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January 24, 2002

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

**Re: Docket No. 00D-1538 - FDA Draft Guidance for Industry; Electronic Records;
Electronic Signatures, Validation**

Dear Sir/Madam:

Wyeth-Ayerst Research, a division of American Home Products Corporation, is submitting written comments on the draft guidance for industry entitled "Electronic Records; Electronic Signatures, Validation" (66 FR 48886, September 24, 2001).

Wyeth-Ayerst is a major research-oriented pharmaceutical company with leading products in the women's health care, cardiovascular, central nervous system, anti-inflammatory, infectious disease, hemophilia, and oncology categories, and is also a major manufacturer of preventative vaccines.

American Home Products is one of the world's largest research-based pharmaceutical and health care products companies. It is a leader in the discovery, development, manufacturing, and marketing of prescription drugs and over-the-counter medications. It is also a global leader in vaccines, biotechnology, and animal health care.

We are submitting the enclosed comments in duplicate. Wyeth-Ayerst appreciates the opportunity to comment on the above-mentioned draft guidance for industry.

Sincerely,



Roy J. Baranello, Jr.
Assistant Vice President
Worldwide Regulatory Affairs

00D-1538
Enclosure

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Title

Please clarify the document's title. It appears that the term *Validation* relates to validation of 21 CFR Part 11; Electronic Records; Electronic Signatures. There should be a distinction of the term *Validation* from the title of the regulation. For clarity, the title of the document should be changed from: "21 CFR Part 11; Electronic Records; Electronic Signatures Validation" to "Validation of Computer Systems Subject to 21 CFR Part 11"

Section 1. - Purpose

We recommend that the paragraph be revised accordingly:

"The purpose of this draft guidance is to describe the Food and Drug Administration's (FDA's) current thinking regarding considerations in meeting the validation requirements of Part 11 of Title 21 of the Code of Federal Regulations; Electronic Records; Electronic Signatures. It provides guidance for industry and is intended to assist persons who are subject to the rule to comply with the regulation. It may also assist FDA *personnel* staff who apply Part 11 to persons who are subject to the regulation enforce the Part 11 regulations."

Subsection 2.2 - Audience

For clarity, we recommend that first bullet point be revised as follows:

- "Persons ~~subject to part 11~~ who create, modify, maintain, archive, retrieve, or transmit electronic records or who utilize electronic signatures;"

Section 3. - Definitions and Terminology

We recommend that the first sentence be revised:

"Unless otherwise specified below, all terms used in this draft guidance are defined in 21 CFR Part 11, and/or in FDA's draft guidance document, "Guidance for Industry, 21 CFR Part 11; Electronic Records; Electronic Signatures, Glossary of Terms," a document common to the series of the guidances on Part 11."

Section 4. - Regulatory Requirements; What Does Part 11 Require?

Reference is made to the second sentence: "To satisfy this requirement, persons must, among other things, employ procedures and controls..."

Please clarify *other things* (e.g., persons with the requisite education, training, and experience; state-of-the art computer systems; etc.) needed to satisfy this requirement?

Subsection 5.1 - System Requirements Specifications

We suggest adding the following bulleted item to page 5 of the draft guidance:

- "Provisioning processes: where lack of information ownership may impact the authorization, integrity and confidentiality of the information being sought on the system."

Subsection 5.2 - Documentation of Validation Activity

The term *thorough* (in the first sentence) is undefined in its relationship to the types of documentation needed to implement and maintain a validated computer system.

Subsection 5.2.3 – Validation Report

Pass/fail results can be a valid outcome for low level testing, such as field lengths, alphanumeric versus numeric. Therefore, we recommend that the language be modified to *ensure that it is not the only result recorded*. High level testing, such as performance may need to be qualified further.

Subsection 5.4.1 – Key Testing Considerations

Live user-site tests are reasonable to expect before rolling an application into production. However, in reality *actual* operating conditions may not be achieved in such a test environment. For example simulated stress testing is common. We therefore recommend that the third bullet be reworded:

- “Live, user-site tests: these tests are performed in the end user's computing environment under actual *or simulated* operating conditions...”

Subsection 5.4.2 -- Software Testing Should Include

The use of the word *contemporary* in the context of *quality standards* seems subject to broad interpretation. Please clarify.

Walk-throughs of program code seem out-of-date as compared to more robust practices such as *code inspections*. However, walk-throughs for System Requirements, Systems Design and Database models are extremely helpful in catching issues before extensive code is developed.

All discussion of inspections and walkthroughs that appear in *Subsection 5.4.2* should be consolidated into and with similar information in *Subsection 5.5 Static Verification Techniques*.

In addition for many vendor-supplied applications the users of the system will not have the specific development language expertise to complete a *code inspection* or *walk-through*. For vendor supplied computer systems, this section should make clear that it is the vendor who typically conducts the structural testing. Otherwise as written, the inference is that the purchaser is responsible for this activity.

The phrase *program build testing* is not defined and may cause confusion. Perhaps the terms *module testing* or *object testing* would be more appropriate.

Subsection 5.4.3 - Expression of Test Results

See comments regarding *Subsection 5.2.3* above.

Subsection 6.1 - Commercial Off-The-Shelf Software

For transparency, we recommend that the first, second, and third sentences be revised as follows:

“Commercial software used in electronic recordkeeping systems subject to Part 11 needs to be validated, ~~just as programs written by end users need to be validated.~~ See 62 Federal Register 13430 at 13444-13445 (March 20, 1997.) We do not consider commercial marketing *information* alone to be sufficient proof of a *computer* program’s performance suitability. The end user is responsible for a *computer* program’s suitability for use in the *regulated regulatory* environment.”

Subsection 6.1.1 - End User Requirements Specifications

We recommend further explanation of the third sentence: “If possible, the end user should obtain a copy of the developer’s requirements specifications for comparison.”

The intent of the sentence appears vague; please elaborate. If the intent were to compare the developer's requirements versus the end user's requirements, then the gap analysis between the two documents in combination with knowledge of the developer's quality assurance program would be used to focus further testing and validation efforts by the end user. The more that is known by the end user about the developer's process, the less the end user must repeat as part of their validation process.

Subsection 6.1.2 -- Software Structural Integrity

The first sentence implies that *end users* should attempt to review the *source code* and deem its adequacy from that review. It seems inappropriate to expect end-users to have expertise in all the possible development languages that were used to code their various systems. End-user efforts would be better spent reviewing a vendor’s client base, financial stability, development methodologies, change control, and associated design and system documentation. Such an evaluation will yield a more complete validation package than code walk-throughs.

The statements regarding the *software’s use history* should be clarified to limit their scope to information available from the software vendor (e.g., defect tracking records) and information in the public domain (e.g., proceedings of user group conferences). Any inference that end users should directly contact other end users (e.g., competitors) could be both inappropriate and awkward; such direct contacts should be made only after vendor authorization.

The phrase, *contemporary standards*, is vague and open to interpretation. It should be clarified.

Subsection 6.1.3 - Functional Testing of Software

We recommend that this section be rewritten to focus on *testing the system against the system requirement document*. Again the expectation that the end user review source code seems unwarranted.

Wyeth-Ayerst Research

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Subsection 6.2.1 - Internet Validation

Since there are handshake mechanisms available that can follow the same path and ensure end-to-end transaction integrity, *delivery acknowledgements via independent paths apart from the Internet* seem impractical and unwarranted.

We suggest adding the following bulleted item:

- *“Use of virtual private networks (VPN) for defined point to point transmissions.”*