

COMMENTS SUBMISSION: DOCKET: 2004D-0440

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Phase Forward appreciates the opportunity to review and comment on this Guidance on Computerized Systems Used in Clinical Trials. In general, the Guidance directly addresses some important issues for the industry, and reflects standard practices and the FDA's experience. However, there are some areas that may need additional consideration. Our comments reflect our experience, and that of many of our customers, in the implementation of enterprise software for Internet-based data collection and clinical data management.

Specific Comments

II. BACKGROUND

Comment: For the sentence in the first paragraph: "To be acceptable, the data should meet certain fundamental elements of quality whether collected or recorded electronically or on paper. For example, data should be attributable, legible, contemporaneous, original ^[4]and accurate".

It is suggested that the acronym (ALCOA) be added the paragraph to provide additional emphasis to the reference.

III. GENERAL PRINCIPALS

Comment: 2. For number (2), under general principles it is recommended that the following statement be added: **For each study, documentation that includes a system description and data flow diagram should be retained at the site.** It is recommended that this statement also be added to section IX. (SYSTEM DEPENDABILITY) paragraph 2.

Comment: 4. and 5. It is recommended that the final guidance combine numbers (4) and (5), or alternatively provide predicate rule references for number (4) "regulatory requirements" for record keeping and record retention.

Comment: In addition, for number (5) it is recommended that it is changed to read: 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. Retaining the original source document, **an electronic copy**, or a certified copy of the source document at the site where the investigation was conducted can assist in meeting these regulatory requirements. In addition it is recommended that the guidance include the following statement from the original guidance pertaining record retention by the investigator: Clinical investigators should retain either the original or a certified copy of all source documents sent to a sponsor or contract research organization, **including query resolution correspondence.**

IV. OVERALL APPROACH TO MEETING PART 11 REQUIREMENTS

Comment: To allow for more consistency with the Part 11 Scope and Application guidance, it is recommended that the first paragraph include legacy systems, and be changed to read: As described in the FDA guidance entitled *Part 11, Electronic Records; Electronic Signatures- Scope and Application* (August 2003), while the re-examination of part 11 is underway, FDA intends to exercise enforcement discretion with respect to part 11 requirements for validation, audit trail, record retention, record copying, and **with regard to all part 11 requirements for systems that were operational before the effective date of part 11 (known as legacy systems).**

V. STANDARD OPERATING PROCEDURES

Comment: For the sake of clarity, it is recommended that that additional information be added to the SOP reference for “Alternate Recording Methods”, i.e. fail to paper.

VI. DATA ENTRY

Comment: VI.A (Computer Access Controls): It recommended that the final guidance provide examples or suggestions as to what it meant by: “established intervals”, “short periods of inactivity”, and “long idle periods”. Left to interpretation, various extremes may be applied depending on the organization (minutes, hours, days, months).

Comment: VI.B (Audit Trails and Security Measures): “justified and documented risk assessment” is referred to several times throughout this document, and the Part 11 Scope and Application guidance. For better consistency, it is recommended that a reference be provided to ISO 14971:2002 Medical Devices- Application of risk management to medical devices (ISO, 2001). It appears the FDA considers this an acceptable methodology for a “justified and documented risk assessment”.

Alternately, a guidance on Risk Assessment for Computerized Systems Used in Clinical Trials is highly recommended.

Comment: VI.B (Audit Trails and Security Measures): It is recommended that the final guidance **delete** the requirement under audit trail to include: ” why changes were made to the electronic record”. This requirement is inconsistent with 21CFR11, and the Guidance for Industry: Part 11 Scope and Application. Neither of these documents have a requirement for “reason for change” under audit trails.

IX. SYSTEM DEPENDABILITY

Comment: IX.A (Legacy Systems): It recommended that the final guidance provide examples or suggestions as to what comprises a legacy system. What core components from the original system (operational prior to August 1997) must be intact and unchanged to “qualify” as a legacy system (operating system, software versions, drivers, data base, hard drive)? It is possible that the system has not undergone changes that prevent it from meeting predicate rule requirements, but has undergone significant changes that render it very different from the “original system” deployed prior to August 1997.