Key risk indicators in eCOA - Considerations for improving eDiary data quality and regulatory compliance

MSR135

CLARIO.

Authors **Bakonyvari, B[1] and Maher, K[2]**

[1] Clario, Budapest, [2] Clario Philadelphia

Disclosure: Both authors are employees of Clario.

Introduction

Electronic Clinical Outcome Assessments (eCOAs) have become an integral component of clinical trials, enabling real-time data collection and reducing recall bias. In particular, electronic diaries (eDiaries) —mobile or web-based tools used by patients to report symptoms or health status— play a critical role by capturing patient-reported outcomes with improved accuracy. However, variability in adherence and reporting can compromise data quality. Regulatory agencies increasingly expect that sponsors implement risk-based approaches—including identifying sites exhibiting markers of poor performance or noncompliance—to monitor eDiary compliance, ensure data reliability, and detect anomalies [1,2,3]. This poster presents key considerations for developing effective Key Risk Indicators (KRIs) for eDiaries focusing on metric definitions, detection of data inconsistencies, and integration into data monitoring strategies.

Methods

We developed and applied a structured process to define eDiary-specific KRIs using illustrative examples from Ulcerative Colitis and Insomnia Disorder trials. The approach included a systematic review of eDiary structure and content, alignment with protocol Schedules of Activities, and identification of eligibility and endpoint requirements supported by diary data to identify any critical points of failure. Each metric was mapped to its rationale, potential actions, and endpoint relevance. The process also incorporated threshold determination, feedback loops with clinical and data teams, and corrective action planning. These steps enabled the creation of protocol-specific KRIs that address compliance, missing data, and data quality risks, supporting their application in regulatory submissions.

The methodology shown in Table 1 contains 6 steps starting at protocol review and ending in the inclusion of the KRIs in the data monitoring plan. Although the table suggests a linear flow, the potential feedback loops with clinical and data teams introduce iteration and flexibility into the methodology. In addition, the methodology starts with the endpoints and revisits them later, as a check point to ensure the KRIs measure what they set out to measure.

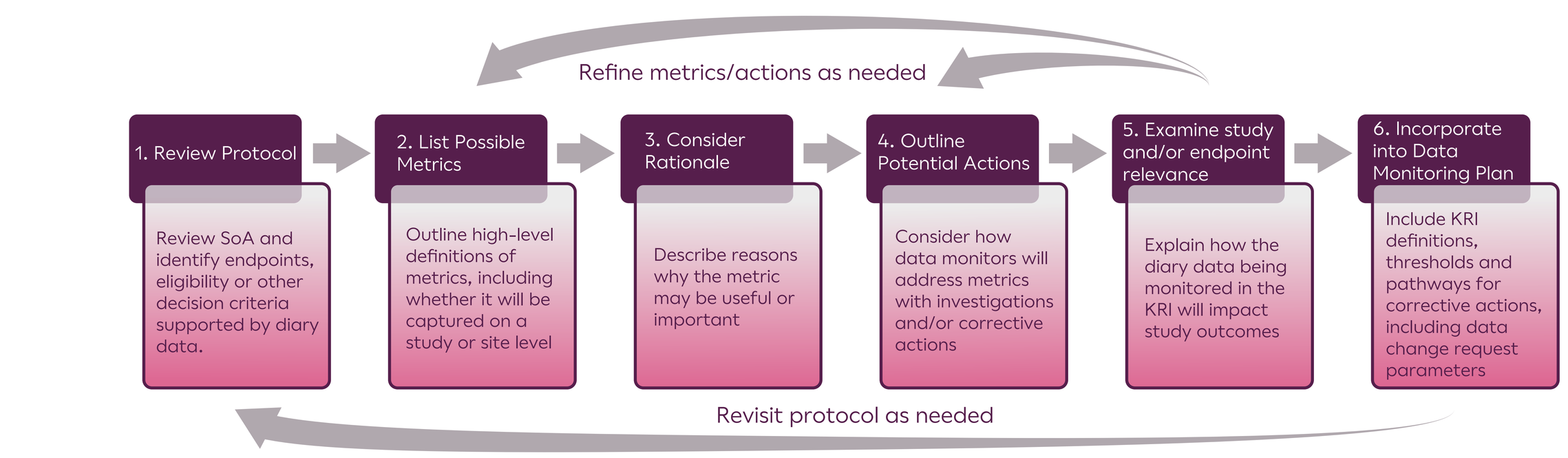

Figure 1: Workflow of KRI definition methodology

Process Steps	Example 1: Ulcerative Colitis	Example 2: Insommnia
1. Review the protocol: Review Schedule of Activities and identify endpoints, eligibility or other decision criteria supported by diary data.	Daily diary data captures symptoms which contribute to modified Mayo Score, used in primary endpoint analysis	Sleep diary compliance is part of eligibility criteria
2. List possible metrics: Outline high-level definitions of metrics, including whether it will be captured on a study or site level	Number of participants in the double-blind treatment period who do NOT have enough diary entries	Rate of participants deemed eligible despite Sleep Diary Compliance <70% in placebo run in period. (Site Level)
3. Consider the metrics' rationale and alert thresholds: Describe reasons why the metric may be useful or important and consider the level of acceptability, beyond which an alert is appropriate.	Not enough diary data will result in the inability to calculate rectal bleeding and stool frequency subscores (which contribute to primary endpoint)	Participants enrolled with sleep diary compliance <70% do not meet eligibility criteria and may have low diary compliance during the treatment phase.
4. Outline potential actions: Consider how data monitors will address metrics with investigations and/or corrective actions	Intervene early if a site shows high rates of missing data by having the site retrain the participants.	Retrain sites on eligibility criteria and the importance of diary compliance; Monitor sites with repeated instances and escalate for oversight review.
5. Examine study and/or endpoint relevance: Explain how the diary data being monitored in the KRI will impact study outcomes	Missing diary data weakens baseline comparability, affecting interpretability of change-from-baseline analyses.	Low compliance may raise concerns about the robustness of PRO data during regulatory review.

Table 1: Examples of methodology use in UC and Insomnia

Metric Description	Rationale	Potential Actions	Endpoint Relevance
Proportion of participants with low diary compliance during the treatment period.	May result in incomplete endpoint data (e.g., symptom subscores not evaluable). Site-level patterns of poor compliance can indicate insufficient patient engagement or inadequate site oversight.	Retrain sites on diary importance and reinforce compliance expectations with patients. Provide additional resources (reminders, engagement tools).	For endpoints dependent on symptom diaries. Low compliance risks non-evaluability, reducing statistical power and interpretability.
Number and proportion of participants missing evaluable diary data in critical time period for score or sub-score calculations.	Prevents calculation of scores or subscores. Indicates inadequate compliance monitoring or lack of site follow-up on missing data.	Investigate reasons for missing diaries (e.g. technical issues, burden, disengagement). Trigger process for additional days of data capture if possible.	Endpoints based on scores or subscores require sufficient diary data to calculate. Missing data reduces evaluability and may bias results if non-random.
Proportion of participants deemed eligible despite not meeting diary compliance inclusion criteria.	Participants entering treatment without verified compliance may remain noncompliant throughout study. Sites with repeated unverifiable eligibility may misapply criteria.	Retrain sites on eligibility and diary verification procedures. Monitor sites with repeated issues and escalate for oversight review.	Incomplete screening diaries risk misclassification, baseline bias, and weaker PRO endpoints under regulatory review.

Table 2: Examples of effective eDiary KRIs that can be applied across many therapeutic areas

Results

Several considerations have been identified as critical for developing eCOA-specific KRIs to ensure alignment with regulatory expectations: KRIs metrics for eDiary Data can highlight potential risks to data quality and support identification of sites or participants in need of intervention.

- Examples of effective metrics include high rates of:
  - Participants with missing endpoint data from diaries
  - Participants enrolled despite diary non-compliance (if included in I/E criteria)
- KRIs should focus on actionable insights – i.e. opportunities to intervene appropriately at a site or
- participant level.
  KRIs, their relevance and their potential actions should be outlined in the study's overall Data Monitoring Plan, in accordance with regulatory guidelines.

Conclusion

The structured implementation of KRIs enhances eDiary data monitoring by supporting regulatory compliance and early detection of assessment inconsistencies at a patient level, excessive completion time, and data plausibility concerns. This enables greater trial efficiency, timely decision-making, and reliable data quality.

1. FDA Guidance for Industry: Oversight of Clinical Investigations — A Risk-Based Approach to Monitoring (2013) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/oversight-clinical-investigations-risk-based-approach-monitoring
2. EMA Guideline on computerised systems and electronic data in clinical trials (2023) https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-computerised-systems-and-electronic-data-clinical-trials_en.pdf
3. ICH HARMONISED GUIDELINE FOR GOOD CLINICAL PRACTICE E6(R3) https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf

Scan the QR code to contact the author