eCOA - Benefits, Challenges, Current and Future Technologies

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Agenda

- Benefits of eCOA
- Challenges for eCOA Providers and Sponsors
- Current and Future Technology
- Questions
What is COA?

**COA definition by FDA:**
“A clinical outcome assessment (COA) directly or indirectly measures how patients feel or function and can be used to determine whether or not a drug has been demonstrated to provide a treatment benefit”

**Includes:**
- Patient Reported Outcomes (PRO)
- Clinician Reported Outcomes (ClinRO)
- Observer Reported Outcomes (ObsRO)
What is eCOA?

- Paper has predominantly been used to collect COA data in clinical trials but *electronic* COA (eCOA) is rapidly becoming the preferred method of data collection, particularly when COA data is being used as the primary or secondary endpoint for a clinical trial.

- FDA PRO Guidance for Industry released in 2009 (Draft in 2006) has been a major contributing factor of electronic PRO’s increasing adaptation.

- In October 2011 FDA conducted a workshop to discuss measurement principles for all COAs used in clinical trials for new drugs. COA was defined and it was made clear that the PRO Guidance requirements apply to all COAs (PRO, ClinRO and ObsRO).
If only we could see the data between visits, we could guide patients to be compliant to the protocol.

By the time we get the data, it’s too late to prevent problems.

Where does the Technology fit into the Process?

Subject at home or clinic

Complete Electronic Questionnaires

Transcribe into EDC or double data entry into CDMS

Source Data Verify

- Data Management
- Statistics
- Clinical Operations
- Upper Management
- Medical Staff
Notable Points Regarding eCOA

- eCOA data is true electronic source data
- Data is hosted by “Trusted Third Party”
- Data model typically determined by sponsor Data Management (DM)
- Copy of data typically transferred to sponsor DM during trial
- Electronic source migrated to sponsor at end of study
- Archives – site and sponsor
Why eCOA?

- Better, Defensible Data/Reducing Regulatory Risks
  - Quality / Security
  - Privacy and discretion for subject
  - Meets ALCOA principles

- Efficiency of Data Handling

- Better Compliance

- Access to data in real-time

- Additional Functionality Not Available with Paper

- ROI compared to paper
“If a patient diary or some other form of unsupervised data entry is used, we plan to review the clinical trial protocol to determine what steps are taken to ensure that patients make entries according to the clinical trial design and not, for example, just before a clinic visit when their reports will be collected.”

FDA Statement from PRO Guidance Doc (Page 14)

FDA PRO Guidance to Industry, December, 2009
eCOA data Meet the ALCOA Standard

- **Attributable**
  - Each user has a unique PIN code
  - Date & Time stamps, Audit trail

- **Legible**
  - Codelist selections, Multiple Choice responses
  - Free-text possible via on-screen keyboard

- **Contemporaneous**
  - Control and/or Eliminate retrospective data entry
  - Typical patient electronic diary entry compliance is >90%

- **Original**
  - PRO data captured directly from subject in electronic form

- **Accurate**
  - Software logic and real-time edit checks prevent incomplete and inconsistent data entries

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Why eCOA?

“Such electronic source data and source documentation must meet the same fundamental elements of data quality (attributable, legible, contemporaneous, original, and accurate) that are expected of paper records and must comply with all applicable statutory and regulatory requirements.”

Why eCOA?

Functionality Not Available with Paper

- Reminder alarms
- Conditional navigation (skip patterns)
- Elimination of extraneous entries in margins
- Automated Instrument Scoring
- Faster study closeout and database lock
- Automated creation of study archives
Why eCOA?

Common Question:
How do the elderly (> 65 yrs.) react to and cope with the technology?

Answer:
Very well, they consistently rank amongst the highest compliant groups.
Why eCOA?

Making life easy for site staff

- Guide site staff to follow visit procedures according to protocol
- Document each step as it occurs
- Reduces possibility of human error
- Eases burden of handoffs between users
Why eCOA?

Cost of electronic vs. paper

- Known / Hidden Costs of Paper
- Intangible Benefits of eCOA

eCOA
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Changing Hardware

- Commercial electronic devices evolve rapidly
- Unlocked devices more expensive
- Devices contain many features not needed for eCOA
- Mixing devices in study can complicate data analysis
- Challenge will diminish as evidence of equivalence mounts
- PRO and ePRO Consortiums beginning to address topic
Converting Paper to eCOA Instrument

- An eCOA developed from a paper version of the instrument should provide data that are equivalent or superior to the original version.

- Further, the eCOA must be measuring the same thing as the original instrument.

- Empirical evidence is required to support both these points.
“Validation” of eCOA Instrument

- As per the FDA PRO Guidance, Page 20: “When a PRO instrument is modified, sponsors generally should provide evidence to confirm the new instrument’s adequacy”. “Modification” explicitly includes “changing an instrument from paper to electronic format”.

- As per the ISPOR PRO Taskforce, Page 14: “…the amount of change that occurs during migration to the electronic platform/device will dictate the amount of evidence necessary to demonstrate that the change did not introduce response bias and/or negatively affect the measure’s psychometric properties.”
### “Validation” of eCOA Instrument

<table>
<thead>
<tr>
<th>Level of Modification</th>
<th>Rationale</th>
<th>Examples</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor</td>
<td>The modification can be justified on the basis of logic and/or existing literature. No change in content or meaning.</td>
<td>1) Nonsubstantive changes in instructions (e.g., from circling the response to touching the response on a screen). 2) Minor changes in format (e.g., one item per screen rather than multiple items on a page).</td>
<td>Cognitive interviewing  Usability testing</td>
</tr>
<tr>
<td>Moderate</td>
<td>Based on the current empirical literature, the modification cannot be justified as minor. May change content or meaning.</td>
<td>1) Changes in item wording or more significant changes in presentation that might alter interpretability. 2) Change in mode of administration involving different cognitive processes (e.g., paper [visual] to IVR [aural]).</td>
<td>Equivalence testing  Usability testing  Potentially cognitive interviewing</td>
</tr>
<tr>
<td>Substantial</td>
<td>There is no existing empirical support for the equivalence of the modification and the modification clearly changes content or meaning.</td>
<td>1) Substantial changes in item response options  2) Substantial changes in item wording</td>
<td>Full psychometric testing  Usability testing</td>
</tr>
</tbody>
</table>
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4 Major Types of eCOA

- Smartphone/Handheld Device
- Site-Based Tablet
- Web-based Portal
- Interactive Voice Response (IVR)
Factors When Selecting eCOA Modality

- Frequency of data collection (Daily, Weekly, at site, event)
- Type of data (Symptoms, Dosing, etc.)
- Use of data – primary or key secondary?
- Number of Instruments / Items per instrument -> Burden
- Patient population – disabilities or impairments?
- Logistics and telecommunication support
Smartphone/Handheld Device

Advantages:

- Portable – reusable
- Provides security, privacy, discretion
- Custom reminder alarms
- Complex edit checks & calculations
- Data entry possible regardless of connectivity
- Automated data sending
- Integration with medical devices
Smartphone/Handheld Device

Disadvantages/Challenges:

- Cost of hardware
- Size of screen
- Short commercial lifespan
- Logistics and inventory
- Need to charge device
- eCOA system access to device control may be restricted (i.e. iPhone™)
Site-Based Tablet

Advantages:

- Large screen - allows near 100% replication of paper instrument
  - Reduced validation requirements
  - Retains format familiar to sites
- Easily accommodates graphics
- Portable and easy to use
- Offline data entry
- Variety of data sending options
Site-Based Tablet

- Disadvantages/Challenges:
  - Cost of hardware
  - Logistics and inventory
  - Site qualification needed for LAN or WiFi sending (firewalls)
Web-based Portal

Advantages:

- No (or reduced) equipment to buy
- Sites, subjects use their own computer
- Very useful for studies with infrequent data collection
- User-friendly for those comfortable with a computer
- Well-suited for large Phase IV studies
- Reminder alerts via email and/or subject’s mobile phone
Web-based Portal

Disadvantages/Challenges:

- Must have active internet connection to collect data
- Varying screen sizes and resolution make standardization challenging
- May stratify population along economic lines
- Private area for subjects to complete assessments at site?
IVRS – Interactive Voice Response System

Advantages:

- Accessible and easy to use for most populations
- Easy to deploy
- Additional equipment not typically needed
- Works nearly anywhere
- Minimal Training Requirements
- Voice prompts can reduce literacy requirements of subjects

Best suited for brief, simple questions
IVRS – Interactive Voice Response System

Disadvantages/Challenges:

- Many people are weary of automated systems
- Multiple response options reach limit of short term memory
- Cannot accommodate VAS or images
- Migrating from paper often more difficult – visual to audible format
- Further studies needed to assess whether transfer of written modality to audible yields equivalent data
Flexible Hybrid Systems

Home diary on Handheld Device

Database Web Portal Access to Study Data

Site-based assessments on Tablet

Web-based assessments on computer & mobile phone
Past, Present …. Future?
Future of eCOA – Device Independent

- Screen size concerns will lessen as experience is gained
- Use of subject’s own device will nearly eliminate need to purchase hardware
- OLED screens will result in mobile devices with roll-out screens – eliminating current screen-size restrictions
Concept Mobile Products

Just Google "flexible screen"
Lifestyle Monitoring and Integration

- Integration with medical devices
  - Automated glucometer / insulin pumps
  - Barcode scanners for dietary intake information
  - 3D Digital cameras and video –
    - Wound care
    - Dermatology
    - Injection site-reactions
- Medication adherence
Questions?