TrialDriver

Visual Data Management for Global Clinical Trials

Electronic Investigator Forms

E-CRFs for on-site data entry and global data transmission

User Guide

Version 3.5

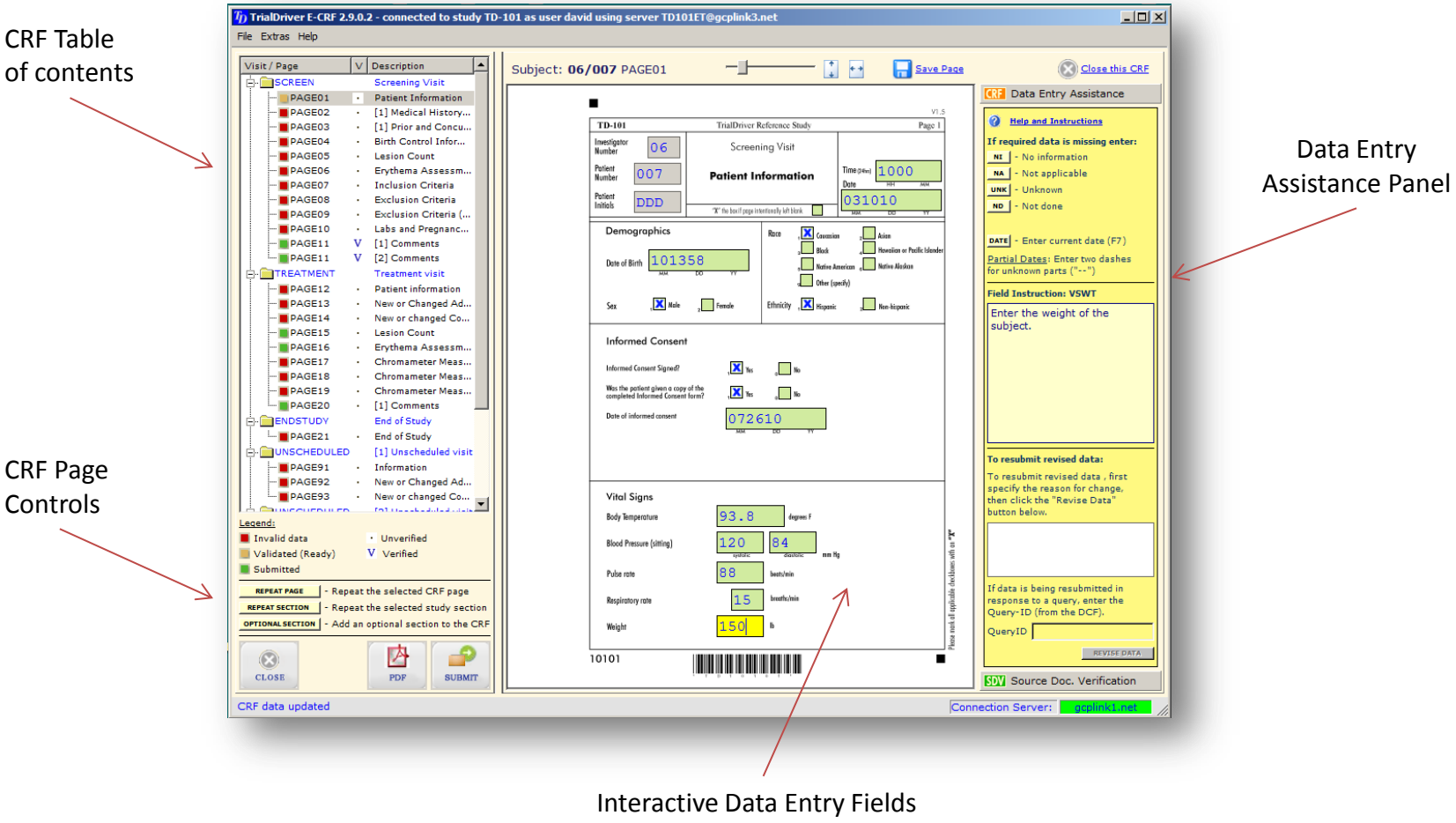
Table of Contents

www.trialdriver.com

TrialDriver eCRF - Table of Contents

Introduction

TrialDriver E-CRF were conceived to leverage the experience that clinical investigators and monitors already have with paper CRFs. The on-screen metaphor of a paper-based CRF book is maintained throughout. Data is entered into interactive CRF fields and is validated at every keystroke - color coding displays the validation status. Data is entered and saved continuously online. When ready, it is submitted to the study database in a batch mode. PDF printouts of CRF pages, patient CRF books and blank CRFs are all available on demand. Source Document Verification can be performed remotely online or on-site against printed copies of the electronic forms in the same way as in any other, paper-based study. Full 21CFR11 compliant audit trails are maintained locally and on the central study server.



Getting Started

TrialDriver E-CRFs are stored on a central study server, which are accessed using the TrialDriver E-CRF client application. Before starting work with a TrialDriver E-CRF, you need the following

- The TrialDriver E-CRF client application must be installed on a PC running Windows XP, Vista or 7
- The PC should have a broadband internet connection. *(Note: If behind a Firewall, port 3306 should be open)*
- The PC can optionally be attached to a printer if E-CRF pages will be printed and stored in the patient files

Standard PC with:

- Microsoft Windows XP, Vista, 7
- TrialDriver E-CRF Client Application

Broadband Internet Connection

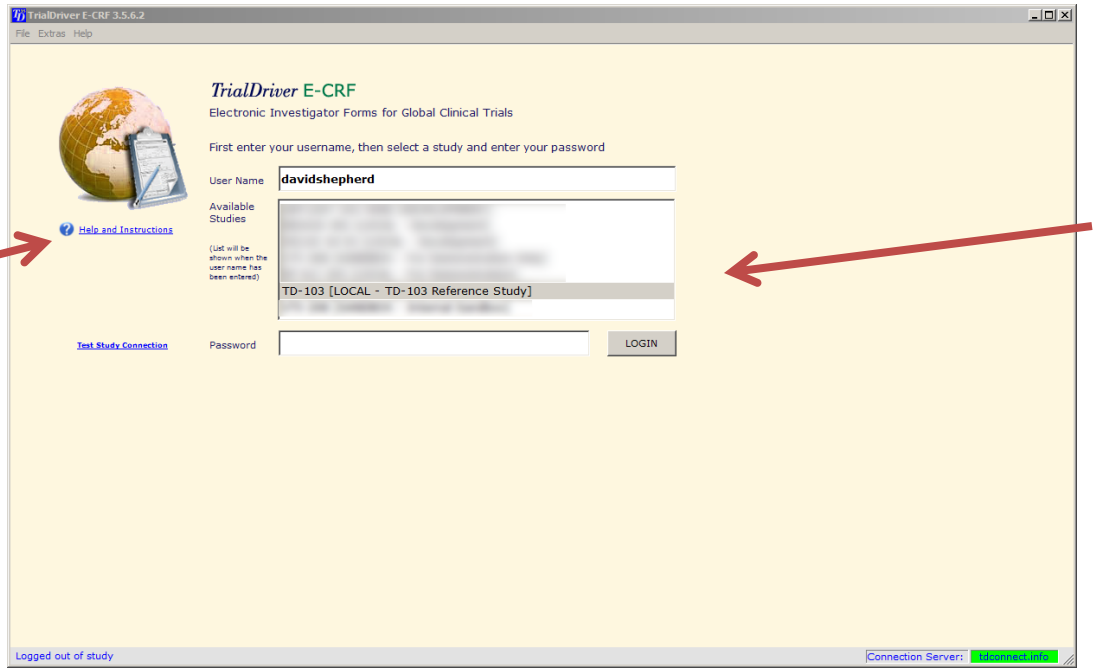
Printer

Logging in to the E-CRF

TrialDriver E-CRFs are password protected. When you launch the E-CRF application via the desktop icon, the first screen will ask you to provide your username and password, which will have been provided to you by the data management team. Based on the user name you provide, you will be presented with a list of studies to which you have access.

IMPORTANT: The TrialDriver E-CRF client requires internet access at all times.

Online help is available in all screens where you see this message



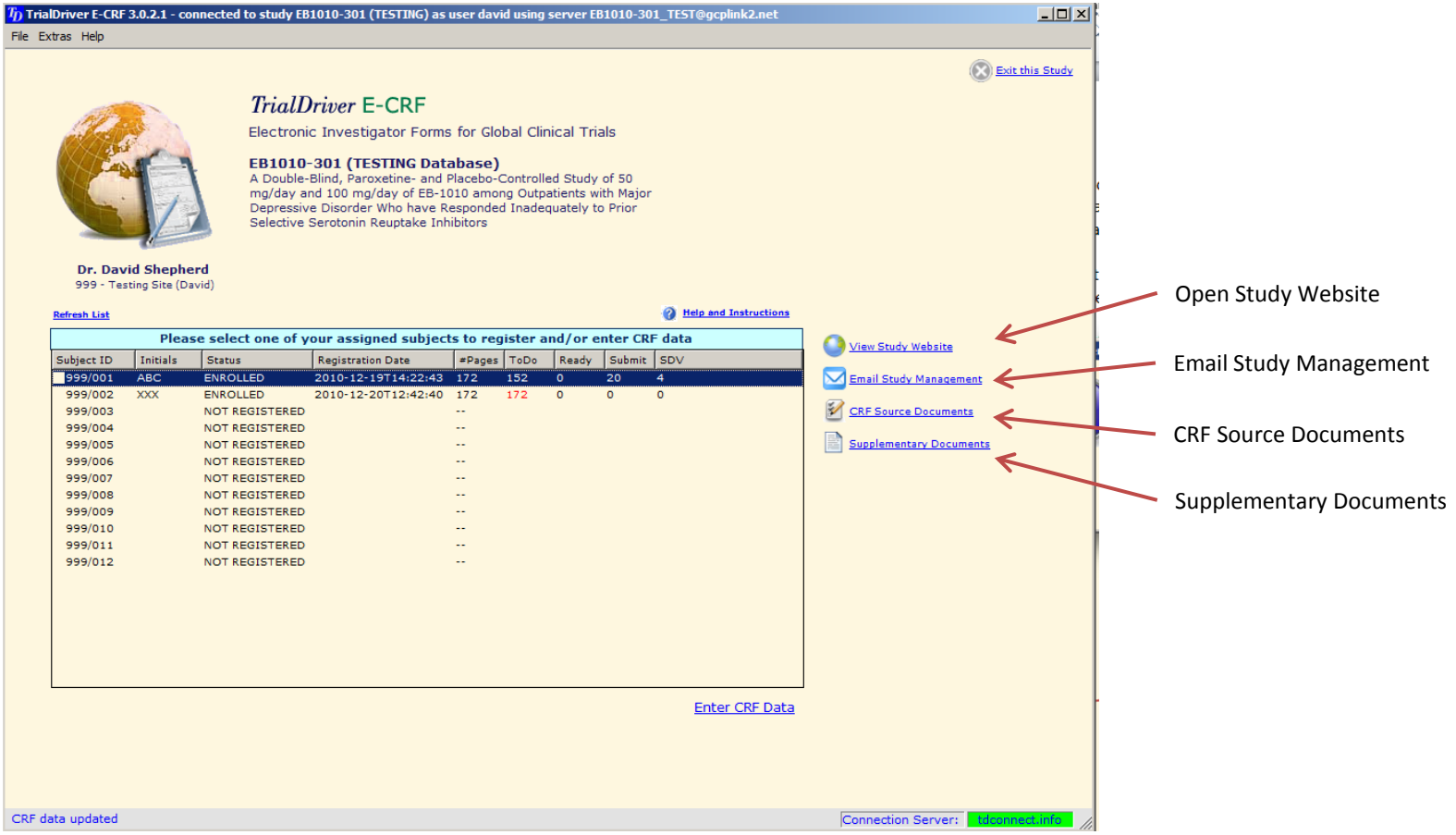
LOGIN TO E-CRF

1. Enter your assigned user name, then
2. Select the study with which you want to work, then
3. Enter your password and click the LOGIN button

If this box is green then your internet connection is good

The Study Main Page

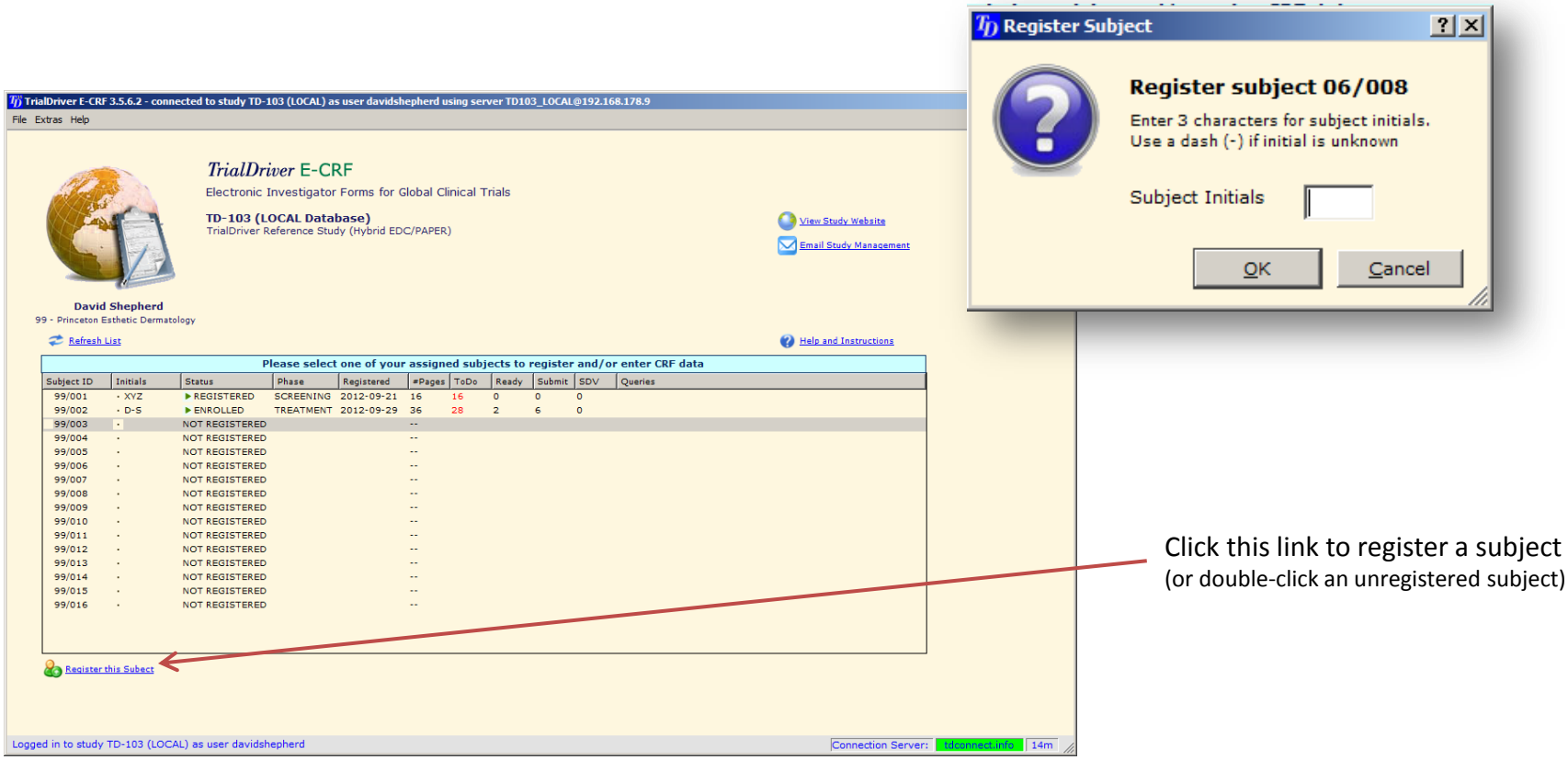
After successfully logging in to the study, you are presented with a list of your subjects. Four additional links provide access to study resources: "*View Study Website*" opens a web page dedicated to study management. "*Email Study Management*" opens your email program. "*CRF Source Documents*" provides access to the source documents for this study, which you can print and fill in prior to entering the data in the E-CRF. "*Supplementary Documents*" provides a list of miscellaneous documents which you can print.



Registering and Enrolling Study Subjects

TrialDriver E-CRFs can include CRF books for multiple subjects. The subjects are pre-configured by data management and are presented in a list. At first all subjects are marked as “NOT REGISTERED”. Select a subject in the list and click the “Register this Subject” link. This will display a dialog in which you will enter the initials of the subject you are registering.

If the study design calls for a screening procedure to be undertaken, the subject status after registration will appear in the list as “SCREENING”, otherwise the subject status will be “ENROLLED”. To complete enrollment for a “Screening” subject, click the “Enroll this Subject” link.



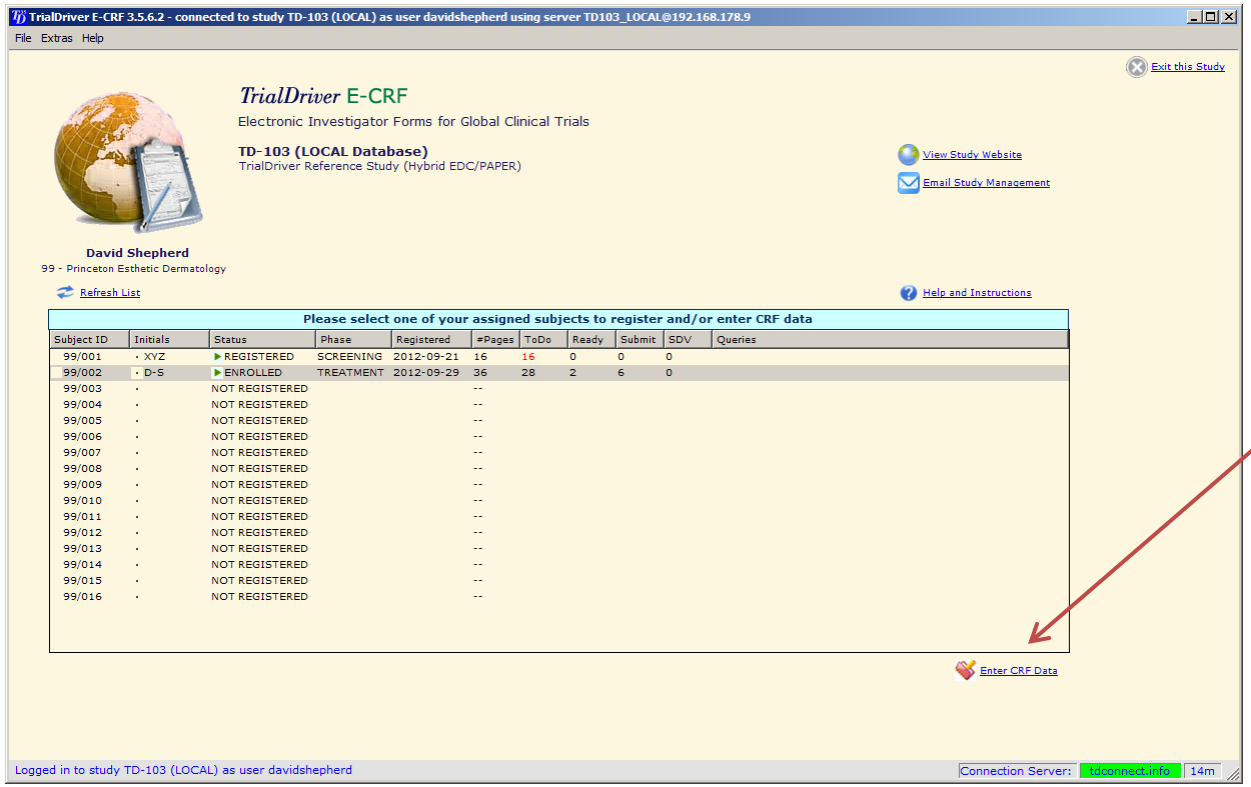
Click this link to register a subject
(or double-click an unregistered subject)

Selecting a Subject for Data-Entry

Select one of your registered or enrolled subjects from the subject list and double-click it, or click the "Enter CRF Data" link.

Don't forget:

- A "SCREENING" subject will only have the CRF screening visit.
- An "ENROLLED" subject will have the entire CRF book.

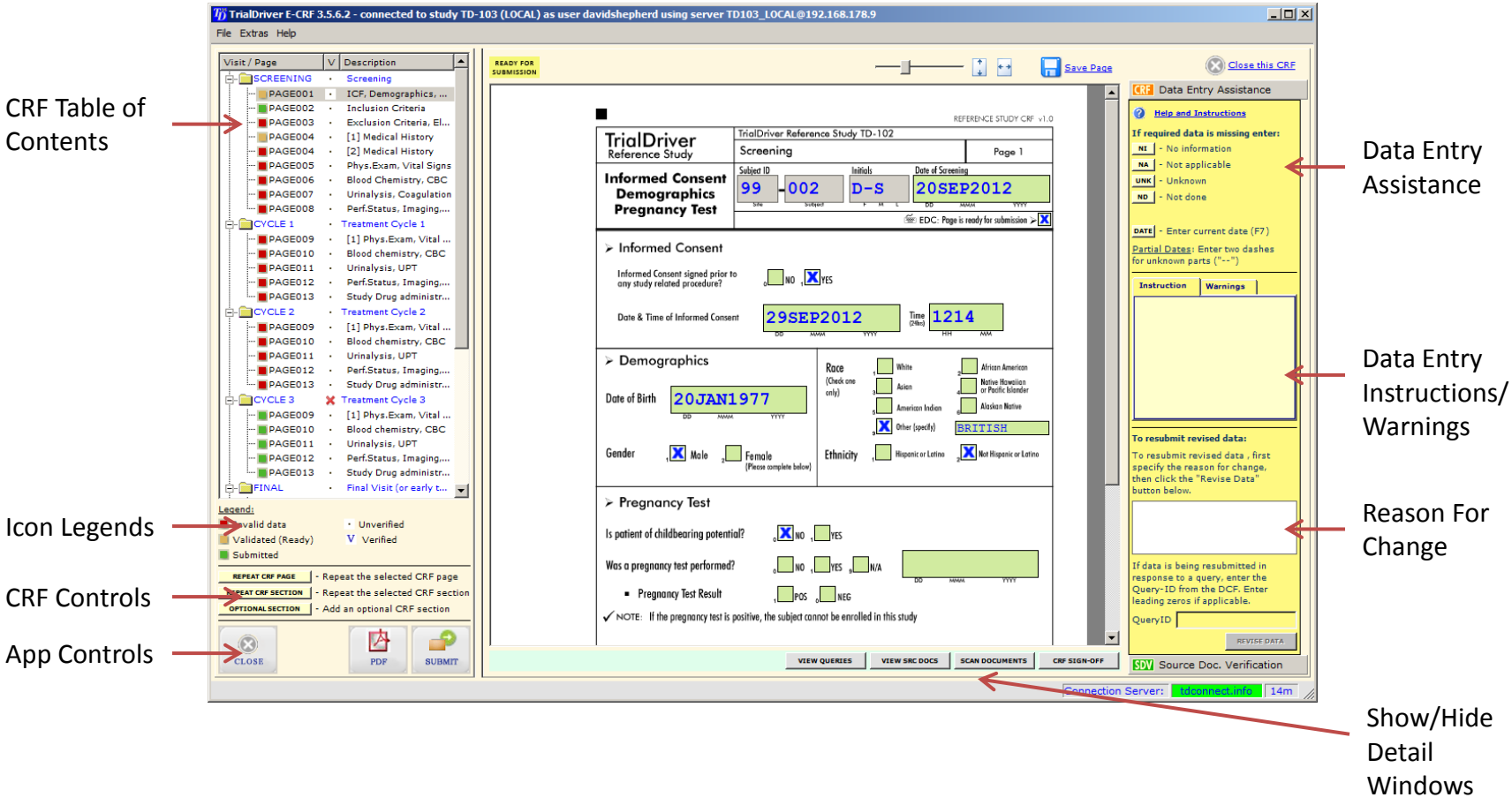


Click this link to perform data entry for a subject subject
(or double-click the subject list entry)

Navigating the E-CRF (Main Screen)

The E-CRF screen is divided into 3 main areas:

- At left is the CRF Table of Contents (TOC). Click an entry in this list to display the corresponding CRF page. Beneath the TOC are controls which allow to create repeating pages and sections, create PDFs and submit CRF data
- In the middle is the image of the CRF page, overlaid with interactive data input fields. Page Zoom controls are at top.
- At right is Data Entry Assistance panel and the "Reason for Change" box, which enables data re-entry for pages which have already been submitted.

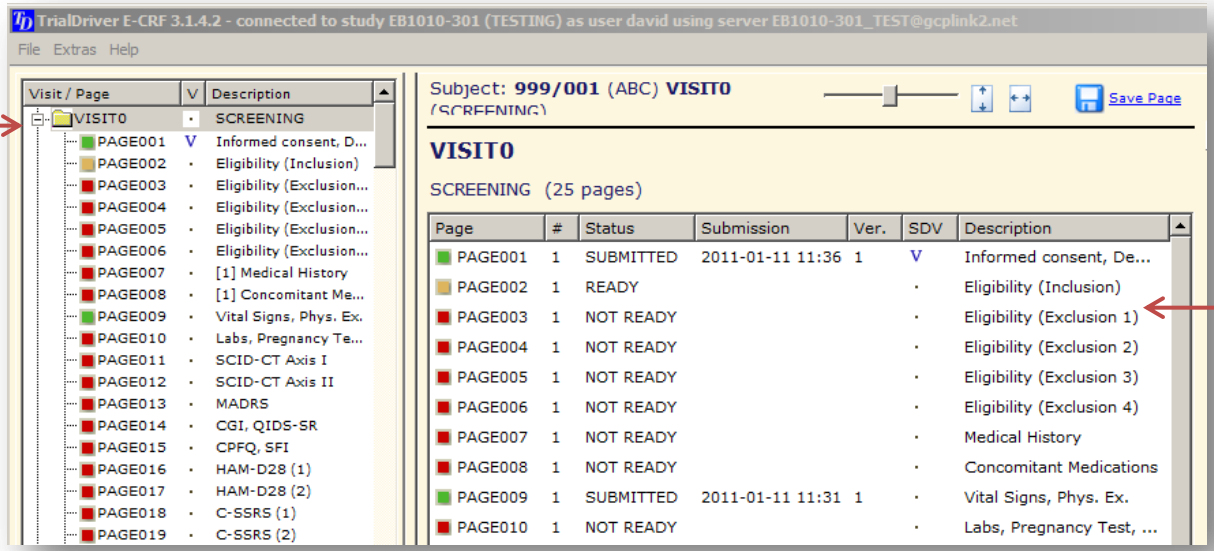


Navigating the E-CRF (Visit Summaries)

Clicking on a Visit item in the E-CRF Table of Contents displays a Visit Summary

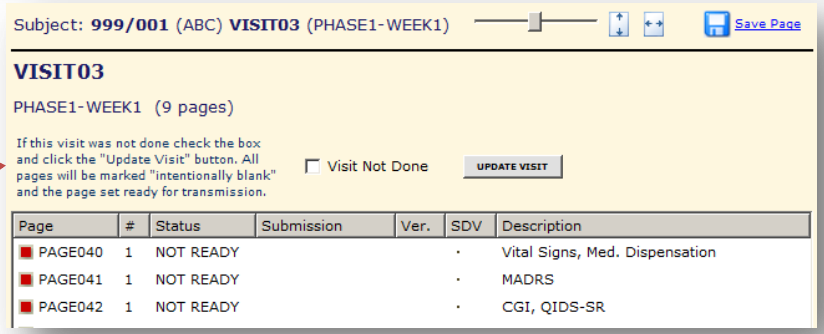
- The list display the page name, page status, submission and SDV details and the page description.
- Some visits (but not all) are allowed to be marked “Not Done” – in this case extra controls will appear on the visit summary sheet. (if a subject terminates early, this can be useful to mark all visit pages ‘Not Done’ in one operation)

Click a Visit item in the Table of Contents to display the summary sheet

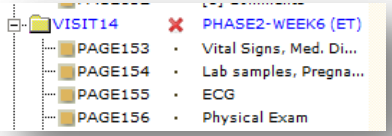


Double-Click a page item to navigate to that page

If the visit is allowed to be ‘Not Done’, extra controls appear on the summary sheet



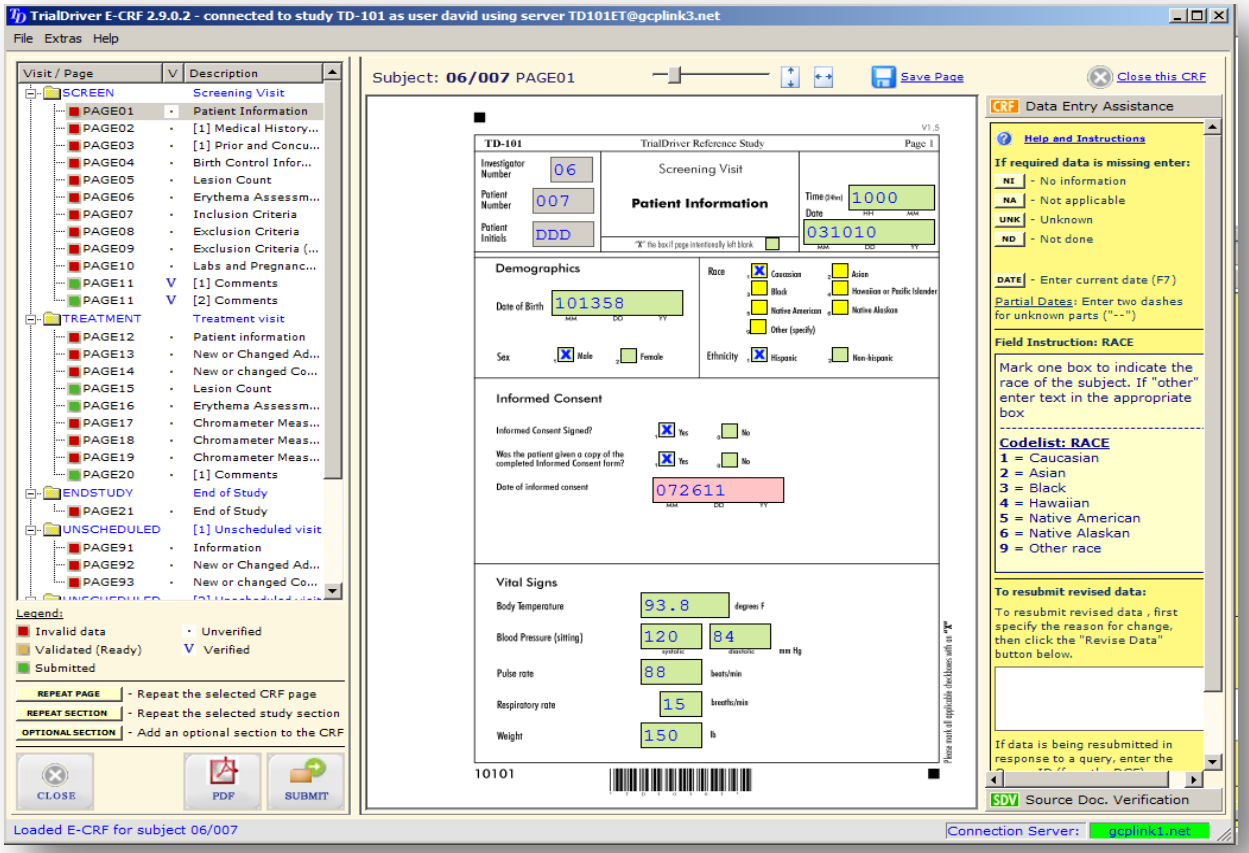
If a visit has been marked ‘Not Done’, a red cross appears next to the visit name



Entering Data into the E-CRF (basics)

- Click in an interactive data field to activate it. The active field is colored YELLOW.
- GREEN colored fields contain valid data, RED colored fields are invalid
- GREY colored fields are Read-Only
- Use the TAB and BACK-TAB key to jump from one data field to the next or previous one.
- Data are entered into TEXT fields and CHECKBOX fields.

NOTE: Page data are saved to the study server whenever you change page or exit the E-CRF. If you want to save data more frequently, click the "Save Page" link

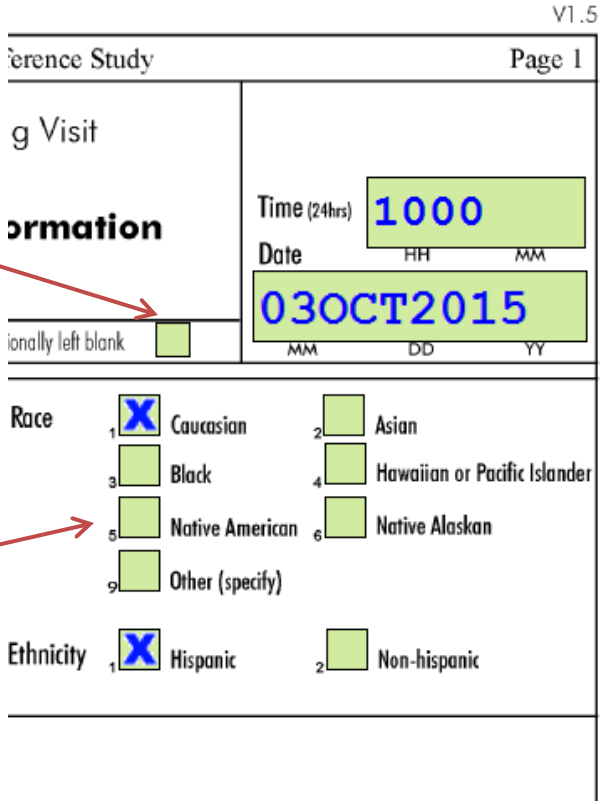


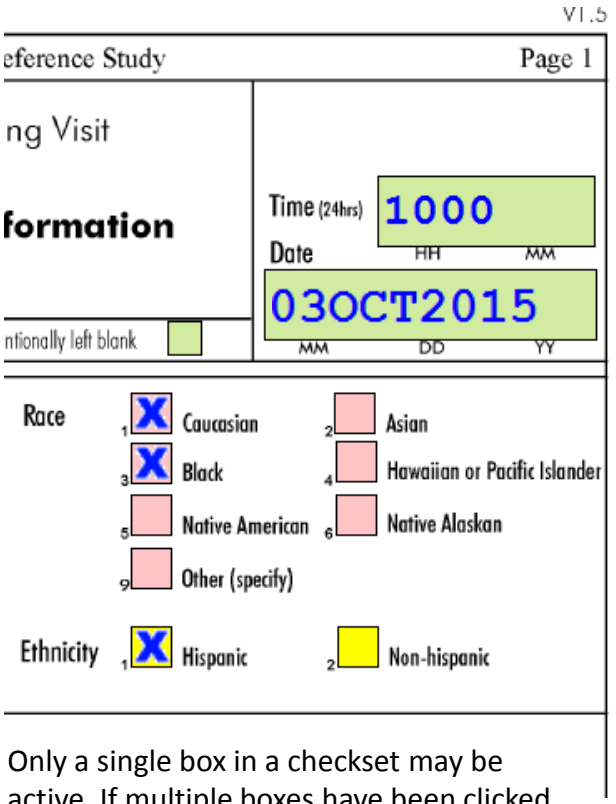
Entering Data into the E-CRF (Checkboxes and "Checksets")

- There are two types of data entry field: Text Entry and Checkbox Entry.
- There are two flavors of checkbox: Single checkboxes and sets of checkboxes (checksets)
- To check or uncheck a box with the mouse, just click in it
- To check a box using the keyboard:
  - For a single checkbox, the SPACE key will toggle the box on or off
  - For a set of checkboxes ("checkset"), hitting the number key displayed next to the box will activate that box

A single checkbox can be toggled by clicking in it, or by pressing the SPACE key

A box in a checkset can be activated by clicking in it, or by pressing the key corresponding to the number printed next to the box

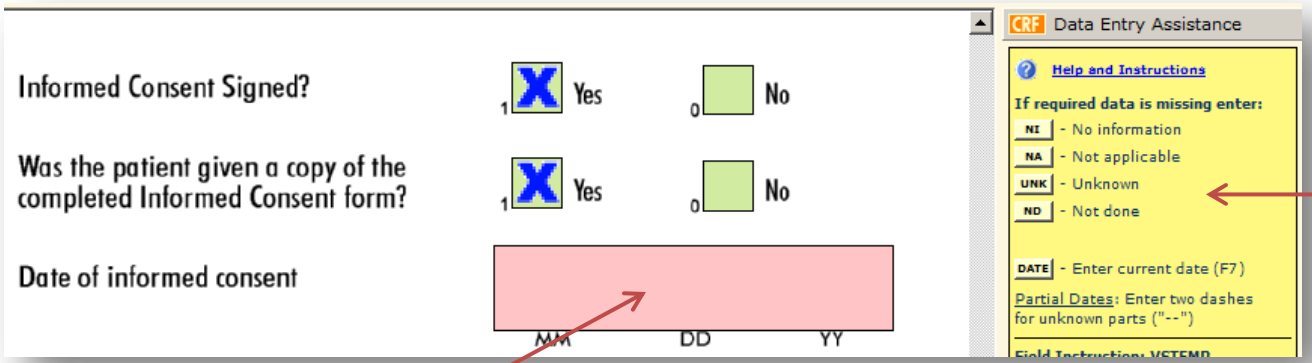




Only a single box in a checkset may be active. If multiple boxes have been clicked, the checkset is displayed in **RED** color, indicating invalid data

Entering Data into the E-CRF (Missing Data)

If a field is empty and displayed in **RED**, this means that the field may not be empty. If however you have no data for this field, then you must indicate this by choosing one of the codes which indicate missing data. There are four such codes which are listed in the Data Entry Assistance area at the right of the screen. Enter the code into a text entry box or, if the field in question is a checkbox, click the appropriate button in the assistance area.



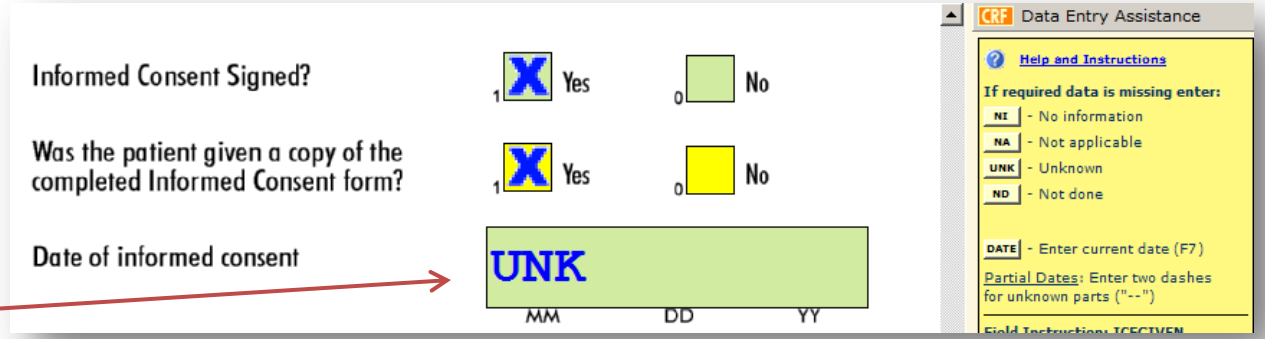
The "missing data" codes are listed in the data assistance area. They are:

NI - No Information
NA - Not Applicable
UNK - Unknown
ND - Not Done

Enter the code text into a text box, or click the button for the appropriate code

This field is displayed in **RED** because it may not be left empty. So long as any field on a page is red, that page cannot be submitted to the study server.

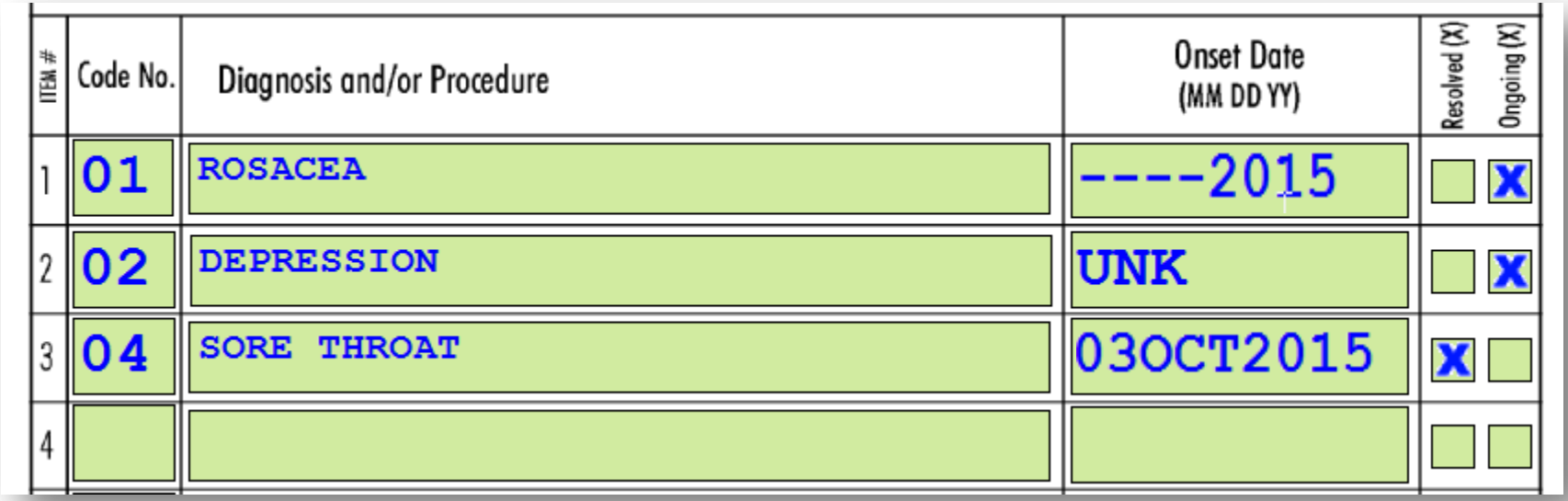
If no data is available for the field, enter one of the "missing data" codes into the box, which will turn the field green



Entering Data into the E-CRF (Partial Dates)

Sometimes you will not be able to provide complete dates.

- If you know the year, but the day and/or month are missing: Enter two dashes for the missing parts
- If the date is completely unknown: Leave the field blank or enter UNK



ITEM #	Code No.	Diagnosis and/or Procedure	Onset Date (MM DD YY)	Resolved (X)	Ongoing (X)
1	01	ROSACEA	----2015		X
2	02	DEPRESSION	UNK		X
3	04	SORE THROAT	03OCT2015	X	
4					

Entering Data into the E-CRF (Repeating Pages and Sections)

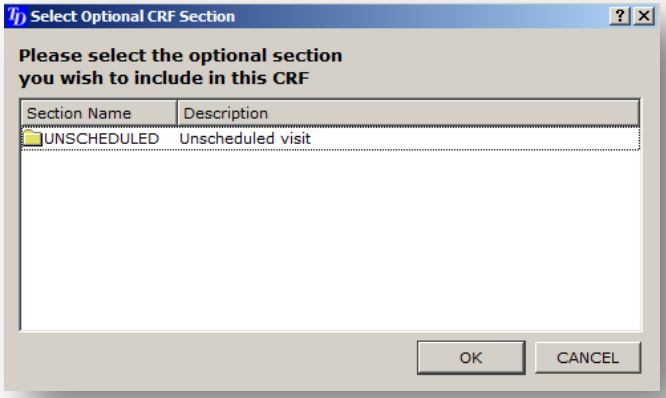
Some pages in a CRF are designated as “repeating pages”. Such pages are typically “logging” pages such as Medical History, Concomitant Medications and so on. If you need more entries than will fit on a single page:

1. Select the page you are interested in from the Table of Contents
2. Click the “REPEAT PAGE” button

Similarly, some studies may have complete sections (visits) which repeat an indeterminate number of times. To create a new repeating section:

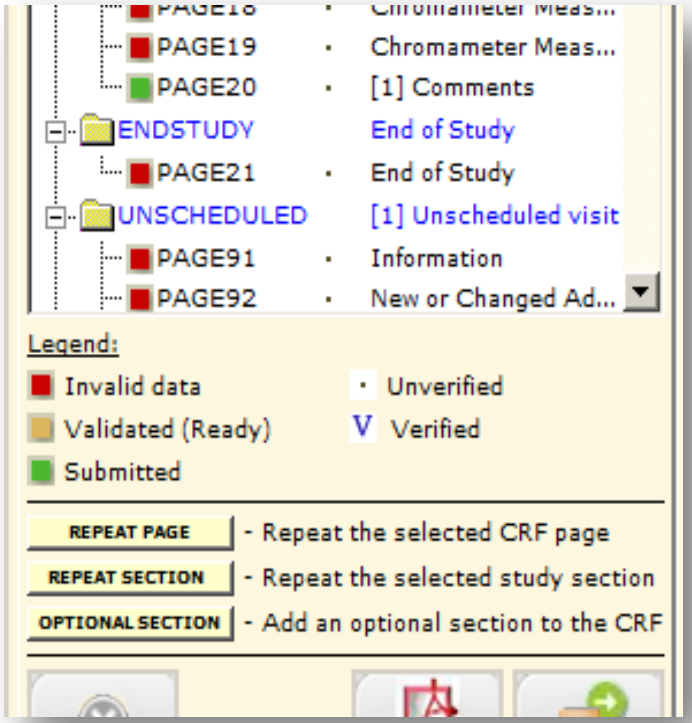
1. Select any page in the section you are interested in
2. Click the “REPEAT SECTION” button

Some studies may contain optional (or unscheduled) sections which do not automatically appear in the subject CRF. To include such a section, click the “OPTIONAL SECTION” button. This will open a selection list containing all such sections which are defined for the current study.



Optional Sections Dialog

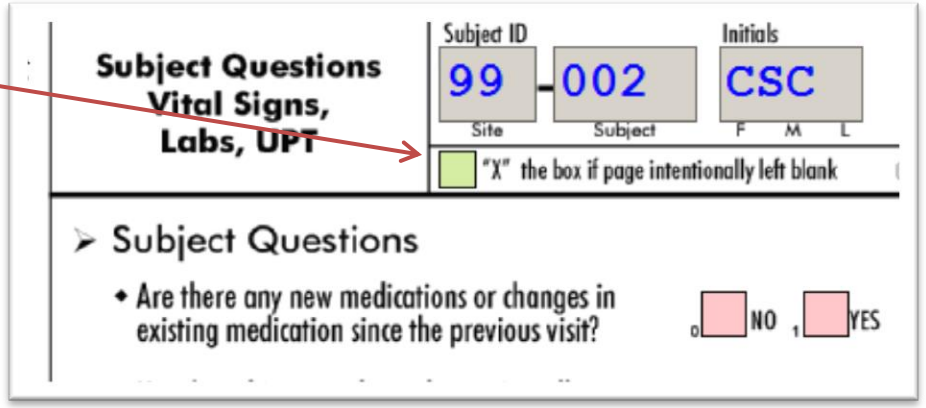
Repeat Controls →



Pages and Visit Not Done

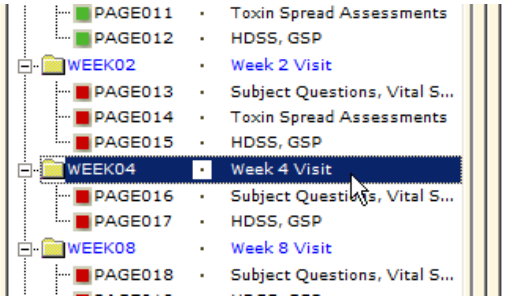
Many eCRF pages (but not all) can be marked as being “intentionally blank”. When you mark a page as “intentionally blank” you are saying that there are no data at all to be recorded on the page – effectively the page is “not done”.

The CRF page headers contain a check box which, when checked, will override all edit checks and make the page ready for submission



If all pages of a given visit may be marked as “intentionally blank”, then the entire visit may be marked as “not done”, as follows:

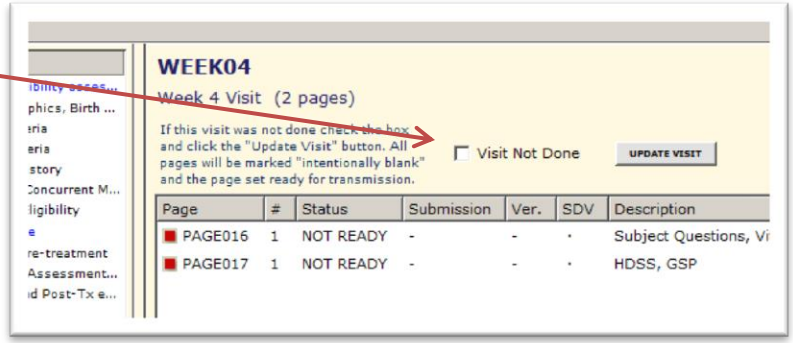
1. Select the visit entry from the eCRF Table of Contents.



Select the visit entry

2. Check the “Visit Not Done” box and click “Update Visit”

   All pages of the visit will be marked as “intentionally blank” and the pages made ready for submission

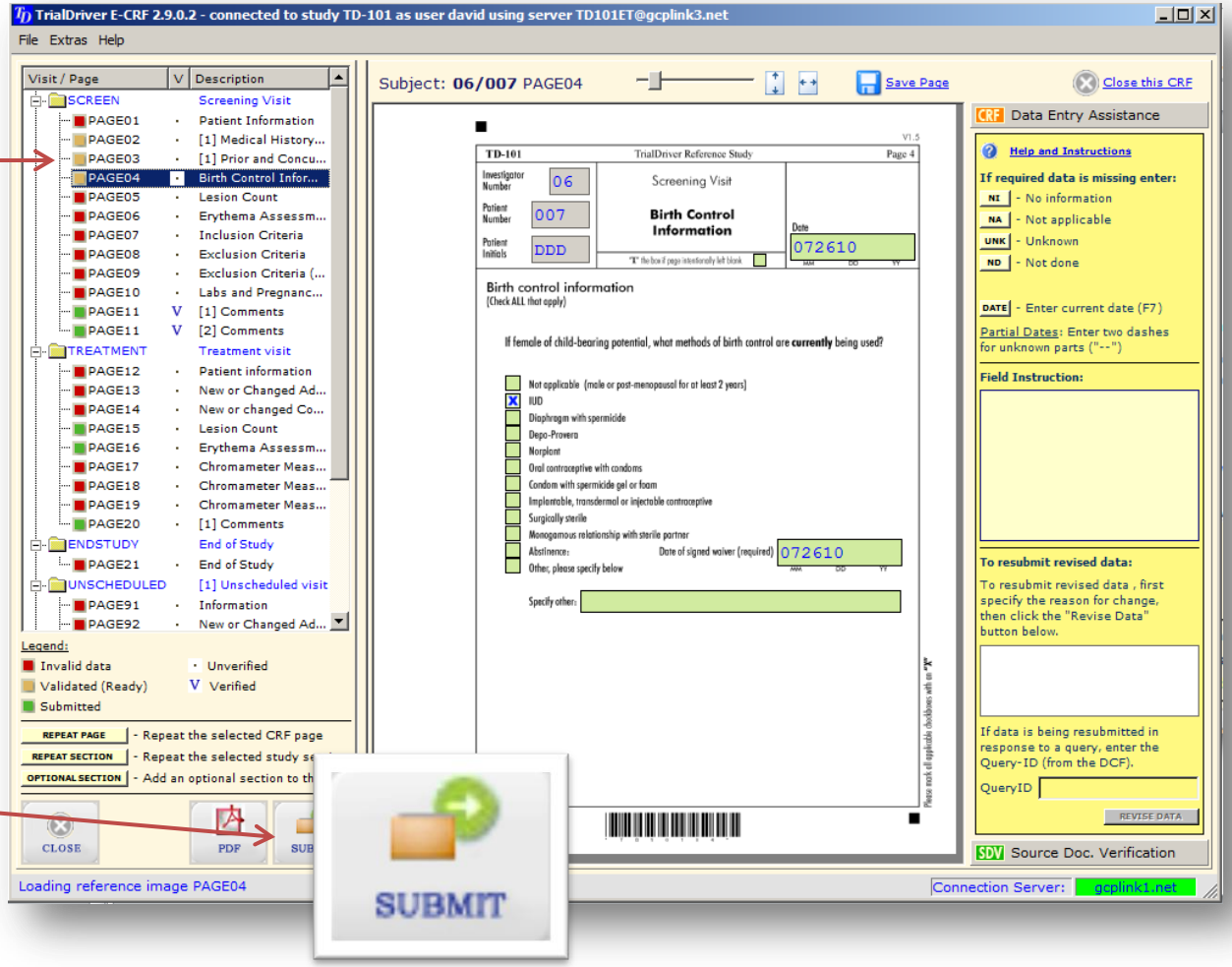


Submitting Data to the Study Server (How to submit data)

When all the fields on a page are displayed in **GREEN**, this means that the page is ready to be submitted to the study server. Click the "SUBMIT" button at bottom right to initiate the data submission process. There is no necessity to submit pages one at a time – all pages which are ready for submission will be submitted at once. A dialog is displayed which tracks the progress of the data submission - at the end a message is displayed "Data successfully submitted". If an error message is displayed, please communicate this to the data management team.

Pages which are ready to be submitted to the Study Server have a **YELLOW** icon in the Table of Contents

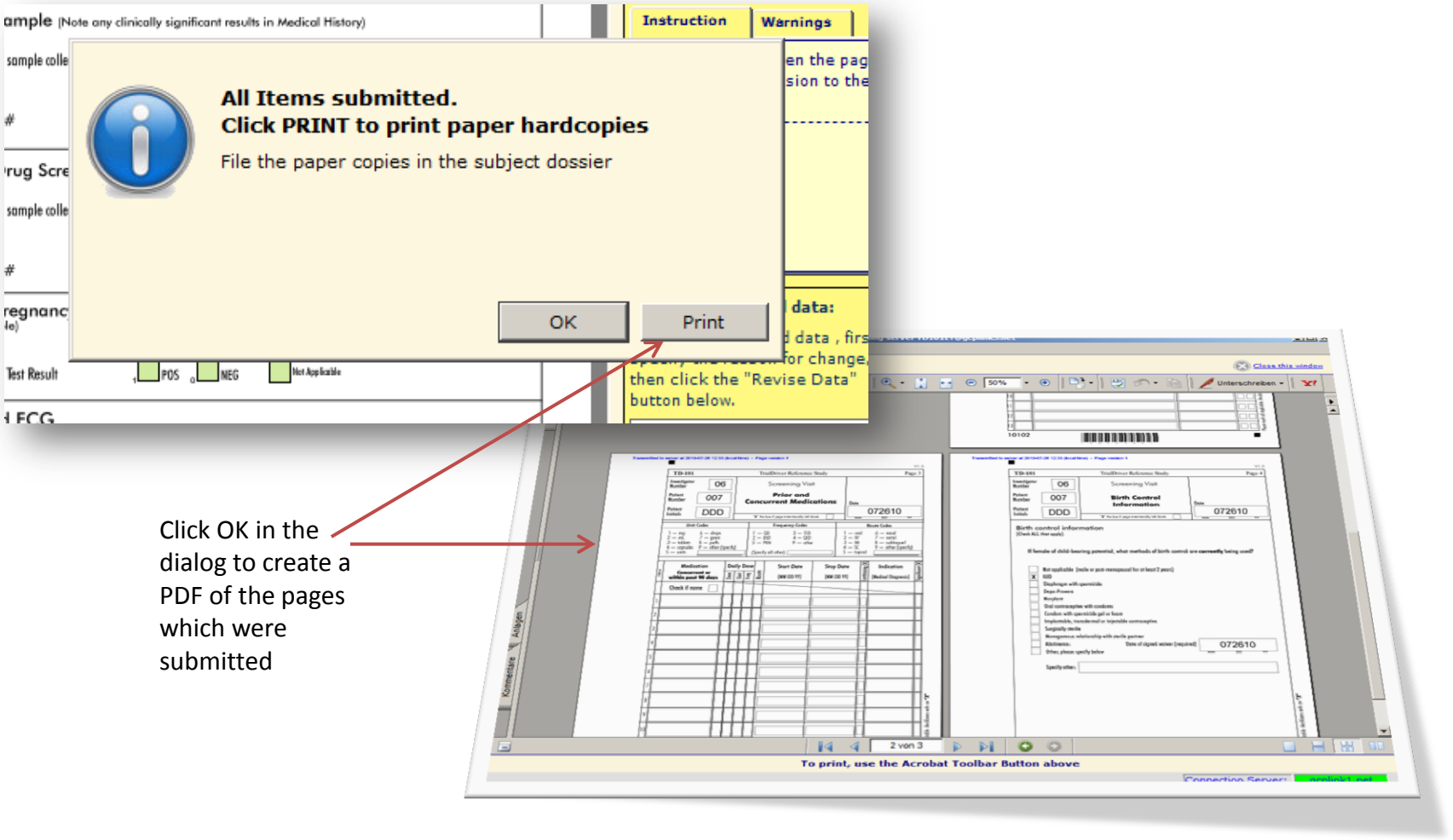
Use the **SUBMIT** button to start data transmission



Submitting Data to the Study Server (After data are submitted)

During data transmission a dialog is displayed indicating the progress. When the transmission is complete a message is displayed which allows you to choose to create a PDF of the submitted pages. This PDF can then be printed and the hard copies stored in the subject dossier. For reference, the CRF page is imprinted with the date and time of transmission.

Choose OK is you do **not** require a PDF at this point (you can create the PDF later if you wish)



Click OK in the dialog to create a PDF of the pages which were submitted

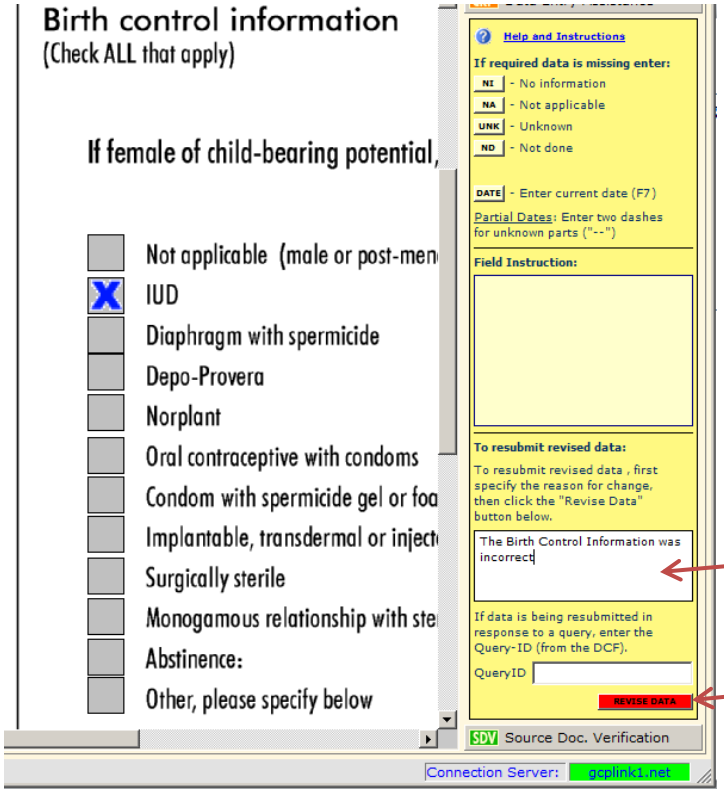
Submitting Data to the Study Server (How to re-submit updated page data)

After a page has been submitted, it is locked and no further data entry is allowed on it. All the fields are GREY, indicating their Read-Only status. The only exception to this rule concerns “logging” pages, which are expected to be updated periodically.

If you must revise data on a locked page, do the following:

- Select the page in the Table of Contents
- Enter a Reason for Change in the Data Assistance panel.
- Click the **REVISE DATA** button

The Page will be reactivated and you can change data. The page must now be re-submitted.



Optionally you can enter a “Query ID” if the data is being changed because of a data query.

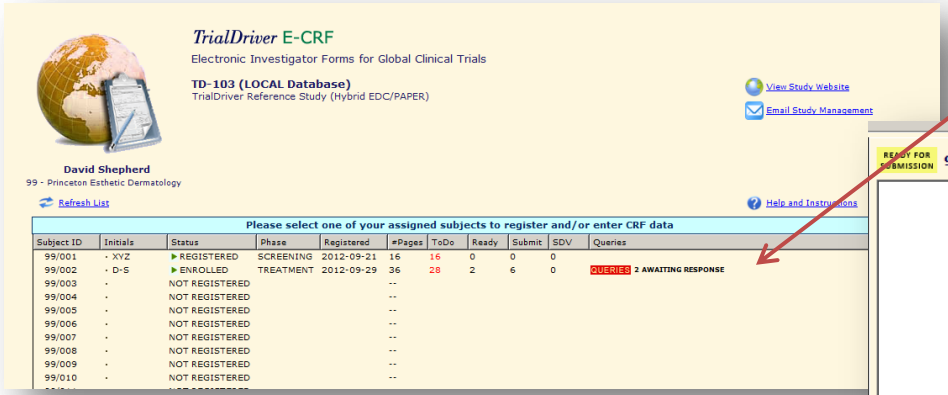
Enter the **Reason For Change** here, then

Click the **REVISE DATA** button to re-enable the page

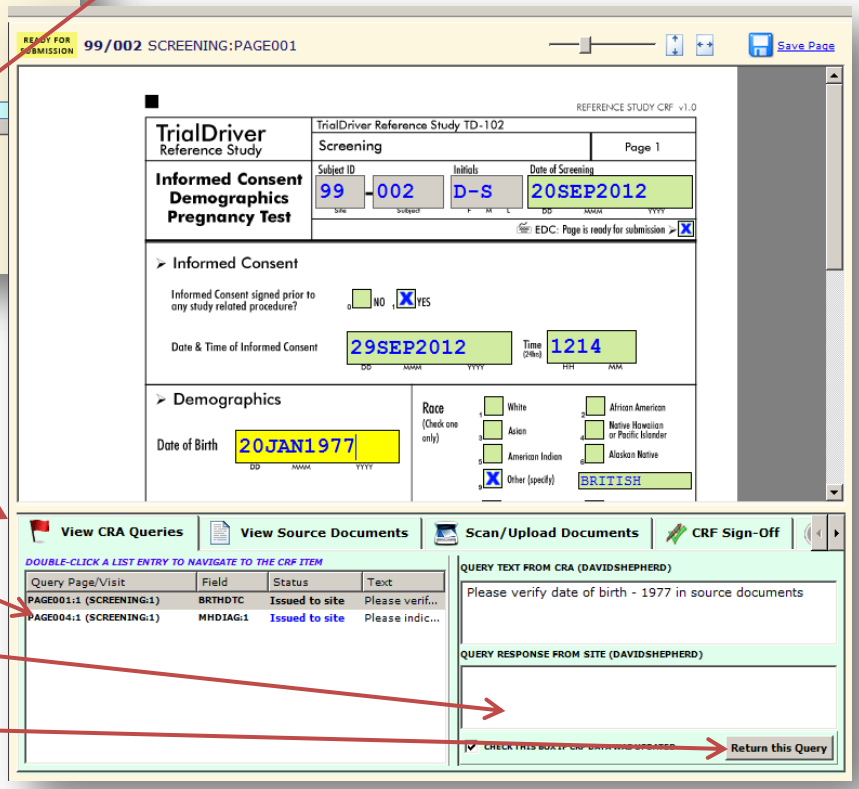
Dealing with Data Queries

Data Management may issue queries against data you have submitted. The TrialDriver E-CRF client allows you to view the Data Clarification Forms (DCF) online and to respond appropriately to them.
The sequence of operations is:

- The presence of a query is indicated by a flag in your subjects list.
- Open the CRF and click the “View Queries” button to see the queries list.
- Review each query in turn. Decide if you will make changes to the data.
- If YES, make the data changes. If NO, enter a brief comment. Finally click the “Return This Query” button



Active queries are flagged in the subjects list.
Open the subject CRF to view the queries



Open the “View Queries “ window by clicking the button beneath the CRF image

Queries are listed in the left hand panel. Select a query to view the query text. Double-Click a query to navigate the CRF to the queried item

Enter your response to the query in the right-hand panel. Or just click the checkbox to indicate that you have made data changes

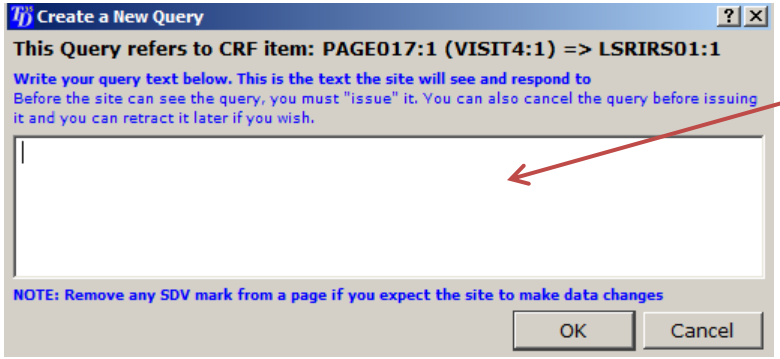
Finally click the “Return this Query” button

Creating Data Queries (For study monitors and CRAs)

When a CRA is monitoring the eCRF, either on-site or remotely, he/she can create online data queries.
This is a two-step process: You first "create" the query and then you "issue" it to the site.

To **create** the query, the sequence of operations is:

- Open the Queries window by clicking the "View Queries" button beneath the CRF image.
- Navigate to the page where the query is to appear and click in the relevant data field (it turns yellow)
- Click the "Create Data Query" button – an editing window opens…



Enter the text of your query in the edit box and click OK.
You will have opportunity to change this text before you "issue" the query.
Click "OK" to save the query

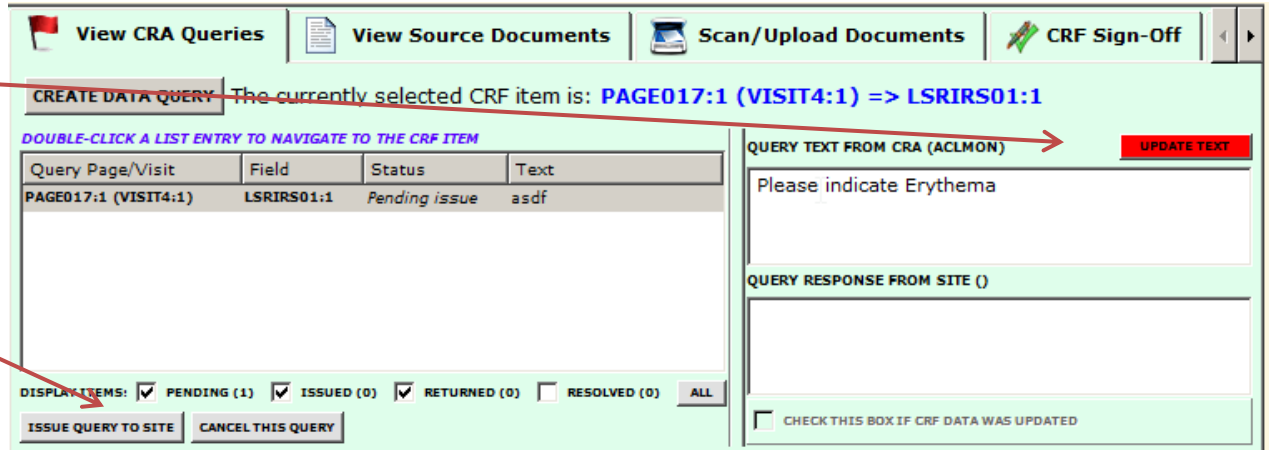
To **issue** the query, the sequence of operations is:

- Select the query from the list of "pending" queries.
- Click the "Issue Query to Site" button

You can edit the query text before issuing it. Click the red "Update Text" to save your edits

Click the "Issue Query to Site" button so that the site can see your query

You can also cancel the query before issuing it

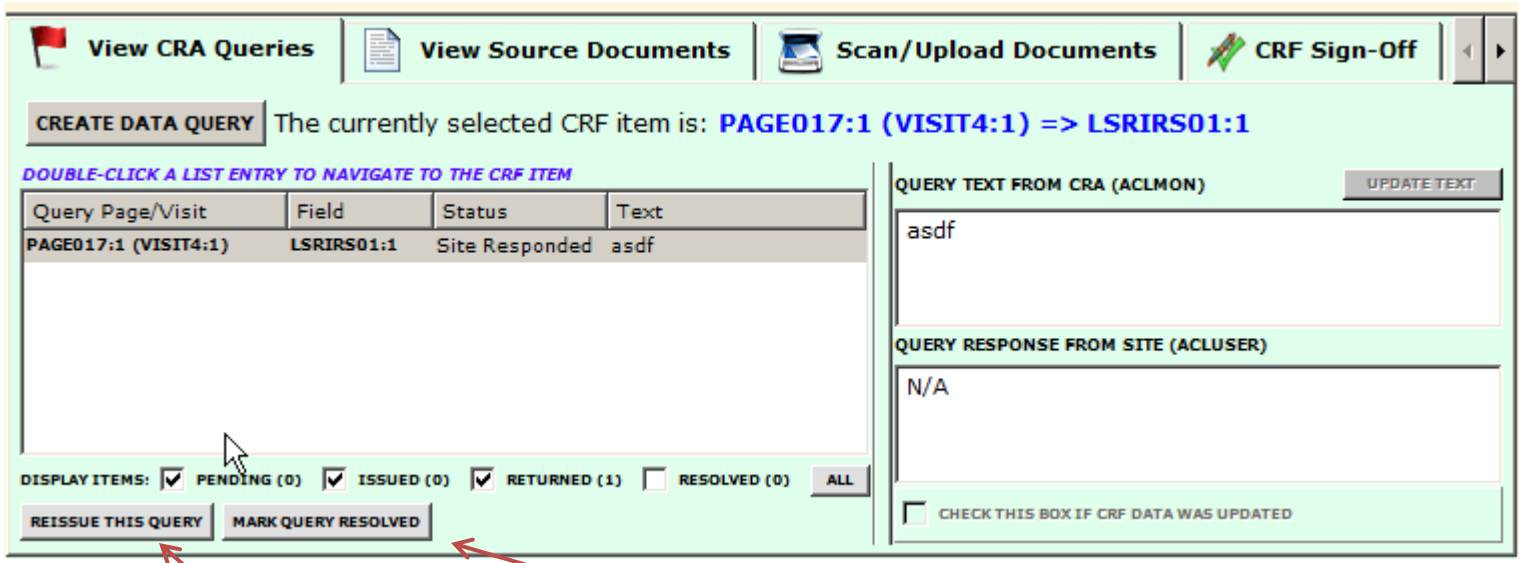


Resolving Data Queries (For study monitors and CRAs)

After a site has responded to a CRA query, it is flagged with "Site Responded" in the queries list. The CRA will now review the site response and either (1) Mark the query as resolved or (2) re-issue the query with an updated query text.

To **resolve** the query, the sequence of operations is:

- Open the Queries window by clicking the "View Queries" button beneath the CRF image.
- Locate any returned queries in the queries list. The list can be filtered to show only returned queries.
- Double click the query to navigate to the relevant CRF page. Click the "Mark Query Resolved" button.



To re-issue a query, click this button.

You can change the text of the query before it is re-issued.

Click this button to **resolve** the query and remove from the queries list.

You can filter the queries list to display resolved queries also. By default they are hidden

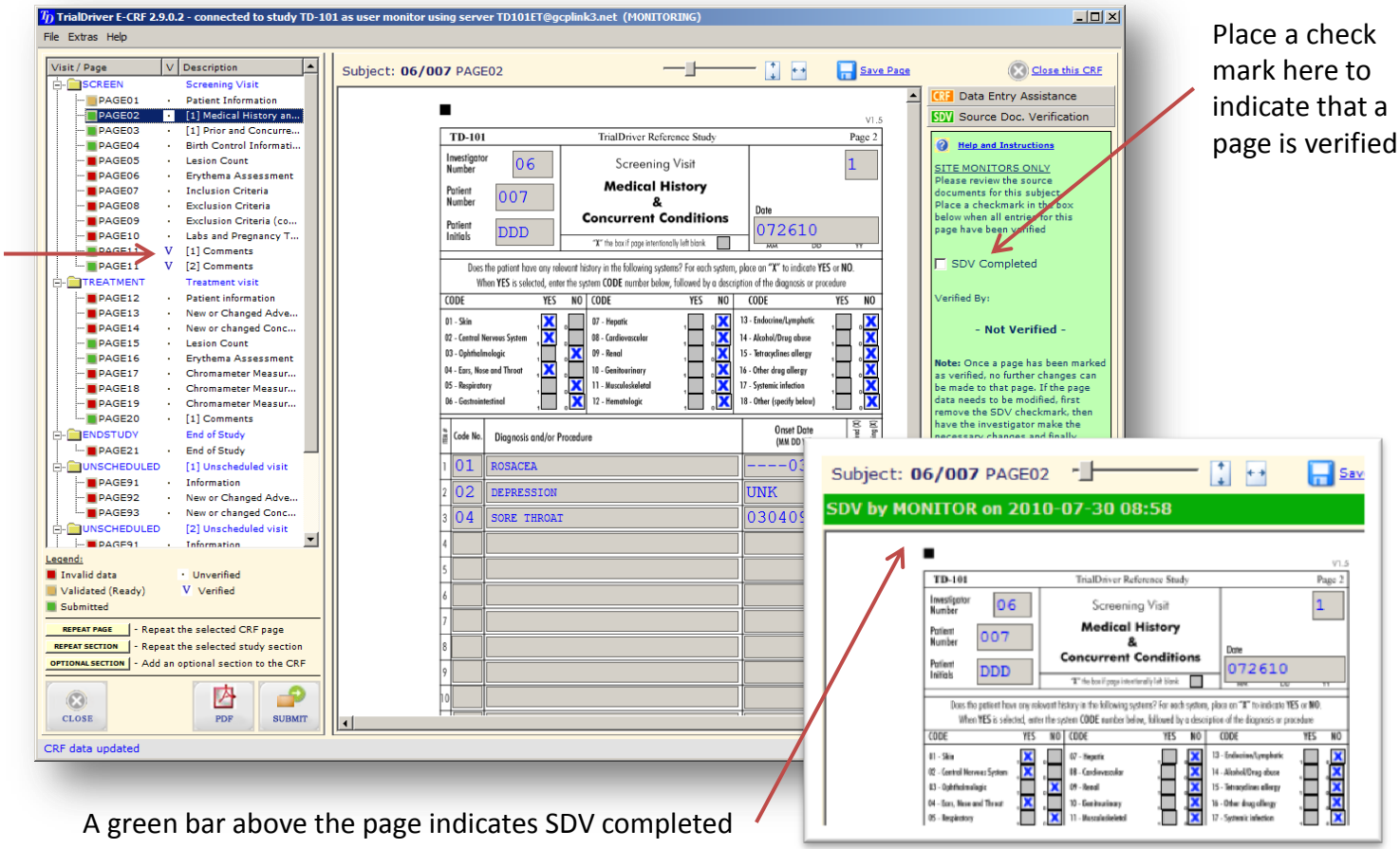
Source Document Verification (For study monitors and CRAs)

Study monitors can perform Source Document Verification (SDV) on TrialDriver E-CRFs. Monitors are provided with special login credentials which prevents them from entering data into the E-CRF but enables an SDV mode, so that they may provide an indication that they have compared the data in the E-CRF with those in the source documents and have found them to match.

Once the monitor has verified an E-CRF page, that page is completely locked and its' data cannot be modified – not even if a reason for change is given. If a page must be modified, the monitor must revoke the verification, which then enables the page again. After the change has been made, the verification process must be repeated.

A "V" icon next to a page indicates that SDV has been completed for that page.

No further changes can be made



Place a check mark here to indicate that a page is verified

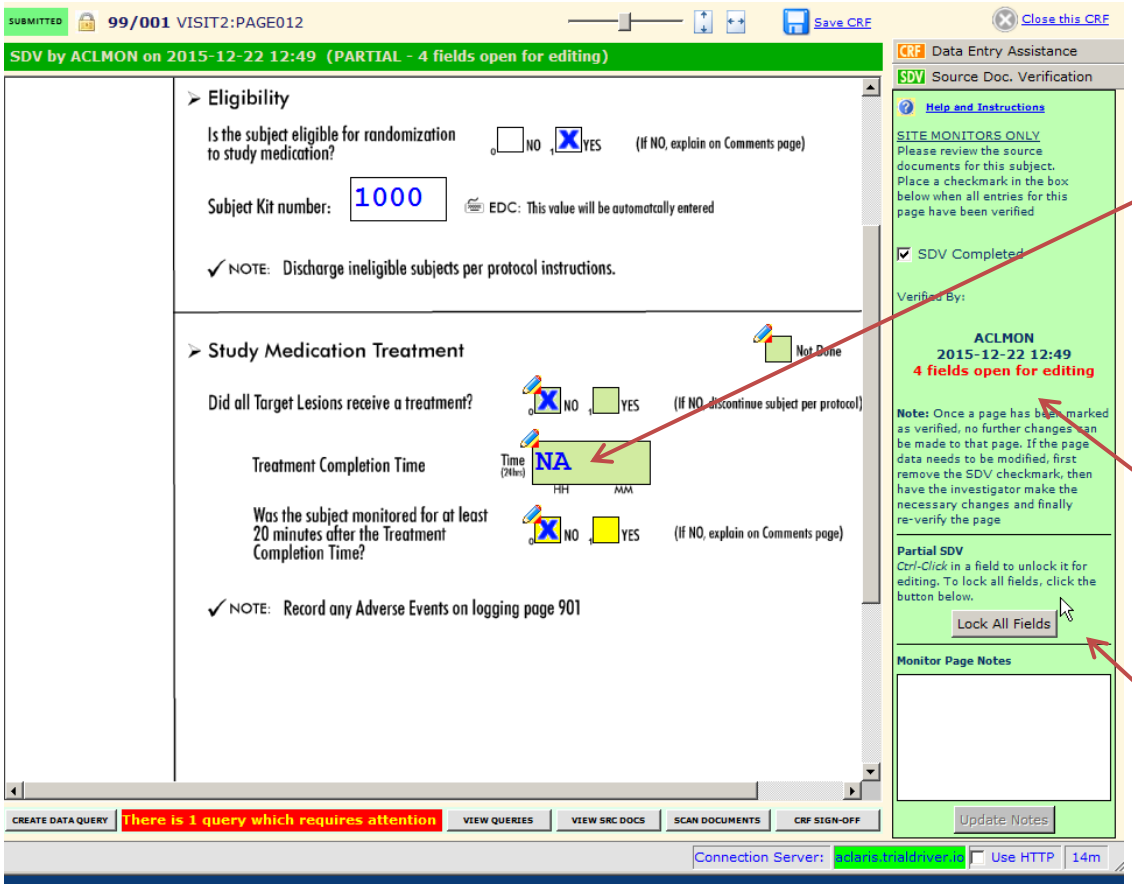
A green bar above the page indicates SDV completed

Partial Source Document Verification (For study monitors and CRAs)

Normally SDV is performed page-by-page. Once a monitor has placed an SDV mark on a page, all data fields are locked.

Occasionally individual fields need to be updated on a page which has previously been SDV'd. The monitor must update the SDV status of the page to allow this. If the SDV mark is completely revoked, then all fields of a page can potentially be updated.

Alternatively, individual fields on a page can be "opened" for editing while leaving all other fields locked, so that the monitor only need re-SDV the intended fields and not be concerned that other data may have changed.



To unlock a field for editing, CTRL-click in the field with the mouse.

An Icon is displayed next to the field.

CTRL-click again to lock the field and remove the icon

A message indicates how many data fields are open for editing

To re-lock all fields, click the "Lock all Fields" button

Investigator Sign-Off

- When a subject CRF is completed, the investigator is requested to sign-off on that CRF
- Not all users are allowed to sign off – only Pis and Sub-Investigators
- PIs can sign and unsign an eCRF – Study Coordinators can also unsign, but not sign.
- When the eCRF is signed off, the pages are locked to prevent further changes. The signature must be revoked ('unsigned') in order to make further changes

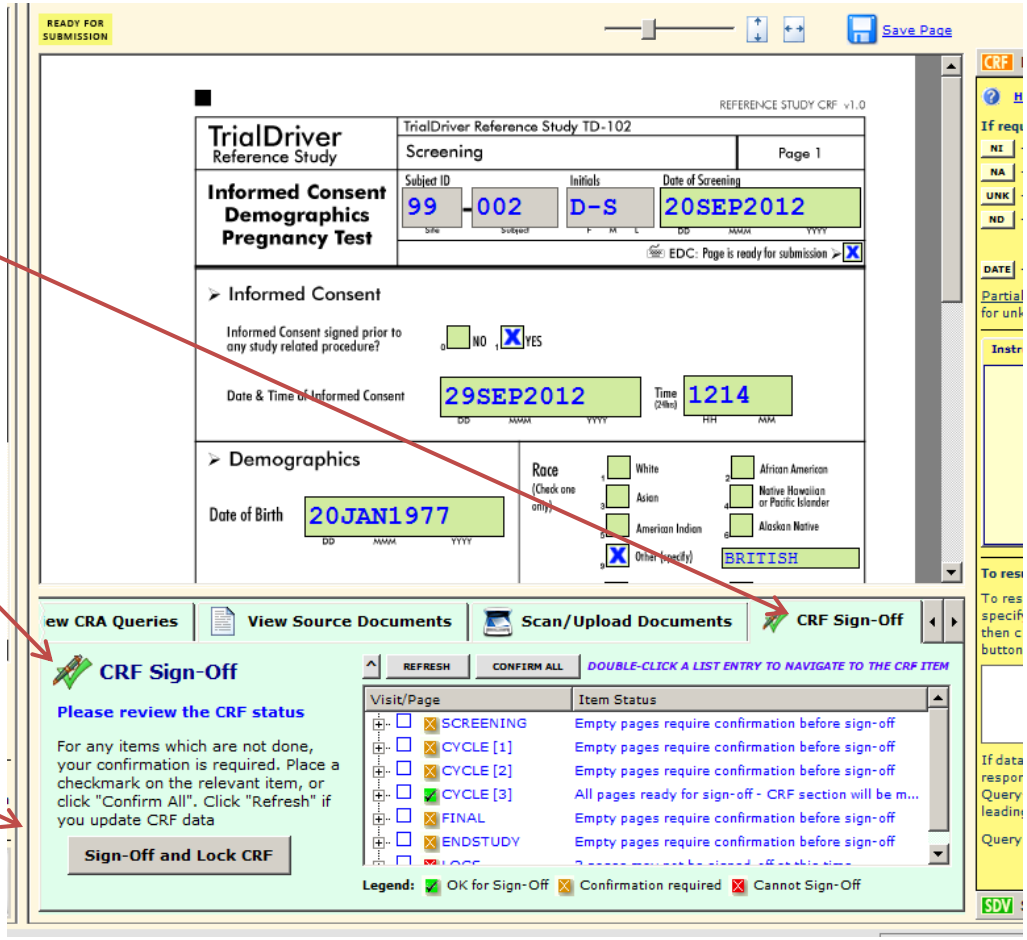
Click the CRF Sign-Off button beneath the CRF image to open the Sign-Off window

An overview of the Sign-Off status of the CRF is displayed

Specifically the Investigator is asked to confirm that any empty pages and visits are intentionally blank.

Place a checkmark next to items which require confirmation – or just click the "Confirm All" button

Finally click the Sign-.Off button. Any remaining pages and visits will be marked blank and submitted to Data Management. The CRF will be locked from further changes.



Creating PDFs

You can create PDFs of the CRF pages at any time. These can then be saved to your local disk, printed or emailed. PDFs are created which display the data you have entered.

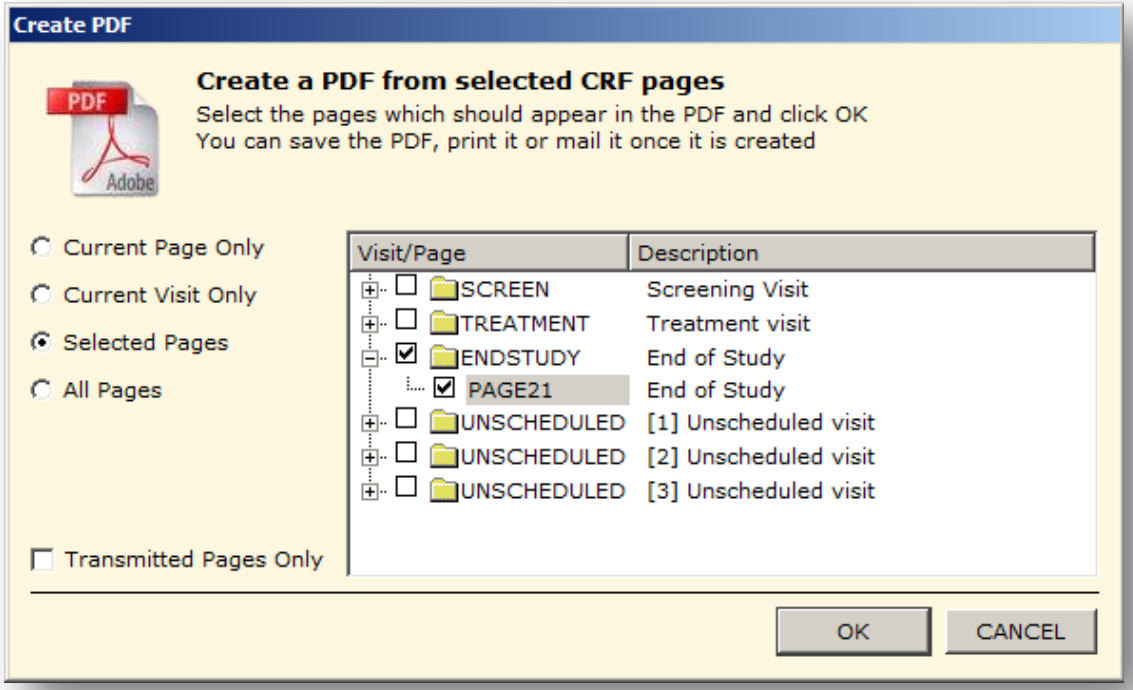
Click the PDF button in the Page Controls area (bottom-left of screen). This will bring up a dialog which allows you to determine which pages should be printed

Your options are to create a PDF containing:

- Only the current page
- All pages in the current section
- Selected Pages – mark the pages you require in the list at right
- All pages

Additionally you can elect to include only those pages which have been submitted to the Study Server. Leaving this option unchecked will also include empty pages

The PDF will be displayed in an embedded PDF Reader window. Click the "Close this Window" link to return to the interactive CRF

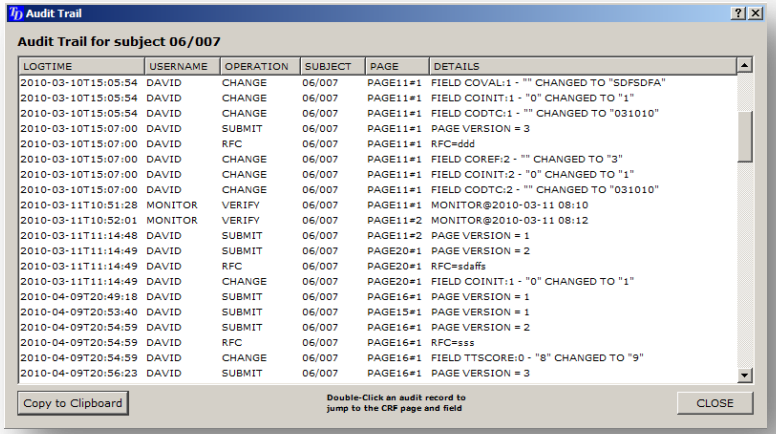


Miscellaneous Options

Some miscellaneous options are available under the menu option "**Extras**". These are:

View Audit Trail

Select this option to display a list of all logged operations for the current subject.
Choose "**Copy to Clipboard**" to copy the list in a comma delimited format (suitable for loading into Excel).
Double-click any list entry to hyperlink to the associated data field (if applicable)



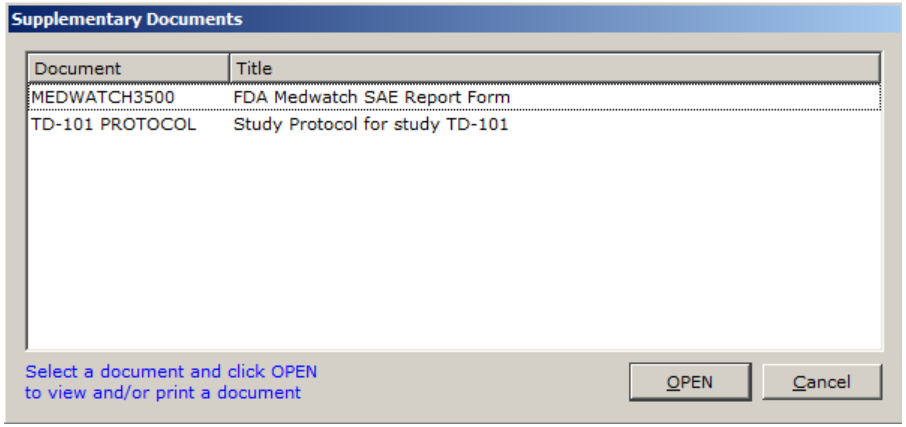
Print Blank CRF

Choose this option to display a PDF of the entire CRF. The PDF will not contain any subject data

Supplemental Documentation

Choose this option to display a list of "supplemental documentation" associated with this study. These are PDFs which pertain to the study, but are not part of the CRF proper.

Select a document and click the **OPEN** button to display it in the PDF viewer, from where it may be saved or printed.



Technical Information

EDC Client

The TrialDriver EDC client is a native Windows application which is installed on the user's laptop or PC. (It does not run in a web browser). It can be installed on multiple machines. (On a Mac it can run under a Windows emulator such as Parallels)

The EDC client is available in an installer program which can be downloaded from one of our websites. (Link will be communicated separately).

By launching this installer program locally, the actual EDC client will be installed and configured. This installation will require administrative rights on the local computer. To launch the EDC client a desktop icon will also be installed.

Server Configuration

The TrialDriver EDC client connects to an Oracle/MySQL database server. The DBMS infrastructure runs in the Amazon Cloud (US east coast region). The server has an explicit TCP endpoint-url in the Amazon Cloud which replaces a fixed IP address (which the server does not have). Additionally a DNS alias is available which points to this endpoint via a CNAME record. These URLs are sponsor-specific and are communicated to you separately.

Firewall Configuration

Any Firewall at your site will need to allow outgoing connections to the TCP endpoint-url on port **3306** (MySQL standard port)

Encryption

Data are encrypted (AES-256) both on the wire (in-motion) and in the study database (at-rest). They are only ever decrypted in the EDC client program and other back-end data management tools.