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User Acceptance Testing of Clinical Databases

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The clinical database tells the story of the clinical trial. During the study, the project team will make many clinical and business decisions based on the clinical database. It is a primary deliverable for the project team.

Before data can be collected in a study, the clinical database has to be developed and tested by a CRO, another service provider, or an internal team. Even then, it is still not ready to go live. First, it must pass user acceptance testing (UAT) to make absolutely, positively sure that it fits the study's needs. Only then can it go live.

Any database changes after "go live" will be not only expensive, but they can also result in missing or inconsistent data, create opportunities for confusion, require replacement of critical forms for sites, and interfere with other key deliverables, including a finished database that includes all pertinent data in a usable form. No one wants to waste valuable resources updating documents, retraining staff, and migrating the database to address problems that could have been identified and corrected via a thorough UAT review.

Additionally, while a CRO or other service provider might build and test the clinical database, according to International Conference on Harmonization Guideline for Good Clinical Practice ICH E6, "The ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor."[1] The recently finalized ICH E6 (R2) guideline adds, "The sponsor should ensure oversight of any trial-related duties and functions carried out on its behalf."[2]

Since the study team knows the study best and will be most affected by any problems in the database, UAT is essential.

UAT starts with a database that has already been tested by the developers, so those tests do not all need to be repeated. Instead, the UAT team should take a risk-based approach with supplemental testing. Such an approach should focus attention on critical data points and keep the following questions in mind:

- Will site personnel find the electronic case report form (eCRF) easy to use?[3]
- Will the statisticians have what they need to analyze the data?
- How well will the query tools and reports aid CRAs in monitoring subject safety and protocol compliance, especially when monitoring remotely?
- Will related system components like IVRS and coding modules work smoothly with the database?

A risk-based approach should also consider the UAT team's previous experience with the database development team and a detailed understanding of how the development team tested the database.

The following recommendations for UAT are based on the author's experience and the Society of Clinical Data Management book, Good Clinical Data Management Practices.[4]

Study Structure

The foundation of the database is the structure, which is based on the protocol, which reflects the study design.

- Verify that the time and events table in the clinical database is consistent with the protocol's schedule of activity.
- Do not rely solely on paper documentation of study structure. Confirm that the study structure in the database generates the correct EDC forms for each visit, including unscheduled visits, if allowed.
- The database structure should organize data so it can be easily understood and analyzed. Do not collect unnecessary data, e.g., information about site payments, that have nothing to do with the clinical data.
- Watch for duplicate data, which might have to be reconciled. Inconsistent duplicate data can create uncertainty and generate errors.
- Any external data that will be imported into the clinical database for further analysis will have to be reconciled with eCRF data of the same type. For example, if sites enter abnormal lab results in the eCRF, it will have to be reconciled with data imported by the lab. If the lab can provide timely data, abnormal lab results need not be entered manually into the eCRF.

Data Quality and Standards

You can improve data quality by using data standards, created internally or, preferably, by a standards organization. The Clinical Data Interchange Standards Consortium (CDISC) has developed standards to facilitate acquiring, submitting, exchanging and archiving clinical data and metadata. CDISC provides a library of Clinical Data Acquisition Standards Harmonization (CDASH) forms free of charge. Using these forms will streamline tabulation of clinical data for FDA submission. Most EDC vendors support CDASH standards, and some even provide libraries of pre-designed standard forms. Confirm and possibly verify that eCRF forms comply with CDASH.

Make sure any guidelines for users are clear and correct. Do they agree with online help in the eCRF? For example, instruct sites on when and where it is appropriate to use a "missing" code for missing data. Use edit checks to help enforce the rules. Obtain feedback from sites on the forms and instructions (and even involve them in UAT), and remedy any problems as quickly as possible.

Ask the development team about its testing process. Ask to see their edit-check testing documentation. Data for test cases might be available. Verify that all data validations, especially for critical variables, have been correctly implemented.

Review codelists for compliance to standards and consistency with the protocol. Codelists often populate drop down lists and radio buttons in the eCRF, so remove inapplicable answer choices, since their presence could generate errors.

Do not just test the unique forms. Make sure every form's edit checks work for all visits where the form is used.

Data Extracts

In addition to testing the eCRF, look at the output — the data extracts. Meaningful field names will make testing and use of the data easier.

Review the content and structure of each extracted file. Confirm that test data appear for every form and field as expected in extracts, such as SAS data files, reports, listings, etc. Make sure the field lengths, units, number of significant digits (especially for lab data), date formats, and back-end calculations flow consistently from the forms into the database and

then into the data extracts. Truncated text is relatively easy to see, but truncated numbers require extra attention. Confirm any blinding or view restrictions, as well.

Workflow

The workflow for reviewing, monitoring and cleaning data is critical to the success of a clinical study. Obtain from the development team a document that details the rights assigned to each EDC role. Have someone from the UAT team perform each role's task in the workflow to confirm the workflow setup on each form and field is correct.

Simulate the role of study coordinator. Confirm that the eCRF flows logically within and across the forms. Verify that data entry feels natural. Include instructions within the forms. Confirm that the forms work smoothly on that type of device if a device other than a standard desktop computer will be used. Ask the Lead CRA or an experienced site monitor to assess the flow of source verification with the eCRF forms.

Ensure that reports are informative for the study's medical monitor(s) and, if one exists, the data and safety monitoring committee (DSMC). Show sample reports to pharmacovigilance team members for their feedback.

System Components

Many external tools and systems, such as randomization, provisioning, medical coding, lab administration, and safety, can be used in conjunction with EDC systems. These system components can be error prone, especially with manual processes. Ask the development team to provide documentation for its testing of these components. Validate these system components with the same rigor as the core EDC system.

For example, if you are using an external system to administer lab data, thoroughly test the lab setup according to approved specifications. Confirm that standards, lab mappings, unit dictionaries, ranges, clinical significance flags, etc., are correctly applied. Ensure that any lab data that can be entered manually in any eCRF form follows the same specifications.

Conclusion

CROs generally welcome sponsor participation in UAT. They appreciate positive feedback for a job well done and value constructive feedback that prevents problems that could be difficult to remedy later in the lifecycle of the trial.

It is vital to perfect the clinical database before the study starts, so any shortcuts in user acceptance testing do not create costly delays later.

References

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