Remote Monitoring of Clinical Trials and EMRs

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What is your primary role?
Session Objectives

• Discuss requirements necessary for remote monitoring in a HIPAA compliant manner.

• Evaluate how operations can be impacted by remote monitoring.

• Describe the benefits, risks and limitations of remote monitoring.
“Providing Remote Access to our EMR?”
“Why not?”
Remote evaluation carried out by sponsor personnel or representatives (e.g., clinical monitors, data management personnel, or statisticians) at a location other than the sites at which the clinical investigation is being conducted.

Centralized monitoring processes can provide many of the capabilities of on-site monitoring as well as additional capabilities.

So centralized monitoring includes various approaches not performed on-site.
Some of FDA Examples

- Routine review of submitted data (looking for missing data, inconsistent data, data outliers, and potential protocol deviations).
- Conduct statistical analyses to identify data trends not easily detected by onsite monitoring, such as: standard checks of range, consistency, and completeness of data; checks for unusual distribution of data within and between study sites.
- Analyze site characteristics, performance metrics (e.g., high screen failure or withdrawal rates, high frequency of eligibility violations, delays in reporting data), and clinical data to identify trial sites with characteristics correlated with poor performance or noncompliance.
- Verify critical source data remotely as described in the monitoring plan, in cases where such source data are accessible, or where CRF data are, according to the protocol, source data.
- Complete administrative and regulatory tasks. Such tasks include, for example, verifying continuous institutional review board (IRB) approval by reviewing electronic IRB correspondence.
- Performing portions of investigational product accountability, such as comparison of randomization and CRF data, to preliminarily assess whether the subject was administered or dispensed the assigned product and to evaluate consistency between investigational product receipt, use, and disposition records;
- Verifying whether previously requested CRF corrections were made.
Some of FDA Examples continued

- Communication with sites
- Informed Consent Form review
- Informed Consent Process review
- Original source data review
- Source data verification
Does FDA cite an investigator for deficiencies in compliance with 21 CFR Part 11?

At this time, FDA does not intend to assess a site's EHRs' compliance with 21 CFR Part 11 during routine BIMO inspections at Clinical Investigator sites.

There are many ways for Clinical Investigator sites to comply with all applicable predicate recordkeeping rule requirements, although there is no prescribed nor formally endorsed method for managing records in electronic format.
Adequate controls should be in place to ensure confidence in the reliability, quality, and integrity of the electronic source data. The determination of whether a computer system used in a clinical investigation is suitable for its intended purpose might not be under the control of the clinical investigator(s) or sponsor (e.g., EHRs). The performance standards for these computer systems may be regulated by other authorities and under the control of, for example, healthcare providers or institutions.

**FDA does not intend to assess the compliance of EHRs with part 11.**

[but guidance refers to ALCOA. How ALCOA is accomplished in electronic records vs. paper has differences.]
Review: FDA Requires Investigators

- To prepare and maintain
  - **Adequate and Accurate** case histories for each individual enrolled in a clinical trial, whether on active treatment or on control.

- Case histories
  - record **All** observations and data **pertinent** to the clinical study that are necessary for **reconstruction and evaluation** of the trial.
  - Include **case report forms and supporting data** including,
    - i.e. 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.

- These data must be:
  - **Original** records or “certified” copies of the original records.
Pertinent Source

- **Use of multiple platforms of source** at sites:
  - Paper (medical charts less, but source worksheets, research charts)
  - Electronic
    - CRFs (when used as original source)
    - Diaries / eIC
    - EMRs (many times on **more than one system**, example clinics vs. hospital; hospital vs. lab/radiology; research vs. managed care).
  - Research may not have been part of the site’s integration to an electronic record
  - Scanned / .pdf
  - Emails

- **Challenge**: ensuring you are being disclosed all pertinent source with remote monitoring.
  - **Solution?**
Quality: ALCOA

• FDA uses the following attributes for assessing the quality and integrity of the data during inspection or review of that data.
  – Attributable: identified with specific subject and recorder (not de-identified!)
  – Legible
  – Contemporaneous: Data recorded at the time they are generated
  – *Original*
  – Accurate

• In any form . . .
  – Paper or Electronic

• *FDA's acceptance of data depends on FDA's ability to verify the quality and integrity of the data during FDA onsite inspections and audits.*

(FDA Guidance 2007 Computerized Systems & FDA Guidance 2013 eSource)
<table>
<thead>
<tr>
<th>ALCOA Standard</th>
<th>Paper</th>
<th>EMR</th>
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<tbody>
<tr>
<td>A: Attributable</td>
<td>Can link the data or supporting source with unique subject and the author. Paper record with delegation log, and subject other subject source. Predated, during, post pertinent information</td>
<td>Same. Common to have a combination of paper and electronic records.</td>
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<td>L: Legible</td>
<td>Can you read the handwriting of the author / subject?</td>
<td>Is the information encrypted and if so can you read on the screen and does the data print legibly and does it support attributable-ness?</td>
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<td>C: Contemporaneous</td>
<td>Things are written at the time they occur.</td>
<td>If the records are converted from paper to electronic, does it support attributable and Does the system date-time-stamp; audit trail to be sure can verify timing to support predicate rule and also protocol compliance.</td>
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<td>O: Original</td>
<td>Pertinent info is documented first. If copied and supplied as source, confirmation that exact copy with all the same attributes as the original. Some call this “certification” process. Not the same as a “shadow file”, unless specified differently = unverified. If something is located in a medical chart and the sight also writes it in a study source document, both are source. Duplication of documentation is not a good practice.</td>
<td>Same as paper, but pertinent info may be documented first in an electronic record, (EMR or eSource for the study). If printouts are supplied by the site, these are like shadow files and need to be confirmed as a copy with all the same attributes as the original.</td>
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<td>A: Accurate</td>
<td>Source should accurately support the CRFs, and various source should not contradict one another.</td>
<td>Same. Also, some EMRs are prepopulated with past information or demographics about the subject. Caution, some records prepopulate past vital signs and other info that may not be contemporaneous and conflict with other data.</td>
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Remote Monitoring per Monitoring Plan Definitions

• Depends how the sponsor defines things.

• Example:
  • SDV (source data verification) = verifying data quality and human subject protections
  • Some refer to this now as SDR (source data review), or
  • SDV = checking for transcription errors between source and eCRF. Identifying a distinction between SDV and SDR.
Regarding Remote Monitoring

- What are the pros and cons for investigation sites, sponsors, and subjects? In theory, how could you make these all PROs?

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<tr>
<th>Sponsors:</th>
<th>Sites:</th>
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<td>data integrity.</td>
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<td>Other</td>
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Appropriate Remote Monitoring

- Access to EMRs on-site is a challenge. Now asking for remote access may be thought to be too risky.

- Compliance with Predicate Rules (sponsor and sites)
  - FDA, HIPAA, local and regional requirements, etc.

- Supported by clinical quality systems at BOTH sponsor and site
  - Talent
  - Training
  - Procedures / templates and tools
  - Communication plans, including escalation related to thresholds
  - Linked to Risk Assessment and monitoring
  - Refer to the EMAs 2013 Reflection Paper for Quality Risk Management.

- Flexibility to various project and individual site differences.
**Logical and Defensible Decisions**

**Covered Entity:**
- If asked to defend the rationale of the use and disclosure of PHI, could this be provided in audit / inspection?
- The HIPAA Privacy Rule does not say you cannot provide remote access to PHI.

**Sponsor:**
- Meets FDA investigator requirements (sponsor oversight)
- Provides access to quality data / Supporting
Remote Access to Source & Challenges

1. eCRF (encouragement in two guidance documents to use CRF as original source when able).
   - Challenge: 1) maintenance of original by site, 2) eCRF system capabilities.
   - For record retention requirements and also for completeness of the medical records.

2. Remote access to PDFs
   - Email attachment
   - Shared area, e.g., Cloud
   - Challenge: 1) **PDFs not automatically a certified copy**, 2) same challenges as remote access to EMR
Remote Access to Source & Challenges

3. Use of a sponsor created electronic source documentation for the study
   - Can link to eCRF; can build in remote review logistics
   - Challenges: SAME Challenges as remote access to EMRs and PDFs emailed
   - For CEs, this is PHI.
   - Is this everything that is “pertinent”? 

4. Remote access to EMR
   - Challenge: 1) security of the PHI, 2) policies of the covered entity (CE), 3) CE risk assessment 4) capabilities of various EMR systems

Future Industry / Regulatory Goals: Population of eCRF from EMR
HIPAA De-Identified Health Information

- De-Identified Health Information = Not PHI
  
  - Includes 18 identifiers and derivations (e.g., names and initials, respectively)

- Once de-identified Not governed by HIPAA

- But not the same as redacting information (black magic-marker) for things such as safety event follow-up where names are removed from copies of medical records and initials / study numbers are replaced before scanning or faxing from site to sponsor.
• Identifiers derived from HIPAA restricted Identifiers are not acceptable for clinical trial data verification and support of quality characteristics for data (ALCOA).

• Also not easy or affordable . . . De-identification must be verified by statistical verification with expert certification kept on file for 6 years, or removing all of the 18 identifiers determined by HHS.
This “middle” option between de-identified and fully identifiable information allows investigators to retain the following data elements in a data set:

- **Town, city, state, and the 5-digit zip code** (but not street address);
- **Dates** such as birth date, admission date, discharge date, and date of death; and
- **Unique numbers, characteristics, and codes.**

Data Use Agreement is one that a covered entity (CE) may use to allow for a Limited Data Set to be used and disclosed for a particular purpose only **without individual (subject) authorization.**
HIPAA Limited Data Set & Data Use Agreements continued

• Should be supported by CE SOPs related to compliance with the applicable regulations (45 CFR 164.514 (b)).

• Data Set is LIMITED and does not meet the source data disclosures needed for most FDA regulated studies.
  • There are 16 types of identifiers that are allowed to be included.

• A Data Use Agreement must meet the requirements within 45 CFR 164.514 (b).

• The regulations refer to limited data sets used for certain practices, like research, but within the CE or provided to a business Associate (BA) to provide a service for the CE.
• May see being uses by sponsors: Remote Monitoring

• Receipt of source documents. Sending PDFs for example.

• Caution about these types of uses.

• Sponsors are not business associates.

• Data use agreement may not be what is needed to accomplish the goals intended.

• Instead . . .
HIPAA Authorizations and CTAs

- HIPAA Authorizations for Use and Disclosure of PHI for Remote Monitoring
  - Include obtaining permission for disclosure by CE and use by outside entity (sponsor) noted in the authorization.
  - Includes what information (PHI) and what purposes.
  - Notes that the collected information will no longer be protected under HIPAA
  - Therefore, no de-identification has to take place.
  - Minimum necessary clause in HIPAA NOT applicable.
HIPAA Authorizations and CTAs continued

- HIPAA Authorizations for Use and Disclosure of PHI for Remote Monitoring
  - Challenges:
    - Adequate assurances from sponsors of the security and behavior of their staff
    - Acceptable to the current SOPs and local requirements of the CE or region.
    - Security risk assessments required by CEs and may not weigh the risk acceptable. *(Security Rule requirement for CEs)*
    - CEs interpretation of the plausibility of this can vary, just like the EMR capabilities and security features.
  - Solutions?
Site Policy / Procedure Needs to Support Remote Review

- Site: working with electronic systems
  - Own systems
    - EMR
    - Remote Access
    - Source, including Certified Copies
  - Sponsors systems
    - eCRFs
    - Source
    - Monitoring / auditing
Examples of Some Potential Workflows

• Sponsor Initiated:
  – PDFs on “cloud” secure access
  – Ask for emailed PDFs
  – Other technology

• Site Initiated:
  – Advantages
One Example: VOS Solution

App

Platform

Streamer

CRA

SITE COORDINATOR

Firewall

Compliant Datacenter
**WORKFLOW PROCESS**

**TRADITIONAL**

1. Monitoring Visit Planning
2. Travel
3. Monitoring visit to the site
4. Travel back
5. Monitoring Report

**VS**

**VOS**

1. Monitoring Visit Request
2. Connection to the site
3. Virtual monitoring visit
4. Switch off and report

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The Train is Moving & We Need to Get On! Collaboration
System Level

• Partner / Collaborate

• Evaluate Current Quality Systems

• Establish Standards and Definitions (SOPs, templates, tools)

• Talent, Technology

• Maintain Data for Improvement from study to study

• Share!
Study Level
Pre-study, During, Post F/U

- Protocol, Monitoring Plans / Site Study Execution Plans
- ICF, Authorization language
- Pre-study evaluations bilateral risk assessment
- CTA / Budget
- Others?
Share Your Experiences
Remote Monitoring

A Site Perspective
Pre-Epic Monitoring

• On-site

• eBrowser access (monitor provided unique login for duration of visit)

• Access requested by clinical research coordinator at least 10 days before scheduled monitor visit

• Ability to restrict date range
Post-Epic Monitoring

• Period of using Release to Inspector (static PDF report)
• Currently using Duke MedLink (Epic CareLink)
• On-site electronic access (monitor provided unique login)
• Access must be requested at least 10 days prior to visit
  – Requested by coordinator via REDCap survey
  – System automatically sends notifications and required confidentiality agreement
• Monitor must sign separate confidentiality agreement
• No ability to restrict date range (may not be necessary for many studies)
Duke MedLink

Use these tabs to navigate to the various kinds of information in the chart.

Click the date to view more details.
Challenges to Remote Monitoring

• **No model to follow**
  – Not currently used at most other Academic Medical Centers
  – Will need to create our own policies and procedures
  – What will we require of sponsor and monitor?

• **Security implications**
  – Where will they be monitoring? Office? Home? Starbucks?
  – Less accountability than on-location where coordinator is within eyesight

• **Reporting/Audit implications**
  – How will we audit? How frequently? Which group (Health System or School)?
  – If monitor intentionally accesses information that he/she shouldn’t, what are the implications for future remote monitoring for that sponsor?

• **Burden/Cost shifting**
  – Depending on processes put in place and sponsor requirements, may require additional work from site’s coordinators
  – Will need to recover these costs in budget negotiated with sponsor
Considerations for Remote Monitoring

• Duke currently working with Epic to develop real-time audit capability

• Requiring sponsor to sign separate addendum to the clinical trial agreement detailing terms of remote access to Duke MedLink

• Potentially requiring monitor to be in closed office or conference room*

• Can address regulatory issues through consent, but question of how much risk institutions are willing to bear (likely institution’s name in the news, not the sponsor or CRO)

*http://jop.ascopubs.org/content/9/1/e13.full
How does the HIPAA Privacy Rule impact the accessibility of original source when found in an EHR?

• Covered Entity (CE) vs. non-covered entity
• Office for Civil Rights (OCR)
• CE: PHI use and disclosure by PHI for treatment, payment and operations (T.P.O.)
  – Research as treatment that requires use and disclosure of PHI
  – Authorizations for Use and Disclosure of PHI

• CEs required to have policies related to HIPAA, but should not restrict the site from complying with FDA requirements
  – Assess at pre-study and determine if original pertinent source can be monitored/accessed

• Minimum Necessary clause only applicable without authorizations for T.P.O.
• ALCOA and supporting source documents
More Questions?
Thank you!

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