Final Guidance on Electronic Source Data in Clinical Investigations

Promoting eSource Data Capture

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FDA Webinar
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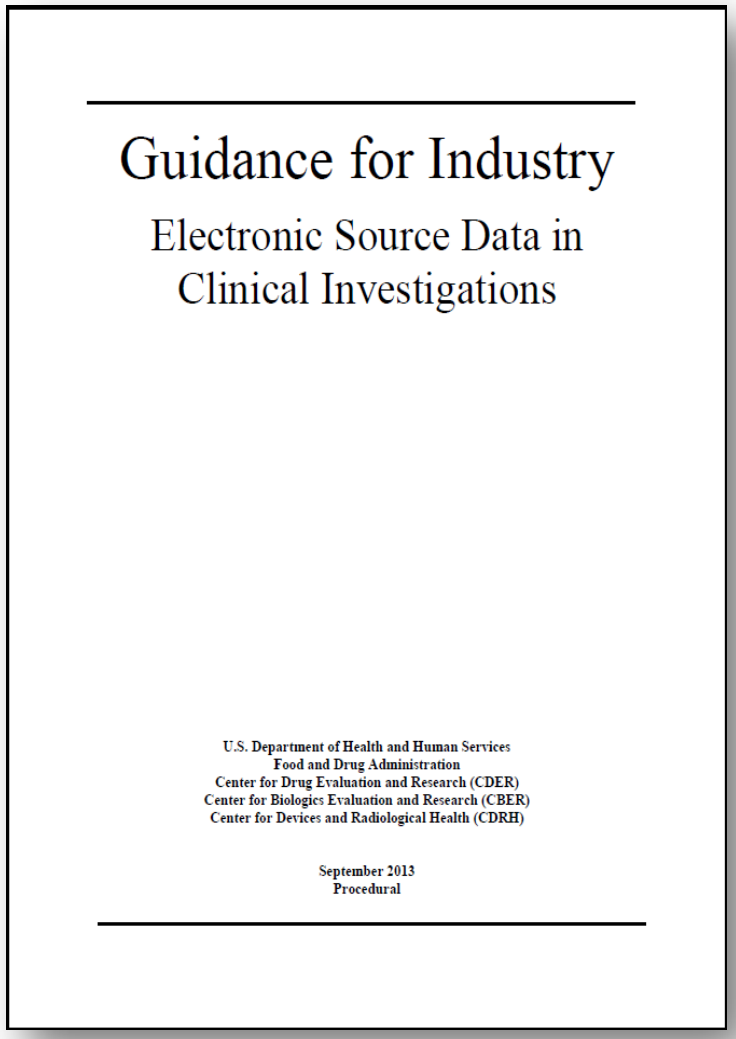
Electronic source data in clinical investigations

Topics

- Why eSource?
- eSource Guidance Development
- Key Definitions
- Source Data
- Source Data Capture
- Data Review, Retention, Access
- Computerized Systems
- EMA Reflection Paper and FDA eSource Guidance
- Q & A

Why eSource?



Guidance for Industry

Electronic Source Data in Clinical Investigations

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

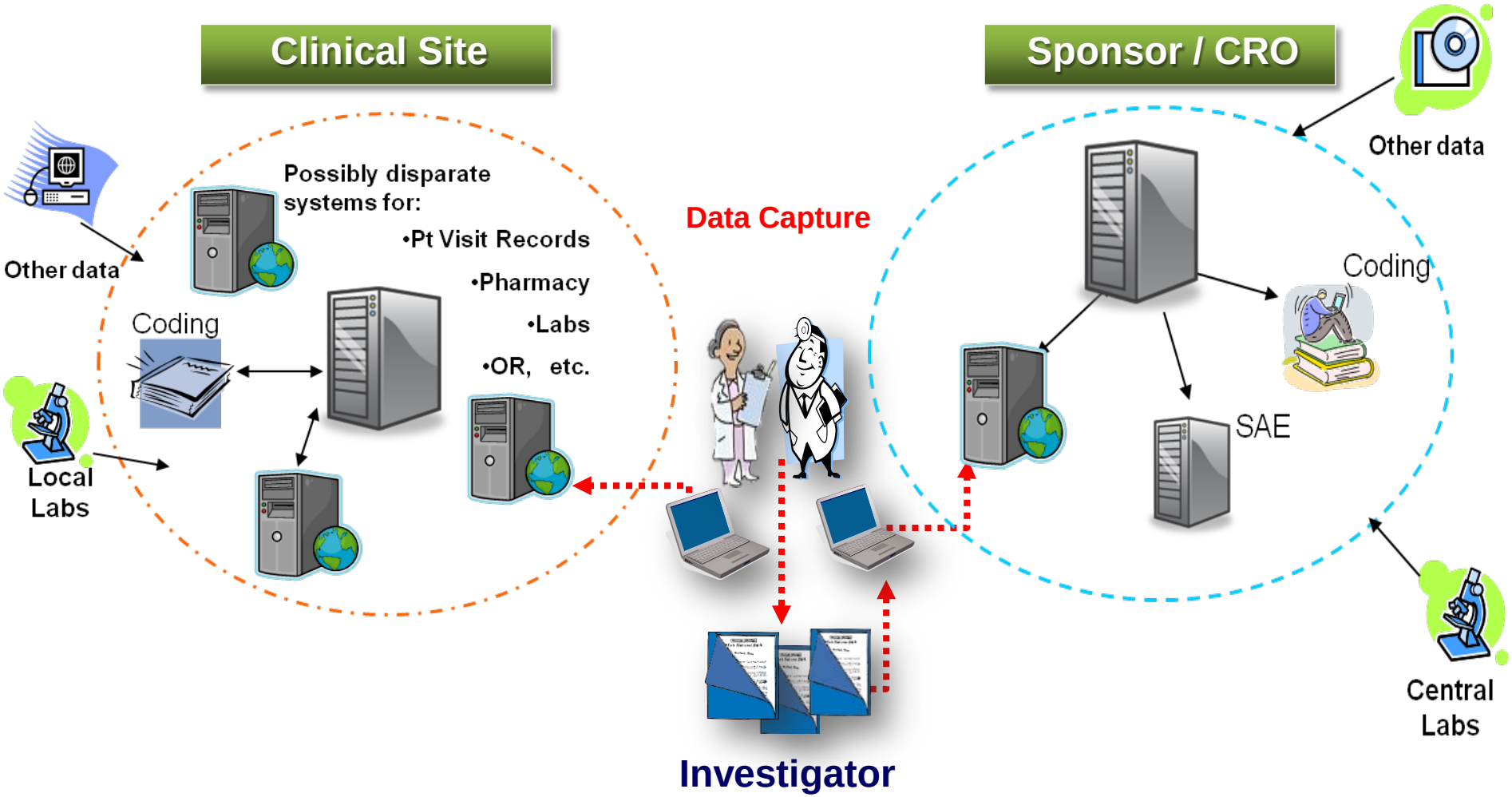
September 2013
Procedural

"…promotes capturing source data in electronic form…,"

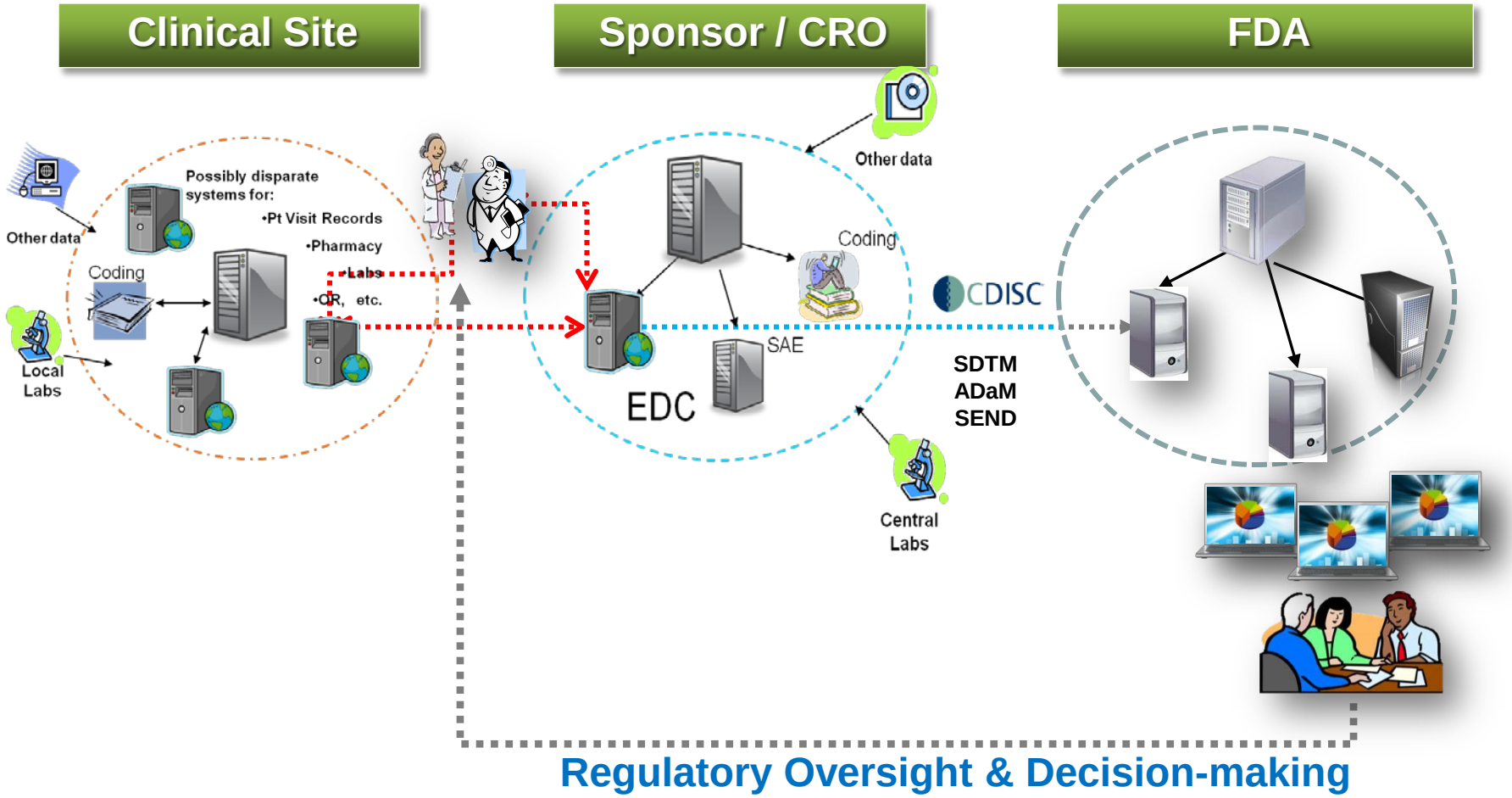
[assists] *"in ensuring the reliability, quality, integrity, and traceability of electronic source data."*

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM328691.pdf

Why eSource? … *to eliminate "shadow" CRFs*



Why eSource? …*to promote direct entry into eCRFs and No Paper*



eSource Guidance Development

- *Electronic Source Documentation in Clinical Investigations:* ***Initial Draft 2011***
  - Major concerns / issues / frustration focused on:

    - Investigator sign-off required prior to Sponsor's review
    - eCRF as a single CDMS System
    - Prescriptive tone with respect to clinical data management
    - Data exchange provision using HL7

  - *Decision to revise and issue another Draft.*

- *Electronic Source Data in Clinical Investigations:* ***Revised Draft - 2012***
  - **90** Day Comment Period
  - **37** organizations (e.g., tech providers, sponsors, CROs, including PhRMA and BiO)
  - **367** Comments…*thoughtful and positive*
  - **65%** focused on Data Capture and Data Review

… we were headed in the right direction!

Key Definitions

- **eSource Data Capture: Key Definitions (1)**
  - **eCRF**
    - Generally, an eCRF is an EDC system used by a clinical site to collect data on study subjects.
    - For this guidance, the eCRF is not a concept, but rather it is viewed as clinical system, i.e., an *electronic record.*
    - The capture, review, management, analysis, and reporting on a clinical study does not occur in any **single** system, such as the eCRF.

- **eSource Data Capture: Key Definitions (2)**
  - **Data Originator**
    - **device** (e.g., blood pressure monitor)
    - **instrument** (e.g., ePRO instrument)
    - **system** (e.g., EHR, laboratory system)
    - **person** (e.g., investigator, radiologist, subject)

Authorized to enter/ transmit source data into the eCRF.

- **eSource Data Capture: Key Definitions (3)**
  - **Data Element**
    - Variable-level data, *i.e.*, the smallest unit of observation for a subject.
      - e.g., diastolic blood pressure, HbA1c value, pain intensity score.
    - Each data element is associated with an *authorized* data originator.
    - *Nothing new here*… this is common in audit trails!

- **Data Capture: Key Definitions (4)**
  - **Data Element Identifiers (DEIs)**
    - Audit trail
      - Who entered / transmitted and When?
      - What changes were made? When? Why?
    - Data entered / transmitted to the eCRF should have DEIs.
      - DEIs are applicable, for example, to
        - » Laboratory data that are transmitted directly to the **eCRF**.
        - » Data entered directly into the **eCRF** by authorized site staff.
    - No implied recommendation that audit trails are transmitted “downstream” from one clinical system to another.

Source Data

Source Data…

All information in original (or certified copies) records of clinical findings, observations or other activities in a clinical investigation. (p.2, esource; 21 CFR 312.62(b))

Access to source data is critical to the review and inspection of the study…

…**So Know Your Source!**

Source Data should be…

- A
- L
- C
- C
- Accurate

See WHO Handbook for Good Clinical Research Practice (GCP), 2005; FDA Guidance on Computerized Systems in Clinical Investigations, 2007.

ALCOA

- **A**ttributable
  - Who entered the data?
  - *Audit trail!*
- **L**egible
  - Electronic data & metadata in human-readable form
  - Modifications should not obscure prior entries
  - *Audit trail!*

ALCOA

- **C**ontemporaneous
  - The time of data entry into the eCRF should be close proximity to the time of clinical activity.
  - *Audit trail!*
- **O**riginal
  - Earliest record
  - Changes and / or corrections should not obscure prior entries.
  - *Audit trail!*

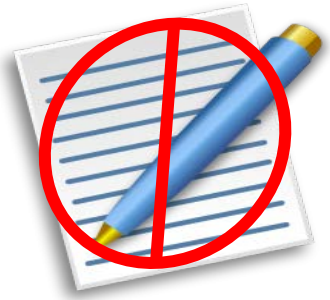
ALCOA

- **A**ccurate
  - eCRF should be a valid representation of the source data.
  - Corrections should be documented.
  - Quality control measures / processes.
  - *Audit trail!*

Source Data Capture

- **Data Capture: *Source Data Capture***

1. Transcription of Data From Paper or Electronic Sources to the eCRF
   - Duplication of data sources
   - Increased likelihood of data errors
   - Potential for delayed access to data
   - **Worst Case!**



2. Direct Entry of Data into the eCRF
   - No intervening paper step needed
   - Less confusion on what is source
   - Decreased likelihood of data errors
   - **Best Case!**

- **Data Capture: *Source Data Capture***

3. Automatic Transmission of Data from Devices or Instruments Directly to the eCRF
   - No paper required
   - Improved data quality and availability
   - Documentation of Source is important (e.g., intervening data management process)
   - **Best Case!**
4. Transmission of Data from PRO Instruments to the eCRF
   - No paper required
   - Improved data quality and availability
   - Documentation of Source is important (e.g., intervening data management process)
   - **Best Case!**

- **Data Capture: *Source Data Capture***

5. Direct Transmission of Data From the Electronic Health Record to the eCRF
   - Virtually, no paper required.
   - Improved data quality and availability.
   - Documentation of Source is important (e.g., intervening data process).
   - EHRs are not regulated by FDA.
   - FDA does not intend to assess compliance of EHRs with **21CFR part 11**.
   - **Best Case!**

Data Review
Retention of Records
Data Access

Data Review

- Investigator conducts the trial
  - Completed eCRF (each subject) should be reviewed and signed prior to submission to FDA.
  - Data must have DEIs that reflect modifications / corrections post-sign-off.

Retention of Records

- Clinical investigator retains control of the data.
  - Control by investigator is independent of sponsors
  - Investigator provides access to source data
  - Paper sources transcribed into the eCRF must be retained.

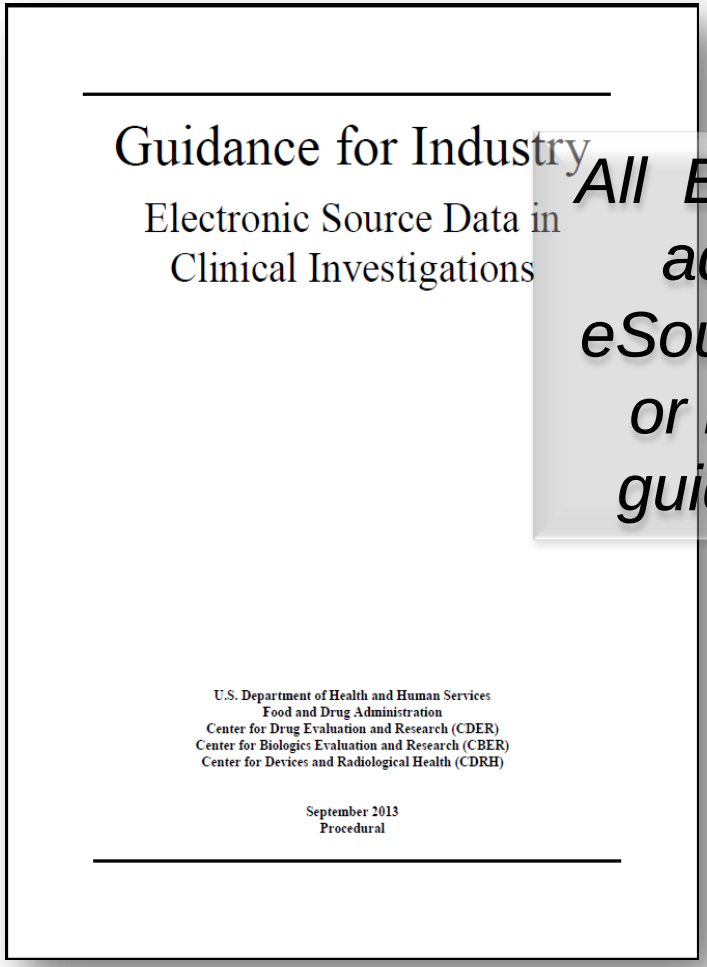
Data Access

- Sponsors, CROs, DSMBs, and other authorized personnel can view data in the eCRF
  - Review of subject's data during the conduct of the trial is important (e.g., safety, protocol violations, data errors, trial efficiency)
  - List of those authorized to have access to data.

Computerized Systems Used in Clinical Investigations

Regardless of the jurisdiction of the regulatory authority (in some cases none) there should be adequate controls to ensure confidence in the reliability, quality, and integrity of the source data.

FDA eSource Guidance and EMA Reflection Paper



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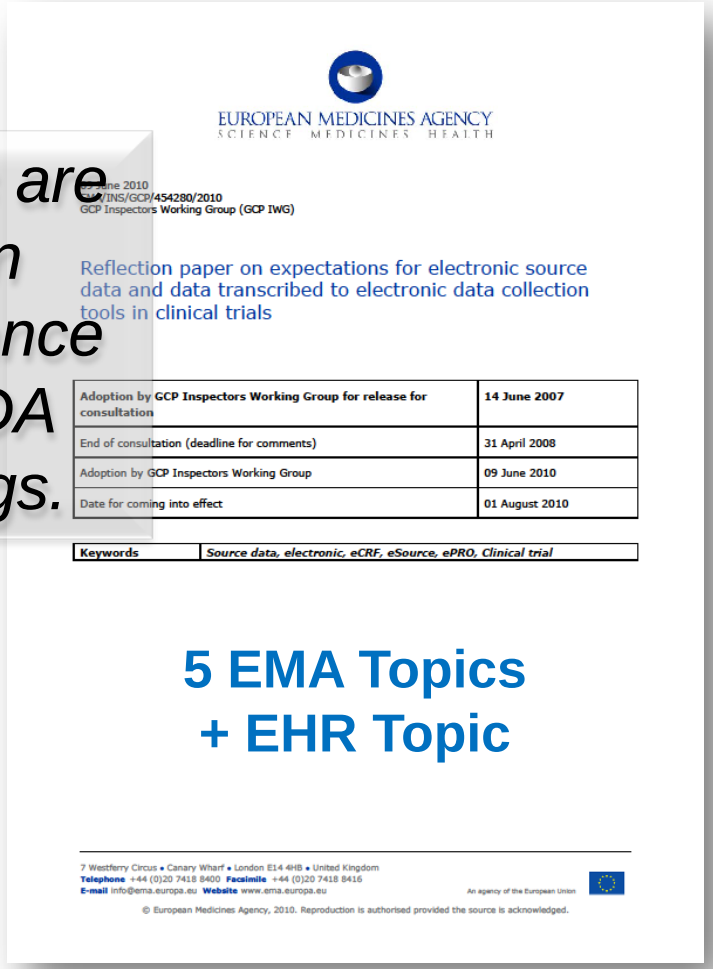
All EMA topics are addressed in eSource Guidance or in other FDA guidance / regs.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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GCP Inspectors Working Group (GCP IWG)

Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials

Adoption by GCP Inspectors Working Group for release for consultation	14 June 2007
End of consultation (deadline for comments)	31 April 2008
Adoption by GCP Inspectors Working Group	09 June 2010
Date for coming into effect	01 August 2010

Keywords	*Source data, electronic, eCRF, eSource, ePRO, Clinical trial*

5 EMA Topics + EHR Topic

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