
Web-Based DataFax

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Why Web-Based DataFax?

- Decision makers investing in electronic data collection (EDC) systems.
 - Primarily Web-based.
 - Reduces time required to collect data.
 - Increases data quality.
- DataFax perceived as a “bridging” technology from paper to EDC.
 - Paper-based system utilizing fax.
 - Batch (asynchronous) instead of real-time (synchronous).
- Extend applicability of DataFax

Concept

Replace sending a paper CRF through a fax machine with sending an electronic CRF (e-CRF) through the Web.

Extending the DataFax Paradigm to the Web

Standard DataFax

Fill in paper form

Sign form

Fax form

Fax QC notification

Correct original
& fax

Web-based DataFax

Fill in electronic form

Digital/Electronic signature

Submit form

Electronic QC notification

Correct electronic form
& resubmit

Assumptions

- Sites have “modern” computing equipment (e.g. no MSDOS/Windows 3.X or Mac II machines).
- Sites have Internet/Web access & email.
- Sites are responsible for all required client software.
- Sites are responsible for electronic source documents.

Constraints

- Must use commercially available software at the sites.
- Must use DataFax “as is”; no “backdoor” programming.
- Must follow DataFax asynchronous submission paradigm.
- Must automatically convert existing study plates to electronic CRFs (e-CRF).
- Must address US Federal regulations.

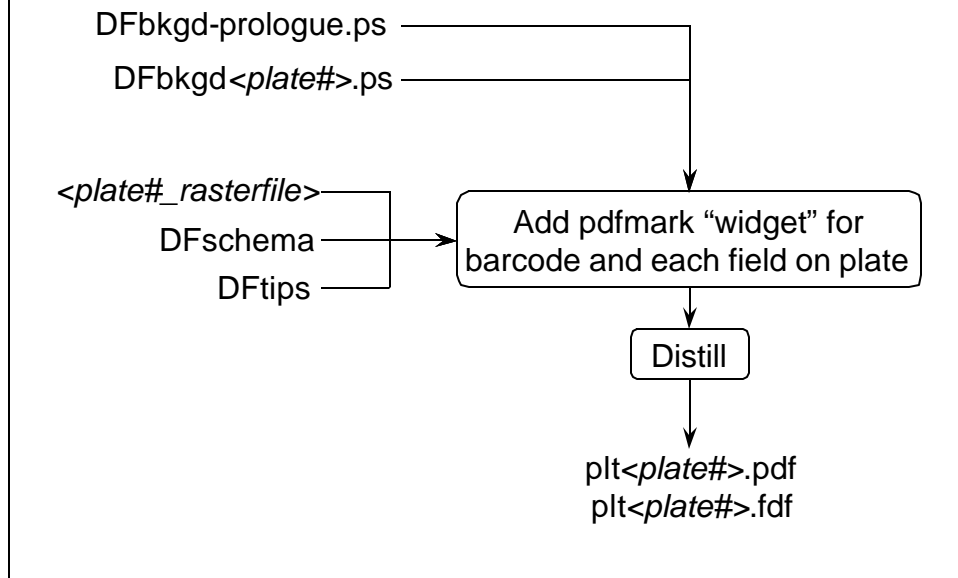
Client-Side Methodology

Method	Advantages	Disadvantages
HTML	<ul style="list-style-type: none">• Simple (too simple?)	<ul style="list-style-type: none">• No easy way to create fields
Java	<ul style="list-style-type: none">• Powerful• Complete control of development	<ul style="list-style-type: none">• Custom code• Client-side Java unreliable
✓ PDF	<ul style="list-style-type: none">• Supports forms• Conversion tools available• Document management tools available	<ul style="list-style-type: none">• Adobe in control

Plate Conversion

- **DataFax**
 - Postscript/raster files provides physical layout.
 - DFTips gives field locations on plates.
 - DFschema describes the data fields.
- **Tools**
 - Adobe Acrobat Distiller
 - Ghostscript (www.cs.wisc.edu/~ghost/)
 - Perl (www.perl.com)
- **Pdfmark**
 - Manual (partners.adobe.com/asn/developer/acrosdk/docs.html)
 - Primer (www.pdflib.com/pdfmark/index.html)

Conversion Process



PDF Plate Features

- Physical page layout same as paper
- Fields
 - Barcode included as hidden fields
 - DFSTUDY
 - DFPLATE
 - DFSEQ (unless defined as first data field)
 - All fields defined in DFtips included in form
 - Fields formatted as defined in DFschema
- Buttons
 - RESET
 - SUBMIT

Conversion Example

The image shows two versions of a web form titled "On Study". The left form is a complex, multi-column layout with many checkboxes and text input fields. The right form is a simplified, single-column layout with fewer fields and a more organized structure. An arrow points from the left form to the right form, indicating a conversion or redesign process.

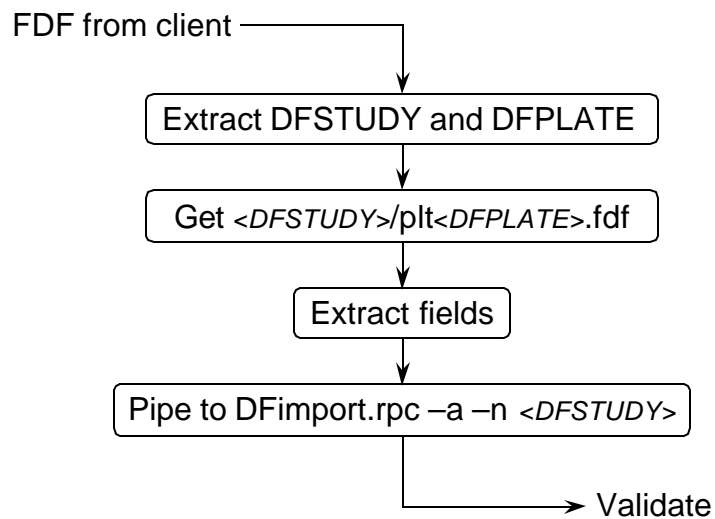
Server-Side Methodology

Method	Advantages	Disadvantages
Perl	<ul style="list-style-type: none"> • Fast development cycle • Easy to debug 	<ul style="list-style-type: none"> • Security tends to be a problem
✓ Java	<ul style="list-style-type: none"> • Powerful • Server-side Java very successful • Good security 	<ul style="list-style-type: none"> • Longer development cycle • Complicated debugging

Server Architecture

- **Web Server**
 - Apache HTTP Server (httpd.apache.org)
 - Apache JServ (java.apache.org)
- **Java**
 - Sun Java 1.2.1 – Java Virtual Machine (java.sun.com)
 - IBM Jikes 1.06 – Java Compiler
(oss.software.ibm.com/developerworks/opensource/jikes/project/)
- **Acrobat (PDF)**
 - Acrobat Forms Data Format (FDF) Toolkit
(partners.adobe.com/asn/developer/acrosdk/forms.html)

Server Process



Implementation Issues

- QC notification
- Managing source documents and signatures
- Data collection process: real-time vs. batch
- Federal regulations and guidelines
- Standard Operating Procedures

QC Notification

- **Standard DataFax**
 - QC Reports faxed to site.
 - Site fax number in Centers DB.
 - Manual faxing an option.
- **Web-Based DataFax**
 - QC Reports emailed to site.
 - Email address captured at login (Centers DB in DataFax 4.0?).
 - QC Reports automatically presented when site logs in.

Source Documents

- **Standard DataFax**
 - All CRFs maintained in patient binders at the site.
 - Corrections to CRFs are noted, initialed or signed, dated, and re-faxed.
- **Web-Based DataFax**
 - All e-CRFs maintained in “electronic patient binders”, *i.e.* PDF files, at the site.
 - Corrections to e-CRFs are noted, digitally signed, saved as a separate page and resubmitted.
 - Adobe Acrobat Business Tools 4.0 (or Acrobat 4.0) provides functionality.

Data Collection Process

- **Real-Time**
 - Synchronous process; QCs must be resolved immediately.
 - Reduces typographical and transcription errors.
 - Does not reduce problems with the data.
- **Batch**
 - Asynchronous process; QCs can be investigated and corrected with subsequent submission.
 - Typographical and transcription errors not caught until validation. “Smart” forms, such as PDF, could catch these.

Federal Regulations and Guidelines

- Title 21 CFR Part 11 - Electronic Records/Signatures
- FDA Office of Regulatory Affairs: Guidance for Industry, Computerized Systems Used in Clinical Trials
- On-going dialogue between government and industry about practical implementation.

Title 21 CFR Part 11 – Electronic Records/Signatures

- **Scope**
Applies to "...records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted, under any records requirements set forth in agency regulations." §11.1(b)
- **Enforcement**
Compliance Policy Guide (CPG) Section 160.850 entitled "Enforcement Policy: 21 CFR Part 11; Electronic Records; Electronic Signatures."
- **Compliance (from CPG Section 160.850)**
"Failure to establish and maintain procedures to control all documents that are required by 21 CFR 820.40, and failure to use authority checks to ensure that only authorized individuals can use the system and alter records, as required by 21 CFR 11.10(g)."

Pertinent Sections

- **21 CFR 820.40: Quality Systems Regulations, Document Controls**

“Each manufacturer shall establish and maintain procedures to control all documents that are required by this part.”
(www.fda.gov/cdrh/devadvice/part820.html)
- **21 CFR 11.10(g): Controls for closed systems**

“Use of authority checks to ensure that only authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand.”
(www.fda.gov/ora/compliance_ref/part11/www.access.gpo.gov/nara/cfr/waisidx_00/21cfr11_00.html
www.21cfrpart11.com)

Computerized Systems Used in Clinical Trials (FDA)

II. DEFINITIONS

Electronic Case Report Form (e-CRF) means an auditable electronic record designed to record information required by the clinical trial protocol to be reported to the sponsor on each trial subject.

III. GENERAL PRINCIPLES

- D. When original observations are entered directly into a computerized system, the electronic record is the source document.
- E. The design of a computerized system should ensure that all applicable regulatory requirements for recordkeeping and record retention in clinical trials are met with the same degree of confidence as is provided with paper systems.

(www.fda.gov/ora/compliance_ref/bimo/ffinalcct.htm)

Regulatory Implications

- Systems and processes used to create, modify, maintain, store, retrieve, transmit and archive e-CRFs must be secure, regulated and auditable to the same degree of confidence as provided with paper systems.
- Study documentation must identify all software and hardware used in the study.
- SOPs must completely describe all processes including when and how they will be used.
- Compliance will be determined on a case by case basis (CPG Section 160.850).

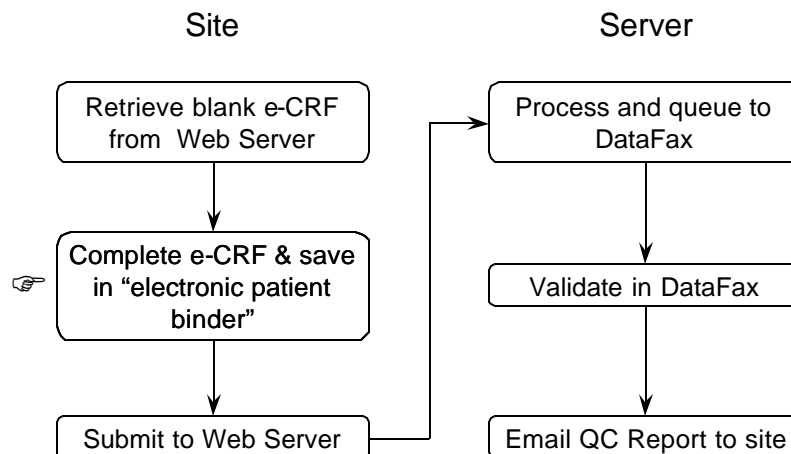
Standard Operating Procedures

- **Ensure system integrity**
 - Describe how access to the system is granted and revoked.
 - Describe how the system is maintained.
 - Describe when and how the system is audited.
 - Describe contingency plans.
- **Data collection and handling**
 - Describe how e-CRFs are completed & submitted.
 - Describe how e-CRFs are corrected & resubmitted.
 - Describe training and certification process.

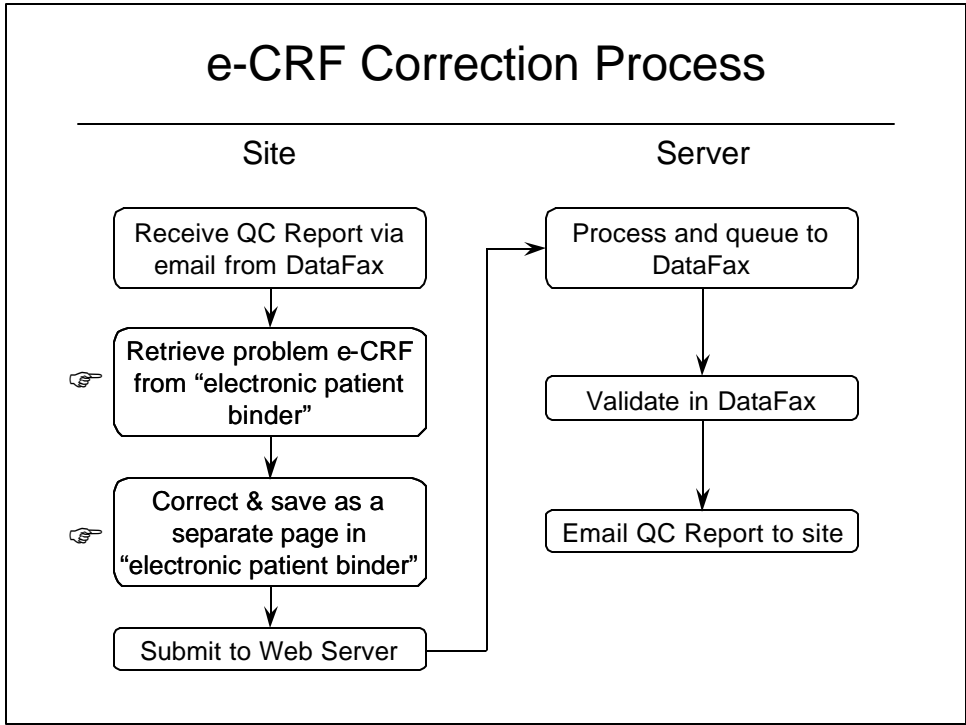
Implementation

- Sites manage source documents.
 - All e-CRFs are created, stored and managed at the site.
 - Specific method is the responsibility of the site.
- Tools
 - Adobe Acrobat Business Tools 4.0 or higher (Adobe Acrobat 4.0 or higher)
 - Web browser with Acrobat defined as application for PDF files.
 - Email

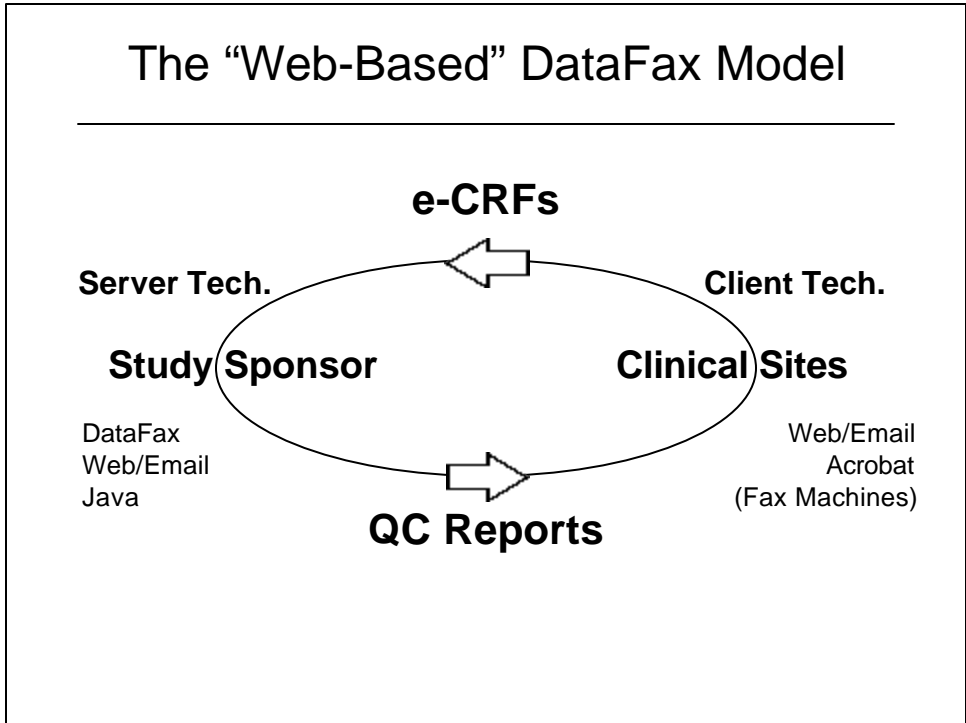
New e-CRF Submission Process



e-CRF Correction Process



The "Web-Based" DataFax Model



Future Plans

- Implementing edit checks at submission
 - Batch edit checks against DFin.dat.
 - Return QC Report as an immediate response to submitted e-CRF.
- Collecting data at the source
 - Can use anything that will run Acrobat Business Tools.
 - Handhelds (e.g. PalmPilot, Handspring)
 - Tablet computers (e.g. Fujitsu)
 - Laptop/Notebook computers.
 - Javascript edit checks.

Summary

- Web-based DataFax is an “electronic” implementation of the DataFax data collection paradigm.
- Demonstrates that DataFax is much more than a “bridging” technology.
- Positions DataFax to participate a “paperless” future.