Barriers to Adoption of Electronic Collection of COA-based Endpoint Data in Clinical Trials

Eighth Annual
Patient-Reported Outcome Consortium Workshop

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Disclaimer

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Session Objectives

- Provide updates on two ongoing ePRO-related studies (BYOD vs. Provisioned Device and EQ-5D-5L Measurement Equivalence)
- Share aggregated data from a questionnaire provided to member firms of the PRO Consortium to identify barriers to adoption of electronic collection of COA-based endpoint data in clinical trials
- Present responses and discuss potential solutions to these barriers from the perspective of the ePRO Consortium member firms
- Present an example of a sponsor's successful approach to promoting and supporting eCOA data collection in clinical trials
- Provide a perspective on eCOA from a sponsor's clinical operations team

Session Outline

- Introduction
- Bring-Your-Own-Device (BYOD) and EQ-5D-5L Update
- Survey on Adoption of Electronic Collection of Clinical Outcome Assessment Data
- Barriers to Adoption of Electronic Collection of COA-based Endpoint Data in Clinical Trials: ePRO Consortium's Response
- (ex)Sponsor Perspective: What Worked for eCOA Uptake
- Adoption of Electronic COA from an operational perspective
- Question and Answer

Session Participants

Moderator

- *David S. Reasner, PhD* – Vice President, Data Science and Head, Study Endpoints, Ironwood Pharmaceuticals

Presenters

- *Bill Byrom, PhD* – Senior Director of Product Innovation, ICON Clinical Research and ePRO Consortium Industry Vice Director
- *Alexandra I. Barsdorf, PhD* – Director, Rare Disease, Patient & Health Impact, Pfizer, Inc.
- *Kelly McQuarrie, BSN* – Director, PRO Team, Janssen Pharmaceuticals
- *Sue Vallow, RPH, MBA, MA* – Vice President, Patient eSolutions, MedAvante, Inc.
- *Marieke Manders, MSc* – GCDO Trial Leader, Immunology – Janssen Research & Development

Panelist

- *Serge Bodart, MS* – eCOA Subject Matter Expert, Biomedical Systems

Bring-Your-Own-Device (BYOD) and EQ-5D-5L Project Updates

Bill Byrom, PhD, Senior Director of Product Innovation, ICON Clinical Research

BYOD Project Update

- In December 2016, the PRO Consortium and ePRO Consortium launched a measurement project titled *Comparability of Provisioned Device vs Bring-Your-Own-Device in Subjects with COPD*.
- The objective of the study is to test the equivalence of PRO data collected on a provisioned device versus Bring Your Own Device.
- C-Path has launched a limited duration project group in which representatives from the ePRO Consortium, PRO Consortium, and Clinical Outcomes Solutions (selected consulting group) participate.
- IRB approval was received on February 28, 2017; user acceptance testing (UAT) is anticipated to begin in Q2 2017.

EQ-5D-5L Project Update

- Funded in part by a EuroQol Research Foundation grant, this ePRO Consortium study's objective is to provide empirical evidence to support the measurement equivalence of EQ-5D-5L data collected on various data collection modes (i.e., paper, handheld, tablet, interactive voice response [IVR] system, and Web).
- Due to challenges in the deployment of the IVR system, data using this mode was not available. Additional funding was allocated by the ePRO Consortium to ensure IVR data are collected.
- User acceptance testing (UAT) was completed in April 2017; the target date to complete data collection is May 2017.

Survey on Adoption of Electronic Collection of Clinical Outcome Assessment Data

Alexandra I. Barsdorf, PhD, Director, Rare Disease, Patient & Health Impact, Pfizer Inc.
Disclosure: Alexandra I. Barsdorf is an employee of Pfizer, Inc. All material presented reflects the opinion of the presenter and not Pfizer, Inc.,

Kelly McQuarrie, BSN, Director, Patient Reported Outcomes Team, Janssen Global Services, LLC.
Disclosure: Kelly McQuarrie is an employee of Janssen Global Services, LLC. All material presented reflects the opinion of the presenter and not Janssen Global Services, LLC., its subsidiaries, or its shareholders.

With acknowledgement of the ePRO Subcommittee

eCOA Adoption Survey

- Rationale for Conducting Survey
- Questionnaire Development and Survey Method
- Questionnaire Content
- Participant Background
- Survey Limitations
- Barriers of eCOA Adoption

Rationale for Conducting Survey

To understand the perceptions of and factors considered by various functional roles supporting clinical trials and other studies when choosing a clinical outcome assessment (COA) data collection mode

- *Characterize and understand preference for paper vs. electronic data collection*
- *Identify barriers to adoption of electronic data collection for COAs*

Questionnaire Development and Survey Method

- Developed by ePRO Subcommittee
- Piloted among several member firm colleagues
- Revised items based on early feedback
- Introductory Email with survey link distributed to C-Path PRO Consortium Committee Representatives from Member Firms (N=26)
  - *Representatives distributed internally within each member firm*
- Questionnaire conducted via Survey Monkey
  - *Anonymous to respondent and company affiliation*
- Data evaluation and interpretation

Questionnaire Content

- Introduction and definitions
- 12 items
- Questions 1-6
  - *Items to elicit preference for mode of data collection and rationale for selection*
  - *Items to identify real and perceived barriers and reasons for adoption/non-adoption of* eCOA
- Questions 7-12
  - *Characterize participant background*

Questionnaire Content

- **Preferred mode of collection** of COA data in general (paper or electronic) and free text to describe why.
- Top 5 Factors:
  - ***Most important when determining the COA data collection mode*** to use in a study
  - ***Most critical for successful eCOA implementation***
  - ***Most critical to you when choosing an eCOA company***
- Indicate to what extent **each of the following considerations is important to you when selecting a mode of COA** data collection ("not important" to "extremely important")
- ALL that apply:
  - **Reason(s) preventing you from using eCOA technology** in studies.
- Free text:
  - Any **additional comments regarding a challenging experience** you may have had or that you heard of related to eCOA implementation

Summary of Participant Background

Current Functional Area (n=116)

- clinical/medical scientists (27.6%)
- health outcomes/outcomes research (19%)
- clinical trial operations (14.7%)
- *Limited response from regulatory, programming, procurement and study monitors*

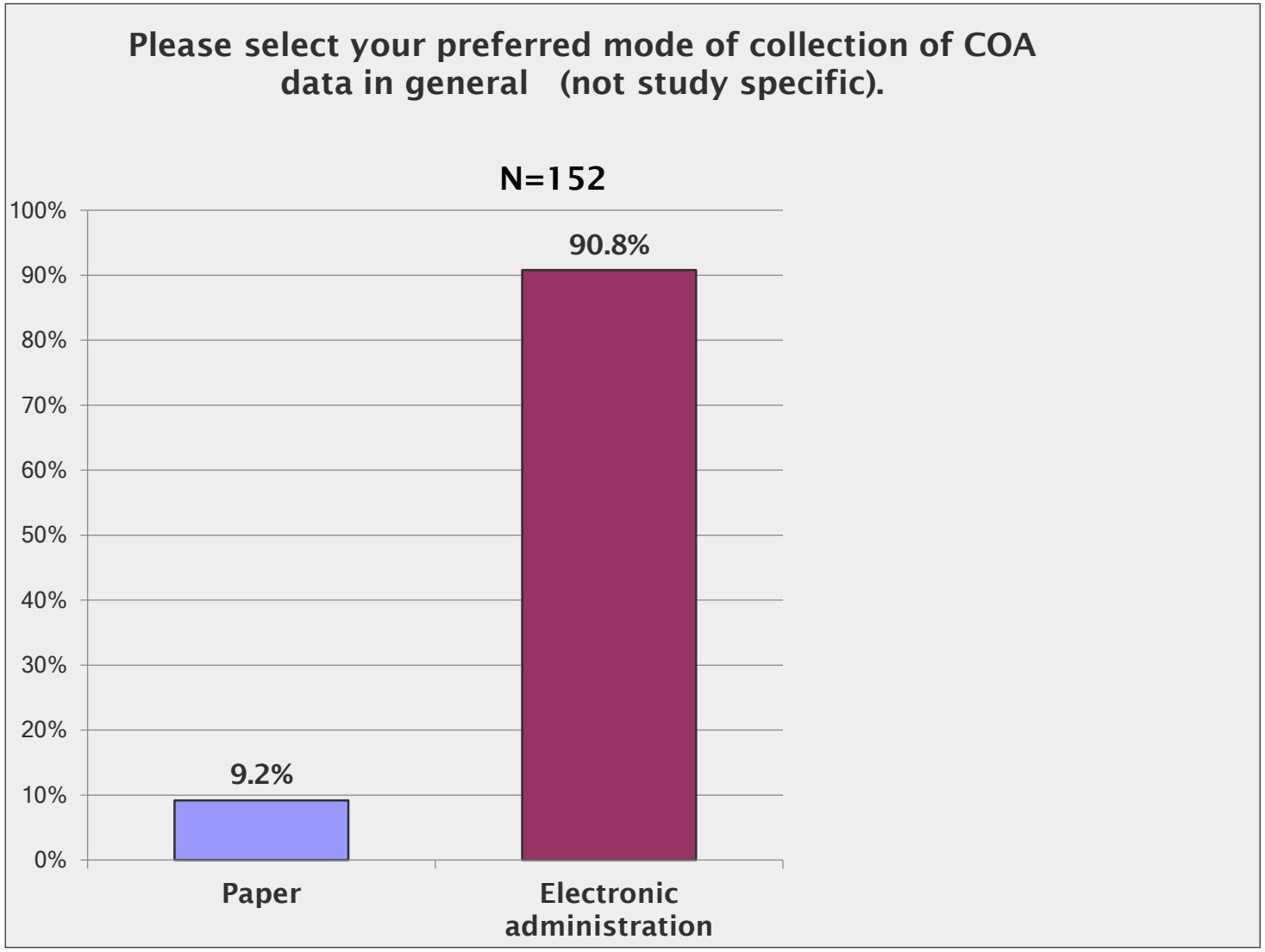
Therapeutic Experience (n=115) - allowed for multiple responses

- *Well represented across different therapeutic areas*
- oncology (48.7%)
- cardiovascular/metabolism (47.0%)
- neuroscience (42.6%)
- rheumatology (38.3%)
- rare disease (32.2%)

Generally an experienced group of respondents, Overall (n=118)

- > 15 years of experience in the industry = 52.5%
- >15 studies in past 10 years = 56.4%

Preferred Mode of Collection of of COA Data



Limitations of Survey

- Not a representative sample
  - Survey site link was distributed only to PRO Consortium member firms
  - Majority of respondents had > 15 years of experience in the pharmaceutical industry and >15 studies in the past 10 years
  - Likely that people who have an interest and experience in COA were more likely to respond

Barriers to eCOA Adoption - Industry

Review of Barriers to be addressed in subsequent presentations

- Necessary lead time/time preparing for eCOA for a study
- Cost and funding needed to implement eCOA
- Regulatory concerns
- Site receptivity/burden and site and patient training and re-training plan
- Patient receptivity or burden and consideration of patient population
- Data integrity, device failure, no paper backup

To be addressed in this presentation

- Lack of internal resourcing and study team familiarity/experience (e.g., effective UAT)

Barriers to eCOA Adoption
Lead time

- 62.4% (64% of those who prefer paper) responded that ***"Adequate lead time for solution design and sponsor"*** is one of the top 5 most critical factors for successful eCOA implementation
- 41.9% (43% of those who prefer paper) responded that ***"Time preparing eCOA for a study"*** is preventing them from using eCOA
- 40. 6% (43% of those who prefer paper) responded that "***Necessary Lead Time"*** is one of the top 5 most important considerations when selecting mode
  - *"long set-up timelines"*
  - *"timing for set-up is longer than other data vendors"*

Barriers to eCOA Adoption
Cost or Funding for Implementation

- 44.5% (57% of those who prefer paper) responded that **"cost (perceived and/or actual)"** is one of the top 5 most important considerations when selecting mode
- 40.2% (57% of those who prefer paper) responded that **"funding needed to implement eCOA"** is preventing them from using eCOA

  - *"Cost is an important component for the initial study but once you have it setup, there are cost saving with subsequent studies"*
  - *"Cost and lead time to program or validate new instruments"*

Barriers to eCOA Adoption
Regulatory Concerns

- 16.2% (14% of those who prefer paper) responded that **"Regulatory concerns"** are preventing the respondent from using eCOA

  - *"Regulatory hurdles/delays implementing study start up timelines have been my reason not to choose eCOA."*
  - *"Regulatory acceptance is not always guaranteed especially if there have been found to be any data errors."*
  - *"Unsure of potential regulatory challenges"*

Barriers to eCOA Adoption
Site-Related Issues

- 80% (71% of those who prefer paper) responded that **"Site and Patient Training and Re-Training Plan"** is one of the top 5 factors most critical for successful eCOA implementation
- 45.6% (28% of those who prefer paper) responded that **"Site feasibility (including familiarity)"** is one of the top 5 factors most critical for successful eCOA implementation
- 28% (21% of those who prefer paper) responded that **"Site Receptivity/Burden"** is one of the top 5 most important considerations when selecting mode

  - *"Efficient and knowledgeable help desk as well as repeated site training and support is key to success"*
  - *"Challenges in site training and establishing comfort with device….."*

Barriers to eCOA Adoption
Concerns about the Patients

- 46.1% (57% of those who prefer paper) responded that **"Patient Receptivity or Burden"** is one of the top 5 most important considerations when selecting mode
- 29.7% (21% of those who prefer paper) responded that **"Consideration of Patient Population"** is one of the top 5 most important considerations when selecting mode

  - *"Working in an elderly population made paper much easier as they may not be able to interact with our limited approved technology."*

Barriers to eCOA Adoption
Concerns of Data Integrity and Quality

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Security with Paper

- *"No forgetting to charge the battery, no forgetting the password, no issues with wrong time/date stamp, faster, cheaper."*
- *"Never had missing data issues using paper in my trials with many PRO instruments over 2 years of clinical trial time frame."*
- *"No chance of malfunction of the e-devices"*

Device Failure

- *"hardware failure leading to missing data"*
- *"device issues, issues with quality data capture and cleaning "*
- *"Even with eCOA, there is still the chance that captured data will be incorrect, and that assumptions made when designing a tool are not accurate"*
- *"Extremely poor experience with device failures"*

Barriers to eCOA Adoption
Need for a back-up

- 19.5% (28% of those who prefer paper) of the respondents selected **"providing a non-paper back up solution in the event of device failure"** as one of 5 factors that are most critical when choosing an eCOA company.

  - *"Need for paper back-up"*
  - *"Acceptable back-up solutions are needed based on program specific objectives."*

Barriers to eCOA Adoption
Poor Experience

- 15.4% (28% of those who prefer paper) responded that hearing of **"Challenges from Others/Previous Poor Experience**" are preventing the respondent from using eCOA

- 14.5% (14% of those who prefer paper) responded that **"Previous Poor Experience"** are preventing the respondent from using eCOA

  - *"1 negative experience (perceived or real) can lead to internal communication which scares others from choosing ePRO"*
  - *"some teams have a negative perception of set up challenges, particularly if they have not done it before or have had a bad experience."*

Barriers to eCOA Adoption
Internal Resourcing and Experience

- 18.8% (28% of those who prefer paper) responded that **"Lack of Internal Resourcing"** are preventing the respondent from using eCOA

  Dedicated group of *internal PRO/COA scientific subject matter experts*

  - Yes = 72.4%

  Dedicated group *of internal technology experts* to support the implementation of eCOA

  - Yes = 52.5%

- 49.6% (57% of those who prefer paper) responded that **"Study Team Familiarity/Experience"** is one of the top 5 most critical factors for successful eCOA implementation

Experiences to Help Address this Barrier

- More training and hands on experience; with a recognition that User Acceptance testing (UAT) provides this opportunity to the internal team
- Greater reliance on vendor expertise to help companies ensure thorough and efficient UAT
- Educating teams to help them understand the true value of the investment of time, cost and resources
- Conducting lessons learned for internal process improvements
- Sharing of best practices to increase confidence across therapeutic areas
- Ensuring clear responsibilities across the interdisciplinary team

Barriers to Adoption of Electronic Collection of COA-based Endpoint Data in Clinical Trials: ePRO Consortium Response

Bill Byrom, PhD, Senior Director of Product Innovation, ICON Clinical Research

Perceived Barriers to eCOA Implementation

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Perceived Barriers

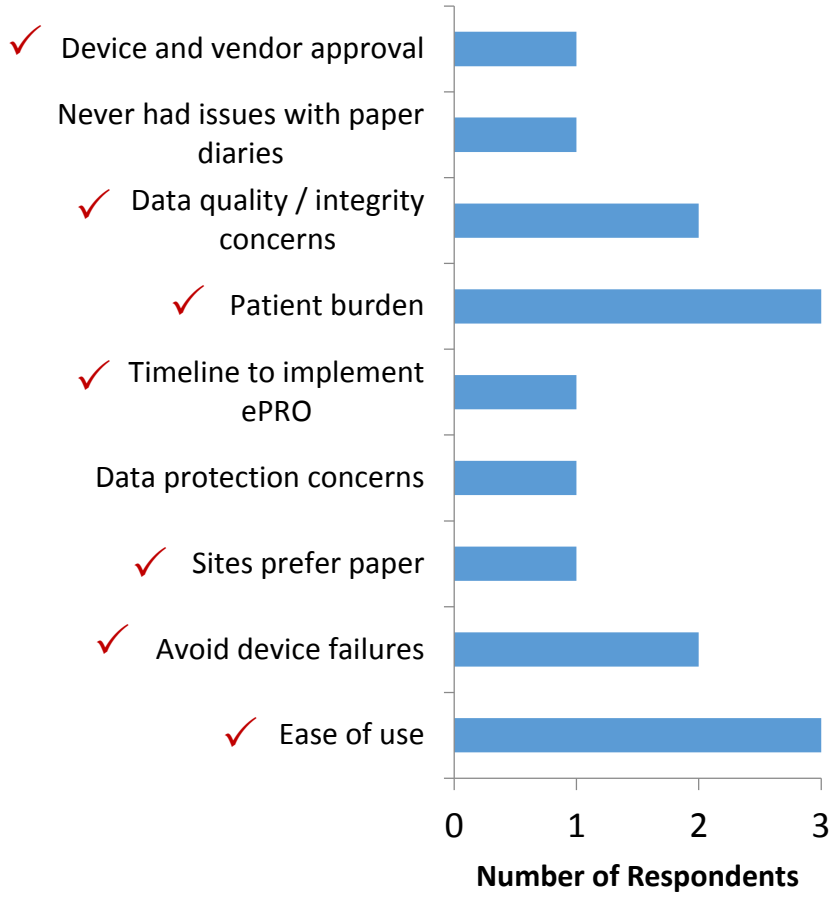
- Lead time: how to plan for eCOA implementation
- Cost and funding needed to implement eCOA
- Regulatory concerns
- Helpdesk support
- eCOA vendor project management
- User Acceptance Testing (UAT)
- Site and patient training/re-training
- Site and patient receptivity/burden
- Data quality / integrity
- Device failure

14/152

9%

of respondents prefer paper for COA data collection

Reasons for preferring paper

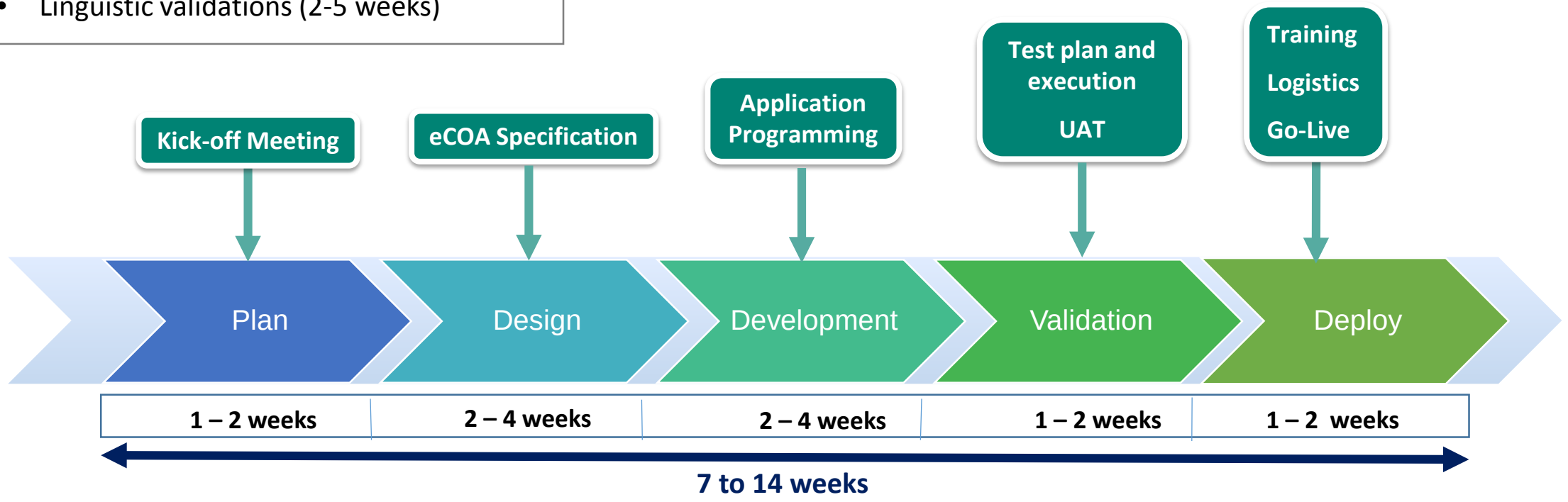


Perceived Barrier: Lead Time for eCOA Implementation

Instrument Management (8 – 12 weeks)

- Licensing
- Instrument migration measurement equivalence study (cognitive interview or equivalence study) (8-12 weeks)
- Linguistic validations (2-5 weeks)

- ePRO implementation timelines are in line with other eClinical systems
- Early consideration is recommended to ensure author licensing and migration requirements can be considered and planned where needed
- It is important to ensure adequate time is provided for the implementation



This timeline is an estimate based on ePRO Consortium member experience and will vary from study to study

Perceived Barrier: Cost to Implement eCOA

Measuring the true cost of paper diaries

- Sponsors must consider the hidden costs of paper when comparing paper to eCOA
  - Paper diary design
  - Printing, shipping, and storage
  - Additional monitoring time by a clinical research associate
  - Physical collection of paper diaries
  - Database development
  - Double-data entry and validation or source data verification (if site data entry)
  - Query resolution process / data cleaning
  - Extended time for database lock
  - Storage and archiving for 15+ years
- Some of the staffing costs associated with using paper are likely to be absorbed internally by sponsors, whereas using eCOA is a very visible external cost

The cost of paper may be more than financial

- eCOA saves time, provides higher-quality data, evidenced assessment timeliness, better "true" compliance
- Cost of missing or invented data

Information in practice

Patient non-compliance with paper diaries

Arthur A Stone, Saul Shiffman, Joseph E Schwartz, Joan E Broderick, Michael R Hufford

Doctors often ask patients to recall recent health experiences, such as pain, fatigue, and quality of life.[1] Research has shown, however, that recall is unreliable and rife with inaccuracies and biases.[2] Recognition of recall's shortcomings has led to the use of diaries, which are intended to capture experiences close to the time of occurrence, thus limiting recall bias and producing more accurate data.[3]

The rationale for using diaries would be undermined if patients failed to complete diaries according to protocol. In this study we used a newly developed paper diary that could objectively record when patients made diary entries in order to compare patients' reported and actual compliance with diary keeping. For comparison, we also used an electronic diary designed to enhance compliance in order to assess what compliance rates might be achieved.

Methods and results

We recruited 80 adults with chronic pain (pain for ≥3 hours a day and rated ≥4 on a 10 point scale) and assigned 40 to keeping a paper diary and 40 to an electronic diary. On satisfying the eligibility criteria, each patient was assigned to the next training session for which he or she was available, regardless of which diary it was for. We conducted one training session for each diary each week, with each training session for the paper diary matched by time and day of the week with an electronic diary training session. Participants were paid $150 and gave their informed consent; patients given the paper diary were not told that compliance would be recorded electronically.

The paper diary comprised diary cards bound into a DayRunner Organizer binder. The cards contained 20 questions drawn from several common pain instruments and included fields to record time and date of completion. The diary binders were unobtrusively fitted with photosensors that detected light and recorded when the binder was opened and closed; these were extensively tested and validated. The electronic diary was a Palm computer with software for data collection in clinical trials and presented identical pain questions via a touch screen and recorded time and date of entries. This system (invivodata) incorporated several features to maximise compliance, including auditory prompts, and has demonstrated good compliance.[4]

Patients were instructed to complete daily entries at 10 am, 4 pm, and 8 pm within 15 minutes of the target times. With the electronic diary, entries could not be initiated outside the designated 30 minute windows. We considered paper diary entries to be compliant if they were made within the 30 minute windows. A more liberal secondary outcome allowed a 90 minute window around the target times. Reported compliance was based on the time and date that patients recorded on their paper diary cards. Actual compliance was based on the electronic record (from the record of diary binder openings for paper diaries). Paper diary entries were deemed compliant if the binder was opened or closed at any point during the target time window. We also assessed "hoarding" with the paper diary, defined as days when the diary binder was not opened but for which diary cards were completed.

After three days' familiarisation, the participants began 21 days of diary keeping with weekly feedback. Participants completed an average of 20.5 days, and the table shows compliance rates. With the paper diary, reported compliance was 90%, but actual compliance was 11% (20% with the wider 90 minute window). With the electronic diary, actual compliance was 94%. Hoarding was common with the paper diary: 32% of days contained no diary openings, yet reported compliance (30 minute window) for these days was 92%. Most of the 40 patients (75%) had at least one day of hoarding.

Compliance rates for 80 patients' record keeping in paper and electronic diaries

	Paper diary (n=40)	Electronic diary (n=40)
30 minute window		
Total No of episodes*	2445	2435
No of excluded episodes	126	7
Mean per cent compliance (95% CI)†		
Actual‡	11 (8 to 14)	94 (92 to 96)
Reported	90 (86 to 94)	
90 minute window		
Total No of episodes	2445	
No of excluded episodes	134	
Mean per cent compliance (95% CI)†		
Actual	20 (14 to 25)	
Reported	96 (92 to 98)	

*Participants using paper diaries should have completed 2445 diary entries within the designated time windows. Of these, 114 were eliminated because the diary was open for more than 45 minutes, and 12 were eliminated because laboratory visits overlapped with time windows. Participants using electronic diaries should have completed 2435 entries, but 7 overlapped with laboratory visits.
†Compliance statistics were calculated separately for each participant and then averaged.
‡Compliance was significantly higher in the electronic diary group (t(78)=29.97, P<0.0001).

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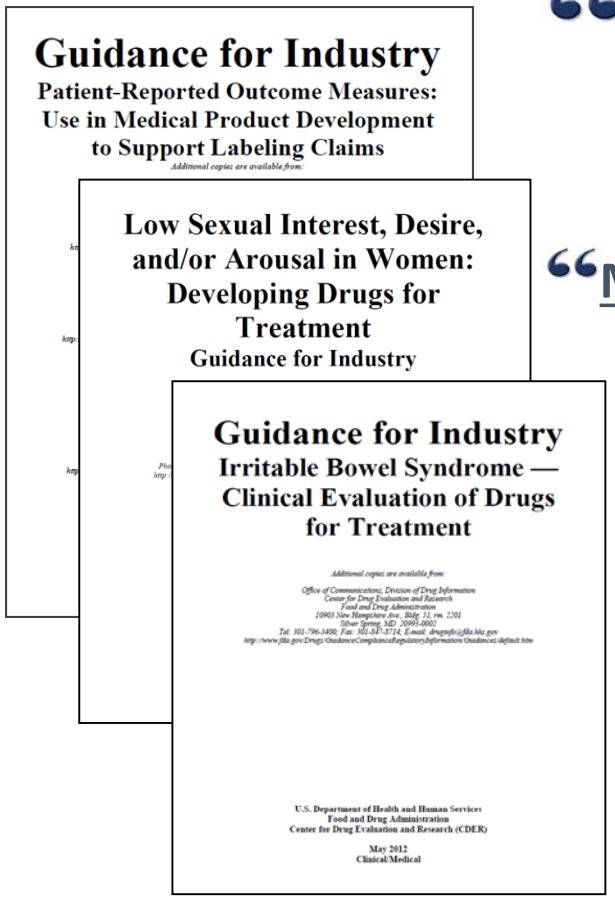
BMJ 2002;324:1193–4

BMJ VOLUME 324 · 18 MAY 2002 · bmj.com

1193

Stone AA, Shiffman S, Schwartz JE, Broderick JE, Hufford MR. Patient non-compliance with paper diaries. *BMJ : British Medical Journal*. 2002;324(7347):1193-1194.

Perceived Barrier: Regulatory Concerns



"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."

"**Missing data is a major challenge** to the success and interpretation of any clinical trial."

"Sponsors should consider … procedures used to **avoid missing data**."

"We prefer use of an **electronic format** with reminders or alarms, when appropriate and feasible, to ensure **real-time data capture and limit missing data**, as well as to **accurately capture the timing of the assessment**."

"Sponsors should choose a format for daily sign or symptom assessment (e.g., **interactive voice response or personal digital assistant**) so that patients can evaluate their IBS signs or symptoms on a daily basis throughout the trial."

US Food and Drug Administration. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims. December 2009. www.fda.gov/cder/guidance/5460dft.pdf
US Food and Drug Administration. Draft guidance for industry: Low Sexual Interest, Desire, and/or Arousal in Women: Developing Drugs for Treatment. October 2016. www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM526362.pdf
US Food and Drug Administration. Guidance for industry: Irritable Bowel Syndrome — Clinical Evaluation of Drugs for Treatment. May 2012. . https://www.fda.gov/downloads/Drugs/Guidances/UCM205269.pdf

Perceived Barrier: Help Desk

"Main issue would be inadequate helpdesk support to sites / patients by the ePRO vendor ....nothing will raise concerns to senior mgmt than having a site complain they couldn't get the technology to work in front of a patient and the helpdesk were slow to help etc."

Help desk/Tech Support

- Better trained on protocol specific issues
- Must be able to cover 24/7 in all languages (more than one location involved)
- Must be familiar with study requirements and able to provide real-time assistance to sites and/or subjects
- Replacement of devices should be considered if issue is too long
- Bugs exist. Software is not perfect. Vendors are however now working with far more reliable technology than 5 years ago

Site support

- Site issues are often related to device set-up and configuration
- Mitigated with better and regular Investigator Training

Patient support

- Over 95% of patient support enquiries relate to PIN / password reset – easily addressed by the helpdesk or via the solution itself

Perceived Barrier: User Acceptance Testing (UAT)

> User acceptance testing is the process by which the clinical trial team determines if the system meets expectations and performs according to the system requirements documentation.

- UAT is not a complete re-validation effort conducted by the clinical study team
  - Does the system meet the design specification?
- eCOA vendors are able to support sponsors in conducting UAT by providing assistance with development of test scripts and attending UAT sessions
- Some CROs are able to perform UAT on behalf of the Sponsor study team
- Sponsors should also consider:
  - Outlining a test timeline and plan
  - Identifying a group to test the system
  - Actively participating in the training provided by the eCOA vendor

The ePRO Consortium is currently developing a best practices document to further define UAT, its importance, and recommendations for a successful process.

*Zbrozek A, Hebert J, Gogates G, et al. Validation of electronic systems to collect patient-reported outcome (PRO) data: Recommendations for clinical trial teams: Report of the ISPOR ePRO systems validation good research practices task force. Value Health 2013:16:480-9.

Perceived Barrier: Site Training/Re-training

The ePRO Consortium is currently developing a manuscript on best practices for site and patient training.

- Training site personnel (investigators and staff)
  - Develop a training curriculum that reflects the structure and logic of the measure, error messages, the assessment schedule, workflow, and integration of the electronic systems where appropriate (e.g. using wearables in combination with mobile device)
- Training models include
  - Face-to-face training: e.g. Investigator meeting and site initiation (train the trainer)
  - Remote training
  - Interactive web-based training
- Provide training materials and manuals that can be used as reference throughout the course of the trial
- Certify site proficiency and provide additional support/training to site personnel with low proficiency measured by brief examination of key concepts

Perceived Barrier: Patient Training/Re-training

The ePRO Consortium is currently developing a manuscript on best practices for patient and site training.

- Training patients
  - Develop a training curriculum that reflects how to: navigate the screens, address error messages, explains the assessment schedule, demonstrates how to correctly complete the rating scales to be used in the study, and how to move forwards and backwards in an assessment
  - The training should include technology-specific topics, such as turning the device and off, charging the device, data transmission, importance of passwords and device security and how to obtain technical support
- Training models include:
  - One-to-one training with site personnel
  - Interactive electronic training on device or via web
- Provide training materials/usage guides that can be used as reference throughout the course of the trial
- Patient proficiency measured by demonstration of the ability to use the device as required by study

Perceived Barrier: Site Receptivity/Burden

- Negative attitudes towards eCOA among clinical staff are often linked to previous experiences with device failure using older hardware and less robust software
  - Vendors are now committed to leveraging well understood consumer technologies to design a user experience that is more engaging to clinic staff and patients
- Feedback from clinical staff on the usability of eCOA systems is generally positive
- Training of clinic staff to ensure they are comfortable and confident with technology can have a significant impact on site acceptance.

Voiding diary [1]
Physician preference: 100% (n=6) preferred ePRO to paper

[1] Sussman, R. D., Richter, L. A., Tefera, E., Park, A. J., Sokol, A. I., Gutman, R. E., Iglesia, C. B. (2016). Utilizing Technology in Assessment of Lower Urinary Tract Symptoms: A Randomized Trial of Electronic Versus Paper Voiding Diaries. *Female pelvic medicine & reconstructive surgery*, *22*(4), 224-228.

Perceived Barrier: Patient Receptivity/Burden

- Patients find ePRO systems easy to use and many prefer them to paper. This is just as true of older adults and those unfamiliar with computers as it is of younger computer users. [1]
- Older adults find ePRO easy to use for both screen-based systems and IVR. [1]
- **The ePRO Consortium has included a patient burden questionnaire in its ongoing EQ-5D-5L equivalence study.**

Rheumatoid Arthritis [1]

- Patients aged 32 – 83 years
- In general, patients preferred the electronic version over the paper, and this was **true for the older as well as the younger patients**

Psoriatic Arthritis [3]

- 53 patients
- 99%: ePRO acceptable
- 96%: "very easy" or "quite easy"
- Site-based tablet instrument

Daily menstrual diary [2]

- 3-month daily diary, n=25

Various populations [4]

- 167 patients with experience of both paper PRO and ePRO trials
- 77.3% preferred ePRO
- 76.1% had high agreement that ePRO makes dairy participation easier
- 73.1% had high agreement that ePRO-use makes them more willing to participate in future diary completion.

[1] Tiplady, B., Goodman, K., Cummings, G. et al. Patient-Patient-Centered-Outcome-Res (2010) 3: 179-183.
[2] Johannes C et al. Ann Epidemiol. (2000) 10: 457.
[3] Elash C et al. Equivalence of Paper and Electronic Administration of Patient Reported Outcomes: a Comparison in Psoriatic Arthritis. Value in Health (2015); 18: A342
[4] Ross J, Holzbaur E, Wade M, Rothrock T. Patient Preferences: Pro Mixed Modes-ePRO Versus Paper. Value in Health. 2014 Nov; 17(7):A515.

Perceived Barrier: Data Integrity and Data Quality

Data Integrity

- Electronic systems allow data to be attributable, legible, contemporaneous, original and accurate (ALCOA)
  - Timeliness of data entry is measurable and controllable
  - Extraneous, unclear or conflicting data is eliminated
- eCOA vendors are bound by 21 CFR Part 11 (audit trails, ID, passwords)
  - Vendors are responsible for implementing authentication measures, ensuring data integrity use of passwords
  - Audit trails are available in all systems and data encryption does not allow for any alteration of the data during transmission.

> “Never had missing data issues using paper in my trials with many PRO instruments over 2 years of clinical trial time frame.”

Data Quality

- Data transmitted immediately / as soon as signal available
  - Enables pro-active compliance encouragement
- Data automatically date/time stamped
- Completion windows to prohibit data entry beyond instrument recall period
- Perceived diary completion data quality and missing data may be significantly over-estimated with paper diaries. *

* Stone AA, Shiffman S, Schwartz JE, Broderick JE, Hufford MR. Patient non-compliance with paper diaries. *BMJ : British Medical Journal*. 2002;324(7347):1193-1194.

Perceived Barrier: Device Failure

- Device failure is less of an issue than with early eCOA solutions using older hardware and less robust software
  - Vendors now leverage modern consumer mobile technology that has high reliability
- Vendors should procure quality devices from reputable suppliers and implement software using quality control before shipment to avoid device failures
- Vendors should ensure that spare devices are available at the site or in the country and can be shipped within a suitable timeframe (e.g. 24 hours)

Example

- 4,000 patient trial
- Manufacturer quoted device failure rate < 1%
- Study device failure rate = 0
  - Each device primed before shipment
- 20-30 broken screens during study
  - Eliminated by device cases / screen protectors

The ePRO Consortium is developing a manuscript titled "Best Practices for Avoiding Paper Backup when Implementing Electronic Approaches to Patient-Reported Outcome Data Collection in Clinical Trials."

Conclusions

- The benefits of using ePRO far outweigh the challenges

- Most perceived barriers can be overcome by:
  - Building in adequate planning and preparation time
  - Timely site training, in addition to the Investigator meeting, which includes easy to use reference guides
  - Effective QC of device installations pre-shipment
  - Responsive site-facing helpdesk

- Sponsors should consider these factors at the vendor selection phase

(ex)Sponsor Perspective: "What Worked for eCOA Uptake"

Sue Vallow, VP Patient eSolutions, MedAvante
(formerly Sr. Director & Head, Patient Focused Outcomes at GSK)

Background to eCOA "Revival" at GSK

- 2012 – Very few studies / teams using eCOA
- Patient Focused Outcomes (PFO) team created in 2013
- eCOA was needed, to ensure proper implementation of the PFO strategies
- Pulled together a cross-functional team of key stakeholders: "ePRO Revival Team"
- ePRO Revival Team conducted survey on eCOA use revealed:
  - Perception of high cost
  - Lack of upfront planning
  - Lack of eCOA expertise

Efforts to Increase eCOA Uptake

Diagnosing

- eCOA revival team
- Survey
- Interviews
- Cost Model

Communication

- Vendor Refresh
- Management Alignment

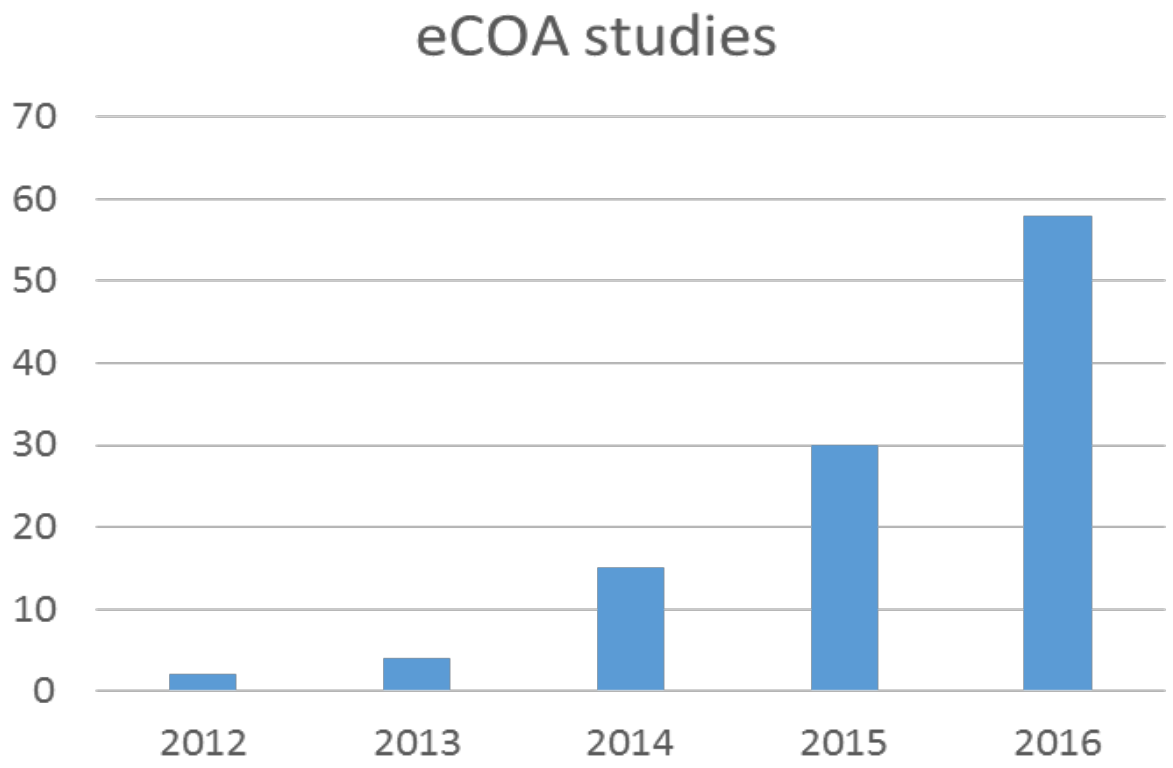
Education & Execution

- Cost model
- Awareness Days
- PFO Team advocating
- eCOA Director

Embedding

- eCOA in goals
- Studies with great data
- Team took on eCOA tasks
- Continued education

Impact of Efforts to Increase eCOA



Acknowledgments:
The GSK PFO Team Circa 2013-2016

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Eric Schnitzer

Maggie Tabberer

Megan Turner

Robyn von Maltzahn

Adoption of Electronic COA from an Operational Perspective

Marieke Manders, GCDO Trial Leader

Immunology Portfolio Delivery Operations, Janssen Research & Development

My eCOA Journey

Mid **2013**, did I wish to implement eCOA in a Phase 3 rheumatoid arthritis (RA) study?

- Three roles required for Primary Endpoint:
  - Joint Counts - **Independent Joint Assessor**
  - Assessment of pain (VAS), global disease activity (VAS), physical function (HAQ-DI) - **Patient**
  - Global Assessment of Disease Activity (VAS) - **Investigator**
- At Wk 16, **joint count improvement** determined treatment allocation by IWRS

I scheduled 1:1 meetings with:

- 6 peer Trial Leaders with eCOA experience
- They all recommended to use eCOA, not paper
- Data Management Lead: data cleaning would be my responsibility

Conclusion:

- I decided to implement eCOA and focus on **device** functionality, **training** and **data review**

My eCOA Journey

- F2F kick-off meeting with eCOA vendor
- Investigator Meetings
  - Preceded by F2F training of **CRAs** to familiarize them with device first
  - 1.5 hours site staff training in break-out sessions to allow **hands-on time** with the device
- Supply shipments
  - eCOA quick start-up guide (1 page laminated card) was included

- Site Initiation Visit
  - CRAs trained site staff and assisted with device set up and user role set-up
  - In case of booster visits: eCOA retraining was provided
- During the study
  - **eCOA Vendor Portal /IWRS review instructions** were created and revised when needed
  - A **Central Monitor** was assigned
  - Weekly checks were performed as the study progressed

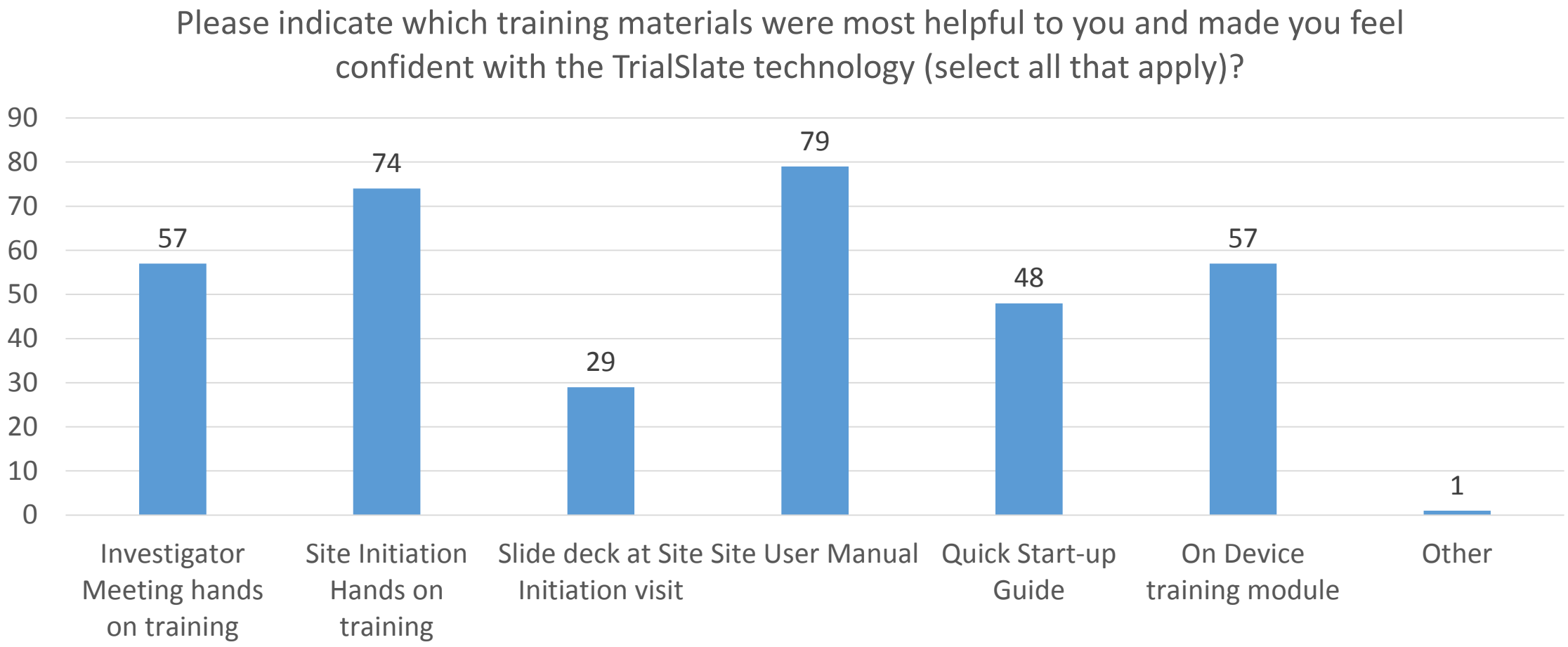
My eCOA Journey

What was checked by the Central Monitor?

- **Screening Joint Counts** visible in eCOA Portal for every new subject?
  - If not: retraining was provided
  - Retrospectively entered joint assessments were SDVd
  - Were there any duplicate subjects?

- From **Enrolment** onwards
  - Joint count eligibility criteria met?
  - Variation of not-evaluable joints over time as expected?
  - Joint assessment **dates** in eCOA Portal consistent with IWRS visit **dates**?
  - Apart from joint counts, were all other ePRO and eClinRO assessments visible?
  - Did the **Early Escape** status at Week 16 in eCOA Portal match with status in IWRS?
- No issues were faced during DBL
- After DBL, a **Site Survey** was sent

Responses from Site Survey on Training



102 sites were approached; 146 surveys were returned

Completed by: Investigators (78), Study Coordinators (38), Independent Joint Assessors (29), Site staff member not actively using TrialSlate (1)

Panel Discussion and Q & A

Moderator

- *David S. Reasner, PhD* – Vice President, Data Science and Head, Study Endpoints, Ironwood Pharmaceuticals

Presenters

- *Bill Byrom, PhD* – Senior Director of Product Innovation, ICON Clinical Research and ePRO Consortium Industry Vice Director
- *Alexandra I. Barsdorf, PhD* – Director, Rare Disease, Patient & Health Impact, Pfizer, Inc.
- *Kelly McQuarrie, BSN* – Director, PRO Team, Janssen Pharmaceuticals
- *Sue Vallow, RPH, MBA, MA* – Vice President, Patient eSolutions, MedAvante, Inc.
- *Marieke Manders, MSc* – GCDO Trial Leader, Immunology – Janssen Research & Development

Panelist

- *Serge Bodart, MS* – eCOA Subject Matter Expert, Biomedical Systems