Deploying ePRO Instruments in Clinical Trials: Challenges and Solutions

J. Jason Lundy, PhD – C-Path
Tara Symonds, PhD – Pfizer Ltd
Cindy Howry, MS – Bracket
Valdo Arnera, MD – PHT Corporation

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Presentation Outline

• Introduction – Jason
• ePRO Challenges – Tara
• ePRO Solutions – Cindy and Valdo
Benefits of Electronic Data Capture

• Electronically adapted PRO instruments (ePROs) have the advantages of:
  – less administrative burden;
  – avoidance of secondary data entry errors;
  – easier implementation of skip patterns; and
  – more accurate and complete data.
• May increase participation of subjects from typically underrepresented groups, such as those of lower income or lower literacy

Considerations for ePRO Migrations

• Characteristics of the patient population and therapeutic area
  – functional and cognitive abilities/limitations
• Characteristics of the instrument
  – Setting where the instrument will be completed (e.g., subject’s home)
  – Length of items, structure of response set, subject burden
  – Use of multiple modalities within a trial (i.e., mixed modes)
Considerations for ePRO Migrations

- Infrastructure for electronic data collection
  - Cellular signals, internet connectivity
- Language and translations
  - Assume that translated text will take more space (i.e., more characters) than US English
  - Certain formatting does not translate well (e.g., fonts, capitalization, and underlining)
- Benefits that do not exist on paper
  - seamless skip logic, real-time edit checks, calculations, and alarms

Recap

- Advances in electronic data capture should enhance the data collection process for both investigators and subjects
  - Evidence is necessary to verify the alternate mode of data collection does not lead to different results than what would otherwise be reported by the subject
- Careful consideration of the data collection strategy prior to migration is necessary
- Industry best-practices continue to evolve
Deploying ePRO Instruments in Clinical Trials: Challenges
Tara

...and Solutions
Cindy and Valdo

Outline

• Starting Out
• Developing the ePRO solution
• Launching the ePRO
• ePRO in the field
• Conclusions
Starting out...

- Critical to understand exactly what is required - RFPs
  - ePRO should be described in the clinical trial protocol
    - Which endpoints, mode, frequency of collection etc
  - Clearly outline detailed requirements as early as possible:
    - Documentation needed (e.g. detailed screen/call flow for ALL patient facing elements including error messages; site and subject manuals)
    - In built programming (e.g. time windows, alerts and alarms, languages needed)
    - Actual measures (e.g. Number of screens, questions)
  - All too often the timelines and budget spiral out of control because of added elements that were not foreseen
    - E.g. modem’s for each site because of lack of wireless connection
  - Task Ownership Matrix helps identify what is necessary and likely time to complete
  - Understand population of the study: elderly, children, adolescents, cognitively impaired
- Review of past experiences for similar studies
  - In country issues for technology, IRB requirements etc

Starting out...

- Internal Alignment
  - ePRO “Champion” within pharmaceutical or biotech company to help facilitate buy-in and rationale for ePRO rather than paper
- Protocol Details
  - Use of ePRO specified in the protocol
  - ePRO provider needs to understand the protocol
- RFP/Proposal
  - Include as much information as possible for ePRO provider related to countries, languages, # of sites/subjects, and data management plan
  - If using peripheral devices, like glucometers, peak flow meters and barcode scanning have actual samples available
- Plan early for ePRO – Cannot be an afterthought
Developing the ePRO

- TOM – who does what, when
- Device Testing
  - UAT is a given by all
  - Feasibility and Usability are not normally included by the e-vendor
    - Essential that at least feasibility is completed e.g. download connection is available, toll free numbers work
- Site Training
  - Usually conducted at IM – ensure they sign into this specifically
  - If site is not live within 6-weeks further training completed
  - On-going training throughout the course of the study – site personnel change
  - Training materials essential for both site and patient
    - Remember – need to train the sites to train the patients, not just to use the systems themselves
- Patient Training
  - Layman terms with good graphics, translated, quick reference guide for technical terms (e.g. Modem, USB Port)
  - Includes how to use the devices/technology AND how to complete the PRO appropriately
- Helpdesk – 24/7 in local language!
- Data management early involvement to inform correct structure of database for reporting

Developing and Configuring ePRO...

- Kick Off Meeting (KOM) - Critical
  - Face to Face meeting
  - Internal and ePRO provider- all areas including Data Management, Health Outcomes, (if using peripheral devices) Vendor, and ePRO “Champion”
    - Communicate Roles and Responsibilities for Sponsor and ePRO Team
    - Updates on Priority of Countries and Languages
- Setup for Training for Patients, Sites and Monitors
  - Discuss Options for Training
  - How will you know who has been training?
- Discuss Project Lifecycle and Plan
  - Who What When Where
  - Screen Shot Documents for Submissions
  - UAT Activity – who is responsible for what
Developing and Configuring ePRO....

Project Lifecycle

Launching the ePRO

• Ensure sites are well trained and training materials are ready
  – Patients in local language
  – Sites in local language as well – PI not necessarily doing the enrolment
Nothing can be as emphasized as the need for an adequate Training

- One size does not fit all
  - The IM should – whenever possible – stay the cornerstone of the training
  - e-Learning
  - Training & Practice device
  - 24/7 support
  - Documentation, whenever possible in local language

Launching the ePRO

- Devices have arrived at the sites – customs issues in some countries
Knowledge of worldwide Logistics is a major component of ePRO

- Anticipating “Risk-Countries” and Keeping updated with ever-changing regulations is key
- Zero-Risk does not exist due to the very nature of the way Customs operate

<table>
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<th>Prep Time</th>
<th>Transit Time</th>
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<td>60%</td>
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Launching the ePRO

- Create FAQ in webportal to address common questions from sites – can be updated throughout study
- Monthly site newsletter can also address common ePRO issues/questions as they arise during the study

Investigators Portals are becoming more and more frequent

- FAQ to address common questions from sites is one of the main features as well as frequent newsletters
ePRO in the field

• Compliance reporting is a positive because it allows early intervention with non-compliance – site/patient issues

Compliance Reporting is key!

• E-mail alerts
• Graphical and global representation for all the sites in all the countries
• Big brother report: Who is looking at their data and who is not
Compliance Reporting is key!

Overall Compliance By Country

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<tr>
<th>World Region Name</th>
<th>Total Countries</th>
<th>Total Sites</th>
<th>Total Subjects</th>
<th>Total Diaries Expected</th>
<th>Total Diaries Received</th>
<th>Total Diaries Pending</th>
<th>Region Compliance</th>
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<td>6</td>
<td>59</td>
<td>761</td>
<td>360,031</td>
<td>307,235</td>
<td>17,086</td>
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<td>254</td>
<td>2,205</td>
<td>1,028,980</td>
<td>961,313</td>
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<td>3</td>
<td>21</td>
<td>5,212</td>
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<td>49,243</td>
<td>44,203</td>
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<td>43</td>
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<td>155,145</td>
<td>17,010</td>
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<td>4,440</td>
<td>84.85%</td>
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ePRO in the field

- Helpdesk, monitoring of types of problems logged. Allows early intervention to rectify common issues.

Monitoring of logged issues

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<th>Case ID</th>
<th>Created Date</th>
<th>Created Time</th>
<th>Case Number</th>
<th>Case Name</th>
<th>Status</th>
<th>Category</th>
<th>Type</th>
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<th>Group</th>
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<td>HD0000000154738</td>
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<td>23 Jan 2012</td>
<td>12345</td>
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<td>SitePad Tablet Transmission Errors</td>
<td>Initialization Error</td>
<td>Problem</td>
<td>Tier 3: Product</td>
<td>SitePad is not accepting static IP address. Site type in all information is IP address. Prim and Sec DNS, subnet and gateway. Then they fall finish. When they go back into the network menu, the menu is blank.</td>
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<td>14 Apr 2012</td>
<td>12346</td>
<td>B Pitt</td>
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<td>SitePad Tablet Transmission Errors</td>
<td>Initialization Error</td>
<td>Problem</td>
<td>Tier 3: Product</td>
<td>SitePad is not accepting static IP address. Site type in all information is IP address. Prim and Sec DNS, subnet and gateway. Then they fall finish. When they go back into the network menu, the menu is blank.</td>
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<td>12347</td>
<td>A Jolie</td>
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<td>Problem</td>
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<td>SitePad is not accepting static IP address. Site type in all information is IP address. Prim and Sec DNS, subnet and gateway. Then they fall finish. When they go back into the network menu, the menu is blank.</td>
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<td>Client Services Training Task</td>
<td>eDCF</td>
<td>Request</td>
<td>Study Support Center</td>
<td>SC from site 12350 wanted to know how an eDCF was to be approved in StudyWorks.</td>
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<td>12349</td>
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<td>SC from site 12350 wanted to know how an eDCF was to be approved in StudyWorks.</td>
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</table>
ePRO in the field

- Site wants to change ePRO data entry – what should the policy be?

Changing Data?

- There should be an agreement from start about which changes can be accepted
- Usually patient entries cannot be changed
- Exceptions are e.g. visit dates, patient initials or other demographics
- Under control of the investigator at all times
ePRO in the field

- Logpads can fail
  - Do not provide a paper copy?
  - Process for shipping out new devices quickly
  - Sometimes though not feasible to have patients come back
    - Better to have paper than not?
  - Glitches in the system will be found
    - Process for sorting these out and rolling out a new version of the program
- Paper version used by sites
  - Now have to deal with this data
  - Databasing
  - Reconciliation of both paper and electronic diary information at same visit

Paper Back-ups

- An idea that makes sense at first
- But “a pillow of laziness”
- It is in my opinion that “no data” is better than paper data
- Incorporating paper data in a study raises the concern of “mixed modes”
- If paper diaries are forbidden, it is important to explain “why?” right from the start
Conclusions

• If nothing else, remember ......
  – At the outset be as specific as possible about the requirements for the ePRO solution
  – Training of both site and staff is absolutely essential
  – Feasibility is important and ideally usability
  – Contingency planning for problems with the device in the field
    • Replacement devices vs paper