MEDIDATA / Rave

WHITE PAPER

A Review of the Changing Trends and Use of eCOA in Clinical Trials

Table of Contents

The availability of new technology, maturing digital organizations, and increased adoption by regulators are major factors driving the digital transformation of electronic clinical outcome assessments (eCOAs). Sponsors can leverage flexible and integrated eCOA tools to benefit from quicker study start-up times, higher-quality data, increased efficiencies in study management, enhanced patient-reporting experiences, and cost savings.[1]

This white paper provides an overview of industry and regulatory eCOA trends that are converging to expand the adoption of eCOA for clinical trials. The latter part of the paper provides a summary of Medidata's Rave eCOA, which is a flexible solution that is easy to use, contains a global library of preconfigured and preapproved eCOA questionnaires, accurately captures patient outcomes data, and is built on the Medidata Rave Clinical Cloud's unified data platform that creates a single source of truth for all study-related data. Collectively, these features are enabling sponsors to employ Rave eCOA to enhance the patient-reporting experience, and in the process, create trials that are maximally patient focused while reducing the burden on sites and clinical teams.

Industry Trends

EXPANDING USE OF COA IN CLINICAL RESEARCH

Over the past decade or so, a confluence of factors has led to the continued growth of COA in clinical trials, including the following:

- An increased focus on the role of patients in clinical trials
- Efforts to better understand the impacts of disease and their respective treatments on the symptoms and outcomes from a patient's perspective
- Regulators' increased acceptance of and reliance on the patient perspective to evaluate treatment effectiveness
- Payers' increased reliance on the patient perspective to analyze the cost effectiveness of new treatments, especially in an environment of increasing treatment costs

Importantly, COA data are progressively being used not only to develop confirmatory nonprimary endpoints but also for labeling as primary endpoints. For instance, one analysis showed that 16.5% of new U.S. Federal Drug Administration (FDA) drug approvals between 2011 and 2015 had a patient-reported outcome (PRO) included in the labeling, and 76.7% of the PRO labeling was based on primary endpoints.[2] Another report highlighted disparities in the use of COA across therapeutic areas; it was shown that PRO labeling remains uncommon for oncology drugs overall and that there were even variations in the evidentiary standards used by different regulators (i.e., the FDA and EMA) to assess PRO data from oncology clinical studies.[3] It is worth highlighting ruxolitinib for myelofibrosis—it was the first oncology drug to be approved based on the exclusive use of PRO data as the endpoint for a supporting label indication and continues to represent a great model for achieving approval of novel anticancer agents using PRO-related data.[4]

Overall, the growth of eCOAs in clinical trials has been encouraged and adopted by patients, sponsors, regulators, and payers, and a part of the digital transformation in clinical trials, which is the focus of the next section.

TRANSFORMATION OF COA TO eCOA

While validated COAs have traditionally been developed and administered on paper, the sustained drive to continue to make clinical trials more patient focused has led to a significant upward trend in the use of eCOAs. eCOA is the recommended and preferred method to collect COAs and also plays an important role for patient-centric drug development.[5,6,7] Furthermore, several studies have also demonstrated the measurement equivalence of COA instruments between paper and electronic formats.[8]

The increasing use of eCOAs is consistent with the overall application of more digital technologies within clinical trials, which can expedite patient enrollment, increase patient compliance, and enable advanced trial data analytics.

While the eCOA landscape is certainly continuing to evolve as more and more COAs transform to digital, it remains true that they can be delivered using a range of technologies that are convenient and easy, boost compliance, and satisfy regulatory security requirements, while delivering more accurate data as compared to paper COAs. In addition, data can be captured using one or more of a variety of options that are already familiar to patients (trial provisioned or on the patient's own devices), including smartphones, tablets, wearables/sensors, web apps, and interactive voice response systems. The trend of using a patient's own device (also referred to as "bring your own device" [BYOD]) can provide additional cost savings and reduce the burden of managing the devices. However, sponsors need to consider some of the challenges associated with BYOD trials (e.g., patients may delete the app, turn off notifications, or lose the phone during trial),[9] and in some cases, a mixed BYOD/trial-provisioned model might be ideal.[10]

In addition, major multistakeholder initiatives, such as the Electronic Patient-Reported Outcome (ePRO) Consortium formed by the Critical Path Institute (C-Path), are leading the way by developing best practice recommendations for ePRO dataset structure and standardization. Other collaborative efforts, such as the one between Medidata and Mapi Research Trust (MRT), seek to standardize MRT's library of eCOA questionnaires in the Medidata Rave eCOA to create a clearinghouse of MRT's library of more than 470 eCOA forms and their respective translations so that forms do not need to be custom made and retranslated every single time.

Overall, the recognized benefits of eCOAs include the following:

- Increased patient compliance and engagement
- Data that are more accurate relative to paper COAs (reduced inconsistencies and transcription errors)
- Enhanced communications between patients and sites/clinicians
- The ability to collect additional data streams using technologies such as wearables
- Amenability to remote collection, which can enhance patient safety, minimize patient and site burden, and still maintain data integrity

THE VALUE OF eCOA DURING TIMES OF UNCERTAINTY

In response to concerns related to the COVID-19 (coronavirus) pandemic, numerous pharmaceutical companies have funneled significant effort and investment into programs seeking to develop new therapies and vaccines to meet the extraordinary demand for safe and effective treatments.

Implementing eCOAs in these clinical studies can not only shorten study start-up times and facilitate the collection of COA data on a global scale but also allow data to be gathered remotely to maintain data integrity while permitting patients to remain engaged with a trial. Both of the latter points are critical elements given the social distancing requirements in effect.

Regulatory agencies have put forth guidance documents that outline a variety of recommendations that can minimize the negative impact of the pandemic on clinical trials, including considerations for implementing remote COA data collection.[11,12]

In addition, C-Path recently released a document that covered risk mitigation strategies for the collection of PRO data that were originally intended to be obtained through clinical sites.[13] A number of mitigation strategies were recommended for patients no longer going to clinical sites who needed to complete questionnaires, including providing access to web-based systems or an app on their own devices (BYOD). These efforts can maintain data integrity and uphold the benefits of ePRO. Several challenges were also cited, and we encourage interested readers to consult the decision tree provided in the document for a more complete discussion of the pros and cons of the recommended approaches.

Overall, sponsors that are able to implement an effective eCOA strategy are well positioned to reap the benefits associated with improved operational efficiencies and innovations that are being realized solely through new data streams, trial designs, and advanced trial data analytics.

Regulatory Trends

Major regulatory authorities, such as the FDA and the EMA, have long adopted the view that the patient perspective should be a facet built into the drug development process. This has been persistently encouraged and reinforced over the years, and these agencies have published dozens of guidance documents that recommend using COA data to support label claims in new drug or marketing authorization applications. It follows that increases in digital adoption are being embraced by regulators and favoring the inclusion of eCOA data in new applications.

For instance, to fulfill its commitments with the 21st Century Cures Act and PDUFA VI, the FDA has exerted significant effort to advance its patient-focused drug development (PFDD) program, which is intended to inform how stakeholders can best develop and apply methods to gather, use, and submit meaningful patient experience data to advance drug and device development while maximizing the utility of these data for regulatory decision-making.[14] This effort includes developing a series of methodological PFDD documents, including recommendations related to technologies to collect, capture, store, and analyze COA data. Specifically, there are four PFDD guidance documents in development, with the first two available in draft form:

1. **Guidance 1: Collecting Comprehensive and Representative Input**

2. **Guidance 2: Methods to Identify What Is Important to Patients**

3. **Guidance 3: Selecting, Developing or Modifying Fit-for-Purpose Clinical Outcomes Assessments**

4. **Guidance 4: Incorporating Clinical Outcome Assessments into Endpoints for Regulatory Decision Making**

Collectively, these documents provide further regulatory leadership on the use of patient experience data, especially with respect to COA data, including technologies to collect, capture, store, and analyze such data (a Guidance 4 topic).

As indicated earlier, there are data to suggest that different regulatory agencies can have unique evidentiary standards, such as the different methods to assess PRO data from oncology clinical studies reported by Gnanasakthy et al. (2018).[15] Further, most approved labeling claims from the FDA and EMA are for symptoms; health-related quality of life (HRQL) claims are less common, although the EMA has granted more than the FDA. These are important considerations for sponsors to account for from a strategic perspective.

Traditional eCOA Solutions: Effective But Limited Applicability

Among the commercially available eCOA solutions, the extent and maturity of electronic data collection varies across types of COA (ObsRO, ClinRO, PerfO, and PRO). Further, stand-alone solutions can sometimes require considerable effort to initiate a study and integrate with other disparate technologies. As BYOD trials continue to gain traction, flexibility in eCOA technology will be key to ensuring full accessibility across different devices and safeguarding against some of the most common concerns associated with BYOD trials.

Choose an eCOA Solution that Solves Today's Implementation Challenge

Rave eCOA is a modern mobile solution for collecting clinical outcomes assessments with smartphones or tablets. Available as an iOS or Android app, Rave eCOA provides a single-system deployment model that can simplify builds and lower costs. Rave eCOA eliminates the need for managing multiple stand-alone solutions and streamlines patient data capture efforts with the only unified eCOA platform solution already integrated with Rave EDC.

Endnotes

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