Use of Electronic Health Record Data in Clinical Investigations

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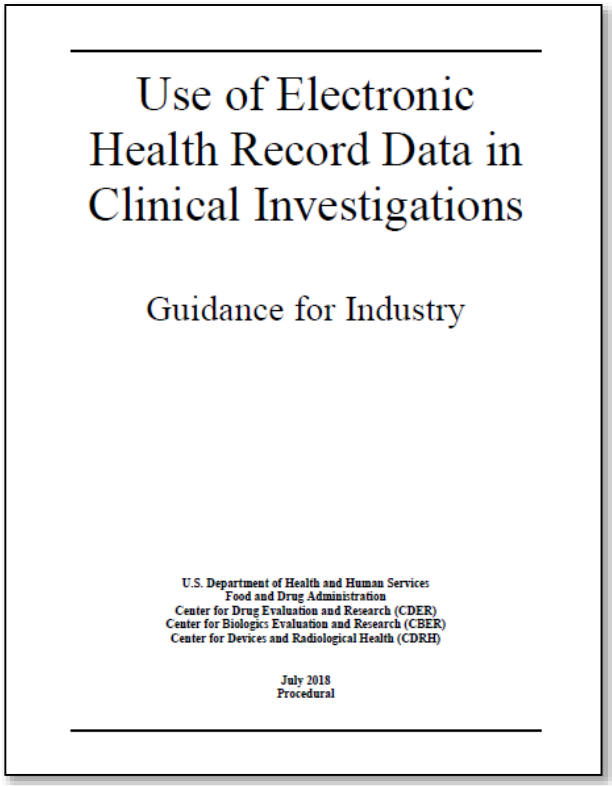
Overview of Today's Presentation

- Why did we write this guidance
- Challenges and opportunities with the use of EHR data in clinical investigations
- Interoperability and integration of systems
- Best practice for ensuring the quality and integrity of EHR data in clinical investigations


Use of Electronic Health Record Data in Clinical Investigations

Guidance for Industry

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)

July 2018
Procedural

What is the standard for case histories?

- Predicate rule 21CFR312.62
  - -An investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes.
- In the paper environment this was satisfied by:
  - Clinical notes by investigators
  - Physical copies of pertinent information from the patient's paper records
  - Physical reports from laboratories, imaging services, other consultants

Why did we write this guidance?

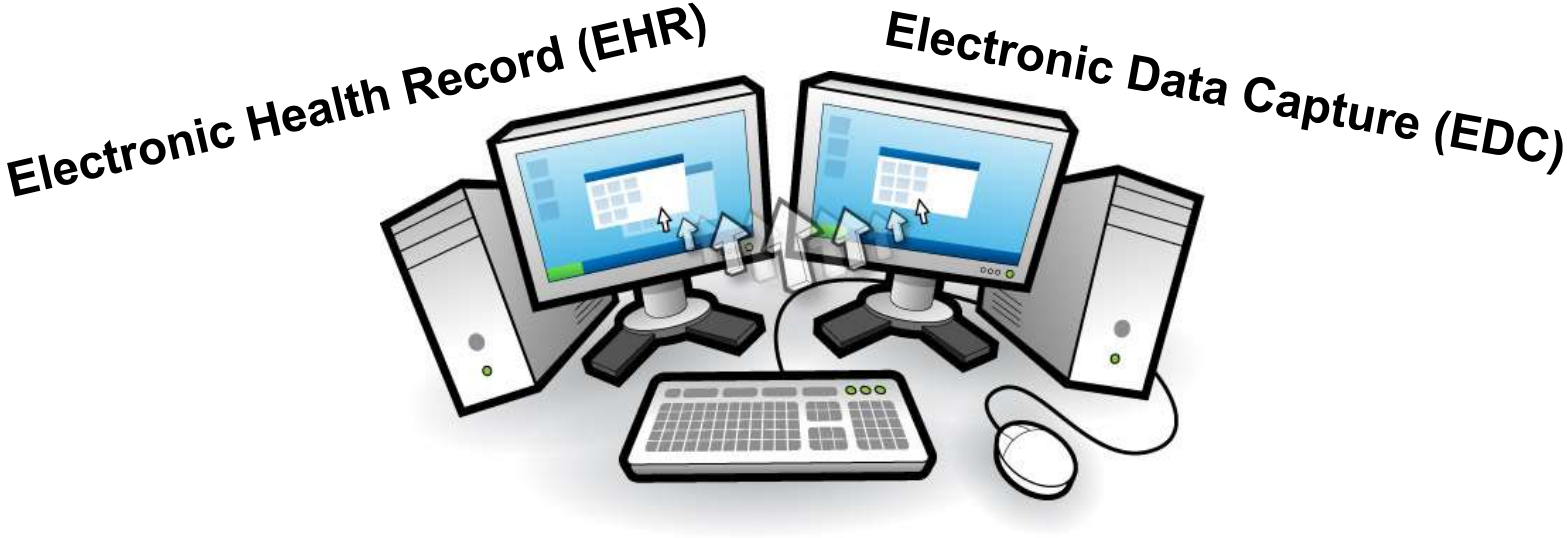
- Many patients and caregivers are involved in both clinical care and research, yet the record systems used for care and research are separate
- This disconnect leads to inefficiencies:
  - Data must be separately entered into two different systems- duplication of work, transcription errors
  - Things may happen to a patient in a trial that healthcare providers need to know, and things may happen during clinical care that researchers need to know but these two worlds are not communicating
  - Follow-up of patients in the clinical care environment may reveal important findings on safety and efficacy of new medical products that are not captured in the framework of a clinical trial

The Challenge

- Paper hospital charts and progress notes have been used in the past to satisfy FDA's requirements for patient records
- Electronic health records provide a new technological opportunity to integrate health care and research
- EHRs are not regulated by FDA (owned and managed by healthcare providers) - *FDA does not intend to assess compliance of these systems with part 11*
- Existing standards for EHRs which meet clinical criteria for safety and reliability may satisfy many FDA requirements clinical records
- Challenge:
  - How can they satisfy FDA's regulations on electronic records, audit trails, data attributability, record retention and patient confidentiality?

The Opportunities

- Pure data extraction e.g. patient demographics
- A source of real world data in clinical investigations
- Integrated systems where investigator and clinician use the same system



Interoperability And Integration Of Systems

Mitra Rocca

Interoperability

The ability of two or more products, technologies, or systems to exchange information and to use the information that has been exchanged without special effort on the part of the user

EHR and EDC Systems Integration

- Noninteroperable
- Interoperable
- Fully integrated

Noninteroperable Systems

Require manual transcription of ***data elements*** from the EHR to the eCRF or the paper case report form

Interoperable Systems

- Enable electronic transmission of relevant EHR data to the EDC system
- An interoperable EHR and EDC system could provide access to additional patient information populated from other clinical information systems

Fully Integrated Systems

Allow clinical investigators to enter research data directly into the EHR systems

EHR and EDC Systems Integration

Four Recommendations

1. Use of open, consensus-based Data Standards
2. Exchange of structured and unstructured data
3. Validation
4. Data From Multiple EHR Systems

Recommendation 1:
Data Standards

- Leverage the existing open data standards for the data exchange between EHR and EDC systems
- Ensure that the integrity and security of data are not compromised

Recommendation 2a:

Exchange of Structured Data

- Exchange of structured data between EHR and EDC systems so that data may be entered once at the point-of-care and used many times without manual re-entry or manual source data verification
- Ensure that the structured data elements obtained from the EHR correspond with the protocol-defined data collection plan

Recommendation 2b:

Exchange of Unstructured Data

Consider the reliability and quality of unstructured EHR data and the appropriateness of using it as critical source data, such as study endpoints

Recommendation 3a:
Validation

- Ensure that the interoperability of EHR and EDC systems functions in the manner intended in a consistent and repeatable fashion and that the data are transmitted accurately, consistently, and completely
- Ensure that software updates to the sponsor's EDC systems do not affect the integrity and security of EHR data transmitted to the sponsor's EDC systems

Recommendation 3b:

Validation and Data Quality Plans

- Address the interoperability of the EHR and EDC system and the automated electronic transmission of EHR data elements to the EDC system
- Periodically check a subset of the extracted data for accuracy, consistency, and completeness with the EHR source data and make appropriate changes to the interoperable system

Recommendation 4:

Data from Multiple EHR Systems

If data from multiple EHR systems from different health care organizations and institutions are integrated with EHR data at the clinical investigation site, data from another institution's EHR system may be used and transmitted to the sponsor's EDC system provided that data sharing agreements are in place

Best Practice for the Use of EHR Data in Clinical Investigations

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Office of Scientific Investigations
Division of Clinical Compliance Evaluation/CDER/FDA
Good Clinical Practice Assessment Branch/Team 3

December 6, 2018

Overview

- Use of Office of the National Coordinator for Health Information Technology (ONC)-certified EHR technology
- Use of EHR technology not certified by ONC
- Data integrity controls that should be in place when using EHR data in FDA-regulated clinical investigations
- How to apply eSource principles to EHR data use in clinical investigations
- Considerations for informed consent
- Inspection, record keeping, and record retention requirements

ONC-Certified Technology

- FDA does not intend to assess EHR systems for compliance with 21 CFR part 11
- Performance standards are regulated by other authorities
  - For example, in the U.S., HHS's Office of the National Coordinator for Health Information Technology (ONC) that oversees Health IT
- FDA encourages the use of certified EHR systems together with appropriate policies and procedures for their use

ONC-Certified Technology

- Advantages of certified technology
  - Aimed toward ensuring interoperable data sharing
  - Required to meet certain privacy and security protection requirements for an individual's health information (see 45 CFR 170.314(d)(1) through (8) and 45 CFR 170.315(d)(1) through (11)

Part 11 Controls for Electronic Systems

System Attributes

- Access control
- Audit trails
- Record retention
- Record copying
- Encryption

System Performance

- Validation
- Operational checks
- Authority checks
- Device checks

System Users

- Appropriate training
- System documentation
- Adherence to SOPs

ONC Certification -- Privacy and Security Protection Requirements at 45 CFR 170.314(d)(1) through (8) and 170.315(d)(1) through (11)

- Authentication
- Access Controls (and automatic access time-out)
- Authorization
- Auditable events (including audit trails to track changes to a record)
- Tamper-resistance (encryption)

System Attributes

Recommendations
ONC-Certified EHR Technology

- Sponsors should include in their data management plan
  - A list of EHR systems used by each clinical investigation site in the clinical investigation
  - Sponsors should document the manufacturer and version number of the EHR system and whether the EHR system is certified by ONC

Recommendations
ONC-Certified EHR Technology

- If an EHR system is decertified during the clinical investigation because the system no longer conforms to ONC's certification criteria, sponsors should determine
  - The nature or reasons for the nonconformity
  - Whether it would affect the quality and integrity of data used in the clinical investigation

EHR Technology Not Certified by ONC

- Sponsors should consider whether systems that are not ONC-certified have appropriate privacy and security controls in place to ensure that the confidentiality, integrity, and security of data are preserved
- System attributes
  - Access to electronic systems is limited to authorized users
  - Authors of records are identifiable
  - Audit trails are available to track changes to data
  - Records are available and retained for FDA inspection for as long as the records are required by applicable regulations

EHR Technology Not Certified by ONC

- Sponsors should consider the following risks of using data from systems that do not contain adequate data integrity control:
  - Potential harm to research subjects
  - Patient privacy rights
  - Data integrity of the clinical investigation and its regulatory implications

- If we are not able to verify the integrity of the data, then we may not accept that data to support a regulatory decision

Recommendations

Determining Suitability of EHR Technology Without Certification

- EHR system certification information from other authorizing bodies outside the United States
- Feature and product-specification information from the EHR system vendor

Recommendations
General Best Practice

Sponsors and clinical investigators should ensure that:

- Policies and processes for the use of EHRs at the clinical investigation site are in place
- Appropriate security measures are employed to protect the confidentiality and integrity of the study data

Recommendations
General Best Practice

Sponsors should:

- Ensure study monitors have suitable access to all relevant subject information pertaining to a clinical investigation, as appropriate

- Discuss with the relevant FDA review division any unique issues or challenges encountered relating to the data collection from the EHRs

Recommendations
eSource Principles

FDA

Data Originator

- For EHR data elements gathered during the course of a clinical investigation – data originator is the EHR

Data Modifications

- After data are transmitted to the eCRF, the clinical investigator or delegated study personnel should be the only individuals authorized to make modifications or corrections to the data
- Should reflect the date, time, data originator, and the reason for the change

Data Modifications

- Clinical investigators should review and electronically sign the completed eCRF for each study participant
- If modifications are made to the eCRF after the clinical investigator has already signed the eCRF, the changes should be reviewed and approved by the clinical investigator

Requirements

Informed Consent

- Must include a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained (21 CFR 50.25(a)(5))
- Should identify entities, such as health care providers, clinical investigators, sponsors, contract research organizations, study monitors, and regulatory agencies who may gain access to the patient's electronic health record relating to the clinical investigation

Informed Consent

- Please note that, under the Health Insurance Portability and Accountability Act (HIPAA) privacy rule, FDA does not need permission to inspect records containing health information (see 45 CFR 164.512)
- Informed consent:
  - Should state that FDA may inspect records (21 CFR 50.25(a)(5))
  - Should not state or imply that FDA needs permission from the subject for access to the records

Requirements

Inspection, Record Keeping, & Record Retention

- Clinical investigators must retain all paper and electronic source documents (e.g., originals or certified copies) and records as required to be maintained in compliance with 21 CFR 312.62(c) and 812.140(d)
- FDA must have access to records and may inspect and copy all records pertaining to a clinical investigation in accordance with 21 CFR 312.62, 312.68, 812.140, and 812.145

Inspection, Record Keeping, & Record Retention

- All relevant information in the EHR pertaining to the clinical investigation must be made available to FDA for review upon request (21 CFR 312.62(b), 312.68, 812.140(a), 812.145).
- Available and viewable to FDA as original records in the EHR or as ***certified copies***.
- If necessary, FDA may request to review the EHR audit trail information during inspection

In Summary…

- EHRs offer a rich source of real world data for use in clinical investigations
- FDA encourages the use of EHR data in clinical investigations
- The integration/interoperability of EHRs with the EDC system can increase the quality and efficiency of the clinical investigation
  - Reduced burden on study personnel
  - Reduced possibility for transcription errors (and may increase the accuracy and completeness of the clinical trial data)
- It is critical that sponsors assess the EHR system attributes as well as the policies and procedures for their use that are in place at the clinical investigation site to ensure that the appropriate data integrity and data security controls are employed

Q&A and Resources

Click for:

- Use of Electronic Health Record Data in Clinical Investigations: Guidance for Industry
- Electronic Source Data in Clinical Investigations
- PDF of today's slides
- Additional questions? Email: CDERSBIA@fda.hhs.gov

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