

Demystifying Part 11: A Practical Overview of Electronic Records

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Outline

- The world of laws, regulations & guidances
- Review of 21 CFR Part 11
- Review of Guidances
 - Aug 2003 Scope & Application
 - Sep 2004 CSUCT
- Impact on investigational sites

Disclaimer

- Not speaking for the FDA!
- Do not use these slides as a compliance guide!
- Every site is different, and must be assessed individually!

Regulatory Process

- Acts/Laws
- Regulations
- Guidance
- “Draft” Regulations/Guidance
- Dockets
- Manual of Policies and Procedures (MAPP)

Acts/Laws

- Law of the Land
for example
- *FDA Modernization Act of 1997*
- ...amended the Federal Food, Drug, and Cosmetic Act of 1962 relating to the regulation of food, drugs, devices, and biological products.
- ...recognized the Agency would be operating in a 21st century characterized by increasing technological, trade and public health complexities.

Steve Wilson, FDA

Regulation

- The rules that the FDA writes to translate the spirit of the law into a workable framework
- Are legally enforceable
- E.g., 21 Code of Federal Regulations (CFR) 11
 - Good practice for all computerized processes
 - Sponsors and Government

Guidance

- Represents the Agency's **current** thinking
- Not binding on FDA or the public
- An alternative approach may be used if such approach satisfies the requirements of the applicable statutes, regulations or both.

Included in Background published with Guidances

Draft Regulations & Guidances

- Are not binding during comment period
- *Federal Register* notification
- Public comment period (to the docket)
- Difference between the two processes
 - Regulation – FDA must address comments
 - Guidance – FDA uses the comments as advice

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Manual of Policies and Procedures (MAPP)

- Internal CDER SOPs

For example

- [7600.7](#) Processing an Electronic New Drug Application (Issued 5/31/2000, Posted 6/5/2000)

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Context

- FDA has the authority to inspect all records relating to clinical trials
- “FDA’s acceptance of data from clinical trials ... depends on FDA’s ability to verify the quality and integrity of the data ... whether recorded electronically or on paper. For example, data should be Attributable, Legible, Contemporaneous, Original and Accurate.”

ALCOA

- **Attributable:** the raw data can be traced by signature (or initials) and date to the individual who observed and recorded the data
- **Legible:** the raw data are readable and recorded in a permanent medium, e.g. ink for written records or electronic records that are unalterable
- **Contemporaneous:** the raw data are recorded at the time of observation
- **Original:** the raw data are the firsthand observations, and not a copy
- **Accurate:** an unaltered and correct recording of the observation

www.fda.gov/cvm/guidance/guide85.doc, www.fda.gov/cder/ode4/preind/wu.ppt

One Source of Confusion

- Aug 1997: 21 CFR Part 11 went into effect
- Apr 1999: Guidance for Industry CSUCT finalized
- 2000 – 2002: numerous draft guidances on Electronic Records & Signatures parts of 21CFR11
- Feb 2003: draft guidances withdrawn
- Aug 2003: Scope & Application guidance issued
- Sep 2004: Apr 1999 CSUCT withdrawn and replaced with a revised draft version

21 CFR Part 11 Purpose

- To define good practice for all computerized processes – Sponsors and Government
- To pave the way for submission
 - Systems
 - Guidance
 - Procedures
- “...intended to permit the widest possible use of electronic technology...”

Steve Wilson, FDA

21 CFR Part 11

- Subpart A – General Provisions
 - Scope
 - Implementation
 - Definitions
- Subpart B - Electronic Records
 - Controls for closed systems
 - Controls for open systems
 - Signature manifestations
 - Signature/record linking

21 CFR Part 11

- Subpart C – Electronic Signatures
 - General requirements
 - Electronic signature components and controls
 - Controls for identification codes/passwords

21 CFR Part 11: Subpart A

- Scope
 - Records generated and/or stored electronically
 - Not paper records transferred electronically
 - Equivalence of paper and electronic signatures
 - Equivalence of paper and electronic records
 - Availability for inspection

21 CFR Part 11: Subpart A

- Implementation
 - Can use electronic records & signatures provided inform the FDA of intent and meet validation requirements

21 CFR Part 11: Subpart A

- Definitions
 - Closed system: one where access is controlled and limited to certain individuals
 - Open system: one where access is freely available
 - Electronic (or digital) signature: computer data compilation of any symbol or series of symbols that are the legally binding equivalent of a handwritten signature

21 CFR Part 11: Subpart B

- Controls for closed systems
 - Systems must be validated
 - Records must be viewable in human-readable format
 - Records must be protected and readily retrievable
 - System access must be limited to authorized individuals
 - Secure time-stamped audit trails are required for electronic records
 - Verification of adequate training
 - Signature accountability supported by written procedures

21 CFR Part 11: Subpart B

- Controls for closed systems (cont.)
 - System documentation control
 - Use of checks to ensure validity of source of data input

21 CFR Part 11: Subpart B

- Controls for open systems
 - Ensure authenticity, integrity and if appropriate confidentiality of electronic records

21 CFR Part 11: Subpart B

- Signature manifestation
 - Signed electronic records shall contain associated information identifying:
 - Printed name of signer
 - Date and time signature was executed
 - Meaning associated with the signature
 - To be secured as are closed systems
- Signature linking
 - Linked to records so as to prevent falsification by any ordinary means

21 CFR Part 11: Subpart C

- Electronic Signatures
 - Must be unique to an individual
 - The individual's identity must be confirmed
 - Organization must declare in paper form with traditional signature to the FDA that will use electronic signatures
 - Must be used only by their owners
 - Must have at least 2 distinct components
 - Must be closely administered to prevent false usage

Part 11: Scope and Application Guidance for Industry

- August 2003
- States:
 - We do not intend to take enforcement action to enforce compliance with the validation, audit trail, record retention and record copying requirements
 - Records must still be maintained in accordance with the underlying predicate rules
- Also do not intend to enforce Part 11 for systems in place prior to August 1997
- Part 11 REMAINS IN EFFECT

Part 11: Scope and Application Guidance for Industry

- Issued in response to feedback that requirements would
 - Unnecessarily restrict the use of advanced electronic technology
 - Significantly increase the costs of compliance
 - Discourage innovation with no significant public health benefit
- Particularly applicable to validation, audit trails, record retention, record copying and legacy systems

Part 11: Scope and Application Guidance for Industry

- Implies that requirements remain for
 - Electronic signatures
 - Data integrity
 - System access security
 - Use of operational system checks
 - Assurance of appropriate training & experience
 - Legal accountability for electronic signature use
 - Systems documentation controls

Draft Guidance for Industry: CSUCT

- Computerized Systems for Use in Clinical Trials
- Sept 2004 revision of April 1999 Draft Guidance
- Intended to provide insight into the Agency's application of the Scope & Application guidance
- Primarily aimed at systems used at investigational sites
- Revised to bring it into line with the current thinking on Part 11

The Rubber Hits the Road...

- You've received a letter from a sponsor asking to you to attest to your level of 21CFR11-compliance
 - Sign 'yes, we have affected systems and we are compliant'
 - Sign 'we have no affected systems and are therefore compliant'
 - Sign 'no, we have affected systems and are not compliant, or have not assessed them'

What to do?

- If no formal assessment has been done, then the only possible answer is 'no'
- CRCs and investigators are not equipped to conduct an assessment without assistance
- Contact your institution's IT department, or engage a consultant to assist

Assessing Compliance

- The purpose of the research drives the assessment
 - Independent research, goal is publication only
 - Investigator-initiated, data may be transmitted eventually to the FDA
 - Paper system
 - Electronic system
 - Sponsor-run, data intended for submission
 - Paper system
 - Electronic system

Independent, Publication

- If the data will not be submitted to the FDA, then 21 CFR 11 does not apply
- Still may want to consider assessing systems for quality

Site-initiated, Data to FDA

- Paper system
 - If no computers are used to capture or store the data, no further action probably necessary
- Electronic system
 - Will be impacted at least to some degree, possibly greatly

Sponsor-run

- Paper system
 - If no computers used at any point, no further action probably necessary
- Electronic system – varying impacts
 - EDC data capture – shared responsibility
 - Software like visit scheduling is not affected

Two Aspects

- System design and development
 - Responsibility for compliance lies with system developer/owner
- System usage
 - Responsibility lies with administrators and users

Compliance Still Required

- Electronic signatures
- Legal accountability for electronic signature use
- System access security
- Systems documentation controls
- Data integrity
- Use of operational system checks
- Assurance of appropriate training & experience

Enforcement is Discretionary

- Validation
- Audit trails
- Record retention
- Record copying
- Legacy systems

i.e., primarily system development and administration activities

ALCOA Still Rules!!!

Attributable, Legible,
Contemporaneous, Original and
Accurate

CSUCT Guidance

- Contains many fairly specific statements and recommendations
- Still draft, and many comments were received
- May change in details, but the concept is here to stay

The Bottom Line

- You probably have affected systems
- You are probably not fully compliant
- You may be compliant with the Aug 2003 'Scope and Application' approach
- You may be compliant with the Sept 2004 CSUCT guidance
- Unless you are in IT, or are trained in 21CFR11, you probably don't have the knowledge to answer the sponsor letter

References & Reading

- Note: pay attention to publication date, and interpret the content in light of what guidances had been published
- 21 CFR Part 11:
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11&showFR=1>
- Aug 2003 Scope & Application Guidance:
www.fda.gov/cder/guidance/5667fnl.htm
- Sep 2004 CSUCT:
www.fda.gov/cder/guidance/6032dft.htm
- GCP Guidance:
www.fda.gov/cvm/guidance/guide85.doc