EHR – present challenges in clinical trial use

Readiness assessment and mitigating actions

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Points of interest

- Continued from this morning, remaining points of comparison of EU and FDA guidance specifically regarding EHRs
- Meeting with stakeholders on EDC systems in December
- European initiatives of interest, among others stakeholder meeting in December, member state survey and eSource Readiness Assessment initiative.

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Comparison

EMA	FDA
Source data should be attributable, legible, contemporaneous, orginal, accurate, complete, consistent, enduring and available when needed (ALCOA+) and must meet the regulatory requirements for recordkeeping specified in 28 different local laws. Sponsors and investigators should pay special attention to local legislation with regards to the source data going directly into the eCRF. The EHRs are first and foremost a communication tool for HCPs to ensure communication around the patient.	Source data should be attributable, legible, contemporaneous, orginal and accurate (ALCOA) and must meet the regulatory requirements for record keeping (specified CFR citations)

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Comparison

EMA	FDA
The EMA reflection paper has an added section regarding Electronic Health records. *Clinical trials can be conducted at institutions that use electronic health record systems. In that case the sponsor must assess the systems in use by investigators to determine how well they meet the requirements of GCP including those detailed in the paper. If the systems do not meet the GCP requirements then mitigating actions should be taken as necessary prior to trial site initiation. Examples where the requirements may not be met are discussed in the paper*	The guidance specifies that FDA does not intend to assess the compliance of EHRs with part 11 According to the FDA webinar on this document, the monitor will have to rely on the data presented if he or she does not have direct access to the EHR

EHRs challenges in clinical trials

Clinical trials can be conducted at institutions that use electronic health record systems. In that case the sponsor must assess the systems in use by investigators to determine how well they meet the requirements of GCP including those detailed above. The assessment should include consideration of the potential harm to trial subjects and patient rights and to the data integrity of the trial. If the systems do not meet the GCP requirements then mitigating actions should be taken as necessary prior to trial site initiation.

Examples where mitigating actions may be required:

- Lack of appropriate audit trail
- Direct access to trial subjects' (and not others) entire electronic health records, possible or not?
- Monitors'/inspectors' ability to verify that copies are complete and accurate

Audit trail in EHRs

- Investigator controls may be absent in systems where non-trial healthcare professionals at the investigator site or other location may alter the health records. In this instance the sponsor assessment on the impact to the trial should include whether there is an audit trail of changes made.
  - If there is an audit trail, then a chronological assessment of what was known at the time of a trial decision is possible and therefore the absence of investigator control may have little impact.
  - However, if an audit trail is not available, additional process controls, such as a signed and dated print outs, will have to be introduced to maintain the information. (Requirement 6)

Direct access to trial subjects' (and not others) entire electronic health records

- The monitor, auditor and inspector should have direct access to trial subjects' entire electronic health records whilst the trial site staff should ensure that the medical records of patients who are not trial subjects should not be accessible. (Requirement 4).

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Monitors'/inspectors' ability to verify that copies are complete and accurate

- Whenever copies of electronic health records are provided for the purpose of monitoring/ auditing/inspecting the monitor/auditor/inspector should be able to verify that this copy is a complete and accurate copy of the electronic health record.

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Example of deviation/finding

- The investigator had not given the monitor direct access to the source data i.e. the electronic medical record and the monitor had not verified that printed records which were the basis for source data verification were complete and accurate, ICH GCP 4.9.7. and 5.18.4 (k), (m) (**major)**

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Copying medical records – is it allowed?

2.11 ICH GCP: The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

- Central monitoring
- Adjudication committees
- Others?

Comparison

EMA	FDA
Comment: Direct transmission of data elements from EHR to the eCRF can only take place, if the respective EHR system is adequately validated for that purpose. Lately, a number of promising initiatives and projects have been launched in both European Member States and the U.S., but the majority of EHR systems are currently lacking the required preconditions in respect to validation and reliable protection of data privacy.	Examples of information in the FDA guidance which is not detailed in the EMA reflection paper : •Definition of data element, data element identifier, data element originator etc. with examples •A list of all authorized data originators should be developed and maintained by the sponsor and made available at each clinical site. •FDA has a specific section on direct transmission of Data From the Electronic Health Record to the eCRF •Other guidance: a list of recommended SOPs for electronic systems

European initiatives of interest

- Yearly meeting between GCP IWG and interested parties
- Ad hoc meetings between organisations and the GCP IWG, example:
  - eClinical forum: Investigator Site eSource Readiness Assessment project. a series of questions, with "pre-fill" answers from the site's EHR vendor, suggestions on potential workarounds for areas that may fall short of regulatory expectations. The site can identify if its system and/or processes are compliant with regulations or if additional processes need to be put into place. The site can then share the resulting assessment with research sponsors and regulators without the need for sponsor-specific assessments.
- National initiatives to solve issues specifically regarding electronic health records
- IWG survey among member states on medical records
- eSource stake holders meeting in December

Meeting with stakeholders on EDC systems in December

Some potentially interesting agenda points:

- Independent contemporaneous copy of eCRFs (again)
- Cloud solutions, important considerations
- Electronic Certified Copies
- ePRO
- Things to be aware of when contracting out electronic services

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Cloud solutions

- Who owns the data when stored on vendor's servers?
- What is the attitude to server farms location and sharing of partitioned server with other clients?
- What considerations are given to data protection in the countries where servers may be located?
- How should the cloud data be protected from unauthorised access?
- What consideration is given to back up and restoration? What are the minimum expectations for this?
- What are essential components for consideration in contacts with a cloud service provider?
- What risks do you believe there are in using cloud?
- How is guaranteed that documents and data stored in the cloud are archived and ready for inspection for at least 25 years after the end of the clinical trial (as required by article 58 of the European Clinical Trial Regulation)?

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ePRO

- Definition of source data
- Confirmation of existence of patience entering data
- Back up procedures when using ePROs
- Processes for provisions of the investigator sites with certified copies of the ePR data

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Recent deviations given regarding contracts between sponsors and CROs providing services including electronic systems

- For a number of contracts the following issues were revealed:
  - Split of responsibility was unclear both with regards to tasks but more frequently with regards to responsibilities regarding the Trial Master File (emails, meeting minutes).
  - It is unclear to which standard the CRO will conduct its delegated sponsors' functions.
  - It is not stated that sponsor should have access to conduct audit at the CRO site and that the CRO site could be subject to inspections (national and international authorities.
  - It is not specified that the CRO should inform the sponsor in case of deviations discovered by the CRO which could potentially effect sponsor data.

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Recent deviations given regarding contracts between sponsors and CROs providing services including electronic systems

- It is not clear how reporting of 'serious breaches' should be ensured (responsibility, deadlines etc.). This is already a requirement in some EU countries by law and the EU portal is currently being set up to handle future breaches.
- Information is missing about agreed output (e.g. excel exports, meta data, complete database, ongoing and final delivery to investigators, TMF delivery etc.), NB! Possibility to restore database may be requested.
- Arrangements about decommissioning of the database were not clear

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Questions?

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