Deploying ePRO Instruments in Clinical Trials: Challenges and Solutions

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May 22, 2013

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

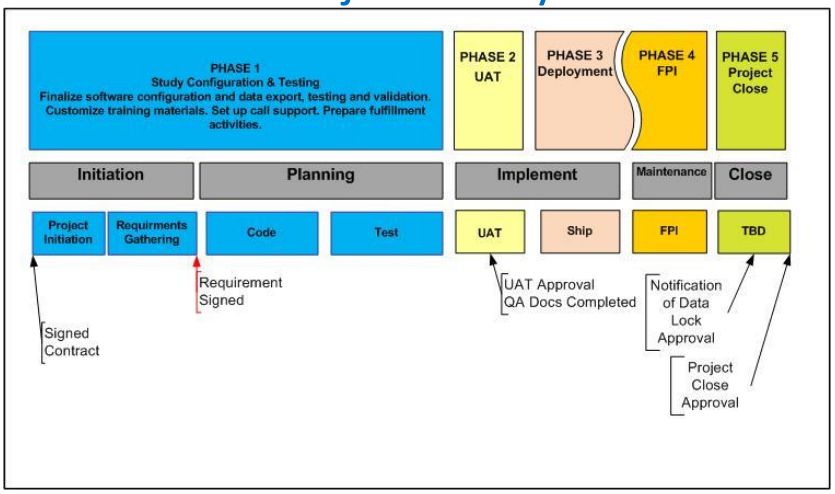
- TOM – who does what ,when
- Device Testing
  - UAT is a given by all
  - Feasibility and Usability are not normally included by the e-vendor
    - Essential that at least Feasibility is completed e.g. download connection is available, toll free numbers work
- Site Training
  - Usually conducted at 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

Knowledge of worldwide Logistics is a major component of ePRO

Country	Rating	Prep Time	Transit Time	Invoice Pre-Approval	Incoterms	VAT	Invoice Value
Bulgaria	2	1d	1w	N	DDU	20.0%	60%
Canada	1	1d	2d	N	DDP	5.0%	60%
Chile	2	1w	1w	Y	DDP	19.0%	60%
Czech Republic	1	1d	4d	N	DDP	20.0%	60%
Estonia	2	1d	5d	N	DDP	20.0%	60%
Germany	1	1d	3d	N	DDP	19.0%	60%
Hungary	1	1d	1.5w	N	DDP	27.0%	60%
Japan	1	2d	1w	N	DDP	5.0%	60%
Korea, South	1	1d	1w	Y	DDP	10.0%	60%
Mexico	2	4d	6d	Y	DDP	16.0%	60%
Peru	2	1.5m	3w	Y	FOB	18.0%	60%
Poland	1	1d	1.5w	N	DDP	23.0%	60%
Romania	1	1d	1w	N	DDP	24.0%	60%
Russia	3	2m	1m	Y	DDU	18.0%	100%
South Africa	2	1w	4d	Y	DDP	14.0%	60%
Spain	1	1d	3d	N	DDP	18.0%	60%
Ukraine	3	2m	1m	Y	DDU	20.0%	60%

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

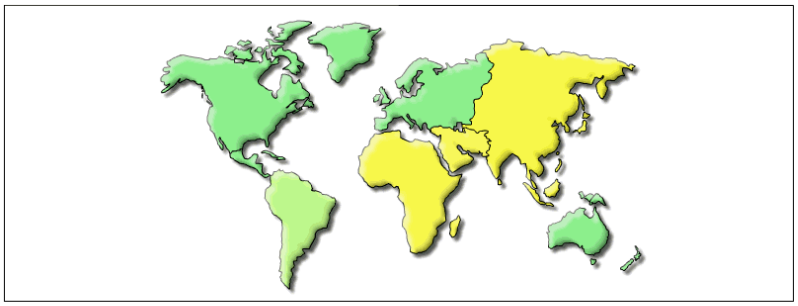
- Compliance reporting is a positive because it allows early intervention with non-compliance – site/patient issues

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

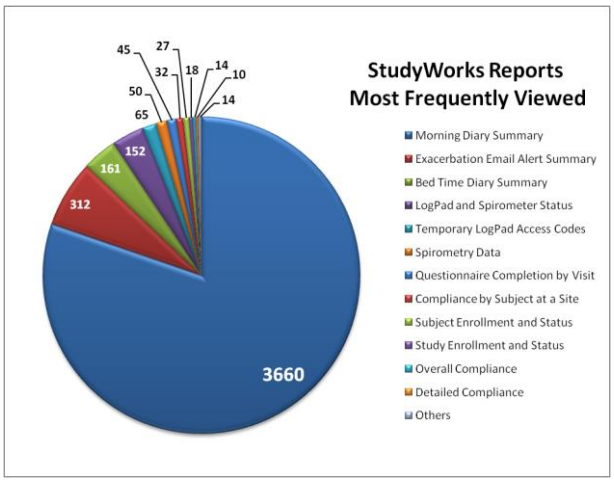
Overall Compliance By Country

Client: PHT Corporation
Study: Demo Study
Display Time: (08 Jan 2011 09:48:15 UTC) (08 Jan 2011 04:48:15 Local)



World Region Name	Total Countries	Total Sites	Total Subjects	Total Diaries Expected	Total Diaries Received	Total Diaries Pending	Region Compliance
Asia	6	59	761	369,931	307,725	17,980	83.18%
Europe	22	254	2,206	1,036,360	961,363	39,049	92.76%
Africa	1	3	21	5,212	4,386	5	84.15%
North America	2	24	140	49,343	44,833	3,744	90.86%
South America	5	43	483	193,145	171,010	8,607	88.54%
Central America	1	3	74	26,423	24,057	228	91.05%
Oceania	2	6	33	13,351	12,306	283	92.17%
Middle East	1	5	107	57,341	48,365	4,540	84.35%

Compliance Reporting is key!



ePRO in the field

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

Monitoring of logged issues

Case ID	Create Date	Country	Site Number	Site Name	Status	Category	Type	Item	Case_Type	Group	Description
HD0000000199044	08-Apr-13	GB	12345	B Obama	Assigned	Data Summary	General Issue	Printing Problem/Question	Request	Study Support Center	Site 12345 - Subjec 001359 - SC called and informed that she is not able to view the prescription modul
HD0000000200077	22-Apr-13				Assigned	StudyWorks	Self Serve Admin	e-Mail Notification	Request	Study Support Center	Pharma Co ABC 1234 - SPM does not receive the account access requests
HD0000000200761	30-Apr-13	GB	12346	B Pitt	Assigned	SitePad Tablet	Transmission Errors	Synchronization Failure	Problem	Study Support Center	sync failure at site 12346
HD0000000200911	02-May-13	GB	12347	A Jolie	Assigned	StudyWorks	Data	Data accuracy	Request	Client Services	Site reported that Dr. A. Jolie's second displayed address in StudyWorks is wrong and has to be removed. This address is visible under
HD0000000200539	27-Apr-13				Closed	StudyWorks	Self Serve Admin	Access Management	Request	Study Support Center	SC Kate Middleton is requesting the protocol number for StudyWorks access.
HD0000000200884	02-May-13	GB	12348	P Simon	Closed	Client Services Task	Training	eDCF	Question		SC asks for more information on an online DCF approval email notification.
HD0000000200881	02-May-13	GB	12349	A Garfunkel	Closed	Client Services Task	Training	eDCF	Request		Site 12349 - SC called and requested how to approve Online DCF
HD0000000200901	02-May-13	GB	12350	J Lennon	Closed	Client Services Task	Training	eDCF	Request	Study Support Center	SC for site 12350 wanted to know how an eDCF was to be approved in StudyWorks
HD0000000200903	02-May-13	GB	12351	P Mc Cartney	Closed	Client Services Task	Training	eDCF	Request	Study Support Center	SC from site 12351 wanted to know how an eDCF was to be approved in StudyWorks
HD0000000154738	23-Jan-12				Closed	SitePad Tablet	Transmission Errors	Initialization Error	Problem	Tier 3 - Product	SitePad is not accepting static IP address. Site types in all information into IP address, Prim and Sec DNS, subnet, and gateway. Then they hit finish. When they go back into the Network menu, the menu is blank.

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 requirement s 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