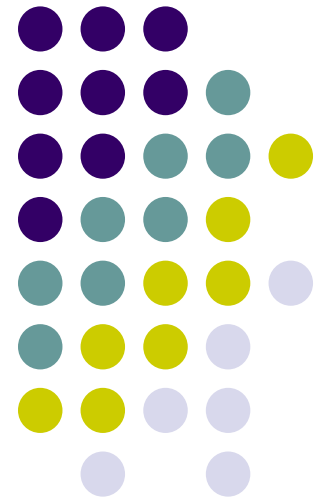# Introduction to C³D

## Harris Corporation

Dec 2016

Introduction

- C^{3}D - **C**ancer **C**entral **C**linical **D**atabase
- eCRFs Instructions Manual
- Support
- Data Entry
- Audit-Trail
- Discrepancy Management
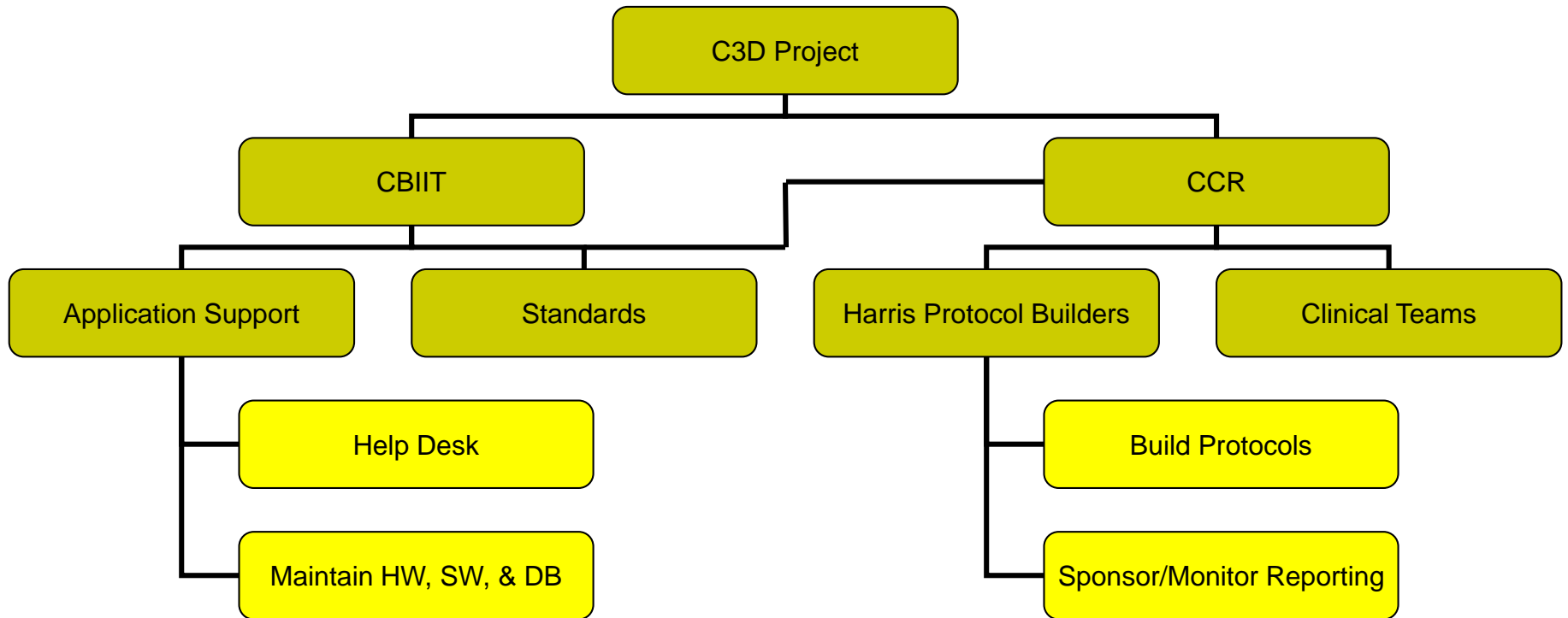- Verification
- Approval
- Lab Loading

What is C³D

- Clinical Trials Data Management System
- RDC (Remote Data Capture) Data Entry
  - Accessible anywhere in the world (via a Windows computer and Internet Explorer).
  - For studies prior with Clinical Center Number prior to 2012: The Java Runtime Environment (JRE) version 1.7.0_45 (or later) is required.
  - The above requirement will no longer apply by mid-2017, when open studies setup in C3D before 2012 will be converted to a new interface – 'RDC Onsite'.
- C³D supports data standardization, reuse, sharing, and interoperability through electronic Case Report Forms (eCRFs) based on Common Data Elements (CDEs)
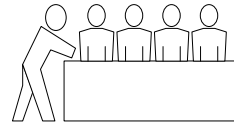- Based on Industry Standard Technologies
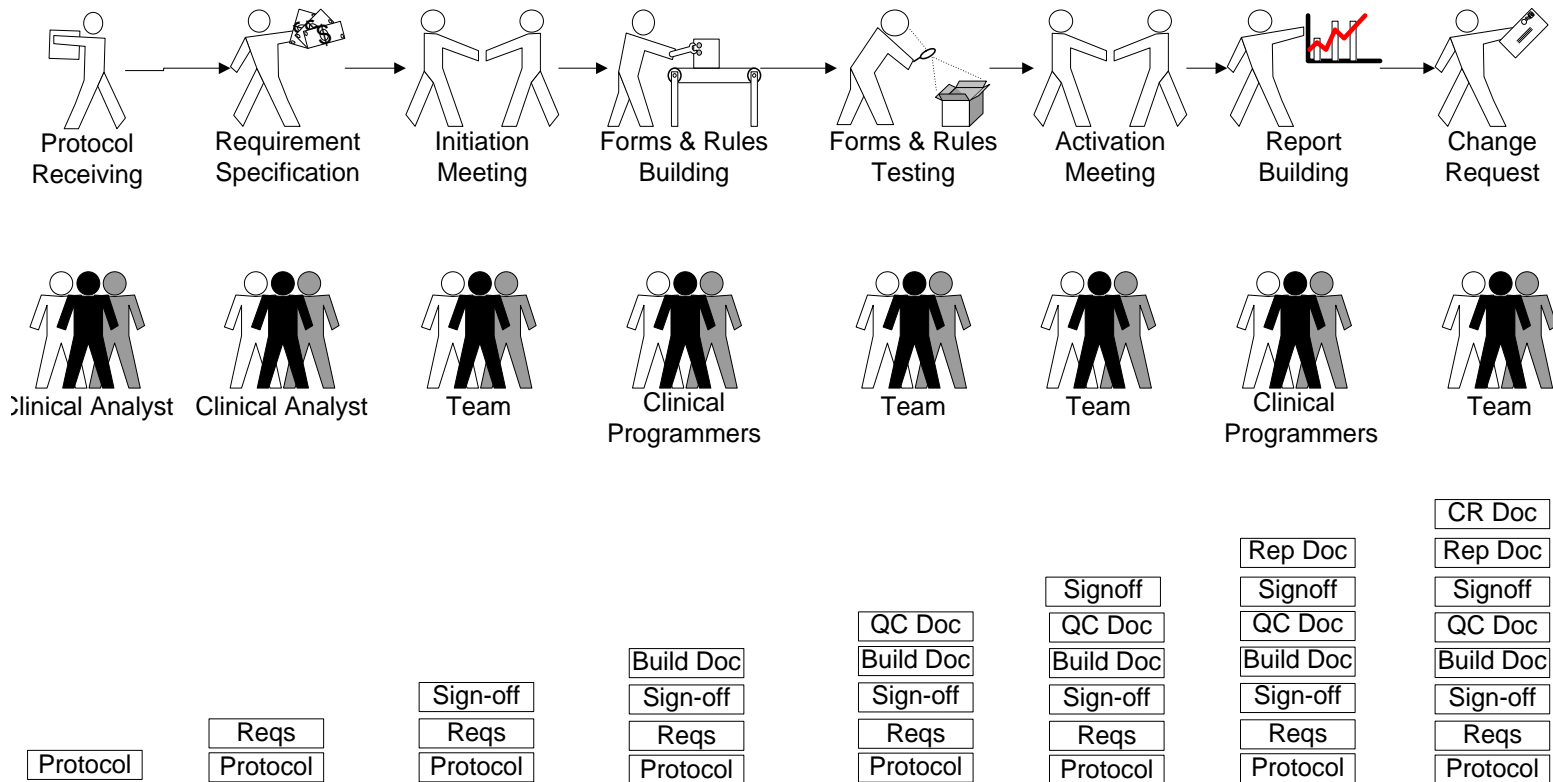
Cancer Central Clinical Database C³D
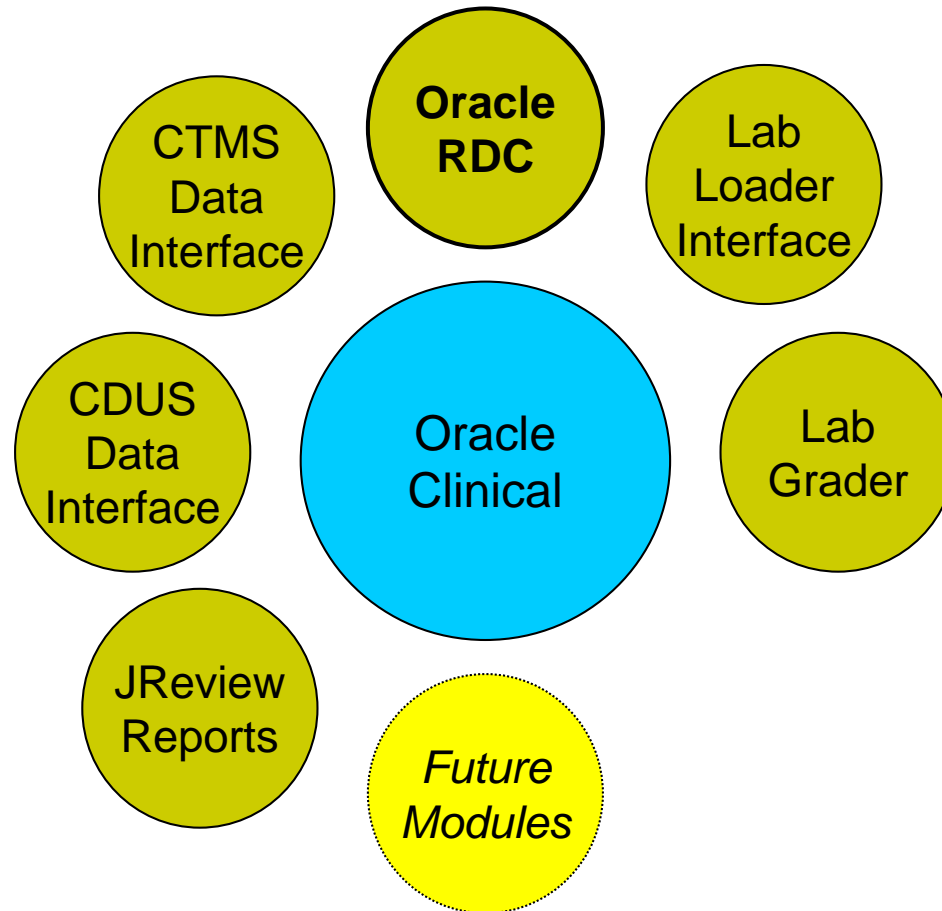
C³D Organization

Designing Protocols in C³D

Control & Configurations Management Group (CCMG)

Protocol Receiving	Requirement Specification	Initiation Meeting	Forms & Rules Building	Forms & Rules Testing	Activation Meeting	Report Building	Change Request
Clinical Analyst	Clinical Analyst	Team	Clinical Programmers	Team	Team	Clinical Programmers	Team

							CR Doc
						Rep Doc	Rep Doc
				Signoff	Signoff	Signoff	Signoff
			QC Doc	QC Doc	QC Doc	QC Doc	QC Doc
		Build Doc	Build Doc	Build Doc	Build Doc	Build Doc	Build Doc
	Sign-off	Sign-off	Sign-off	Sign-off	Sign-off	Sign-off	Sign-off
	Reqs	Reqs	Reqs	Reqs	Reqs	Reqs	Reqs
Protocol	Protocol	Protocol	Protocol	Protocol	Protocol	Protocol	Protocol

CCR Standard Case Report Forms

- Library of Standard Forms & Rules is available as a starting point to build protocol specific forms & rules
- Detailed Instructions are available for each Standard Form https://ccrod.cancer.gov/confluence/x/9QiJAw
- Each Instructions includes:
    - General Description
    - eCRF Screenshot
    - Field Specific Description (Mandatory, Derived, etc.)
    - Validation/Derivation Rules

eCRF Instructions Manual

Home

C3D Portal

Login

Training and Education

Sponsor Reporting

Support

Other Applications Documentation

GLC Web Application Users Manual

TIGER-LC Web Application Users Manual

Contents

- Purpose
- Course Initiation eCRF
- Validations
- Derivations

Purpose

Record course initiation Start Date, Arm, Treatment Assignment Code (TAC) and Treating Institution.

Course Initiation eCRF

Field Name	Description / Instructions	Format
Visit Date[(m)]	Enter the date the course started.	DD-MMM-YYYY
Course #[(d)]	Sequential number of this course of treatment: first course = 1, second course = 2, etc.	5 digits
Start Date of Course[(m)]	Enter the date on which the course was started. This is the date on which a protocol stipulated medication (or treatment) was first administered.	DD-MMM-YYYY

CCR Standard Case Report Forms

- Screening/Baseline Forms
  - Eligibility, Enrollment, PE, Vitals, Baseline Symptoms, Prior Therapies, …
- Courses/Cycles
  - Course Initiation, Study Medication Administration, PK, Course Assessment, PE, …
- Labs
  - Blood Chemistry, Hematology, …
- Ongoing
  - AE, Concomitant Measures, Extent of Disease, …
- Off Tx / Follow-Up / Off Study

C³D Protocol Phases
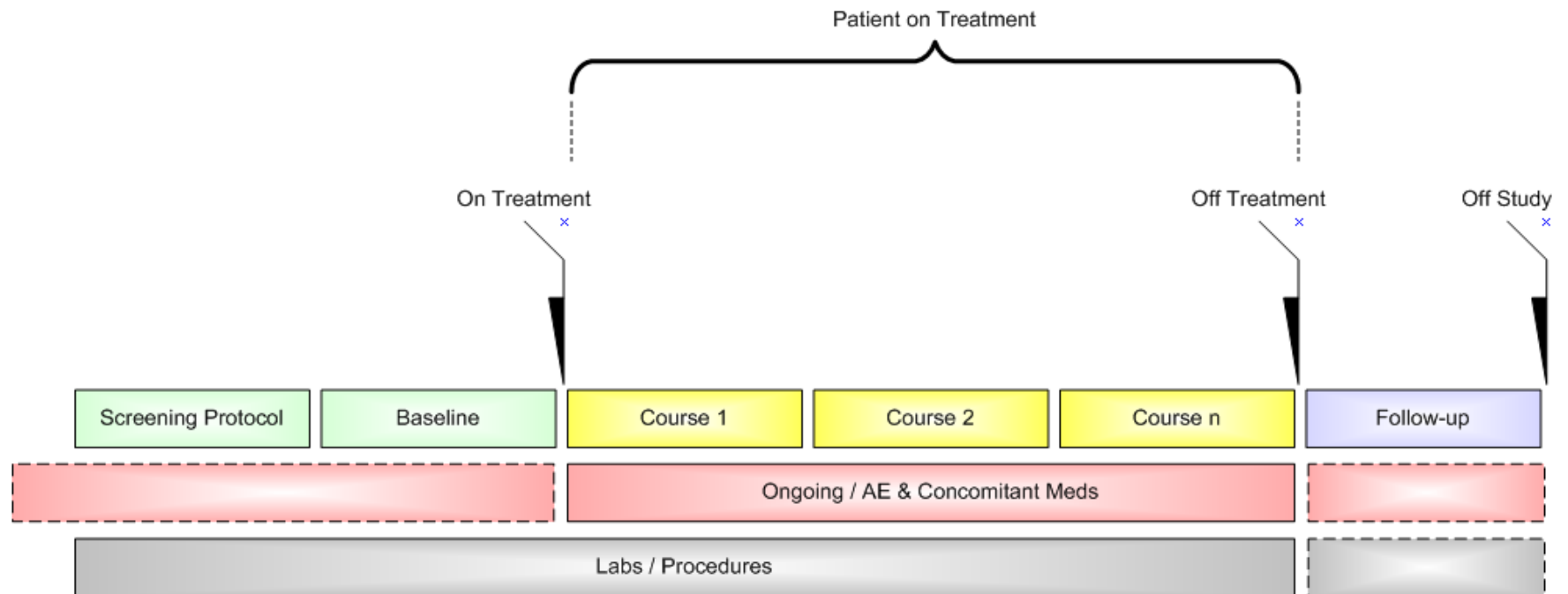
Role Based Access

Access => Role	Browse	Enter Data	Manage Discrepancy	Verify eCRF	Approve eCRF
PI	Yes	No	No	No	No
Research Nurse	Yes	Yes	Yes	Yes	No
Data Manager	Yes	Yes	Yes	No	No
Monitor	Yes	No	Yes	No	Yes
QA	Yes	No	No	No	No
Protocol Builders	Yes	Yes	Yes	No	No

NCI/CCR Confidentiality Agreement – Training Certificate

- At the end of the Training session, print, sign and fax the CCR Confidentiality Agreement to 240-541-4435. You can also scan and e-mail it back to the Trainer.

- Upon receipt of the CCR Confidentiality Agreement:
  - The request for your C3D account, password and access will be submitted. The C3D Help Desk will provision your C3D account within 2 business days.
  - The Certificate you attended the training will e-mailed to you.
  - Keep your signed CCR Confidentiality Agreement and the Training Certificate in your Study's regulatory binder.

C³D Support

- CBIIT provides the first line of support for C³D related issues
- Contact
  - ❑ Email: ncicbiit@mail.nih.gov
  - ❑ Phone: 240-276-5541 (**Toll free**: 888-478-4423)
    - ○ Telephone support is available Monday to Friday, 9:00 a.m. to 5:00 p.m. Eastern Time, excluding government holidays.
  - ❑ Additional Information at: https://ccrod.cancer.gov/confluence/x/KwBYB
- Protocol specific issues are escalated to the Protocol Builder by CBIIT
- Changes to Standards are escalated to Controls & Configuration Management Group (CCMG)

Username & Password

- Username is typically your last name and first name initial.
  Ex: **smiths**
- Password rules:
  - Start with a letter;
  - Must containing **at least one number <u>and</u> one special characters** (Ex:! #);
  - Has to be at least 8 characters long;
  - The following special character could cause problems if used: $ % & ' '' /.
- Production Database is called **ocprod**
- About C^{3}D Password:
  - Do not share the password with others!
  - Password needs to be changed the first time you login.
  - Passwords expire every 4 months and need to be changed.
  - Account gets locked upon three unsuccessful attempts. Contact C^{3}D Help Desk to unlock account and/or get new password.

C³D Login Web Pages

- C³D is Accessible Worldwide

- C³D Production Login Page:
  https://octrials.nci.nih.gov/opa46/rdclaunch.htm

- C³D provides a separate Data Entry environment to test protocol design
  - Test Login page:
    https://octrials.nci.nih.gov/opa46/rdclauncht.htm

C³D Login Web Page

For studies with NCI Clinical Center Number prior to 2012 (ex: 11_C_0001, 10_C_0002), click on the Login button.

Click on Login Button

Login

Oracle Developer Forms Runtime – Web

Window

ORACLE

Logon ✕

Username: _____

Password: _____

Database: _____

Connect   Cancel

Enter User, Password, and Database.
Then click Connect

C³D Activity List

Selecting Activity

- Quick Links to View
  - All Study Data
  - Discrepant Data
  - Site Specific or Patient Specific Data
- Change Study button to choose a Different Study
  - Default Study is preserved from prior login
  - Access to study sites and C^{3}D features are controlled by user role
- Search button used to locate eCRFs based on one or more criterion

- **Quick Tip:**
  - This screen provides a quick review of open discrepancies in your study
  - **It is strongly recommended to work with one patient at a time when performing data entry to avoid entering data in the wrong patient position.**

Selecting Study

Study Access

- Study/Site access and C^{3}D features determined by user role
- User Roles:
  - Data Managers (Performs Data Entry)
  - Research Nurse (Performs Data Entry and Verifies eCRFs)
  - Monitor (Read-only access and Approves eCRFs)
  - Principal Investigator (Read-only access)
  - Reviewer (Read-only access)

Search Criteria

Search Criteria

- Search options:
  - Book - collection of CRFs for a particular version of the protocol (initial version or amendments)
  - Site
  - Patients
    - Range of Patients
  - Visits/Pages
    - Phases, Visits, etc.
  - CRF Status
    - Complete, Discrepant, Verified, Approved, etc.
  - CRF Entry Date Window
    - Entry or Modification Date Ranges
  - Data
    - Data entered in an eCRF

- **Quick Tip:**
  - Protocol Amendments may require different DCI Book. Latest DCI book is the default one. Use Search option to select a previous book.
  - Search Criteria Could be saved for future use.

RDC Spreadsheet

Navigating RDC Spreadsheet

- Spreadsheet Layout
    - Patients along Rows
    - Phases or Visits Tabs along Columns; pull down for additional visits
    - eCRF within Tabs
    - Cells represents an eCRF for the corresponding Patient-Visit
- Tabs can be organized by Study, Phase, & Visit
    - When working with Lab eCRFs, choose to work with Visits instead of Phases or Study.
- Information Tabs for Summary, Discrepancies, Verification, Audit-trail, etc. at the bottom
- Navigation Functions via
    - Menu
    - Toolbar
    - Hot Keys

eCRF Icons
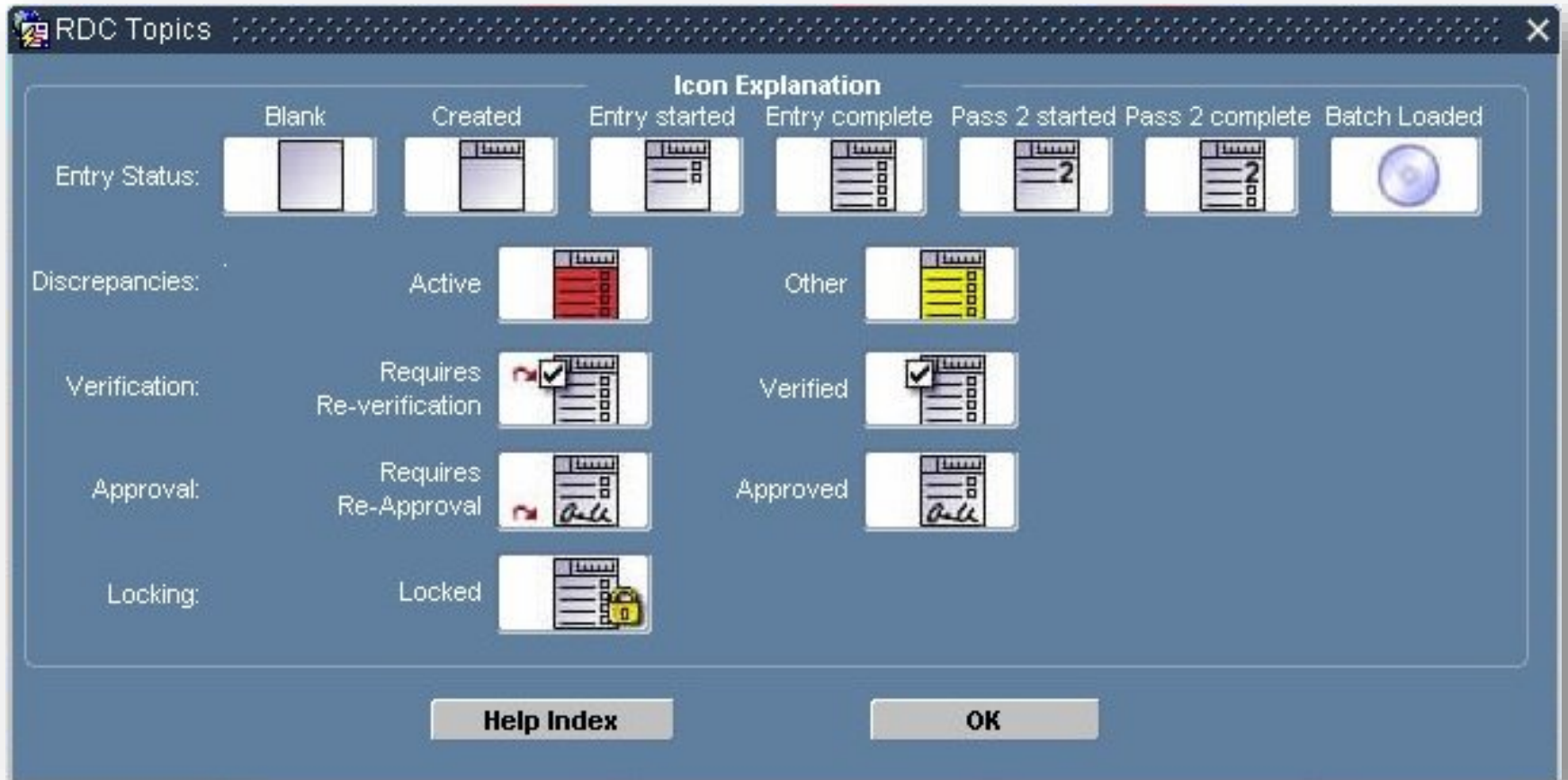
Important eCRF Icons

- Square icon represents manual entry
- Round icon represents automated entry (lab load)
- An eCRF just created, but without data has no lines within the icon
- Partially entered eCRF has lines across half of the icon
- Completed eCRF have lines across the whole icon
- Blank Square icon indicates eCRF has been marked blank
- Red icon indicates one or more open discrepancies

Electronic CRF (eCRF)

eCRF Navigation

- Clicking on eCRF icon open the eCRF
- eCRF may contain tabs for the different sections of the eCRF
- Grey Fields indicates non-enterable fields (Derived, Defaulted, etc.)
- eCRF Scroll Bars indicate additional information
- Ellipsis indicates the field has a Pick List. Click on the ellipsis or press F9 to display the Pick List.

Audit Trail

eCRF specific Audit Trail

Audit Trail

- Audit Trail Tab shows history of all changes made to a specific eCRFs
- Shows current and prior values for each changed eCRF field along with the date of change and the user who made the change

- **Quick Tips**:
  - Auditing Begins after Form is marked complete
  - Do not share user ids and passwords!

Resizing eCRF Window

Click Title Bar to enter Resize Mode

Then Click and Drag the Title Bar to move the window or the sides/corners to resize

Click Done when resizing is complete

Resizing eCRF Window

- Click on the eCRF title bar to enter resize mode
- Click and drag title bar to move window
- Click and drag window edge to expand/ reduce window size
- Click OK when Done

- **Quick Tip:**
  - ❑ Right mouse click on the eCRF title bar to show a pop-up menu with options to move/resize the eCRF window.

Log Out

Log out using Exit
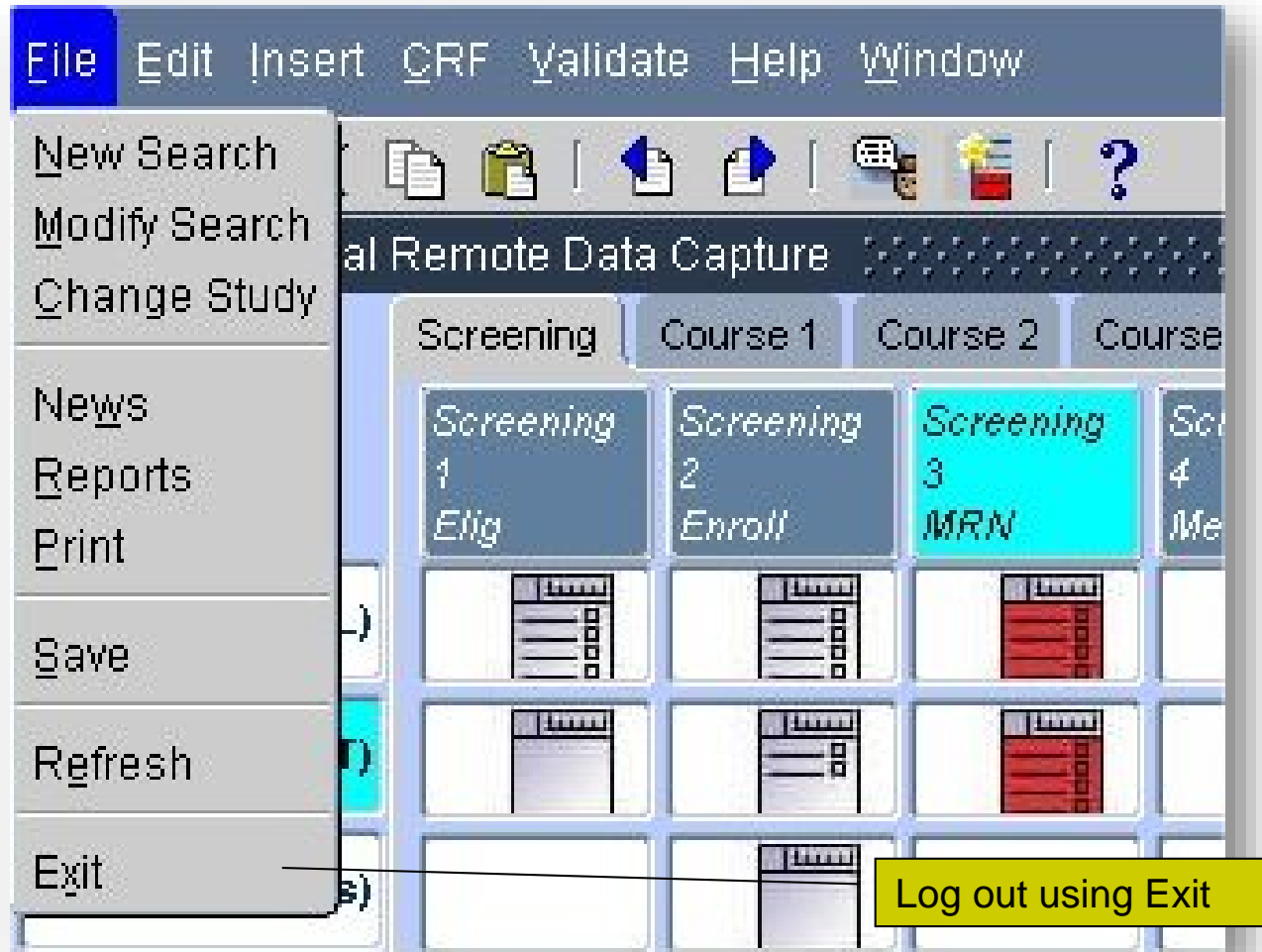
Log Out

- Exit C^{3}D before closing the Browser
- Inactivity for more than 30 minutes logs your out automatically. **Any unsaved work is lost!**

Inserting New Patient

Choose Patient Position

Icon to Insert New Patients

Inserting New Patient

- Click Patient Icon or Select Insert -> Patient from the menu bar
- Choose a Patient Position Number from the pick list
- New Patient Row is Created

- **Quick Tips:**
  - The total number of Patients available for entry are governed by protocol ceiling accrual. Request additional patient numbers if protocol is amended.
  - It is a good practice to use the patient numbers in sync with those assigned by Central Registration Office (CRO)

Starting New Planned eCRF

Starting New Planned eCRF

- Click on an empty cell to insert eCRF and begin data entry
- Resize if necessary

Entering Visit Date

Enter Visit Date and press Tab key

Entering New eCRF

- Click on the empty Cell to insert appropriate eCRF
- Enter the Visit Date
  - **Visit Date is the Lab Sample Collection Date for Lab eCRFs!**
  - Visit Date is <u>mandatory</u> except for Ongoing Visit eCRFs.
  - Partial dates are not acceptable.
  - Consult eCRFs Instructions Manual for eCRF specific guidance:
    - Usually Evaluation Date, Administration Date, Initiation Date, Lab Date, Course Start Date, etc.

Entering Data in eCRF

43

Entering Data in eCRF

- Navigating between Fields
  - Use Tab Key to move to Next Field
  - Use Shift Tab to move to Previous Field
  - Use Mouse Click to navigate to a Specific Field
- Fields with Ellipsis indicate a Pick List (Use the Pick List!)
- Enter Dates as

  - Complete dates for Current Information (ex: 5/23/2014, 5-23-2014 or 05232014)

  - MMYYYY for Prior Information is acceptable when complete date cannot be obtained (ex: 05-00-2014, 05/00/2014, 05002014)

Tabular eCRF

To Delete Selected Row

Number of Rows (Repeats) allowed for entry and displayed are set by Designers.
Table does not have scroll bar.
Use Up/Down Arrow Keys to Navigate beyond the visible rows.

Tabular eCRF

- Fields shown in a grid layout
- Scroll up and down the rows of the table using arrow keys (No Scroll Bars!!)

- **Quick Tips:**
  - ❑ Use the menu option CRF -> Insert Row to insert a row between two rows (below the currently selected row).
  - ❑ **A row cannot be left blank and must be deleted before proceeding to another row**.
    - ○ Select the menu option CRF -> Delete Row.

Using Pick List

Using Pick List

- Fields with Ellipsis contain a Pick List
- Pick List can be accessed by clicking the Ellipsis or pressing the F9 Key
- Searching the Pick List:
  - Start typing in some letter and the list is filtered as you type or;
  - Click on the Find box, enter a some letters surrounded by the wildcard % character (ex: %ypo%) and click on the Find button. Select one of the values.
  - **If the Pick List has more than 1,000 items, items beyond 1,000 cannot be searched after the Pick List is shown.** Close the Pick List and use the wildcard find shown above then press the F9 key or click on the ellipsis. This way the entire list will be searched and matched items shown. The following Pick Lists have more than 1,000 items:
    - CTCAE Term (version 3.0) pick list on the Adverse Events and Baseline Symptoms;
    - Agents in the Concomitant Measures and Medications;
    - Enrollment eCRF Disease Term (only when using comprehensive CTEP list of Diseases);
    - Enrollment eCRF Registering Institute;
    - Course Initiation eCRF Treating Institute.

- **Quick Tips:**
  - If a value is not in the pick list enter it, consult your DM Supervisor. Entering a value that is not on the pick list will create a discrepancy.

Marking eCRF Blank

Marking entire eCRF Blank

Marking Section Blanks

Marking eCRF Blank

- Entire eCRF can be marked Blank
- Individual Sections of an eCRF can be marked Blank
- Checking Blank Flag will erase any entered information from the eCRF/Section
- Blank Flag can be unchecked to enter information

- **Quick Tip:**
  - ❑ It is a good practice to mark Sections that will not have data entered as Blank.
  - ❑ Once all sections of a CRF are 'addressed' (by entering data or marking it as blank) the overall status of the eCRF becomes Entry Complete.

Entering/Viewing Laboratory Data

Entering/Viewing Laboratory Data

- Laboratory Data eCRFs are designed with dedicated Tabs (Hematology, Blood Chemistry, Urinalysis, etc.)
- Additional Lab eCRFs can be viewed by clicking Show Unplanned Events
- Additional Lab eCRFs can be added by:
  - Select the appropriate Lab Visit;
  - Open the patient's last Lab eCRF on the selected visit;
  - Then select the menu option Insert -> Visit
    - **Do not select Insert -> CRF**

Saving eCRF

Saving eCRF

- eCRF can be saved using
  - Toolbar Save Icon (yellow floppy disk)
  - F10 Key
  - File -> Save menu option

- **Quick Tip:**
  - Save Often!! Especially while entering Ongoing Information such as AEs and ConMeds.
  - C^{3}D session terminates without warning if there is no activity for 30 minutes.

Data Entry Change Reason

Data Entry Change Reason

- Change Reason needs to be specified while changing data on completed eCRF

- Change Reason becomes part of the Audit Trail along with date of change and user name

- Comments can be provided in the change reason to further explain

- **Quick Tip:**
  - Do not use personnel/patient names or identifiers in the comments.

What is a Discrepancy?

- A discrepancy is the failure of entered data to pass a validation check as applied by C^{3}D.

- C^{3}D validation checks are defined based on the definition of the fields, logical rules, protocol specifications, and sponsor requirements.

- Discrepancies are tools to assist teams in identifying potential data inconsistencies and facilitate real-time QA of data.

- **Quick Tips:**
  - Discrepancies do not cover 100% of possible data inconsistencies.
  - Clinical judgment may supersede discrepancy logic.

C³D Discrepancy Types

- **Univariate**
  - ❑ Generated during data entry/load when data is in some way different from the Question's definition (e.g. mandatory, length, type, range, pick list, etc.)

- **Multivariate**
  - ❑ Based on a condition on one or more questions as defined in a validation rule
  - ❑ Generated on-line or when validation rules are run (eCRF must be saved as Complete.)

- **Manual**
  - ❑ Generated by data entry operator seeking clarification on data values

Some Typical Discrepancies

Types	Example:	Resolutions
Data Type	Text entered in numeric or date field.	Review Source Document and enter appropriate data.
Length Problems	Too many characters entered.	Use NIH accepted Abbreviations.
Value not on the Pick List	Generic Agent not present in Concomitant Agent Pick List and user typed in an Agent not found on the Pick List.	Search for alternates. Consult Team Lead. Request value to be added to Pick List.
Mandatory Value	Required Field left empty.	Refer to Source Document. Design modification.
Partial/Invalid Dates	00-10-2010 entered, but field requires a full data such as 01-01-2010	Refer to Source Documents. Check Day Month Year order. Check that date is not in the future.

Outstanding Discrepancies in a Study

Outstanding Discrepancies in a Study

- Total number of Discrepancies in a study are shown in the Activity List
- Clicking on the 'Review xx Active Discrepancies' link will present only the Discrepant eCRFs

- **Quick Tip:**
  - Data Managers should manage their discrepancies every morning to help ongoing QA of data.

eCRFs Containing Discrepancies

eCRF Containing Unreviewed Discrepancies are displayed as Red

eCRF Containing Discrepancies

- eCRF containing discrepancies are shown in Red
- It is a good practice to address discrepant eCRF on an ongoing basis

Discrepancies Tab

Discrepancies in the selected eCRF are summarized in Discrepancies Tab

First tab enumerates all discrepancies. Additional tabs provide individual discrepancies details.

Discrepancies Tab

- While viewing an eCRF, clicking on the Discrepancies Tab shows the discrepancies on that eCRF

- The first tab gives the summary of all discrepancies in that eCRF (open and closed)

- Additional tabs provide individual discrepancies details.

Discrepancy Details

Discrepancy Details

- Subsequent tabs show details for each discrepancy
- Open Discrepancies are displayed first and are followed by Closed Discrepancies

- **Quick Tip:**
  - Double Clicking on the Discrepancy Text brings up a pop-up box with the entire message

How are Univariate Disc. Created?

How are Univariate Disc. Created?

- Univariate Discrepancies pop-up is presented during data entry when the entered value does not match the field definition.
    - Mandatory field left empty
    - Text entered in a Date or Numeric Field
    - Too many characters entered
    - Value is not on the Pick List
    - Partial Date entered when a complete date is required
- Data Entry operator can:
    - Cancel the pop-up and fix the value
    - Or accept the discrepancy

- **Quick Tip:**
    - Univariate Discrepancies are reassessed during Batch Validation for Design Changes.

How is a Univariate Disc. Displayed?

How is a Univariate Disc. Displayed?

- Discrepant data is highlighted in Yellow
- Discrepancy text provides the details

- **Quick Tip:**
  - Double Click on the Discrepancy Message Text to view the entire message in a window.

How are Multivariate Disc. Created?

- Multivariate Discrepancies are created based on validation rules programmed in a study
    - <u>Example 1</u>: Create Discrepancy if the entered BSA is not within 10% of the calculated BSA
    - <u>Example 2</u>: Create Discrepancy if Date of Histological Confirmation is before Date of Diagnosis

- **Quick Tip:**
    - Rules available as a standard on each eCRF are summarized in the eCRFs Instructions Manual.
    - Though several standard rules are implemented for each eCRF as specified on the eCRFs Instructions Manual, clinical teams can request them to be turned off or modified to comply with the Protocol.

Evaluation of Multivariate Rules

- Validation Rules are evaluated:
  - ❏ on-line validation rules are evaluated upon completion of a CRF **Saved as Complete**
  - ❏ during an overnight batch validation session for CRFs **Saved as Complete**

- Multivariate Discrepancies are displayed in the same manner as Univariate Discrepancies. The Discrepancy Details panel indicates the type of Discrepancy.

- **Quick Tip:**
  - ❏ Complex rules run overnight.

How is a Multivariate Disc. displayed?

Discrepancy tab

Discrepancy Description

Related Data

How is a Multivariate Disc. displayed?

- Discrepancy is based on one or more fields and is NOT highlighted in Yellow
- Discrepancy tab provides the details
  - Discrepancy Text
  - Involved Clinical Data in the evaluation of the Discrepancy

- **Quick Tip:**
  - The Action pull-down "Go to Data Field" does not work as the discrepancy could be based on more than one field.

How to Address a Discrepancy

Choose Go to Data Field from Pull Down Menu

Fix Data as indicated in the Discrepancy Text

How to Address a Discrepancy

- Review Discrepancy Details
- Whenever possible, use the Action pull down 'Go to Data Field' to jump to the Discrepant Field
- Resolve the discrepancy by:
    - Consulting Source Documentation and;
    - Modifying incorrect data and specifying change reason;
    - Requesting eCRF Design and/or Validation Rule Change.

- **Quick Tip:**
    - System obsoletes univariate discrepancy automatically when data is corrected and complies with design/rules.
    - Multivariate Discrepancies are only re-evaluated during overnight Batch Validation.

Verification & Approval

Verification & Approval

- C³D Verification & Approval functionality offer capability to track QA and Monitoring of eCRFs.

- Verification functionality is available for users with Research Nurse account role.

- Approval functionality is available for users with Monitor account role.

Verification

Verification

- Each eCRF can be verified by clicking on the Verify button
- Verified eCRF Icon has a Checkmark
- Editing a verified eCRF changes its icon to a Re-Verify status
- Edited eCRF can be re-verified
- eCRF Verification Change History is maintained in the Verification pop-up Window

Verification

Verification

Approval

Approval

- Each eCRF can be approved clicking on the Approve button and providing your C^{3}D password
- Approved eCRF Icon has a Signature
- Editing an approved eCRF changes its icon to a Re-Approve status
- Edited eCRF can be re-approved
- eCRF Approval Change History is maintained in the Approval pop-up Window

CRIS to C³D Lab Data Flow

CRIS ➡ **CDW** ➡

Lab Mapping

WBC Count   WBC_SERUM
Basophils   BASO
Hemoglobin   HEMOGLOBIN
WBC Morphology ???

➡ **C3D**

LLI
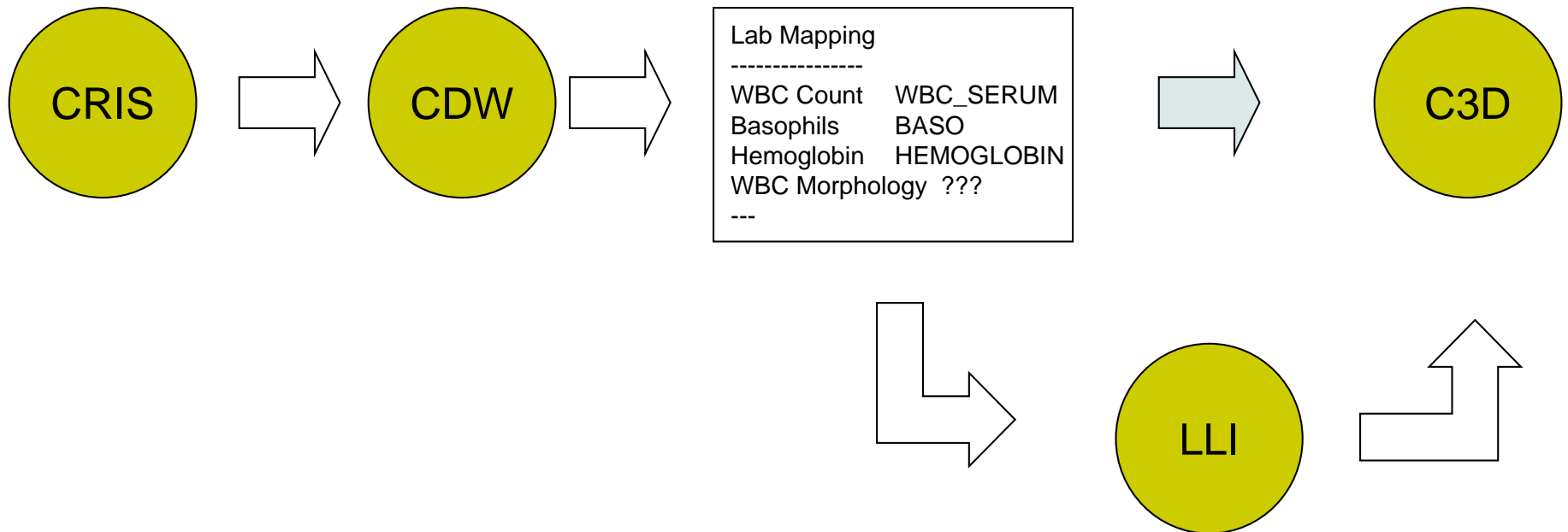
What is LLI?

- LLI is a utility to review and identify specific Lab Test Results to be downloaded from the CRIS/CDW into C^{3}D

- URL: https://octrials.nci.nih.gov/opa46/labloadinter.htm

- Username & Password are same as C^{3}D

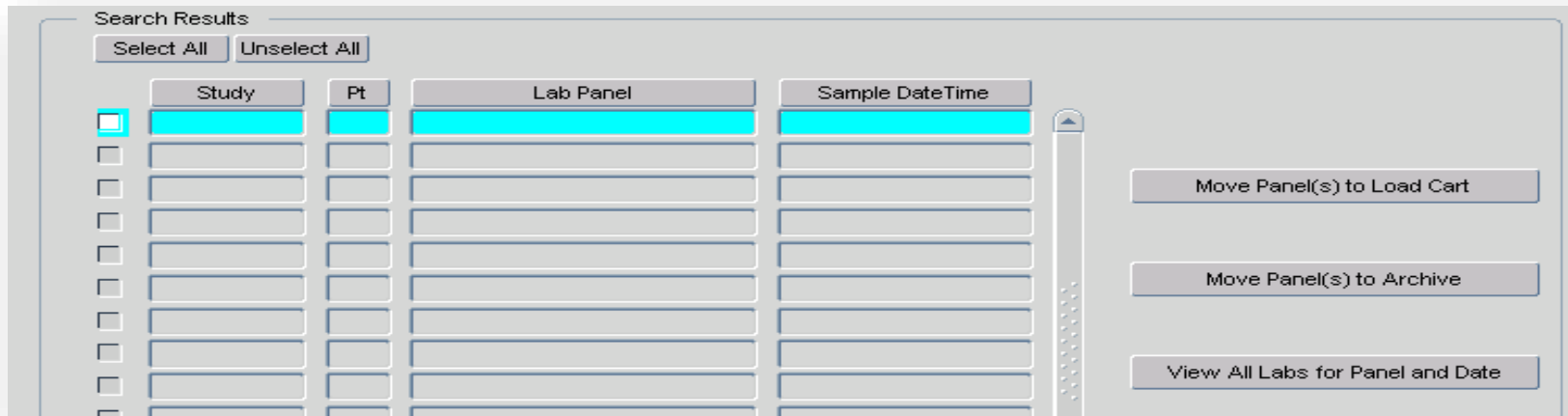# LLI Search Screen

LLI Search Criteria

- **Searching**
  - Can search by Study, Patient Number, Lab Panel, OC Lab Question, Date and/or Time
    - Each search field contains Pick List.
    - Date and Time allows the '%' wild card
    - Date and Time provide the additional option of:
      - "On or Before", "On or After" and "LIKE" comparisons
      - Partial dates can be entered as %NOV%

LLI Search Screen Results

- **Search Results**
  - The result set lists Lab Panels that have at least one lab test available for loading that meet the criteria entered into the search fields.
  - The sort order can be changed using the column headings.
  - Results can be selected/deselected for processing by using the individual select check box or Select Buttons.
  - Entire panels of lab tests can then be moved to the Load Cart or Marked for Archive.
  - Clicking "View All…" button or by double clicking the record presents the Work Cart with specific Lab Test Results for that panel.

LLI Work Cart

- **Work Cart**
  - Shows Entire Panel, including previously loaded and missing Lab Tests
  - The list can be filtered using the "Load Flag" radio buttons.
  - Sort by Lab Test Panel Order (R), Test Name, Results, etc.
  - Results can be selected/deselected for processing by using the individual select check box or Select Buttons.
  - Once selected, the lab tests can be moved to the Load Cart or Archived

Questions?