

Aventis Pasteur



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Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 00D-1538

Draft Guidance: 21 CFR Part 11; Electronic Records; Electronic Signatures, Validation [66 FR 48886, September 24, 2001]

Dear Sir/Madam:

Aventis Pasteur would like to thank you for the opportunity to comment on the above-referenced Draft Guidance entitled "21 CFR Part 11; Electronic Records; Electronic Signatures, Validation". The document describes the agency's current thinking on issues pertaining to validating computer systems subject to Part 11. We offer the following comments/clarification for your consideration.

Section 3. Definitions and Terminology

page 3

We suggest developing and maintaining this as a completed section versus referring to the "Guidance for Industry, 21 CFR Part 11; Electronic Records; Electronic Signatures, Glossary terms."

Section 4. Regulatory Requirements: What does Part 11 Require?

page 3

This section is essentially redundant with 21 CFR Part 11.10 and 11.10(a) and therefore provides the reader with no supplementary information to better interpret CFR requirements. The fact that Part 11 compliance requires validation (what to this reader appears to be the rationale for this section) can be covered in Section 1, "Purpose", thus obviating the need for the section.

00D-1538

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Section 5. Key principles

5.1 System Requirements Specifications

page 4 – 1st sentence

“Regardless of whether the computer system is developed in-house, developed by a contractor, or purchased off-the-shelf, establishing documented end user (i.e., a person regulated by FDA) requirements is extremely important for computer systems validation.”

“Off the shelf” terminology should be described in this guidance, either directly in this section or in Section 3. Note for example that the term “end user” is defined in the same sentence.

There seems to be some inconsistency between “System Requirements Specifications” and “end user requirements specifications”. We believe that “System Specifications” are required depending upon the type of system (i.e. GAMP categories,). Varying deliverables may be required, but they should address specifications.

5.2 Documentation of Validation Activity

page 6

We suggest including a statement somewhere in this section describing how testing and/or assessment of the system’s ability to satisfy end-user requirements (described in Section 5.1) should be incorporated into the subsection 5.2.2 Validation Procedures (i.e., validation protocol(s)).

This section should include a statement related to documentation of equipment installation (typically Installation Qualification protocols and reports).

5.2.1 Validation Plan

page 6

We believe that a specific validation plan may not be needed for simple “Standard Software Packages” systems. Therefore we suggest the following change: “validation documentation should include a validation plan...” should be changed to “Validation documentation should include a validation plan (where applicable)...”

5.2.2 Validation Procedures

page 6

If we understand “System Configuration” as a description of hardware and software settings, we believe that this kind of information may be included in the Design Documentation rather than in the Validation Procedures. Therefore we suggest the following change: “It should describe the computer system configuration, as well as test methods and objective acceptance criteria, including expected outcomes” should be changed to “It should describe the test methods and objective acceptance criteria, including expected outcomes.”

5.3 Equipment Installation

page 7

We suggest placing this information before section 5.2 “Documentation of Validation Activity”. As described above, Section 5.2 should describe documentation requirements for equipment installation.

This section suggests that during Equipment Installation standard operating procedures should be readily accessible. We think that all SOPs should be available during the PQ phase but for sure in place by the time the system goes into production. Only some pertinent procedures (such as the Backup & Recovery procedure) should be needed during Equipment Installation. Therefore, we suggest the following change: “User manuals, standard operating procedures, equipment lists, specification sheets, and other documentation should be readily accessible for reference” should be changed to “User manuals, pertinent procedures, equipment lists, specification sheets, and other documentation should be readily accessible for reference.”

5.4 Dynamic Testing

5.4.1 Key Testing Considerations

page 7 - 1st bullet point

- *“Test conditions: test conditions should include not only “normal” or “expected” values, but also stress conditions (such as a high number of users accessing a network at the same time). Test conditions should extend to boundary values, unexpected data entries, error conditions, reasonableness challenges (e.g., empty fields, and date outliers), branches, data flow, and combinations of inputs.”*

The term “boundary values” should be defined either directly in this section or in Section 3, “Definitions and Terminology”.

It is stated that "*Test Conditions should include not only "normal" or "expected" values, but also stress conditions... Test conditions should extend to boundary values, etc.*" We need to realize that the Vendor Quality program can and should be taken into account when determining the degree of testing required. For example, if the vendor has, in a similar configuration, performed and documented appropriate boundary testing, then an abbreviated testing of conditions may be warranted.

5.7 Independence of Review

page 10

It is imperative that the review of the validation activities is a team-based effort involving all responsible parties. It is agreed that we should not have the entire process performed by the people who build systems. The people that use the systems must be involved with the testing and review of the systems. That is, the people that are accountable for the information managed by the system must be involved in the review of the validation.

Section 6 Special considerations

6.1 Commercial, Off-The –Shelf Software

6.1.2 Software Structural Integrity

page 12

This section provides guidance for end users to perform software structural integrity assessments by either researching software program use history or auditing a supplier's software development program. The last sentence in section 6.1 "Commercial, Off-The-Shelf Software" suggests that software structural integrity assessment (indeed "all of the following...") constitutes a validation requirement for commercial software applications.

Is the expectation then that the information collected in program use history assessment or audits should be part of the validation package, to be either submitted or reviewed upon inspection?

6.1.3 Functional Testing of Software

page 13 – 3rd sentence

“When the end user cannot directly review the program source code or development documentation (e.g., for most commercial off-the-shelf software, and for some contracted software,) more extensive functional testing might be warranted than when such documentation is available to the user.”

This section notes that when end users cannot adequately review source code or development documentation, “...more extensive functional testing” is in order. Some examples of what such testing could include would be helpful in terms of interpreting the intent of this recommendation.

6.2 The Internet

page 13

Discussion about the need to validate the beginning and end-points of a system are critical with internet connected systems due to the openness of the environment. But, we need to realize that changes are continually occurring in the internal infrastructure as well (i.e., LAN, WAN, Hubs, Operating Systems, etc.)

We believe that the document does not provide a great deal of guidance. The concept of computer validation needs to be presented for the different types of systems (e.g. GAMP System Categories.) Many business related applications are continually undergoing changes due to technological advances, changes to the business environment and/or changes to regulations. Approximately 1 page was given to the concept of change management and much of it is vague (such as the discussion on the use of regression analysis and testing).

On behalf of Aventis Pasteur, we appreciate the opportunity to comment on 21 CFR Part 11; Electronic Records; Electronic Signatures, Validation and thank you for your consideration.

Sincerely,

A handwritten signature in black ink, appearing to read "Ricky D. Smith".

Ricky D. Smith
Acting Site Head,
Regulatory Affairs
and Authorized Official

RDS/MWH/kh