

C-Path Collaborative Efforts to Address Specific ePRO Data Collection Challenges

Linda Deal, Shire

*FIFTH ANNUAL
PATIENT-REPORTED OUTCOME (PRO) CONSORTIUM WORKSHOP*

April 29 - 30, 2014 ■ Silver Spring, MD

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Objectives of This Session



- To share the collaborative writing efforts of
 - PRO Consortium’s ePRO Subcommittee
 - ePRO Consortium
- To present collaboration team’s best practices and recommendations for
 - allowing subjects to opt-out of responding to a question
 - i.e. providing patients the option to not respond to a question rather than enforcing completion
 - challenges to source data collection and documentation
- To discuss concrete examples from the perspective of
 - Sponsors i.e. Pharma and Biotech companies
 - Technology providers
 - Regulators
- To share dissemination status beyond this workshop today

Session Participants



Moderator

- *Linda Deal, MS* – Head of Patient-Reported Outcomes, Gastrointestinal Business Unit Lead, Shire

Presenters and Panelists:

- *Paul O'Donohoe, BSc* – Director of Health Outcomes, CRF Health
- *Sarah Fleming, MPH* – Manager, Patient Reported Outcomes, Janssen Global Services

Panelists:

- *Alexandra Barsdorf, PhD* – Associate Director, PRO Center, Outcomes & Evidence, Global Health and Value, Pfizer, Inc.
- *Ari Gnanasakthy, MSc, MBA* – Co-Director, PRO Consortium and Head, Patient Reported Outcomes, Novartis Pharmaceuticals Corporation
- *Jonathan Helfgott, MS* – Associate Director for Risk Science (Acting), Office of Scientific Investigations, CDER, FDA
- *Cindy Howry, MS* – Vice President, eCOA/ePRO Product Management, Y-Prime

Opt-out

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Paul O'Donohoe
CRF Health

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- Goal of group
- Background
- Issues to consider
- Recommendations
- Key questions

- The goal of this group was to:
 - Identify the possible risks of requiring subjects to complete all ePRO items
 - Identify the various different approaches that could be taken to requiring subjects to complete ePRO items
 - Offer considerations and recommendations around opt-out for study teams implementing ePRO
 - Document to be made available on C-PATH website in coming weeks

- Complete and accurate data – cornerstone of any trial
- Paper has recognized issues with missing or inaccurate data
- Electronic solutions are increasingly popular data capture tools
- This has provided study teams a powerful way to collect high-quality patient-reported outcome data

- These new tools have also brought new possibilities
- Key strength of ePRO is the ability to prevent subjects from progressing to the next item in an instrument until they have provided a response to the current item
- Seems to offer the chance of complete PRO data at the close of the study

- HOWEVER, what if a subject is confronted with:
 - Inapplicable questions they cannot answer
 - Questions about work for those who are unemployed
 - Sensitive questions they are unwilling to answer
 - Questions about sexual health
- Risks inaccurate or unreliable data
- Worst case scenario - subject may refuse to continue

- Unlike paper, there is no way to know if a subject has provided an answer just to move on with the questionnaire
- Suddenly our lovely complete dataset is looking a bit too good to be true...

3 possible approaches

1. Requiring subjects to complete all items in all the instruments in the study;
2. Requiring subjects to complete all items used as key endpoints in the study, and allowing the subject to opt-out of responding to some, or all, other items (including sensitive items);
3. Allowing subjects to opt-out of responding to all items in the study.

- Each of the three options have their own pros and cons
- Careful consideration should be given to the quality of questionnaires being used in a study
- Items or questionnaires supporting primary or secondary endpoints should be identified
- Items that may potentially be “unanswerable” (e.g. questions about work for subjects who are unemployed) or “sensitive” (e.g. questions relating to sexual health) should be identified

- Weighing up the importance of data in relation to its support of endpoints, versus the potential difficulty for subjects to answer questions, will help identify the most appropriate approach
- Regardless of the approach taken, if some form of opt-out is allowed the electronic system should be programmed such that subjects actively have to confirm their intent to skip an item
- The approach taken will help in the development of an appropriate statistical plan

- Are there challenges implementing the 3 different approaches on an electronic platform?

- What are some limitations encountered with questionnaires that can impact compliance or missing data?
- What is the possible impact on a clinical trial of enforcing compliance?
- What is the perceived trade-off between complete but potentially inaccurate data, and incomplete data?

- What is the position on requiring subjects to respond to all questions, versus the potential of having missing data which the subject has explicitly chosen not to provide?
- What is the position about the ethical implications of requiring subjects to respond to all questions, or is that purely an issue for IRBs?

ePRO Data Collection Challenges and Prevention Strategies

Sarah Fleming, MPH
Janssen Global Services

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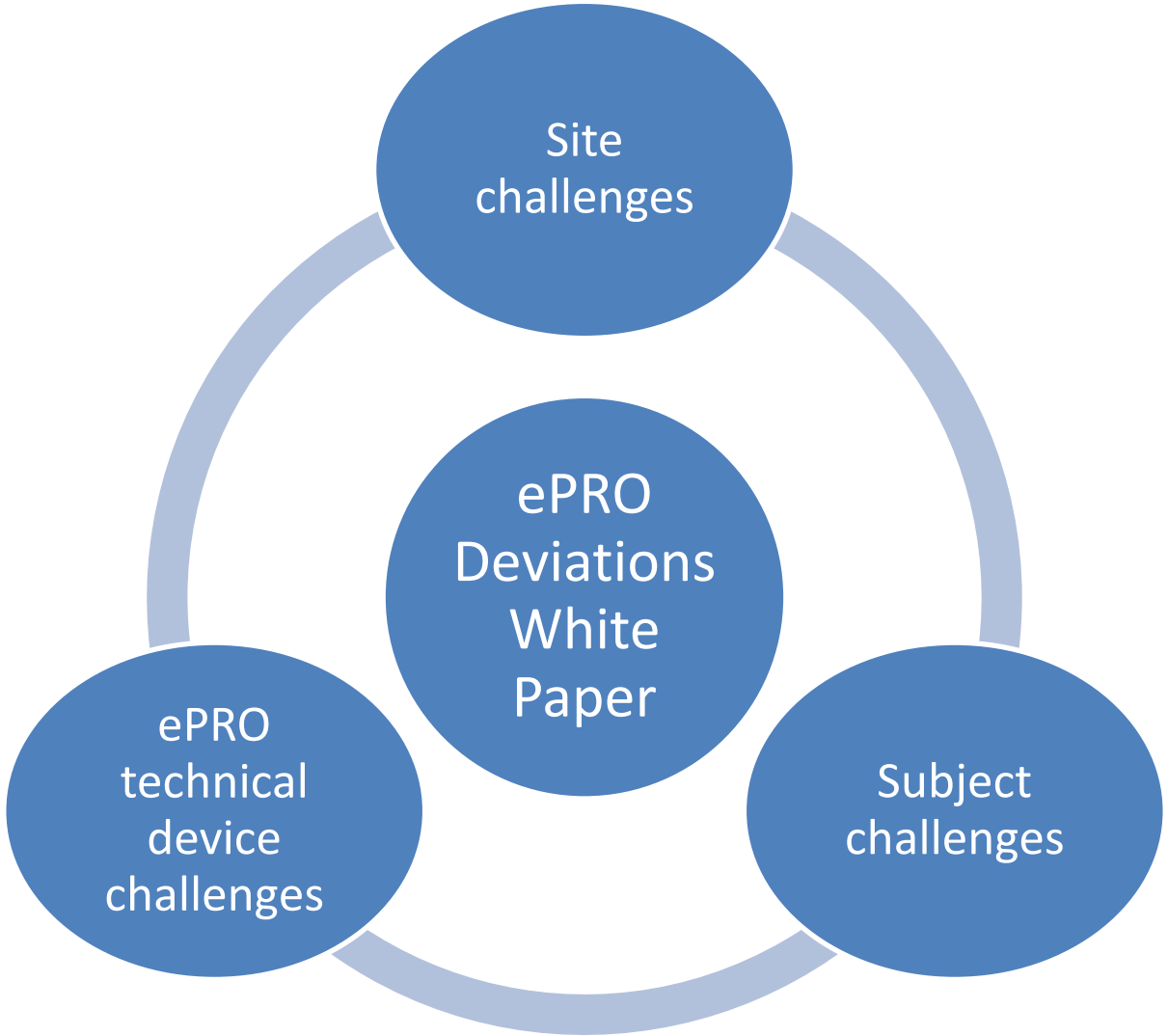
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- Background
- Issues that may come up that risk compromising source data collection
- Recommendations for how to handle these issues
- Considerations for using or allowing paper backups

- Electronic data capture is becoming the preferred method of data collection for all source data (FDA, 2013)
- New challenges with increased use of ePRO
- Topics include:
 - Study site and subject challenges that may lead to deviations from the ePRO data collection plan
 - Provides recommendations to prevent potential problems or corrective actions

Identified challenges to ePRO source data collection



Site Acceptance of and Compliance with ePRO Data Collection



- Clinical study protocol language
 - Eligibility criteria specify ePRO use
 - Data monitoring expectations
- Site staff and monitor training
 - Basic ePRO use
 - Data monitoring online
 - How to train subjects to use devices successfully
 - Procedures for troubleshooting

- Understand time requirements for ePRO completion
- Subjects should be aware of time commitment necessary to complete questionnaires
- Number of devices needed for site based on expected recruitment

Sites should be trained to:

- Check to make sure that devices are charged and functional prior to subject arrival
- Backup devices
- Reschedule subjects if a backup device is not available
- Call ePRO vendor helpdesk

Subject Acceptance of and Compliance with ePRO



- Informed Consent Form – ePRO language
- Device alerts/reminders to the patient
- Site and monitor training
 - Provide reports or email alerts to the sites and/or monitors to be alerted of
 - subject non-compliance, and/or
 - data transmission issues

Subject Comfort and Familiarity with ePRO Modalities



- Emphasize the importance of subject training
- Subject training in person at site
 - Quick reference guide given to all patients

- Site monitor and subject **training** are crucial to the success of ePRO within a clinical study
- **Preparation** and preventive strategies will increase the likelihood of successful data collection

- After implementing all best practice recommendations, deviations may happen
 - ePRO device failure due to either site issues or device issues resulting in
 - Missing data
 - Unauthorized versions of paper sources
 - Mixed modality
- How should these be handled?

Panel Discussion

Paper use in ePRO study



- Sponsor perspective
 - Experience where sites planned to collect paper PROs in an ePRO study
- Vendor perspective
 - Paper collected, responsibility to enter data into the database?
- Regulatory perspective
 - In these situations, what is appropriate from a regulatory perspective when handling these data points? Mixed modality data handling? Paper source entered electronically on the backend for long term data collection?

Discussion and/or Questions?

Session Participants



Moderator

- *Sue Vallow, RPh, MBA, MA* – Senior Director, Patient Reported Outcomes, GlaxoSmithKline

Presenters

- *Kathryn Engstrom* - Data Scientist – Auto Immune, Eli Lilly and Company
- *Jonathan Helfgott, MS* – Associate Director for Risk Science (Acting), Office of Scientific Investigations, CDER, FDA
- *Sue Vallow*

Panelists

- *Valdo Arnera, MD* – General Manager, PHT Corporation
- *Linda Deal, MS* – Head of Patient-Reported Outcomes, Gastrointestinal Business Unit Lead, Shire
- *Jason Eger* – Vice-President, Project Management, ERT
- *Sarah Fleming, MPH* – Manager, Patient Reported Outcomes, Janssen Global Services