

21 CFR Part 11 Guidance

Comments to FDA

Reponses from:

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Introduction

We appreciate the opportunity to respond to the FDA document "Guidance for Industry 21 CFR Part 11: Electronic Records; Electronic Signatures; Validation." It is very useful to have this further guidance to the concisely stated rule. The reference sections are also very helpful.

We include in this document our comments and observations based upon our experiences developing and validating computerized systems for use in clinical trials. We have made some general comments regarding testing and validation procedures. We have focused most of our comments on the use of a computerized system in the user's working environment.

We have structured our comments by first citing the original text, then listing our modification or addition(s), and we end with comments explaining our suggestion.

Section 5.1 System Requirements Specifications

Current text:

- Scanning processes: where a paper...
- Scalability: in a networked ...
- Operating environment: sources of ...

Suggested text:

Add the following bullet:

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- User work process: requirements should include an assessment and understanding of the user's intended or expected work process.

Comment:

The ultimate system requirement is the work a user group needs to perform in the context of a regulated environment. The IT focus on technology can often miss the mark in specifying a system that works well, but does not fit the user's way of working. In other words, a system may function as intended, but not be used properly by the end users. The outcome would then be a risk to data integrity, authenticity, and confidentiality.

Section 5.2 Documentation of Validation Activity

Current text:

Validation documentation should include a validation plan, validation procedures, and a validation report, and should identify who in management is responsible for the approval of the plan, the procedures and the report.

Suggested text:

Validation documentation should include a Validation Plan (describing all the quality actions planned such as training, SOP development, system logs) as well as a Test Plan (describing the approach to be used for evaluating a system's response to normal and stress conditions), Test Procedures (giving specific instructions to testers) and result logs (capturing tester observations of system response), a Test Summary Report, and a Validation Summary Report. These should clearly identify who in management is responsible for the approval of these plans, procedures and reports.

Comment:

As per the IEEE approach that FDA has referenced in past documents, a Validation Plan is separate from a Test Plan, a Test Plan is separate from Test Cases and result logs, and there is both a Test Summary Report and also a Validation Summary Report. Putting everything into one plan causes great confusion. System teams may then define "validation" as being only the testing activity and fall short in audits and inspections for not having system support and user SOPs, work instructions, user training materials and training records, up-to-date system descriptions, documented change control, repeat testing, etc.

Section 5.2.2 Validation Procedures

Current text: The validation procedures should include detailed steps for how to conduct the validation. It should describe the computer system configuration, as well as the methods and objective acceptance criteria, including expected outcomes. The procedures should be reviewed and approved by designated management.

Change section heading to: *Test Plan*.

Suggested text:

The Test Plan should include a strategy for how to conduct testing of the system to relevant specifications. It should describe the computer system configuration being tested, as well as the test methods and objective acceptance criteria, including expected types of test documentation to be produced. The Test Plan should be reviewed and approved by designated management.

We also suggest adding two new sections after the *Test Plan*:

Section 5.2.x Test Procedures

Test Procedure documents should include detailed steps for how to conduct the tests. They should describe objective acceptance criteria, including expected outcomes. The procedures should be reviewed and approved by designated management.

Section 5.2.x Test Report

The Test Report should document detailed results of the testing effort. Whenever possible, test results should be expressed in quantified terms rather than as “pass/fail.” A traceability matrix in the report should link tests back to the requirements being tested. The report should be reviewed and approved by designated management.

Comment: Our proposed modifications and additions for section 5.2.x are based upon our broader suggestion of distinguishing between validation and test plan documents.

Section 5.2.5 Validation Report

Current text: The validation report should document detailed results of the validation effort, including test results. Whenever possible, test results should be expressed in quantified terms rather than stated as “pass/fail.” The report should be reviewed by designated management.

Suggested text: The Validation Report should document detailed results of the life cycle validation effort, including highlights of test results, but covering all other efforts. These would include relevant SOPs, system manuals, system training materials and training records, documented change control and user support practices, audits of system supplier and internal system practices, system description and configuration management, etc. The report should be reviewed and approved by designated management.

Comment: We think that the validation report should cover issues relevant to the proper implementation and use of the system (e.g., training manuals), rather than only the testing efforts.

Section 5.4.1 Key Testing Considerations

Current text:

- Test conditions...
- Simulation tests...
- Live, user-site tests...

Suggest text:

Add the following bullet:

- Results tests: these tests extend beyond the robust performance of the software in the user’s environment, to examining whether the actual results of using the software match the expected results. For example, the software may function as designed, but the users may be unable or unwilling to use the system as intended, yielding undesirable results.

Comment:

Consistent with our comments and suggestion for section 5.1, we have a broad concern about software meeting the users’ needs in their day-to-day work process. If users are unable to integrate a system into their normal work process, or to modify their work process to adapt to a new system, the results obtained from the system will not match expectations. We believe that testing needs to examine whether users are able to use the system in such a manner that it is possible to obtain the desired results. In other words, the ultimate results of using the system cannot pose a threat to data integrity, authenticity, or confidentiality.

Section 5.4.2 Software testing should include:

Current text:

- Structural testing...
- Functional testing...
- Program build testing...

Suggest text:

Addition of the following bullet:

- Outcomes testing: this testing should examine the results of using the software in the user's natural work environment. This type of testing compares actual to expected values obtained in real-world use of the system.

Comment:

Following from our suggestion that testing include an evaluation of whether results meet expectations, we propose a 'formal' testing category of 'Outcomes testing.'

Section 5.6 Extent of Validation

Current text:

- The risk that the system poses to product safety, efficacy, and quality...
- The risk that the system poses to data integrity, authenticity, and confidentiality; and,
- The system's complexity...

Suggested text:

Add the following bullet:

- the implementation and proper functioning of the system in the user's work environment.

Comment:

Consistent with our comments throughout, we believe that the validation effort should include clear direction for users and documentation that the systems works for users in the course of their day-to-day activities.

Section 6.1.1 End User Requirements Specifications

Current text:

End users should document their requirements specifications relative to part 11 requirements and other factors, as discussed above. The end user's requirements specifications may be different from the developer's specifications. If possible, the end user should obtain a copy of the developer's requirements for comparison.

Suggested text:

End user requirements specifications should be documented relative to part 11 requirements and other factors, as described above. The end user's requirements are based on a specific work process and will likely vary somewhat from the market requirements used by a commercial developer's specifications. A close examination of the published system user guide and/or support manual can provide an initial check of system suitability to user needs.

Comment:

We believe it is important to make COTS software validation doable for those defining end user specifications and not to put unrealistic expectations into this guidance. A commercial developer's Functional and Design Specifications are proprietary intellectual property. While they may be available for review during a supplier audit, they will not be available for the end user to "obtain a copy." It would be better to recommend that the End User's specifications be compared to published system manuals and user training materials to check the ability of the system to support necessary requirements. (We made a wording change suggestion in the first sentence of the section because in clinical trial settings end users would not typically write their own specifications.)