Best Practices for the Electronic Migration and Implementation of Clinician-Reported Outcome Assessments in Clinical Trials

Heather Romero[1], Sonya Eremenco[2], Kathleen W. Wyrwich[3], Paul O'Donohoe[4], Dan DeBonis[5], Valdo Arnera[6], Shelly Steele[1], Tom Willgoss[7], Kristina Harris[8], Cindy Howry[9], Mabel Crescioni[10] and Jill Platko[5] on behalf of the Electronic Patient-Reported Outcome (ePRO) Consortium and Patient-Reported Outcome (PRO) Consortium

1. WCG MedAvante-ProPhase, 2. Critical Path Institute, 3. Pfizer Inc, 4. Medidata Solutions, 5. Signant Health, 6. ERT, 7. Roche, 8. UCB, 9. .assisTek, 10. Hemophilia Foundation of America

ePRO Consortium

The ePRO Consortium was established within the Critical Path Institute (C-Path) in 2011 to advance the quality, practicality, and acceptability of electronic data capture methods used in clinical trials for endpoint assessment. The ePRO Consortium's members are firms that provide electronic data collection technologies and services to the medical products industry for capturing clinical outcome assessment (COA)-based endpoints in clinical trials. Current members of the ePRO Consortium are: .assisTek, Clinical Ink, CRF Bracket, ERT, ICON, IQVIA, MedAvante-ProPhase, Medidata, and YPrime.

Objective

The objective is to develop best practice recommendations to address the unique challenges associated with the electronic migration and implementation of clinician-reported outcome (ClinRO) assessments.

Development of Best Practice Recommendations

- The Critical Path Institute's ePRO Consortium and PRO Consortium developed consensus-defined best practice recommendations for electronic migration and implementation of ClinRO assessments in clinical trials based on eCOA expertise, industry standards and relevant literature.
- A series of teleconferences were held to outline the components of a successful electronic migration and implementation of ClinRO assessments.
- The panel of Consortium representatives reviewed current guidance on ClinRO assessment development, ePRO best practices, and current industry trends.
- Best practices for electronic migration of COAs have mostly focused on patient-reported outcome (PRO) measures.
- The proposed best practices are specific to development and implementation of electronic ClinRO (eClinRO) assessments.
- The new recommendations are focused on the study start-up and solution development phases of a clinical trial, See Figure 1.
- Advantages of eClinRO assessments when migrated and implemented according to best practices include:
  - Direct data capture instead of manual data entry from paper
  - Reduced missing data
  - In addition, since ClinRO assessments are completed by qualified clinical investigators, eClinRO assessments reinforce standardized administration across multiple sites and improve interrater reliability and data quality overall.

Best Practice Recommendations

The following are best practice recommendations for electronic migration and implementation of ClinRO assessments:

1) The first step in migrating a ClinRO assessment is to obtain a validated reference scale (i.e., the official version of the scale) and adhere to the validated reference throughout the migration and implementation process.
2) Electronic adaptation typically involves minor changes in layout and content, auto-calculation of scores, and programming of branching logic to adapt to the electronic administration mode (see Figure 1 and 2). Such changes are not likely to have changed the clinician's interpretation of the items and response options of the eClinRO assessment, compared to the original validated reference.
3) Expert eCOA/clinician review should be incorporated throughout the eClinRO solution development process.
4) Training of the user includes training on both the ClinRO assessment and the electronic device.

Evidence needed to support adequacy of electronic migration of ClinRO assessment – see Table 1.

1) Expert review by a clinician/eCOA expert and author/copyright holder review (if possible) are sufficient to support modifications that do not change interpretation (i.e., Classification Level I) during migration.
2) Full psychometric testing is recommended for eClinRO assessment modifications that deviate significantly from the validated reference (i.e., Classification Level II).

- The proposed best practice recommendations for eCOA vendors and clinical trial sponsors will support high quality electronic migration and implementation of ClinRO assessments in clinical trials.
- Criteria to judge complexity of a ClinRO assessment (e.g., low vs. high complexity) can assist industry stakeholders in planning for the development of the eClinRO assessment solution, with the goal of ensuring that a faithful migration is achieved.
- Steps for implementing the eClinRO assessment solution can provide a common framework for industry partners to support planning and coordination of start-up activities. Utilizing these best practices will improve the precision of ClinRO data collected in clinical trials to support product registration.
- When migrated properly, eClinRO assessments can ensure data comparability by keeping the instrument standardized and consistent with its original intent and meaning (i.e., the original validated reference instrument that is typically on paper).

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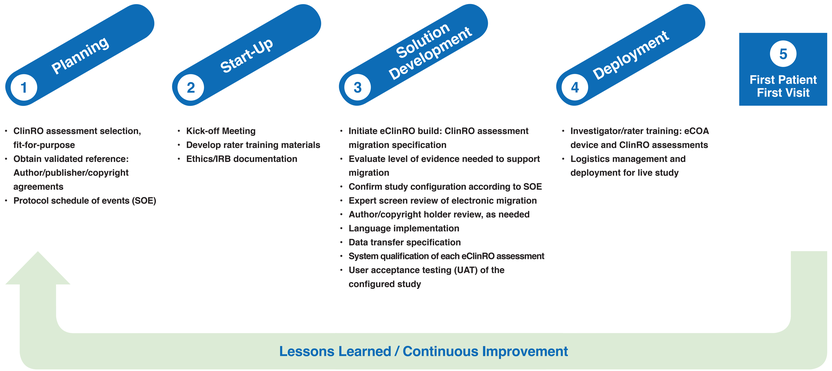
Key Considerations for Electronic Implementation

Implementation

Implementation of an eClinRO assessment in clinical trials involves four phases in the run up to first patient screening date (First Patient First Visit), see Figure 1

Figure 1: eClinRO Study Lifecycle



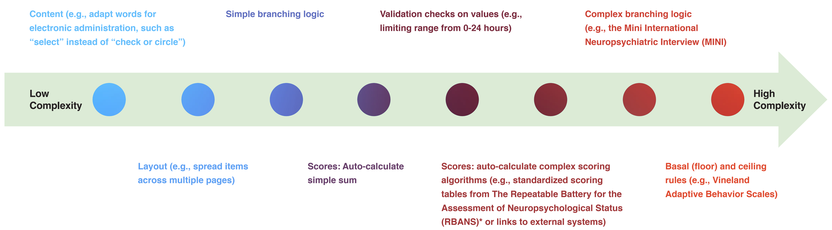
Scale Management

Approach to eClinRO assessment permissions and requirements:
- The electronic migration process starts with obtaining the validated reference from the author/publisher/copyright holder.
- Common sources for validated references: publishers, repositories (such as ePROVIDE), peer reviewed publications, or references in the public domain.

Migration to Electronic ClinRO Platform

- The goal of this process is a faithful migration, such that the clinician completing the ClinRO assessment interprets items the same way regardless of mode of data collection or level of complexity.
- Common migration is from paper to electronic, but may be electronic to electronic.
- Complexity of ClinRO assessment impacts the migration process.
- Elements of ClinRO assessments can be categorized as having low complexity or high complexity, depending on the functionality that needs to be programmed electronically as shown in Figure 2.

Figure 2: Common Elements of Electronic Migration of ClinRO Assessments: Low to High Complexity



Key Considerations for Electronic Implementation (Continued)

Training

- Concurrent with migration and implementation activities is the development of training materials that prepare the qualified investigators to complete the eClinRO assessment
- Training includes two components:
  - Training on the ClinRO assessment
  - Training on the electronic device

The panel recommended coordinating implementation and training to optimize the benefits of eClinRO assessments in the clinical trial setting. The content from investigator training materials and eClinRO assessments should be complementary.

Evidence Supporting the Adequacy of Migration to the Electronic Data Collection Mode

- Levels of evidence needed to support adequacy of electronic migrations of ClinRO assessments are outlined in Table 1.
- The consensus panel proposed that expert review (including user testing) by a clinician or eCOA expert (who has experience with the instrument being migrated) and author/copyright holder review of screenshots (if possible) would be sufficient to support modifications during migration that are unlikely to have changed how the assessment is interpreted.
- It is anticipated that the majority of ClinRO migrations will fall within Classification I.
- Additional evidence in the form of psychometric evaluation was proposed for eClinRO assessment modifications that deviate significantly from the validated reference and essentially create a new measure.

Table 1. Evaluation of Measurement Comparability for ClinRO and eClinRO Assessments: Level of Modification and Supporting Evidence

Classification	Rationale	Examples		Level of Evidence
I	The changes to the instrument are not likely to have changed the interpretation of responses	Validated Reference (Typically Paper) • Manual scores and associated scoring instructions • Paper instruction words (e.g., "check, circle") • Layout multiple items per page • Branching logic, text surfaced • Joint assessment in table format	Electronic • Auto-calculated scores and removal of scoring instructions • Electronic instruction words (e.g., "select") • Layout fewer items per page to fit screen size and translation expansion • Branching logic, programmed • Joint assessment in pictorial format	• Copyright holder approval • Expert clinical/eCOA review
II	The changes to the instrument are likely to have changed the interpretation of responses	• Substantial changes in item wording • Substantial changes in response options		• Copyright holder approval • Expert clinical/eCOA review • Full psychometric testing to support new measure, especially for primary and key secondary outcomes

Disclosures

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

Heather Romero and Shelly Steele: Full time employees of WCG MedAvante-ProPhase
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Cindy Howry: Full time employee of .assisTek
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Valdo Arnera: Full time employee of ERT
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