



Clinical  
Cardiovascular  
Research, LLC

2004D-0440

Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, rm.1061  
Rockville, Maryland 20852

Hello,

Thank you for the opportunity to comment on the Draft Guidance for Computerized Systems Used in Clinical Trials: Docket Number 2004D-0440. We have made an effort to keep comments concise and limited to a single topic. In three cases we have added questions to further elaborate comments.

Best Regards,

Shifu Zhao, Ph.D.  
Manager, Data Operations

Warren Zabloudil  
Senior Network Administrator

Clinical Cardiovascular Research, LLC  
18310 Montgomery Village Avenue  
Gaithersburg, Maryland 20879  
301.208.9100

**OVERALL COMMENT with QUESTIONS:**

Comment: The content of this Guidance overlaps significantly with Guidance for Industry: Part 11, Electronic Records; Electronic Signatures – Scope and Application.

Questions: Could sections VI, VII, and VIII be combined and simplified? Could sections IX and X be combined and simplified?

**COMMENTS with QUESTIONS:**

SECTION III: General Principles – Part 8:

“We recommend that data be retrievable in such a fashion that all information regarding each individual subject in a study is attributable to that subject.”

Comments: (1) That information is attributable to its belonging subject should be a requirement, not an option for a computerized system. (2) In discussions surrounding 21

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CFR Part 11, 'attributable' is typically used to refer to data that can be tracked to the recording persons.

Questions: Should the word 'attributable' here be replaced with an alternative?

#### SECTION IX: Systems Dependability – Paragraph 4:

“We recommend that you base your approach on a justified and documented risk assessment and determination of the potential of the system to affect data quality and record integrity. For example, in the case where data are directly entered into electronic records and the business practice is to rely on the electronic record, validation of the computerized system is important. However when a word processor is used to generate SOPs for use at the clinical site, validation would not be important.”

Comment: The provided example does not fully clarify this issue.

Questions: In the case of locally developed software used to manage a trial but only affect data indirectly; if the company’s risk assessment determined that validation is not important but a subsequent FDA audit disagrees, how is the situation arbitrated? While validation documents are subject to audit, are risk assessment documents indicating validation is unnecessary also subject to audit?

#### COMMENTS:

##### SECTION II: Background:

"Although the primary focus of this guidance is on computerized systems used at clinical sites to collect data, the principles set forth may also be appropriate for computerized systems belonging to contract research organizations, data management centers, and sponsors."

Comment: 21 CFR Part 11 and this Guidance clearly cover any computerized systems used to create, modify, maintain, archive, or transmit clinical data required to be maintained and/or submitted to the FDA. It appears unnecessary to identify a primary category of systems as the ones used at clinical sites to collect data.

##### SECTION III: General Principles – Part 4:

“It is important to design a computerized system in such a manner so that all applicable regulatory requirements for record keeping and record retention in clinical trials are met with the same degree of confidence as is provided with paper systems.”

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Comment: 'The same degree' may be better worded as 'the same or higher degree' given the numerous advantages a computerized system can have over paper-based instruments.

**SECTION III: General Principles – Part 5:**

“Under 21 CFR 312.62, 511.1(b)(7)(ii) and 812.140, the clinical investigator must retain records required to be maintained under part 312, § 511.1(b) and § 812, respectively, for a period of time specified in these regulations.... 6. When original observations are entered directly into a computerized system, the electronic record is the source document.”

Comment: Item 6 should be appended to item 5, thus making a complete and focused principle.

**SECTION III: General Principles – Part 7:**

“Records relating to an investigation must be adequate and accurate in the case of ... (INDs), ... (INADs), ... (IDEs). An audit trail that is electronic or consists of other physical, logical, or procedural security measures to ensure that only authorized additions, deletions, or alterations of information in the electronic record have occurred may be needed to facilitate compliance with applicable records regulations...”.

Comment: This principle seems to be about the audit trail. The discussion can be brief as much is repeated in the following VI.B section.

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