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

Re: Docket Nos. 03D-0060, 99D-1458, 00D-1538, 00D-1543, 00D-1542, and 00D-1539 (Draft Guidance for Industry on "Part 11, Electronic Records, Electronic Signatures--Scope and Application;" Availability of Draft Guidance and Withdrawal of Draft Part 11 Guidance Documents and a Compliance Policy Guide

Dear Sir or Madam:

Attached please find the comments of Purdue Pharma L.P. to the referenced draft guidance documents issued by the FDA on February 21, 2003. Attachment 1 provides our comments to the Scope and Applications document.

We would like to commend the FDA team on the development of this guidance. We appreciate the hard work and effort required in preparing such guidance. We trust that our comments reflect the detailed review we have performed and can be incorporated to make the document even more useful to the industry.

Please be assured that Purdue Pharma L.P. welcomes the opportunity to work with the FDA in preparing and reviewing such guidance on complex issues like 21 CFR Part 11. If I can be of assistance with regard to these comments, please do not hesitate to contact me.

Sincerely,

Albert W. Stockalis

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99D-1458 C16

Attachment

cc: Dr. Theresa Muchnick, Vice President, Corporate QA,
Purdue Pharma L.P.
Dr. Frank J. Sena, Executive Director, Corporate Compliance
Purdue Pharma, L.P.
Dr. Anthony C. Santopolo, Vice President, Regulatory Affairs
Purdue Pharma L.P.

Attachment 1 – Comments on "Part 11, Electronic Records, Electronic Signatures – Scope and Application;" Availability of Draft Guidance and Withdrawal of Draft Part 11 Guidance Documents and a Compliance Policy Guide.

1. Introduction

Lines 32-35:

The statement indicating re-examination of Part 11 with possible revisions, but not indicating any expected time frames for this activity, is too open to misinterpretation and may cause many companies to scale down or even halt remediation projects already commenced. As further reading of this guide makes it clear that this is not the intention of the FDA, this statement, and the one following in Lines 41-44 with respect to legacy systems, need to clearly indicate that such activities should not be halted, if, indeed, that is the intent of the FDA.

Lines 36–38:

Recommend deleting the sentence " We will not normally take regulatory action to enforce compliance with validation, audit trails, record retention, and record copying requirements of Part 11 as explained in the guidance." The sentence gives the impression that the FDA will not enforce compliance in these areas but later the guidance states that these areas will be enforced when related to predicate rules.

2. Background

No comments.

3. Discussion

a. Overall Approach to Part 11 Requirements

Lines 126 – 132 and 218 – 220.

"We intend to enforce all other provisions of Part 11 including, but not limited to, certain controls for closed systems in 11.10 (e.g., ...appropriate controls over systems documentation...)." Is this only applicable to 11.10(k)(1) and not to 11.10(k)(2)? In lines 218 – 220, the guidance states enforcement discretion regarding 11.10(k)(2) which would present an inconsistency in the guidance document.

b. Details of Approach – Scope of Part 11

1. Narrow Interpretation of Scope

Lines 149-156

Need clarification of the statement "merely incidental use of computers in those instances would not trigger Part 11." The FDA should provide examples of "incidental use". (e.g. Laboratory equipment that prints report for paper based batch record yet stores regulated data that may be used for later regeneration of the paper record.)

It appears that the FDA has reinstated the typewriter rule. The guidance in lines 209 – 210 states that "a word processor used only to generate SOPs" which are printed and signed "...would most likely not need to be

validated." Would that apply to a clinical study report, which is printed and signed, also?

2. Definition of Part 11 Records

Lines 158-192

Clarification is needed in this section to distinguish between records composed of raw data or primary data. This section deals with defining the types of records that must be maintained by predicate rules and are maintained in electronic format. Should Part 11 apply to records comprised of raw data (e.g., HPLC data points vs. Chromatograph, drafts of an SOP vs. final approved SOP)?

c. Approach to Specific Part 11 Requirements

1. Validation

Predicate rules do not specifically address the qualification of hardware, but the qualification of hardware is currently an industry expectation. The guidance should address the FDA's position on qualifying hardware in the validation section of the guidance.

Lines 198-201:

The statement indicating that the FDA "intends to exercise enforcement discretion regarding the specific Part 11 requirements for validation for computerized systems" is misleading. It seems to give the impression that validating for Part 11 is no longer as important as it was, whereas in reality the FDA position on validation has not changed, just the approach that should be taken (risk-based).

Lines 203 –210

Need additional clarification on risk-based approach. Will the FDA provide a framework around a risk-based approach covering both business and regulatory risk and their interaction? Can the output of a risk assessment possibly result in the application of a simple qualification test of software in lieu of a full SDLC validation (e.g., software associated with the control of equipment)?

2. Audit Trail

No comment.

3. Legacy Systems

Lines 236-240

The guidance states that the FDA will use enforcement discretion. This section needs to be enhanced with additional definition/information. The guidance should state when the FDA will enforce compliance with Part 11 and what criteria will be used for legacy systems.

The guidance states the agency will not normally take regulatory action to

enforce compliance with any Part 11 requirements. Need clarification of the phrase "not normally". The guidance should provide examples to help clarify the meaning of 'not normally" (e.g. A legacy system which has had vendor supplied upgrades after August 20, 1997. Is this system considered covered by "not normally"?)

4. Copies of Records

Is it permissible to have non-electronic copies of electronic records as the only retained evidence at a clinical trial investigational site?

The guidance section on copies of records may conflict with the record retention section in this area. The section on copies of records talks in general about electronic copies of records while the record retention section states that you can archive these electronic records to non-electronic media such as microfilm, microfiche and paper or to PDF.

5. Record Retention

We endorse the removal of the FDA's objection to the archival of electronic records using non-electronic media.

General

The guidance may confuse the issue of whether or not systems require validation. Part 11 requires systems to be validated. However, validation of systems was required in GMPs before Part 11 in order to meet the predicate rule. Part 11 adds requirements that must be satisfied by the system if the system is to be considered compliant (e.g., electronic audit trails).

- When the FDA is reviewing the Part 11 regulation for modification, the Preamble should be included as part of the review and modification process. Information contained in the Preamble that is affected by the guidance should be included in the guidance. What is the applicability of the Preamble to Part 11 when this guidance is finalized?

The FDA has recalled several guidance documents. The Clinical guidance document Guidance for Industry: Computerized Systems Used in Clinical Trials was not included in the list of recalled guidance documents. What is the applicability of this guidance document as Part 11 guidance changes?

We endorse the risk assessment approach that the FDA is advocating so that focus can be applied to systems that have greater impact on safety and efficacy. Are there plans to reissue guidance on validation, copying of electronic records, maintenance of electronic records and audit trails?