LIONBRIDGE

THE NUANCES OF COA TRANSLATION: PLANNING AHEAD FOR BETTER OUTCOMES

Complex clinical trials require a comprehensive approach to Clinical Outcome Assessments (COAs)—and a plan for translation at every step.

Inside, you will learn:

The variables involved in selecting a COA—and the domino effect on the rest of the trial.

Why it's critical to plan ahead for translation and localization of patient questionnaires, training guides, and other materials that support the use of COAs.

The importance of capturing accurate, quantifiable patient experience data.

The role of linguistic validation and cognitive debriefing in regulatory approvals.

How electronic COAs are accelerating clinical trials—and reshaping the industry.

THE ABCs OF COAs

It's no secret:

Clinical trials are complicated, with a process made all the more arduous by accelerating timelines, escalating costs, rising regulations, and demands for demonstrable data. Yet every trial starts with three simple questions:

A **Is the drug or therapy safe for patients?**

B **Does it demonstrate a treatment benefit?**

C **Do the treatment benefits outweigh the risks?**

Answering these questions—and receiving regulatory approval—relies in large part on data derived from Clinical Outcome Assessments (COAs). By measuring how patients feel and function in their everyday lives, COA tools provide the quantifiable evidence to support therapeutic claims made in drug labeling. Determining the most appropriate COA for a given trial requires pre-study planning to identify stakeholders and minimize variance amid plentiful variables and challenges.

FACTORS SHAPING COA SELECTION IN A CLINICAL TRIAL

- **Trial objectives** – What is the trial's purpose? What are its research questions?
- **COA endpoints** – What will be measured by COAs—symptom severity, physical functioning, impact of disease on daily activities? What is the best way to assess and measure the specific concepts of interest?
- **Target population** – What type of patient will be assessed? What burden does the disease have on patients? Where do they live? What language do they speak? Will translated versions of COAs need to be developed?
- **COA measures** – Are the selected measures fit-for-purpose? Are they reliable, well-defined, and able to detect change over time—so the effect of the treatment can be properly evaluated?

4 TYPES OF CLINICAL OUTCOME ASSESSMENTS

Patient-reported outcomes (PROs)
Report on a patient's health condition directly from the patient, including symptoms and experiences only known by the patient, such as anxiety, pain level, or health-related quality of life.

Top challenges: *patient compliance and retention; data quality and accuracy*

Clinician-reported outcomes (ClinROs)
Report from a qualified healthcare professional based on patient observation and clinical interpretation of observable signs.

Top challenges: *clinician disparities; training resistance; patient-clinician relationship*

Observer-reported outcomes (ObsROs)
Report on a patient's health condition and signs from someone other than patient or clinician, such as a parent, caregiver, spouse, or teacher.

Top challenges: *observer availability; multiple caregivers; data interpretation*

Performance outcomes (PerfOs)
Measurable cognitive or physical tasks performed by the patient and administered by a clinician, such as walking or memory tests.

Top challenges: *patient engagement and motivation*

MORE VARIABLES, MORE CHALLENGES

When it comes to designing clinical trials and determining which COA to use, the variables are endless…

Collecting a wide range of data points	Using an existing, modified, or new instrument	Assessing an innovative therapy
Speaking different languages		
Targeting specific or rare patient populations	Interacting with patients from various cultures across several regions	Grappling with inconsistent technology access

Meanwhile, making that COA determination—and deciding whether to collect COA data on paper or electronically—creates a domino effect on trial costs, patient/clinician/observer burden, and more.

Accounting for these variables is critical. Trial sponsors must reinvent an increasingly complex wheel with each new study to solve a new challenge, with nothing short of regulatory approval hanging in the balance.

And yet, as the wheel spins, sponsors often overlook one variable that greatly affects a clinical trial: translation.

Why Every Nuance Matters

Translation is an integral part of the COA process. By addressing every nuance of translation during study planning and trial design, organizations can ensure proper use of instruments, improve COA performance, and help to maintain regulatory compliance.

In this paper, we'll explore key translation challenges related to COA and trial planning and design. We'll also examine the fast-rising trend of digitizing COAs with Electronic Clinical Outcome Assessments (eCOAs)—and the impact of capturing clinical data electronically.

THE VOICE OF THE PATIENT

Physicians say it often: the patient knows best.

Whether heard at the doctor's office receiving treatment for the flu or in the midst of a clinical trial, the voice of the patient is paramount. That's why the U.S. FDA, in accordance with the 21st Century Cures Act, is developing new industry guidance for methods and approaches of measuring patient experiences and perspectives.

According to FDA draft guidance published in 2018, "patients are experts in their own experience of their disease or condition and the ultimate consumers of medical products. The collection of patient experience data is important because it provides an opportunity to inform medical product development and enhance regulatory decision making to better address patients' needs."[1] The guidance outlines how the collection of patient experience data can:

- Inform clinical trial design and trial endpoint selection.
- Contribute to regulatory reviews, including benefit-risk assessments, potential labeling, and other communications.
- Help the FDA gain a better understanding of the patient experience and expected clinical benefit.

The FDA is expected to finalize draft guidance by 2020, which should serve as a revision or supplement to the 2009 Guidance to Industry on Patient-Reported Outcome Measures. The draft guidance will also address technologies used to collect, capture, store, and analyze patient perspective information.

For now, the implications are loud and clear: COAs must capture a patient's experience accurately and quantifiably.

The Nuances of Hearing—and Understanding—The Patient's Voice

When considering the collection of patient experience data, patient-reported outcomes (PROs) jump immediately to mind. PROs collect data in the form of patient diaries or questionnaires.[2]

Of course, all COAs revolve around the patients. The only way to guarantee that their voices are heard is to ensure the materials used to measure their experience are clear and coherent.

For international clinical trials or those that involve participants who speak multiple languages, that means accurately translating COAs and the information and documentation that support their use—utilizing appropriate translation methodologies so they incorporate the nuances of the target population's culture. This serves to avoid confusion, improve comprehension, and enhance communication while also increasing patient compliance and retention rates. All of which leads to better data collection and more precise clinical trial conclusions.

Enter linguistic validation. This rigorous process, based on ISPOR's methodological guidelines, aims to maintain the content validity and other measurement properties between the original COA and its translated versions—enabling trial researchers to accurately compare outcome data while satisfying regulatory requirements.[3] And it's a process best started early in the trial planning process.

VALIDATING EVERY VOICE

Linguistic validation takes time. Often, it takes a lot of time.

The importance of performing linguistic validation of PRO, ClinRO, ObsRO, and PerfO measures cannot be overstated. Content accuracy and consistency across languages is key to enabling participants across cultures to produce comparable outcome data. That's how data turns into results and results turn into regulatory approvals.

The Nuances of Linguistic Validation: Key Steps

1. DEFINE CONCEPTS

Explain concepts in the source COA measure and provide translation instructions where necessary in order to strengthen the conceptual equivalence of translations and facilitate harmonization across countries.

2. TRANSLATE SOURCE DOCUMENTS

Leverage two professional translators who independently translate documents into the participant's language while also localizing the text to reflect the target group's culture.

3. RECONCILE TRANSLATIONS

Employ a qualified and objective third-party translator to combine the translated documents from each translator and reconcile them into a single document that represents the best aggregate translation.

4. BACK TRANSLATE DOCUMENTS

Leverage a new qualified local-language translator who does not have access to the original text or other reference material to perform back translations of the translated document to ensure maintenance of the original meaning.

5. COMPARE FORWARD AND BACK TRANSLATIONS

Enlist a qualified translator who has not been involved in the back-translation to compare the back-translated version of the COA with the source text to evaluate translation accuracy.

6. ADAPT LANGUAGE

Adapt language that is spoken in more than one country from one language variant to another. Focus on the conceptual equivalence, appropriateness, and acceptance in the target culture.

7. HARMONIZE INTERNATIONAL VERSIONS

Compare different language versions of the COA to detect and rectify any discrepancies in the interpretation of concepts.

8. REVIEW TRANSLATIONS BY A CLINICIAN

Engage a medically-qualified specialist to review ClinRO/PerfO translations to check and refine the accuracy of the subject-specific content as well as medical and scientific terminology.

9. COGNITIVE DEBRIEFING: A KEY BEST PRACTICE STEP

Test PRO/ObsRO translations in cognitive debriefing interviews with a small group of respondents who are representative of the study target population. The objective is to check the respondents' understanding and interpretation of the translation as well as its suitability and relevance for the target culture. Cognitive debriefing interviews are conducted in each respective target country and for each target language and performed by a qualified vendor with experience in qualitative interviewing, in-person whenever possible. This critical step serves as regulatory evidence that content validity and other measurement properties are comparable between the original instrument and corresponding translations.

10. FINALIZE

Make any necessary updates and translations based on cognitive debriefing results, then prepare a final report on the development of translation that can be used in submissions to regulatory bodies.

Note: Linguistically validated translations for many COA instruments already exist, in which case organizations can request usage for trial from the current copyright holder. However, the copyright holder often controls the distribution of existing translations as well and using an unauthorized translation may violate copyright protection. With so many licensing variables in play, often the more feasible course is to engage a language services partner adept at licensing and supporting linguistic validation.

THE IMPORTANCE OF TRAINING

A major challenge for COA implementation is safeguarding for consistency.

Whether the assessments are documented via paper or smartphone, their administration must be standardized by patients, clinicians, and observers across every trial site.

In fact, adequate training for clinicians, observers, and patients themselves is a regulatory requirement that helps reduce errors; minimize variance in ClinRO, ObsRO, and PRO reporting; and maximize data quality. As noted in the FDA's 2009 PRO Guidance, a clinical trial's quality hinges in part on the standardization of instructions and processes by which PRO and other COA are administered. This standardization includes providing consistent training to interviewers, instructions for clinical investigators, and training for patients who are self-administering PROs.

Considering the complexity of many clinical trials—and the potential need for refresher training depending on trial length—COA training creates a burden on the site and stakeholders. However, it's a necessary task that helps organizations even a playing field populated by patients with limited technical capabilities, clinicians with disparate techniques, and observers or caregivers who may differ from one day to the next.

The Nuances of Translating Training Materials

Accurate translation of training documents is vital. After all, if raters and patients don't understand the materials—training videos, interactive didactics, etc.—they won't know how to properly administer the COA measures.

If a training text causes confusion because it has been improperly translated or localized, that adds an even greater burden to trial sites—not to mention added time and cost to the study. By enacting a plan well ahead of implementation, organizations can clearly outline how training will be performed, which materials will be used, and when on-site language support may be needed.

THE RISE OF eCOAs

A major challenge for COA implementation is safeguarding for consistency.

As the cost, complexity, and scale of clinical trials continue to surge, sponsors and other organizations increasingly search for more efficient solutions and more streamlined processes. It's no wonder, then, that the use of eCOAs is on the rise.[4]

Unlike paper-based methodologies, eCOAs leverage digital technologies—smartphones, tablets, laptops—to capture real-time, time-stamped data from patients, caregivers, and clinicians. Collecting outcome measures electronically enhances the integrity and accuracy of data, improves patient engagement, simplifies trial management, and provides stronger support for regulatory approval so sponsors can accelerate drug development.

While the eCOA market steadily marches forward, the debate within the industry on whether and when to implement them is keeping pace. All the benefits of eCOAs come at a cost—from the initial investment in technology to extended timelines, increased training, and ongoing system maintenance and technical support. Other issues include privacy concerns, device failures, data corruption, and Internet access.

The Nuances of a Rising eCOA Trend

There are many benefits to using an eCOA. If trial sponsors decide to gather data electronically, they should plan accordingly by bolstering resources, planning ahead to meet regulatory standards, and having back-up plans in place to address issues with technology.

A big part of that planning involves the translation and localization process. As with paper-based COAs, translating eCOAs and accompanying materials ensures patient experience data is accurately captured, training documents are clearly understood, and the assessment instrument is properly utilized by participants and raters.

The best plan? Partnering with a language services provider that has the expertise and experience to help you better implement eCOAs. A provider recognized by Common Sense Advisory as one of the world's leading translation company, which completes over 10,000 life science translation projects per year. A single partner with the regulatory expertise to ensure accurate, compliant translations for all target markets can streamline your process and reduce inefficiencies and noncompliance.

17% eCOA GROWTH BY 2026

The Electronic Clinical Outcome Assessment (eCOA) Solutions market is projected to grow at a rate of 17.6% by 2026, to reach USD 2.52 billion in 2026 from USD 0.69 billion in 2018.[5]

THE NUANCES OF COA PLANNING AND TRANSLATION

Complex clinical trials—such as multinational studies with diverse patient populations speaking different languages—require comprehensive planning.

It starts with a detailed strategy for Clinical Outcome Assessments that anticipates the unexpected, accounts for every variable, and addresses translation and localization at every step. **Here's how:**

Properly managing the nuances of translation serves to enhance data quality, improve regulatory compliance and acceptance, and bring products to markets faster. To achieve these goals, it's critical to work with a COA partner that has both scientific and linguistic expertise: **a partner like Lionbridge Life Sciences.**

IN A WORLD OF VARIABLES, LIONBRIDGE IS YOUR CONSTANT

Lionbridge Life Sciences has the industry experience and linguistic expertise to take the variables of translation out of your clinical trial equation.

As the world's most experienced language services provider in life sciences, we can help your organization develop a streamlined strategy to support the full range of your COA activities, from pre-study planning through trial start-up and beyond.

Lionbridge has the capacity to:

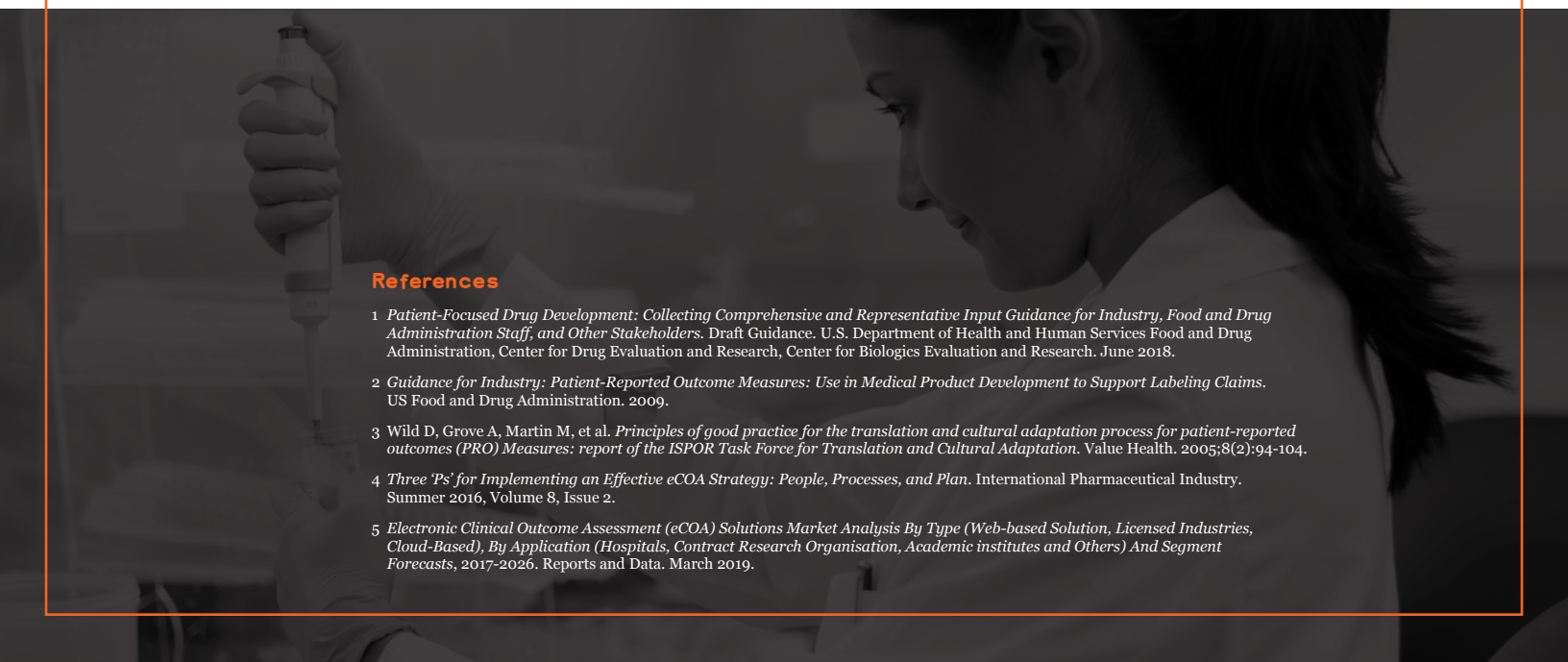
- Support multinational studies of significant scope and complexity.
- Translate and localize materials for remote regions and rare dialects.
- Accommodate requirements across therapeutic areas and populations, including rare diseases and pediatric patients.

Our proven, best-in-class COA solutions—copyright and licensing, rater training support, translation and linguistic validation, eCOA services—are compliant, patient-centric, built to accelerate regulatory approvals, and equipped to meet your global needs.

GET STARTED.

LET'S TALK COAs

OUR EXPERTS ARE READY TO HELP YOUR ORGANIZATION ADDRESS THE NUANCES OF COA PLANNING—AND WHERE TRANSLATION FITS IN.



References

1 *Patient-Focused Drug Development: Collecting Comprehensive and Representative Input Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders.* Draft Guidance. U.S. Department of Health and Human Services Food and Drug Administration, Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research. June 2018.

2 *Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims.* US Food and Drug Administration. 2009.

3 Wild D, Grove A, Martin M, et al. *Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation.* Value Health. 2005;8(2):94-104.

4 *Three 'Ps' for Implementing an Effective eCOA Strategy: People, Processes, and Plan*. International Pharmaceutical Industry. Summer 2016, Volume 8, Issue 2.

5 *Electronic Clinical Outcome Assessment (eCOA) Solutions Market Analysis By Type (Web-based Solution, Licensed Industries, Cloud-Based), By Application (Hospitals, Contract Research Organisation, Academic institutes and Others) And Segment Forecasts*, 2017-2026. Reports and Data. March 2019.

About Lionbridge

Lionbridge partners with brands to break barriers and build bridges all over the world. For more than 20 years, we have helped companies connect with global customers by delivering marketing, testing and globalization services in more than 300 languages.

Through our world-class platform, we orchestrate a network of 500,000 passionate experts in 5,000-plus cities, who partner with brands to create culturally rich experiences. Relentless in our love of linguistics, we use the best of human and machine intelligence to forge understanding that resonates with our customers' customers. Based in Waltham, Mass., Lionbridge maintains solution centers in 27 countries.

LEARN MORE AT
LIONBRIDGE.COM/LIFE-SCIENCES

LIONBRIDGE