# Validating CP-CTNet Study Build in the Medidata Rave **Clinical Trial Data Management Systems (CTDMS)**

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# Introduction

The Cancer Prevention Clinical Trials Network (CP-CTNet) is a program of the National Cancer Institute (NCI) Division of Cancer Prevention (DCP) which performs and provides support for early phase clinical trials. The Data Management, Auditing and Coordinating Center (DMACC) is comprised of partners from the University of Wisconsin – Madison and Frontier Science Foundation and supports the conduct of all CP-CTNet studies. A major component of this support is providing centralized data management and study build expertise.

Although most individuals are aware of the requirement to validate major computer systems under 21 CFR Part 11, an equally important but lesser known requirement is to validate all study builds created within a Clinical Trials Data Management System (CTDMS) environment to show that they are "fit for use" for the specific protocol. Using the same rationale as the typical software development lifecycle (SDLC) validation, the study configured in the CTDMS must be appropriately tested and documented to show that edit checks fire as expected, visits roll out as required, questions are clear and visible and are accompanied with the correct answer fields, and that the data entered into the eCRFs are organized as expected for purposes of reporting or otherwise readying the data for analysis.

CP-CTNet utilizes Medidata Rave as the CTDMS for all network studies. Preparing a study build for data entry is a collaborative effort that begins with review of the protocol developed by a Lead Academic Organization (LAO). Each protocol defines the data that are required to be collected and is the basis for the creation of the System Variable Attribute Report (SVAR), which details each data element that should be present on the set of study eCRFs. Common Data Elements (CDEs) from the NCI Cancer Data Standards Repository (caDSR) are used to define each eCRF question. The use of CDEs ensures that data are collected consistently across all network studies. The SVAR for each study undergoes extensive review by multiple entities before finalization, including: the LAO, DCP, the Regulatory Contractor (CCSA), CDE Contractor (Curator), and DMACC

For CP-CTNet studies, Frontier Science has adapted and improved upon study build and validation processes that had been previously developed for other projects. The use of CDEs and the ability to directly import eCRFs into Medidata Rave from the NCI caDSR have allowed us to streamline the entire build and deploy a study to production in approximately 30 days from finalizing an SVAR, which is a significantly shorter turnaround time than is possible in other projects.

# **High Level Process**

You need to validate and subsequently document that...

- eCRFs collect data required by protocol
- eCRFs are tied to the correct visit
- Number of visits are correct
- Unexpected events roll out the correct form (agent interruption, etc.)
- Edit checks work as expected
- Queries are trigged as expected Data entered on the eCRFs make it to the database in the correct place
- Site permissions are correct



# I The Study Build Validation Process and Considerations

# **STUDY BUILD VALIDATION PROCESS**

The process for validating a study build basically mimics the process for validating a piece of software. CP-CTNet study build validation is carried out by a multidisciplinary team, with each member having expertise in a specific step of the process necessary to produce the end product.



Step 1 – SVAR Review and Approval: A list of requirements base on the needs of the protocol is created for each study build. For example, what data are being collected and when (at what visit)? The DMACC Data Managers utilize the CDEs defined in the SVAR to implement the necessary eCRFs for each study. Each study-specific SVAR undergoes a collaborative review process before the eCRF set is finalized, which includes representatives from the LAO, DCP, DMACC, CCSA, and the CDE Curator. As more eCRFs are built and validated, DMACC will house a library of standard eCRFs to be incorporated in the SVARs used for future trials, which will accelerate this step in the build and ensure consistent data collection across the network.

Step 2 – eCRF Building: The DMACC Data Managers use the CDEs defined in the SVAR to select the appropriate questions to build each eCRF in the NCI's caDSR Form Builder tool. The use of this tool ensures that data being collected across the network is collected in a uniform way. eCRFs are then directly imported from Form Builder into Medidata Rave. In Rave, the Data Managers, Study Builders, and Clinical Programmers work together to define and implement custom edit checks and skip logic that are needed for each eCRF, as well as for the rollout of the visit folders defined by the protocol's Schedule of Evaluations. Before formal validation can take place, Data Managers perform informal testing to ensure that all validation requirements have been accounted for.

Step 3 – User Acceptance Testing: Test cases are created for each requirement to be tested and are outlined in a Testing Plan. The requirements that are tested are both the requirements for the eCRFs themselves, as well as any edit checks. The successful transfer of data between the Registration/Randomization System (Stars) and Rave is also The Data Managers complete each test case, noting any requirements that fail to produce the expected result. Note any cases that do not produce expected results. If testing demonstrates that there are any potential errors with the build, these issues are corrected and the appropriate test case is repeated until it passes.

Step 4 – Complete Validation Documentation: After testing is successfully completed, a Testing Report is created, indicating that the study build has been validated is ready for production. This report acts as a system release report as in software validation and serves as evidence that validation was competed, testing was successful, and that the build is fit for use with the intended protocol.

Step 5 – Deployment to Production: The study is now ready for deployment to the production environment, and invitations to site staff can be sent.

## **CATEGORIES OF EDIT CHECK REQUIREMENT**

<b>Missing Values</b>	For fields where data are always expected, impose a check if blank Specify on requirements document that this field cannot be blank
Simple Range Checks	Identify potential out of range numbers and flag incorrect data Allow to be overridden in the event that the data are correct
Logical Inconsistencies	These are more intuitive and take experience to identify/configure e.g., data of visit must be after date of study start
Cross-form Checks	Programming for these checks is somewhat more complex e.g. adverse event listed as reason for termination but no AE form
<b>Protocol Violations</b>	May require additional tracking or attention during course of study e.g. the listed age for participant renders them ineligible for the study

## USER ACCEPTANCE TESTING (UAT)

A traceability matrix is used to link the requirements for the study to the specific test cases. This demonstrates to an auditor or any other external reviewer that each study requirement was in fact tested and allows the reviewer to locate the test case and/or results if desired.

User Acceptance Testing is the method by which the build is subjected to various data inputs, usually inside and outside of the necessary parameters for a given data field, to ensure that the edit checks and eCRFs display as expected. This is a critical step in the process and the DMACC Data Managers complete this testing, while working closely with Study Builders, as needed, to address any testing issues that may arise.

Testing focuses on ensuring that edit checks roll out as expected for each eCRF and each data field. The chart to the right indicates the types of edit checks that might be tested during user acceptance testing (UAT) of a study build.

Traceability Matrix	
Each requirement for a study build must be tested to verify that the requirement has	been met. The
Traceability Matrix indicate which tests are used for verification and validation of eac	h requirement
Requirement	Test(s)
R1.001, R1.002, R1.003, R1.004, R1.005, R1.006, R1.007, R1.008, R1.009, R1.010, R1.011	AT-76633
R2.001, R2.002	AT-76634
R3.001, R3.002, R3.003, R3.004, R3.005, R3.006, R3.007, R3.008	AT-76635
R4.001, R4.002, R4.003, R4.004, R4.005, R4.006, R4.007, R4.008, R4.009, R4.010,	AT-76636

Describes the organization's approach to Study Build Validation Includes change control provisions Explains what deliverables you produce as part of the process





# **I** The Deliverables

Just as with computer systems validation, there is a minimum set of expected deliverables. The following is a list of deliverables that are required to be created to demonstrate that a given study build was validated within the clinical trial data management system (CTDMS) and that the build (eCRF development) meets the protocol's needs.

## **STUDY BUILD SOP**

### VALIDATION PLAN

- Validation team members and their respective responsibilities One per study
- Describes how this study will actually be validated, in specific
- Describes how you will capture objective evidence of testing
- Summarizes overall study risk

### **SPECIFICATION & REQUIREMENTS**

- List of all the users' specifications, requirements, and expectations for the build
- Based on inputs from anticipated users, the protocol, regulatory needs for the study, and data collection workflows between participating entities

### **TESTING PROTOCOL**

Expected results

Test cases should cover multiple

report forms roll out and that edit

scenarios to ensure that case

checks, etc. fire as intended

Test cases

### **TESTING REPORT**

- Summarizes that all activities as described in the TP were completed as planned
- Can explain any deviations in the process set forth in TP
- Test cases
- Actual results
- Resolutions (if applicable) Evaluation

# I Change Control and Study Build Summary

Change control is administered to a study build if there are subsequent modifications to the protocol. For a study build update, the same process is followed as for a new study, beginning with the review and approval of an updated SVAR. Any change made in the new version of the study build is validated and documented.

Following a standard study build validation and implementation process is essential for ensuring data integrity and data collection consistency across all CP-CTNet studies. All validation documentation is retained within the study's Trial Master File (TMF) and is available to support our robust study build process in the event of an audit or inspection.

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