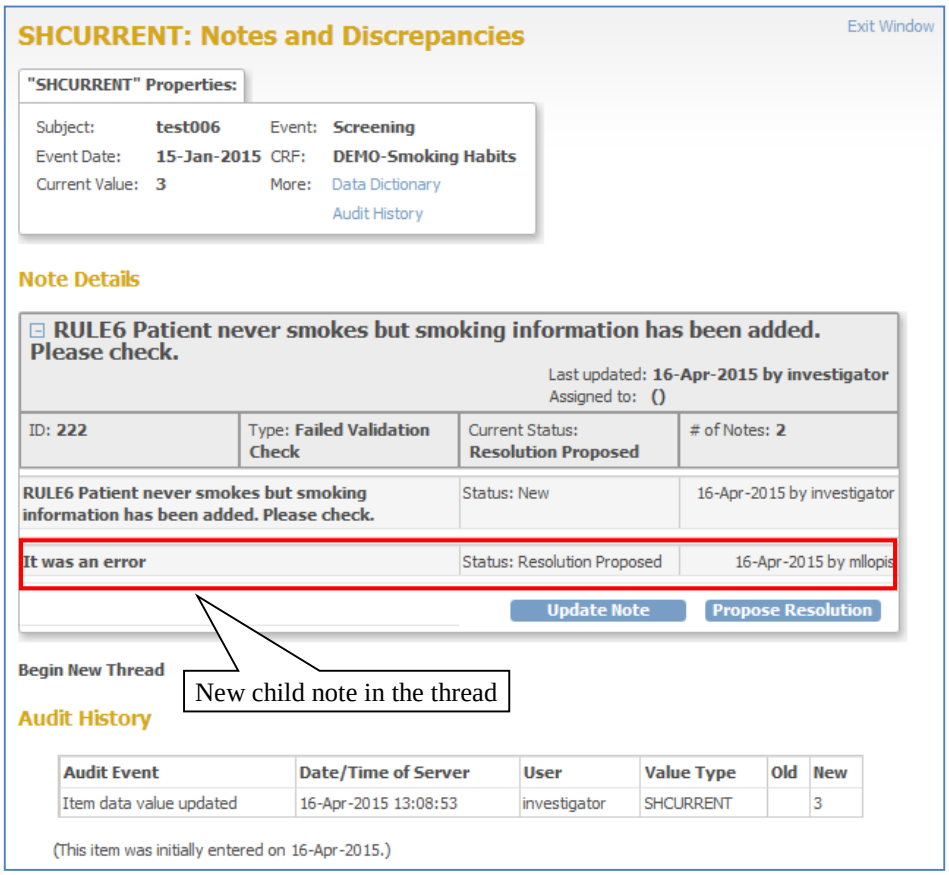


Figure 22

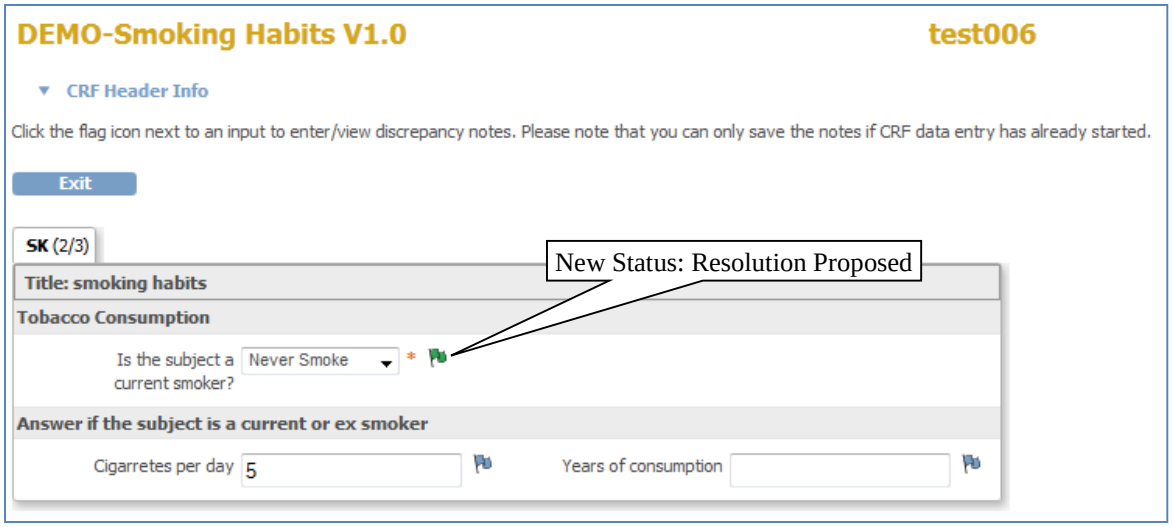


Figure 23

3.1.8.4 Working with individual Discrepancy Notes

This section explains the workflow for a *Failed Validation Check* and a *Query* dividing the process in two phases: creation and resolution.

3.1.8.4.1 First phase: creation

Creation phase is different for Failed Validation Checks and Queries:

- **Failed Validation Checks** are automatically created as follows:

1. If by mistake you enter wrong data in a CRF, mark the checkbox *Mark CRF Complete*, and click the *Save* button, OpenClinica will not save the data instead will prompts you to correct the mistake (Figure 24).

2. If you correct the wrong data and click *Save* again no Failed Validation Check Discrepancy Note will be create.

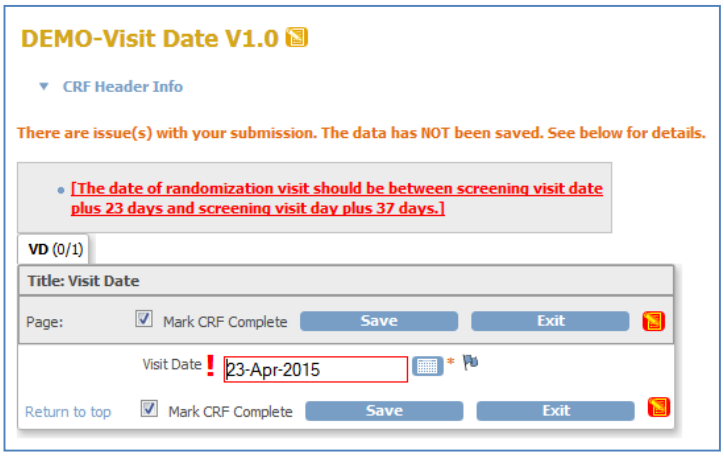


Figure 24

3. If you do not correct the wrong data, or if you do it but continues being incorrect and click *Save* again, OpenClinica will save the data and automatically will create a Failed Validation Check Discrepancy Note (Figure 25).

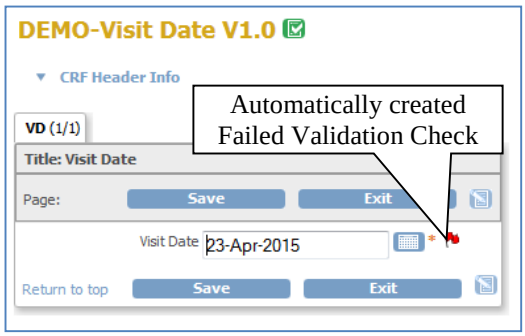


Figure 25

Failed Validation Check creation workflow:

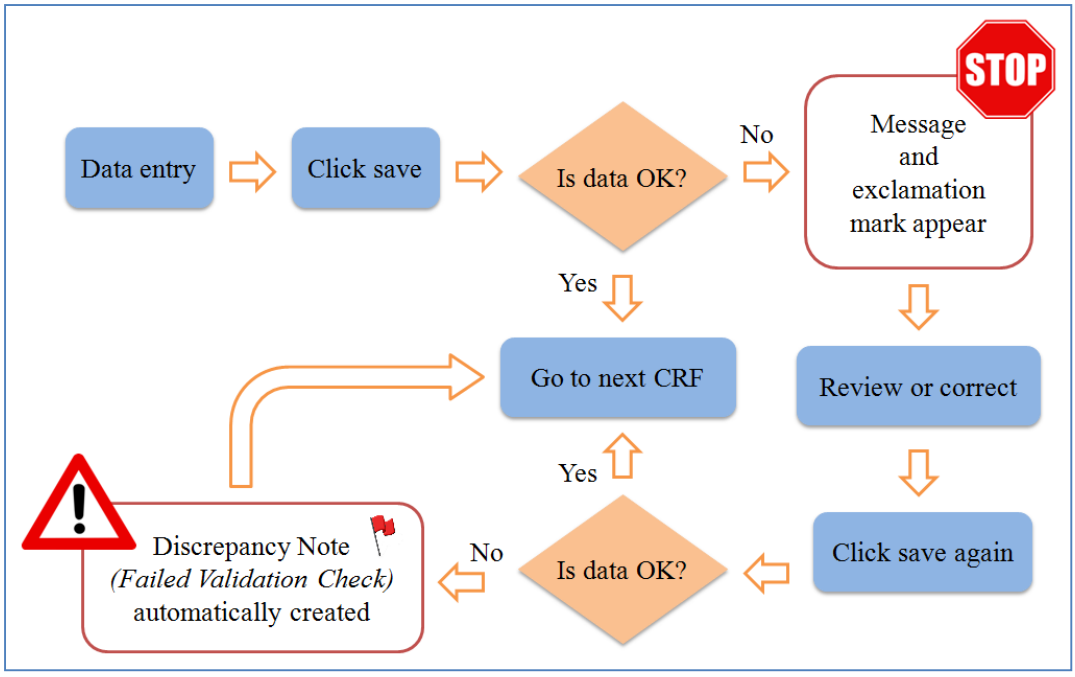


Figure 26

- **Queries** are manually created as follows:

When a Monitor reviews CRF data and needs further information about it, a Query will be manually created and assigned to the Investigator in order to request more information (Figure 27).

1. See Discrepancy Note creation to review how to create Query manually.

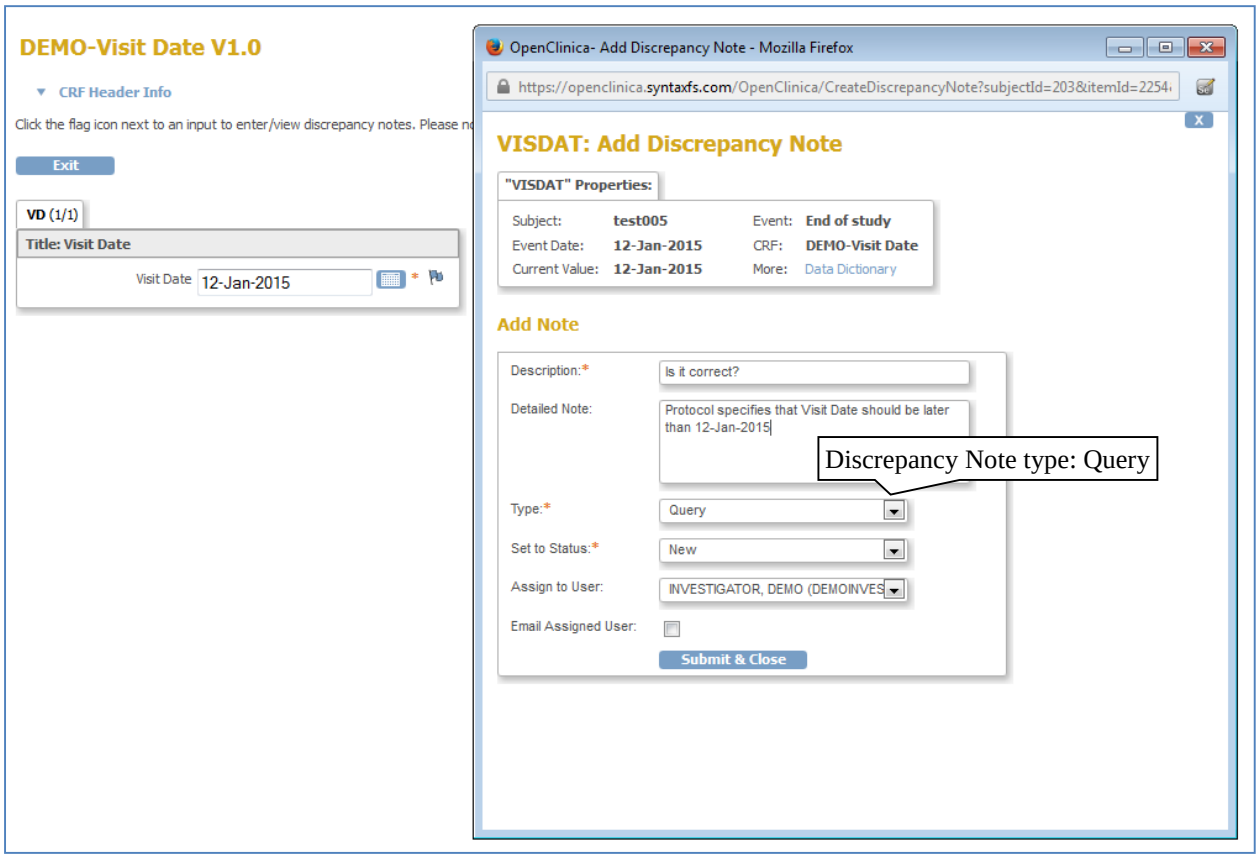


Figure 27

Query creation workflow:

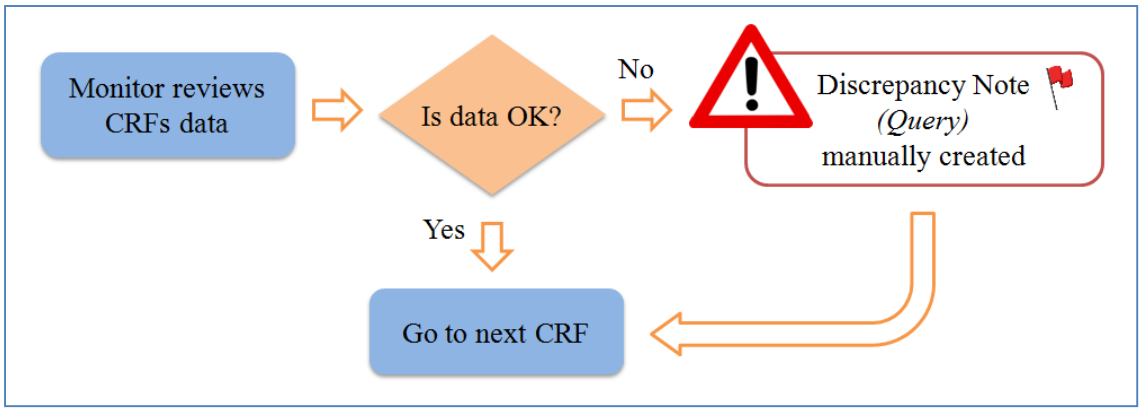


Figure 28

3.1.8.4.2 Second phase: resolution

Resolution phase is the same for both, **Failed Validation Checks** and **Queries**:

1. Review Failed Validation Checks and Queries in the table *Notes and Discrepancies* (navigation bar Figure 2).

2. In the *Resolution Status* column, select *New and Updated* drop-down list and click the *View within Record* icon of the Failed Validation Check or Query you want to correct (Figure 29).

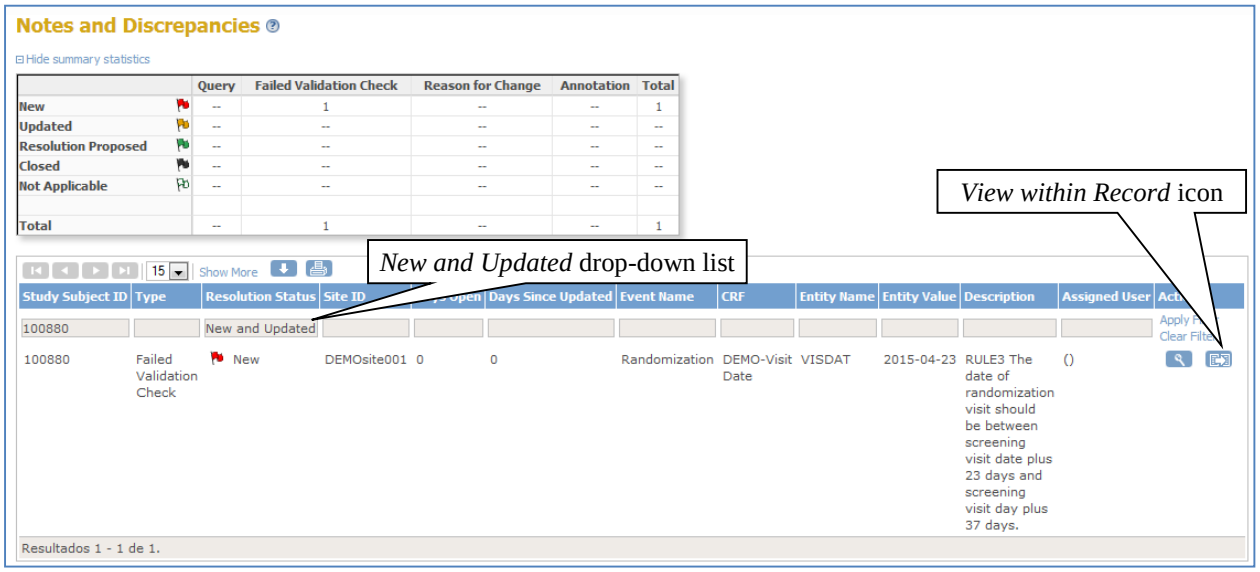


Figure 29

3. OpenClinica will open the *Discrepancy Note window* as well as the *CRF page* of the associated Note, thereby both can be reviewed at the same time (Figure 30).

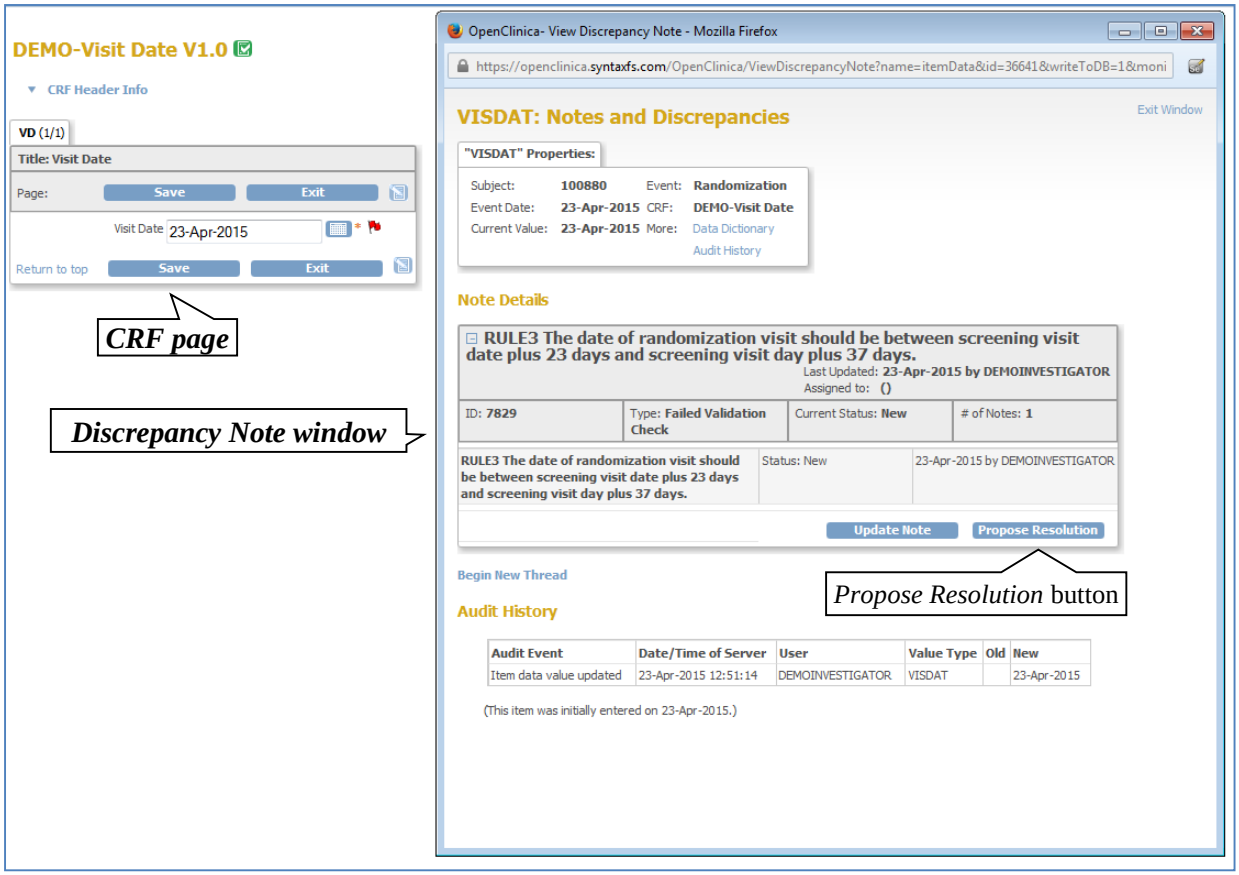


Figure 30

4. After reviewing, two options can be performed:

- **Data are correct and do not need to be modified**: click on the *Propose Resolution* button (Figure 30), complete the *Description* field explaining why data are right, and then click *Submit & Exit* (Figure 31). From that moment proposed resolution can be reviewed by a Monitor.

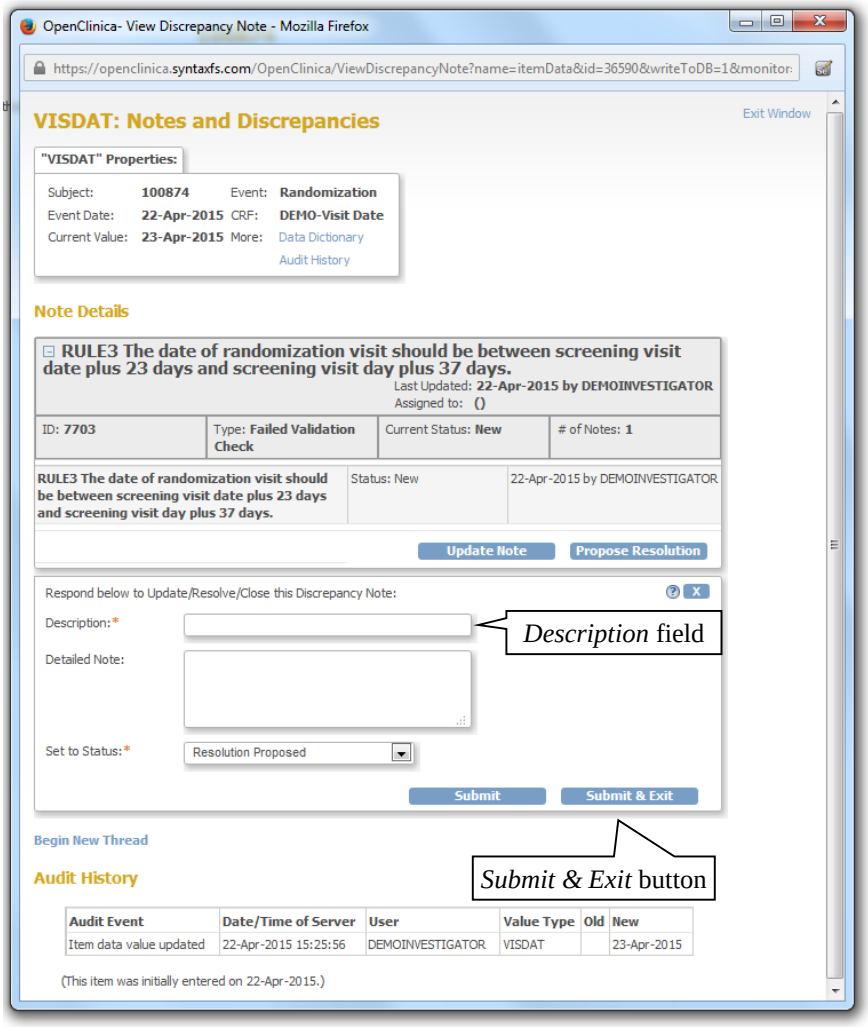


Figure 31

- **Data are incorrect and need to be modified:** close the *Discrepancy Note* window (keeping the CRF page), then modify CRF data, and click *Save*. OpenClinica will notify you about the change in a CRF previously marked as complete (Figure 32).

  Click over the flag to open the *Discrepancy Note* window, and then click on the *Propose Resolution* button (Figure 33).

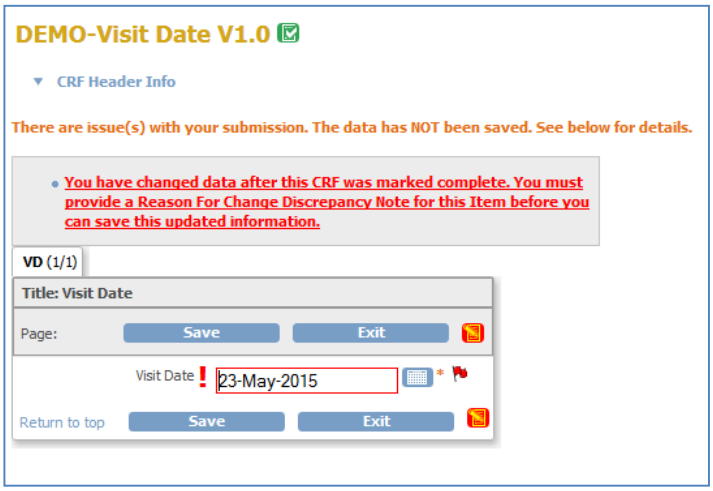


Figure 32

Complete the *Description* field confirming that mistaken data have been corrected, and click *Submit & Exit* (Figure 31).

Finally, click *Save* to finish.

Once saved, the *Failed Validation Check* will change its status as *Resolution Proposed* (green flag Figure 34).

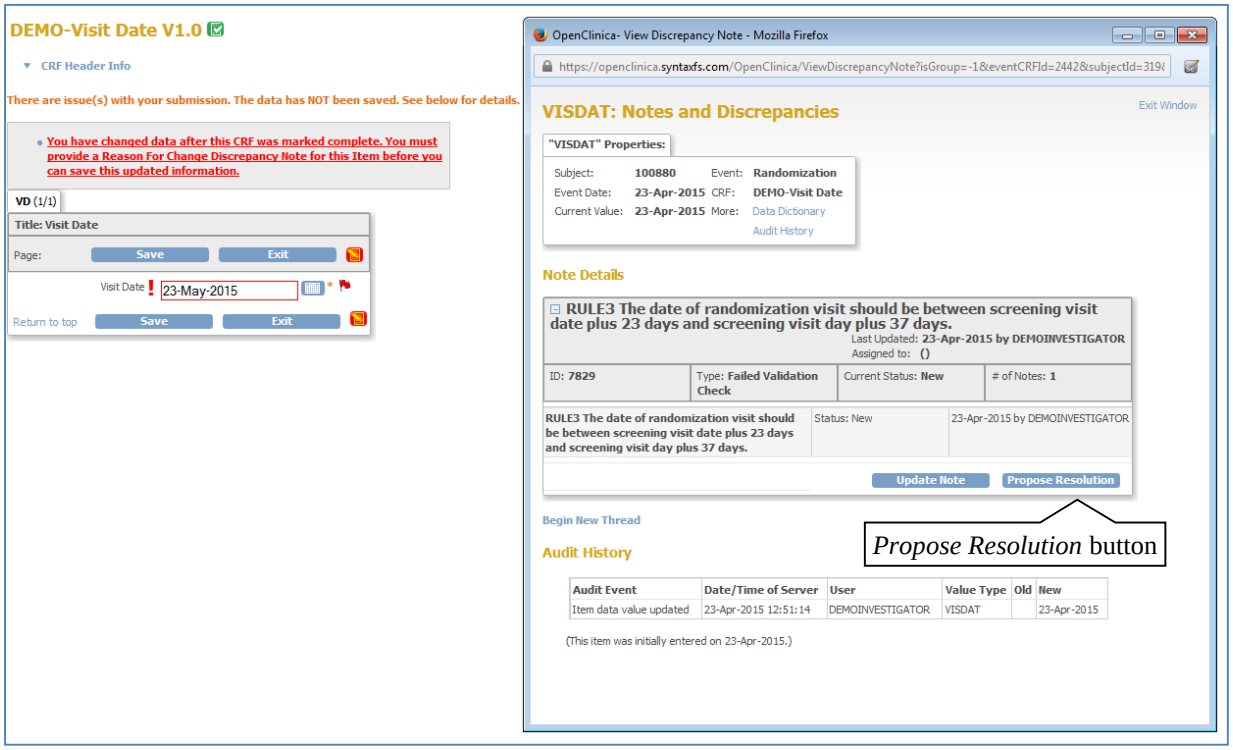
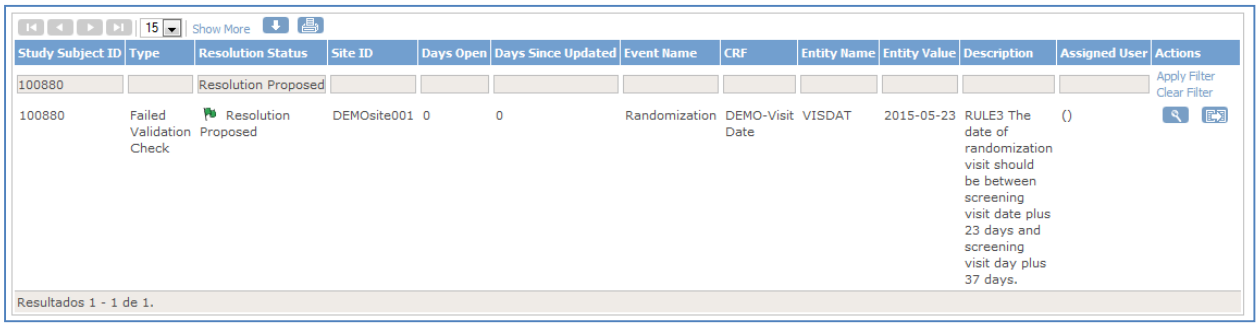


Figure 33



Study Subject ID	Type	Resolution Status	Site ID	Days Open	Days Since Updated	Event Name	CRF	Entity Name	Entity Value	Description	Assigned User	Actions
100880		Resolution Proposed										Apply Filter Clear Filter
100880	Failed Validation Check	Resolution Proposed	DEMOsite001	0	0	Randomization	DEMO-Visit Date	VISDAT	2015-05-23	RULE3 The date of randomization visit should be between screening visit date plus 23 days and screening visit day plus 37 days.	()	

Resultados 1 - 1 de 1.

Figure 34

Failed Validation Checks and *Queries* resolution workflow:

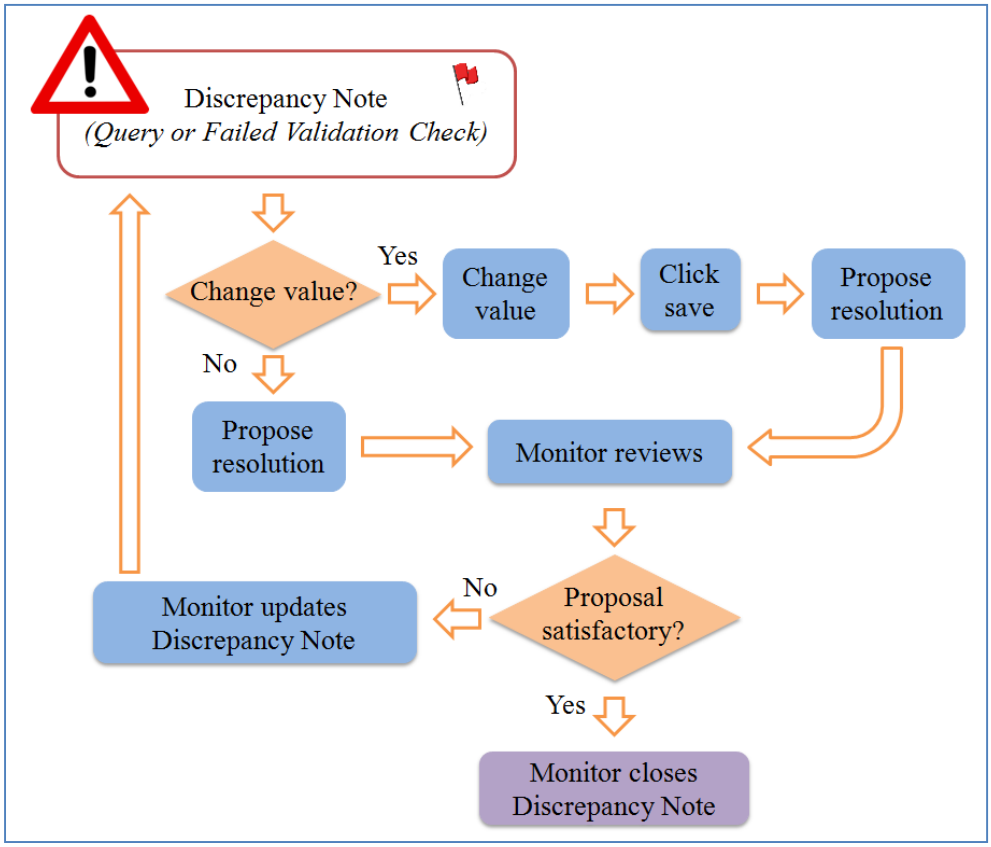


Figure 35