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Validation of Electronic Systems to Collect Patient-Reported Outcome (PRO) Data - Recommendations for Clinical Trial Teams: Report of the ISPOR ePRO Systems Validation Good Research Practices Task Force

ESSENTIAL COMPONENTS OF THE VALIDATION PROCESS

The systems development life cycle (SDLC) is an outline of the activities, tasks, responsibilities and deliverables required to develop a high quality, validated electronic data collection system. The SDLC methodology employed by the ePRO provider should be scrutinized to determine if it includes, at a minimum, these critical elements:

1) system requirements
2) system design
3) coding / tailoring / software development
4) testing by system provider
5) traceability
6) user acceptance test
7) installation/configuration management
8) decommissioning plan

<u>System Requirements</u>

What it is

The purpose of systems requirements documentation is to describe all aspects of the system, regardless of the technology used. The resulting documentation covers the needs of the study protocol, target patient population and clinical staff, and needs to be accepted formally before any system development begins [13].

The system requirements documentation is the blueprint for what the system will do. It enables: 1) the clinical trial team to request changes while the ePRO system is still on paper -- when changes are easy, quick, low risk, and inexpensive to make; 2) the system provider's team to get a clear and thorough description of the system that they need to design, develop and deliver. For example, the programmers, test strategy writers, training developers, etc., need a detailed picture of every aspect of the system to fulfill each of their system validation responsibilities and to ensure that their individual deliverables complement each other properly, resulting in a high quality system for the trial; and 3) the same detailed expectations of

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the system to be understood by both the team and provider. This is especially important during User Acceptance Testing (described later) and during the system's use in the trial.

Other names for this documentation

It can also be called u*ser requirements, functional requirements*, and *user specifications*, among others. Documentation may be in one document or several. Regardless, it is critical to both parties that there is documentation with a very clear, thorough description of all aspects of the system [13,14].

Clinical trial team involvement

The team's involvement is critical during the requirements gathering and definition stage, whether or not the ePRO system will be developed internally, or whether it will be developed by an external provider.

Clinical trial teams who do not have the expertise to write the systems requirements document will usually rely on the ePRO system provider, a consultant, or technical experts inside their organization for producing it. The clinical trial team provides the clinical trial protocol to these experts. In most cases, the team meets with the systems requirements document authors to determine how the system should work to meet the protocol's requirements, as well as the needs of the users at clinic sites, the target patient population, and the stakeholders in the sponsor's organization. Sponsor organization stakeholders include clinical operations, data management, biostatistics, outcomes research or health economics, and regulatory compliance [14].

Items discussed with the clinical team include screen flow (individual screen designs to properly display the PRO items), data entry field edits, data transfer requirements, data file formats, security requirements, as well as compliance with FDA regulation 21 CFR Part 11 [15] on electronic records, electronic signatures and a multitude of other details. The sponsor has to translate regulatory directives into system functionality from data access to reporting to retention for audit and inspection [6].

When a draft of the system requirements document is complete, it is imperative that the clinical trial team provide thoughtful review and feedback to request any necessary changes. These sponsor-requested changes must be made according to an agreed upon timeline to support delivery dates. When the clinical trial team and the ePRO system provider are both satisfied with the system requirements document, in that it correctly and completely includes all system details, key members of the study team sign this documentation, providing evidence of their agreement and approval. Key members of the system provider's project team also sign this documentation to provide evidence of their agreement and commitment to deliver the system as described [13,14].

Why it is important

The system requirements documentation is the basis for all subsequent system validation processes and deliverables. If sections are vague, ambiguous or missing, there will be differences in interpretation and misunderstandings between the clinical trial team and ePRO system provider team members. These differences will then be discovered only later in the user acceptance process, which can result in delays in patient enrollment, risk in the quality and stability of the software, as well as functional issues and deficiencies during the trial. Therefore, it is critical that the document be precise, clear, correct, and complete [13,14,16].

Minimum content

The system requirements document should include everything needed to provide a clear, detailed description of the system. At a minimum, it should show and/or precisely describe all aspects of the system affecting the user, including the instruments selected, screen shots (PDA tablet or Web), voice prompts (IVR), data entry fields, edit checks, error messages, navigation logic, behavior of all buttons (PDA, tablet, or Web), algorithms, alarms, timeouts, security functions, audit trails, electronic signatures, alerts to subjects and site staff, and report designs. Text descriptions of these items must be accompanied by graphics where needed to ensure clarity.

Regardless of the technology to be used for the trial, ideal system requirements documentation should include the following topics: 1) purpose or objective; 2) definitions; 3) referenced documents; 4) assumptions; 5) system and process flows including flowcharts that show the screen flows and related logic for the entire system; and 6) functional requirements. The latter--the heart of the document, may be lengthy, often organized by the user group (e.g., systems requirements for clinic staff), but can be organized in any manner that makes it easy to understand.

This short outline of the functional requirements in system requirements documentation is a sample of content that would be expected for the first screen in a section describing a patient screen flow. Each item in the outline would be followed by a clear and thorough description.

Functional Requirements

Section 1- Patient Screen Flow

1. First Screen- Patient Login
    a. Screen Shot
    b. Data on Screen Banner
        1) Date
        2) Time
    c. Data Entry Fields
        1) Patient PIN number
            a) Check for 4 character numeric and error message
            b) Check for match with subject and error message
    d. Navigation buttons
        1) Cancel button
            a) Data not saved
            b) System takes user to previous screen
        2) OK button
            a) Check for PIN number entered
            b) System takes user to next screen

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Important quality management processes to be aware of

The first important step in developing high quality system requirements is for all members from the system provider and the study team to carefully read and study the trial protocol and any other documents describing the trial and standards of the sponsor. Key members from the system provider team should then lead a collaborative, detailed and thoughtful requirements-gathering discussion to determine how the clinical trial team would like the system to work to support their protocol, data quality and integrity, clinical sites, and staff [13,14].

The individual facilitating the discussion needs to remind the participants that there is always a tradeoff between timeline, cost, and quality.
The more features that are incorporated into the system, the longer it will take and the more costly it will be to build and validate the system.

The requirements-gathering discussion should be followed by a first draft of the system requirements section/document. This first draft should be read carefully by team members on both sides. Another collaborative discussion should follow whereby the clinical trial team provides feedback and requests changes [6, 13, 14]. A requirements-gathering process typically requires at least two revisions of the first draft to produce final system requirements documentation.

If the scope of the approved system requirements exceeds the original assumptions made in planning the project, a revision will be needed in the project plan, which may affect the study timeline and budget. The system provider should provide quality control on the production of the system requirements documentation, such that an independent party familiar with the system requirements reviews the final documentation before it is delivered to the clinical trial team.

System Design

What it is

The design phase involves development of system design documentation providing a complete, clear, detailed, *technical* description of how the ePRO system will be built to meet the needs of the protocol and the users. The documentation serves to communicate to the developer what has to be included as well as what is out of scope of the system. The documentation needs to cover both the context in which the system will operate and the details necessary to free the developer from uncertainty as to how it should be built [13,14].

The ePRO system provider is responsible for developing the bulk of this documentation. The sponsor or CRO responsible for uploading ePRO data to the study database, however, may need to provide specifications for the data transfer files for the ePRO system provider to use when building/configuring the data transfer module.

Software development professionals use the system design documentation to write the programs and/or set technical parameter values for the ePRO system. Some ePRO systems use a base system that is configured for use in a specific study using parameters and settings, with minimal programming of source code to complement the base system.

The initial concept of how to translate the requirements into a viable system may undergo revision as the system is built and subjected to unit tests. As the system is built, the author of the system design documentation needs to communicate effectively with the clinical team and the software development team to ensure that the design to be implemented still meets the requirements of the users [17].

System design documentation needs to cover three principal functions, which correspond directly to the following modules of a typical ePRO system:

- data collection and storage (collection of data by any of several technologies) to be stored on a server controlled by the ePRO system provider);
- web portal and alerts (allowing source data on the server to be displayed, reports to be generated, and alerts to be triggered and sent); and
- data transfer (transformation of stored data into transfer files for sending to the sponsor or its CRO).

Other names for this documentation

It is also known as the *software design specification*, *technical design specification* or *system specification documentation.*

Clinical trial team involvement

The role of the clinical trial team is the review and acceptance of the system design documentation. This role should be clarified early in the life of the project to avoid unexpected delays in moving on to system development. The clinical trial team should seek to clarify areas where the system provider has not correctly interpreted a requirement within the design documentation or has provided an incomplete description of the solution. Where the documentation is difficult to interpret, the clinical trial team should seek assistance from technical subject matter experts, rather than assuming that the specification covers the requirements correctly and fully.

Why it is important

The system design documentation is a bridge between the system's requirements and the software developers. Getting this documentation right is a crucial step to ensure that the software development effort will produce an appropriate solution embraced by the system users and compliant with clinical protocol [6,13,14].

Minimum content

The documentation should cover all three of the modules described above, ideally with a separate document or section for each one. Where a base system is used and the specifications of the base system are not changing, the ePRO system provider should make the relevant portions of that documentation available to the clinical trial team.

The data collection module's system design documentation needs to cover details not already in the system requirements documentation on topics such as the following:

- the logic for handling screens, and
- the logic that controls the logon of the user and flow of control through the screens/scripts;
- edit checks that prevent entry of incorrect data or commands;
- alerts to users, and
- other error handling logic.

In addition, the data collection module's system design documentation needs to cover details not already in the system requirements documentation: 1) for technologies that require sending data to a server, the logic and methods available for data sending, including control processes for assuring that data sent is complete, accurate and not duplicated, and 2) for all types of technologies, the handling of partial/incomplete saving of data to the server (e.g., roll-back).

The web portal module's system design documentation needs to cover design details not already in the system requirements documentation on topics such as the following:

- logon and password security;
- security groups and their authority over data access;
- display of clinical data, including raw data, metadata and audit trails;
- display of and flow between reports, both standard and custom;
- alerts to users and the logic of their triggers; and
- other processes, such as automation of device logistics or data change requests.

The data transfer module's system design documentation needs to cover details not already in the system requirements documentation on topics such as the following:

- timing, frequency and method of data transfer;
- the set of data elements to be transferred and their format;
- the process for transforming data into the format specified by the sponsor or its CRO; and
- control processes for assuring that data transfers are complete, accurate and not duplicated.

Important quality management processes to be aware of

The system provider should provide quality controls on the production of the system design documentation, such that an independent party familiar with the system requirements reviews the documentation before it is delivered to the clinical trial team.

Coding/Tailoring/Software Development

What it is

Coding/Tailoring/Software Development is the process of writing code in a software programming language or assembling and customizing modules of code that have already been developed to meet the needs of a specific trial.

Why it is important

These processes are the building blocks of the computer system that will be used in the clinical trial. Improper execution and documentation of the development process leads to a system that is difficult to maintain and not sufficiently auditable by third parties [12].

Clinical trial team involvement

There is no clinical team involvement due to the highly technical nature of this process. Typically, the clinical trial team communicates through a project manager and/or analyst who ensure the trial requirements are properly translated into specifications for the developers.

Important quality management processes to be aware of

As with any process, the goal is to identify any problems or defects as early as possible and to ensure that they are resolved [11]. In development, there should be a review of the created code that may be executed by one or more technical peers that understand the languages and standards for the development method used (*code review*). Prior to introducing new work into the larger structure of the trial design, the developer (or a peer) should test the individual modules to ensure they perform properly and are meeting the design requirements, constraints and assumptions (*unit testing*) [18].

The discovery of any defects arising from quality processes during software development should be documented with information about the conditions under which the defect occurred to allow for reproduction. See APPENDIX 2: Process Quality Description. The defects should have a clear status (e.g., Open / Assigned / Fixed / Closed) so that they can be corrected in the system and verified by a second party before they are deemed to be resolved. As a system is developed, it should be possible to trace the code created or modules used back to the specific design elements they are implemented to fulfill.

Testing by System Provider

What it is

Testing for all items described in the system requirements document is critical to ensure that a new system meets every agreed upon requirement. The test plan describes the strategy for testing the system to ensure the environment and approach emulates real-world conditions. It also contains a comprehensive set of test cases to cover all systems requirements [7,13].

Clinical trial team involvement

The clinical trial team does not participate in the testing process; it is the responsibility of the system provider.

Why it is important

The programs required to provide systems for clinical trials are many thousands of lines of complex interrelated *code*. Even with highly experienced, highly committed programmers who comply with good quality coding processes, the complexity of most clinical trial systems almost guarantees that early versions of the system will not function in perfect compliance with the systems requirements document. Every system must be thoroughly tested.

System testing is done by following a detailed test plan and test cases. A carefully executed test plan ensures that the system will work as intended throughout the clinical trial [7,13].

Minimum content

The most important sections of a quality test plan are the test strategy and the test cases.

- Testing Strategy:

  This section is typically developed by testing team leaders, and should document the strategy for testing the system in conditions that closely approximate the trial. For example, if a trial with enrollment in 10 countries will last 12 months with a two week run-in period and a nine-month treatment period, the testing strategy needs to describe how the test environment will be created, how data will be collected and verified during the testing phase to simulate these conditions, and how to provide assurance and a high level of confidence that the system will perform reliably during the trial. Furthermore, the testing strategy must document the testing approach to indicate how all requirements in the system's requirements will be covered.

- Test Cases**:**

  Also known as *test scripts*, they are the basis of the testing strategy. They help determine whether the system is complying exactly with the specified requirements.

  Each test case contains step-by-step instructions for a test engineer to enter a set of pre-defined data, as well as a detailed description of the expected results. When executing each test case, the test engineer will indicate clearly whether the actual results equaled the expected results and thus whether the test case resulted in a "pass" or "fail." If there is a "fail," the engineer will document the deviation from the expected results in detail in an issue report, so that the programmer can determine the cause of failure, resolve it, and document the resolution.

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Important testing approaches to be aware of

Multiple testing approaches must be used. This will minimize the risk of system malfunctions and data file issues when the system is used in real-world conditions. The testing process must include the following as applicable for each requirement:

- Positive Testing- A wide range of valid entries and selections are made to ensure valid entries will be accepted by the system.
- Boundary Testing- Entries are made just within the boundary values (e.g., age range) and just on the outside of boundary values, to ensure edit checks on a field are correct.
- Negative Testing- Omissions and/or invalid entries and selections are made to ensure all error conditions are properly handled.
- Load Testing- A large data set of pre-defined, valid data is entered and verified both on a local system and also on remote systems (e.g., data repositories/servers) where the data will be transmitted throughout the trial, through comparison to pre-defined expected data sets. The size of the data set should be large enough to ensure that all related systems -- the local system, the remote systems, the telecommunications system, etc., can all easily accommodate more than the expected volume of data for the study, and still produce accurate results. Load testing is vital to provide evidence that the systems will function properly in a clinical trial.
- Regression Testing- This is critical after a programmer resolves one or more issues. The purpose of regression testing is to ensure the code changes do not damage other parts of the system that were previously working. Regression testing is necessary because code changes can often have unintended consequences on other areas of the software. In cases of substantial code changes, the entire system must be re-tested to ensure a high quality system is delivered. When code changes are very minor, for example to correct a misspelling, or other small error, regression testing can be more limited. The validation team must be very thoughtful about the level of risk introduced with code changes, and use a regression test strategy that will significantly minimize the risk.

Important management processes to be aware of

Test strategies, plans, and test cases should go through multiple management quality reviews and iterations within a system provider’s team. When test cases are executed, system issues or defects will often be found, which must be carefully documented and tracked by the system testers. Programmers will then create and document a new version of the system that contains the changes made to resolve the system defects and issues. A new test strategy will then be created for each new version of the system. This new test strategy should address the risk of software changes on previously performing system functions. Based on this risk assessment, the test strategy will indicate all the test cases that will be re-executed to ensure all defects have been resolved and to ensure adequate regression testing is done to fully address the risk of the software changes and ensure a reliably working system for the trial (7,13).

If there have been carefully executed quality processes by the management of the system provider, only two to three iterations of the test strategy and test case execution should be needed.
The conclusion is a successful User Acceptance Test by the study team, and systems that work as intended during the clinical trial.

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Traceability

What it is

Traceability plays a quality control role by establishing that the software provided meets the user's needs. It ensures that all elements in the systems requirements document are properly 'traced' through to other critical systems validation processes and documents.

A traceability matrix demonstrates that each requirement in the systems requirements document has been accounted for in the design document as well as in the test cases or scripts. It can be used to track: 1) the design (user) requirements for function of the system; 2) the software (functional) requirements that are specified to meet the user's requirements, and 3) the test cases that are used to verify that the end-product meets the software and user requirements.

Testing matrices can take many forms. For example, tracing can be accomplished from a unit test to the design requirements, such as a developer testing a piece of code to see if it works in isolation. Another example is tracing from the test case (formal testing of a specific software specification) to the software requirement.

Why it is important

A traceability matrix ensures that every system requirement has been designed and coded in the software and included in the software test cases. The traceability matrix also ensures that all requirements are exercised by test cases during system and user testing [13,14,17]. Keeping this tracing clear along the way will support both the internal assessment that all design elements have been appropriately tested, as well as support analysis later on if an inspector is verifying validation through testing records of critical design functions.

Most often there is not a single correlation between design requirements, software requirements and test cases. For example, a single design requirement may require several functional requirements to encompass the design feature; a single functional requirement may require several tests cases to verify it is working properly. Therefore, the traceability matrix documents these dependencies between the functional user requirements and the more technical software requirements.

Minimum content

A matrix that traces each systems requirement to a design element and to a test case is the minimum. The matrix can be a stand-alone document or summarized in an approved *test report* showing how the test cases checked for all design requirements.

Clinical trial team involvement

None. Traceability is the responsibility of the system provider. A sponsor may verify and confirm this effort as part of an audit.

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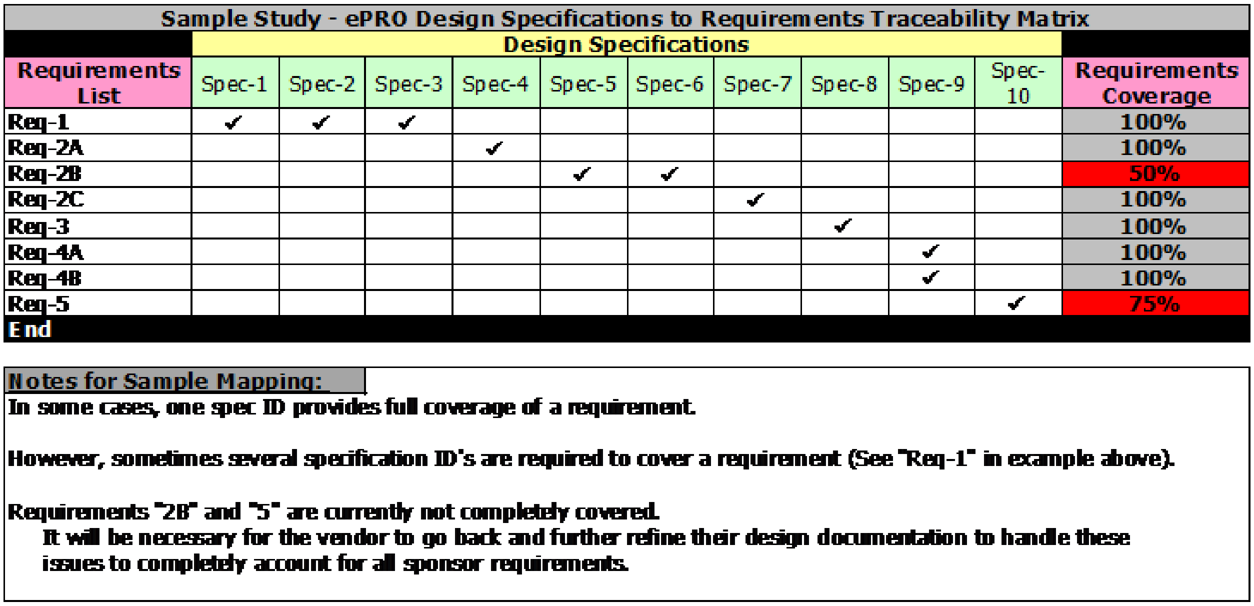
Important quality management processes to be aware of

A thorough traceability matrix prepared at this step can help prevent oversights in the design that will be more difficult and expensive to manage or fix later in the software development life cycle. Like all processes and systems subject to quality control, the traceability matrix should be examined by a system provider employee independent of the development team.



Sample Study - ePRO Design Specifications to Requirements Traceability Matrix

Requirements List	Design Specifications										Requirements Coverage
	Spec-1	Spec-2	Spec-3	Spec-4	Spec-5	Spec-6	Spec-7	Spec-8	Spec-9	Spec-10	
Req-1	✓	✓	✓								100%
Req-2A				✓							100%
Req-2B					✓	✓					50%
Req-2C							✓				100%
Req-3								✓			100%
Req-4A									✓		100%
Req-4B									✓		100%
Req-5										✓	75%
End											

Notes for Sample Mapping:

In some cases, one spec ID provides full coverage of a requirement.

However, sometimes several specification ID's are required to cover a requirement (See "Req-1" in example above).

Requirements "2B" and "5" are currently not completely covered.
It will be necessary for the vendor to go back and further refine their design documentation to handle these issues to completely account for all sponsor requirements.

Figure 1

User Acceptance Testing

What it is

User Acceptance Testing (UAT) is the process by which the clinical trial team determines if the system meets expectations and performs according to the system requirements documentation. If there is an inconsistency between the clinical trial team's expectations and the system provided, it will arise at this point. UAT should not commence until the system provider provides written confirmation that they have completed their role in the validation of the system. It should be noted that UAT is not a complete re-validation effort conducted by the sponsoring clinical trial team. Rather, it is a focused, risk-based approach to testing that allows the clinical trial team to determine if the system complies with the key system requirements (which ultimately reflect the protocol).

Other names for this documentation

UAT is also known as *User Site Testing (UST)*.

Clinical trial team involvement

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The clinical trial team must be heavily involved in developing the testing strategy for the UAT effort. It cannot be left solely to the system provider or a third party. Those who wrote the protocol and provided requirements to the system provider at the start of the project should contribute towards verifying those requirements have been covered [6].

Typically, the clinical trial team has several members involved in executing the test scripts. It can be helpful to include testers who are *not* part of the clinical trial team. Such testers can include proxies for the site staff, who are given the same training planned to be given to study site staff. They can also include proxies for the subjects, who are given the same training that the site staff would give to a real subject. Use of such proxies will help to determine if the system is simple enough to use effectively and if the training materials are adequate. For example, in a pediatrics study, children should ideally be included in determining the usability of the system [6,7].

Finally, the clinical trial team plays a critical role in deciding whether the system is ready to go live by reviewing the discrepancies found in UAT and how the discrepancies are resolved (either by fixing them or agreeing that the discrepancies do not require fixes). Once the clinical trial team has determined that the system is ready for production, they should prepare and sign a formal document that accepts the system as validated for its intended purposes.

Why it is important

UAT is an important step to verify that the system has been built according to the original systems requirements document. A thorough UAT effort also provides the clinical trial team with the opportunity to see how the system is going to function as well as educate themselves on the details necessary to answer questions from study sites and auditors once the system is in production. Furthermore, it helps build the clinical trial team's confidence that the system will function well throughout the trial.

Once completed, a successful UAT will answer three fundamental questions:

1. Was the system designed and built according to the original requirements?
2. Did the original requirements fully cover what the clinical trial team envisioned?
3. Did we build the right diary for subjects to use in this trial? [17].

While it may be tempting for the clinical trial team to rely on the system provider's validation efforts and skip UAT, this would be inconsistent with The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Good Clinical Practice [19] that requires the sponsor to take full responsibility for the quality and integrity of trial data. The sponsor is responsible for implementing and maintaining quality assurance and quality control systems with written SOPs to ensure that trials are conducted and data is generated, documented (recorded), and reported in compliance with the protocol, GCP, and the applicable regulatory requirement(s) [19]. Saving a few weeks in development time is a small price to pay for avoiding negative regulatory inspection findings downstream.

Minimum content

To properly perform a UAT, the clinical trial team documents a testing strategy in a UAT test plan [20]. This strategy will guide the development of test scripts, assignment of the appropriate set of testers, and define the test period (including repeat testing as needed). While this is similar to the system provider's internal validation testing strategy, it is not as extensive.

This plan should mention areas of testing that require extensive testing and those that that require little testing, based on perception of risk [12]. For example, a requirement that the software calculates a score based on the answers in a new daily diary, where that score is used to determine whether a subject is randomized into the study, would be of high importance; such a requirement would require test cases sufficient to cover randomization success and failure. A requirement that the alarm on the device sounds reliably at 5:00 p.m. should require only cursory testing during UAT, because alarms are typically a standard feature of the base software.

Important quality management processes to be aware of

UAT reliability can be improved by the use of a traceability matrix to map the UAT test cases to the original requirements. The matrix provides an efficient method to determine if all of the key requirements are covered by the UAT effort. In addition, independent quality control of the test scripts is important to minimize the risk of using scripts that cannot be executed as designed or will not achieve their specific test objectives [13].

UAT sometimes results in the clinical trial team realizing that the system is functioning as documented and designed, but it is not fulfilling their undocumented expectations or requirements implicit in the protocol. If the clinical trial team feels strongly enough about making changes to how the system currently functions, then the team is required to initiate a "change in scope" process. Requirements are re-documented and the entire life cycle process is followed until another UAT effort is completed. It should be noted that only if there is time, a budget, and a truly important issue, should the clinical trial team consider revising requirements at this late stage, as the first patient / first visit date could be impacted by these changes.

Quality cannot be built into a system by testing. UAT serves as a control gate. If the system provider's process of documenting requirements, designing the system or building it according to design documentation is broken, then a feedback loop between the sponsor and system provider is needed to force improvements in the upstream processes that led to the quality issues in the first place. Such a feedback loop can be implemented by holding "Lessons Learned" meetings and requiring a sponsor and system provider management to address the negative findings from such meetings before the next project begins.

A process needs to be established to require formal documentation of the lessons learned and the steps actually taken to address them. Such an approach will help the system provider to make substantial improvements in their validation processes which should lead to a smoother UAT effort in future projects. Finally, UAT of the ePRO system does <u>not</u> complete the system validation process. Until the ePRO system is installed in a production end-user environment, the process is not considered final [7,8,13].

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Installation / Configuration Management

What it is

The process for the system provider to install the fully tested software, using the methods described above, onto the ePRO device. It includes localizing it for the intended user, providing a user instruction manual, and describing planned system maintenance. It also includes the base and study specific server setup. To ensure that the correct study version is deployed to the right location, a robust configuration/release management process is required. This is true for both the study specific server and client components. Once installed on the target environments, the system can be considered in a state of validation [7].

Why it is important

Because many clinical trials are global, ePRO deployment with the correct software version and local settings can be complex. The configuration process is important to ensure that the "final," "as-tested" version(s) of a system and settings are deployed correctly (e.g., the Punjabi version with correct language(s) and time zone is in Punjab, India). It is also important to make sure that physical accessories, such as power sources, are appropriate for the trial site and that training or user materials are in the appropriate language(s).

Clinical trial team involvement

The clinical team should be cognizant of the ePRO provider's processes for configuration management, deployment and logistics of shipping to multiple global sites. Clinical team input is needed to ensure that the correct localized product is shipped to the site.

Important quality management processes to be aware of

The ePRO provider's installation and configuration team should be using a carefully developed quality-controlled checklist to manage the software installation on each ePRO solution. The checklist provides documentation for the settings on each device and internal quality reviews of the settings and accountability of the installation and configuration staff.

Finally, a statistical QC sampling of patient devices is recommended to ensure that the devices and accessories designed for a region are correct. The end result is to ensure that the clinical team has deployed an ePRO system to collect data from patients globally that can pass regulatory review [7,13].

Decomissioning

What it is

Decommissioning is the process for the system provider to retire or decommission a system for both data and services when a clinical trial ends. The decommissioning process ensures that all open items are dispositioned and closed. This is the final step in the validation process. It is comprised of the following steps:

1. data completion - assurance that all patient data that have been collected are uploaded from the patient devices to the ePRO provider's central database. This is followed by disabling further data upload and locking of the database for download in coordination with study team needs.
2. device returns (PDA-specific) - accounting of the returned devices as well as cleaning (both SW and surface), recycling for additional trials, or disposal.
3. documentation - assurance that the inventory of all required validation documents and records exist in the vendor archive repository.
4. notifications – notifying all internal and external support parties and cancelling services that are no longer necessary.

Why it is important

Decommissioning ensures that the devices, systems, and services set up for a trial are no longer in use, all collected data has been transmitted to the study team and that only official copies remain.

Clinical trial team involvement

The team should be cognizant of the ePRO provider's decommissioning processes. This confirms privacy, confidentiality, and avoids unintended or erroneous data collection.

Important quality management processes to be aware of

The ePRO provider's decommissioning team should be using a carefully developed quality-controlled checklist that provides documentation for the process on each device, internal quality reviews of the process, and provides accountability for the staff executing these processes [7,13].

CONCLUSION

Validation of electronic systems to collect PRO data is a critical component for a clinical trial's regulatory approval. This report addresses the technical nature of the ePRO data collection systems and validation process, as well as how the process is shared by the trial sponsor and ePRO system provider. As a result, the report should enhance the understanding of clinical trial sponsors of the requirements for a technology review to provide a basis for comparison of different ePRO system providers and their respective service offerings.

APPENDICES

Please see original report as per footer below.

REFERENCES

Pages 16 – 18

Excerpted from:
Zbrozek A, Hebert J, Gogates G, et al. Validation of electronic systems to collect patient-reported outcome (PRO) data - Recommendations for clinical trial teams: Report of the ISPOR ePRO systems validation good research practices task force. *Value Health 2013:16:480-9*
http://www.ispor.org/sigs/ePROsystemvalidationsg.asp

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