



From Information to Insight:

Harnessing Centralized Monitoring in RBQM to proactively
identify and mitigate risks in Clinical Trials

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The Imperative for Effective Risk Based Quality Management (RBQM)

- Exponential increase in trial data volume.
- More endpoints and decentralized elements.

Growing Data Complexity



- 100% SDV $\neq$ 100% Quality
- Reactive, costly and late issue detection.

Traditional Monitoring Limits



CENTRALIZED MONITORING (CM):
Key enabler of RBQM



RBQM is essential to ensure data quality and patient safety in an increasingly complex clinical trial landscape.

Critical to Quality Factors (CtQFs)

- Focus on what truly impacts patient safety and data integrity

Key Risk Indicators (KRIs)

- Early signals to detect emerging risks

Quality Tolerance Limits (QTLs)

- Thresholds to trigger timely action

Data Quality Assessments (DQAs)

- Identifies unknown risks beyond KRIs and QTLs

Together, CtQFs, KRIs, QTLs and DQAs enable a proactive, data-driven approach to quality by shifting monitoring from reactive to predictive.

Central Monitoring Strategies - Insights from Clinical Trial Case Studies:

Why RBQM matters?



Trial Data Reliability

- Detects inconsistencies and atypical patterns early



Subject Safety

- Identifies safety signals across sites and patients



Endpoint Integrity

- Ensures sufficient, high quality data for valid conclusions

Centralized Monitoring Use Cases

Vitals Analytics

- Within-patient variability
- Cross-patient and site level comparisons

Assessments (Time/Date Analysis)

- Visit window deviations
- Data fabrication or backdating risks

Investigational Product (IP)

- Compliance Trends
- Missed doses and overdose detection

Vitals (Within/Across patient variability)



Aim: Identifying clinically meaningful and significant variations in vital signs that may indicate:

- ✓ Potential subject safety concerns
- ✓ Data irregularities or measurement bias



Central Monitoring approach

Data Evaluation

- Heart Rate
- Blood Pressure
- Temperature

Analytics Performed

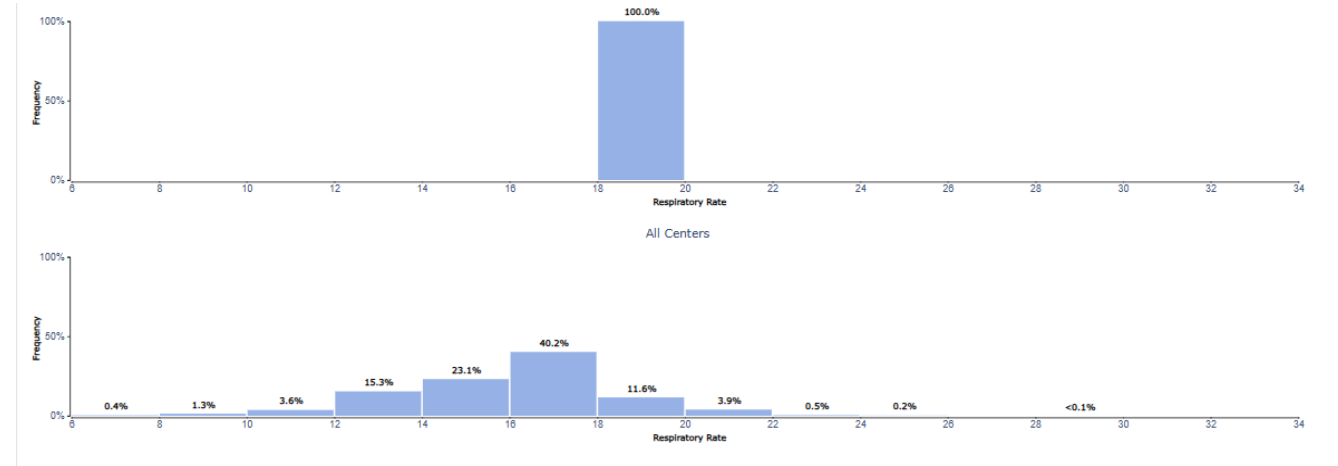
Within-patient trend analysis
Across patient trend analysis
Outlier and pattern detection using algorithms

Risk Interpretation

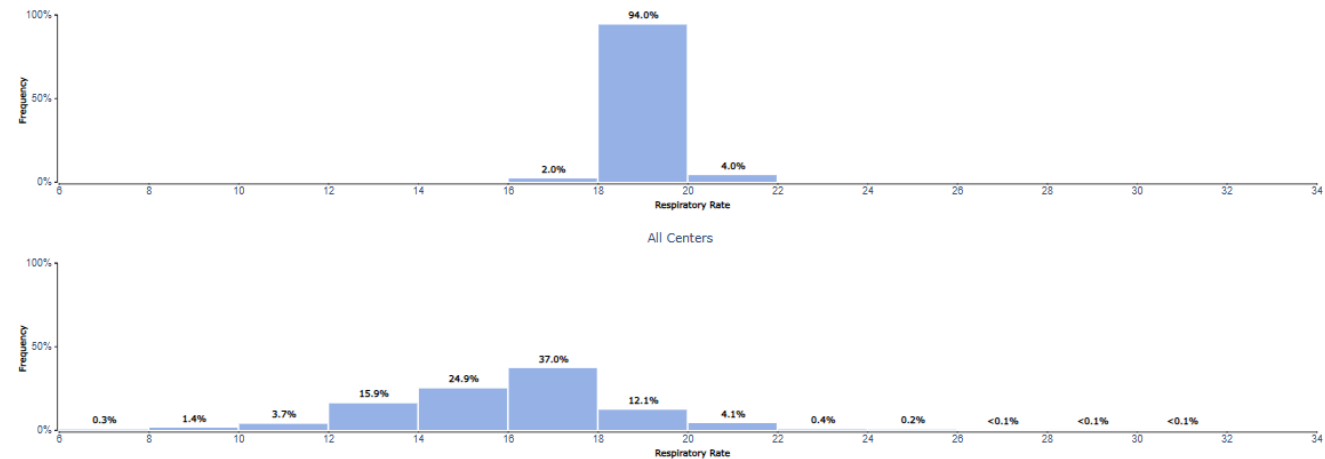
Distinguish expected physiological variability
Flag deviations exceeding predefined thresholds

Case Study - Vital Signs - Respiratory Rate (Higher Rate of Propagation)

Internal Patient Identifier	Visit Name	Respiratory Rate
118000	Day 1 (Visit 5)	18
118000	Day 1 (Visit 5)	18
118000	Week 4 (Visit 6)	18
118000	Week 4 (Visit 6)	18
118000	Week 8 (Visit 7)	18
118000	Week 8 (Visit 7)	18
118000	Week 16 (Visit 9)	18
118000	Week 16 (Visit 9)	18
118000	Week 20 (Visit 10)	18
118000	Week 20 (Visit 10)	18
118002	Day 1 (Visit 5)	18
118002	Day 1 (Visit 5)	18
118002	Week 4 (Visit 6)	18
118002	Week 4 (Visit 6)	18
118002	Week 8 (Visit 7)	18
118002	Week 8 (Visit 7)	18
118003	Day 1 (Visit 5)	18
118003	Day 1 (Visit 5)	18
118003	Week 4 (Visit 6)	18
118003	Week 4 (Visit 6)	18
118003	Week 8 (Visit 7)	18
118003	Week 8 (Visit 7)	18



Next month outcome after CM intervention:



Central Monitoring observation:

- ✓ 03 subjects – multiple visits per subject.
- ✓ RR recorded as 18 breaths/min at every visit.
- ✓ No within-patient or across patient variability observed.

Why this triggered review?

- ✓ RR is a physiological parameter and expected to vary.
- ✓ Identical values across visits suggest systemic propagation.

Case Study – Vital Signs (Pulse Rate)

Data from a Respiratory Infection trial:

Subject #	Pulse Rate
Subject 1	112
Subject 2	72
Subject 3	48
Subject 4	104
Subject 5	96
Subject 6	88

What is your finding for the given data set?

KEY OBSERVATION

All the recorded values are divisible by 4.

No odd number respiratory rates observed.

Possible Explanations Identified

- Measurement Practice Variability:
Pulse Rate measured for 15 seconds and multiplied by 4.
Instead of direct 1 minute observation as per protocol.
- Process Standardization Bias
Use of rounding or shortcut measurement techniques.
Site level habit rather than subject-driven variability.
- Training or SOP gap
Inadequate understanding of protocol-defined measurement method.

Outcome after CM intervention:

- Targeted Site Action:
Site contacted for clarification and retraining.
Measurement procedure reviewed and reinforced.
- Data Quality Impact:
Improved variability in subsequent data.
- RBQM Value Demonstrated:
Early detection without on-site visit
Focused intervention instead of blanket SDV.

Assessments - Ensuring Timeliness and Consistency



Assessments (Time/Date Analysis)



Aim: Maintaining consistency and reliability of assessments according to protocol-defined timeframes.



CM Approach:

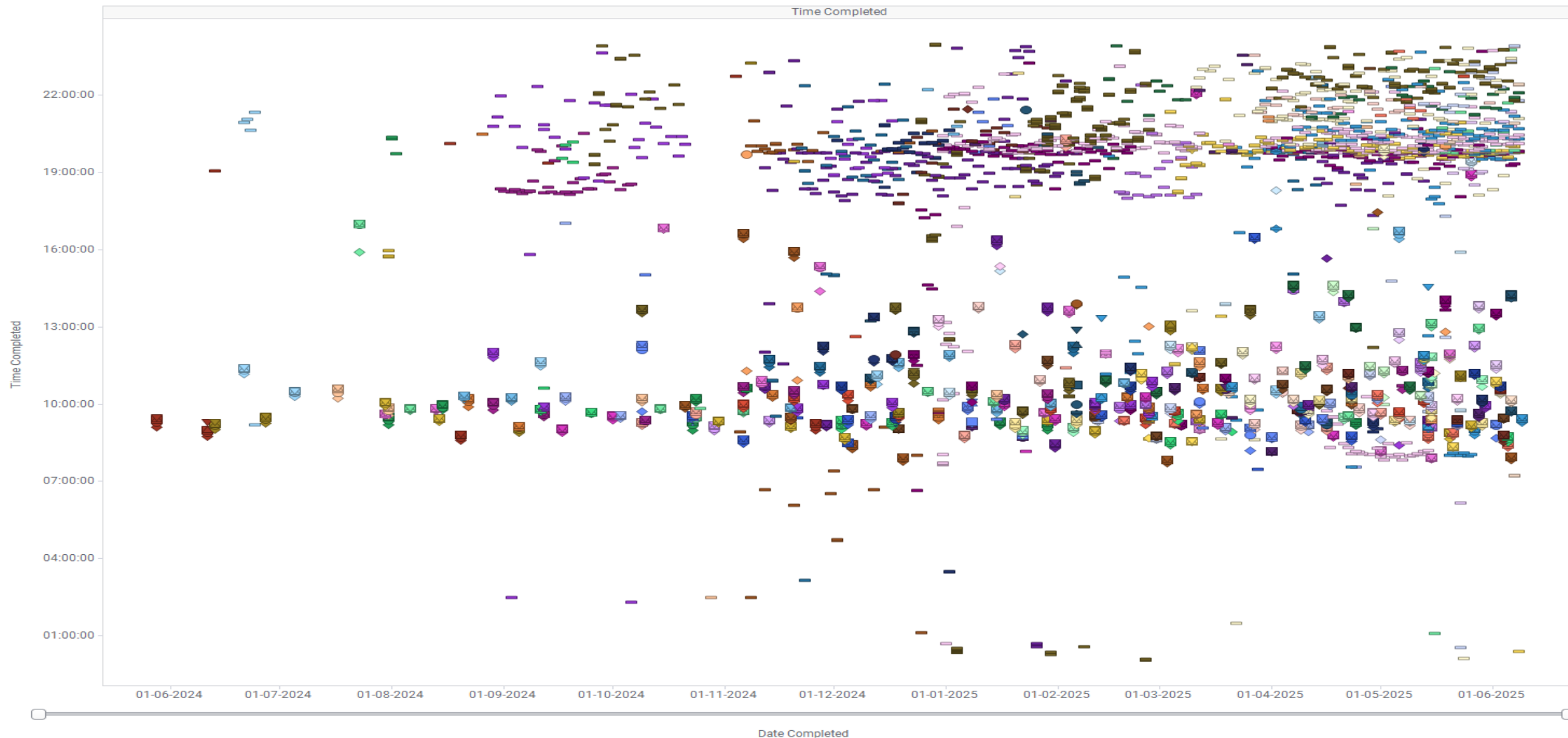
- CM focuses on ensuring assessments are carried out in alignment with protocol-defined timeframes.
- Identifies risks introduced by delays, missed assessments, or deviations that affect data quality.

Example Scenarios:

- Central monitoring highlights data entries made at improbable times (e.g., weekends, late nights) not consistent with typical site patterns.
- Especially concerning if these entries reveal suspiciously uniform results, indicating potential data manipulation.

Case Study 1 - Time & Date Analysis

Time Completed vs. Date Completed



Scenario 1: ePRO Assessments to be completed during onsite visits



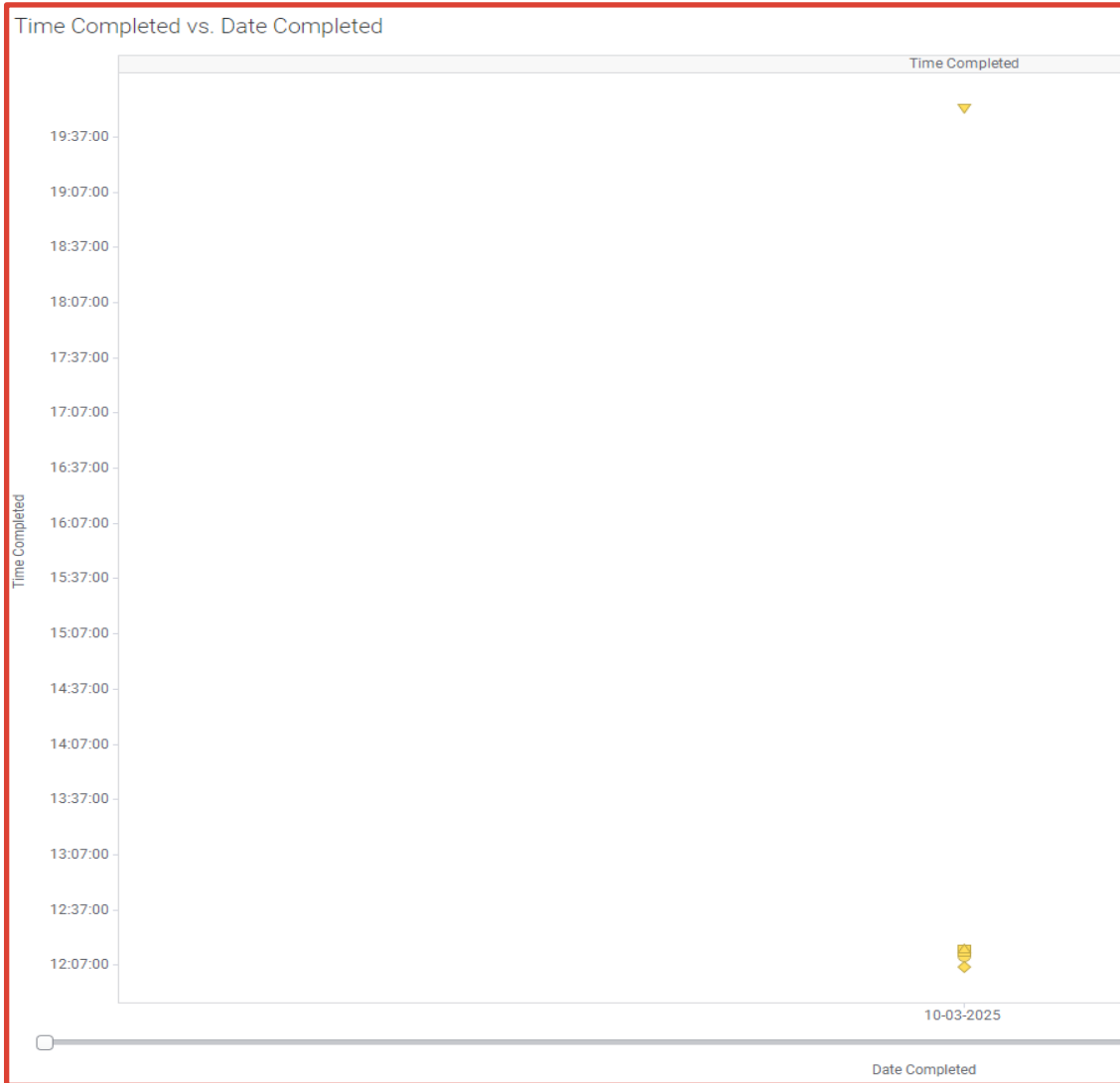
Data Signal Observed:

- Data analyzed-
 - ePRO completion date and time stamps
 - Visit type: Onsite clinic visit
 - Expected completion window: During clinic hours
- Observed pattern-
 - Visit date: 11-March-2025
 - ePROs completed around 22:09 (10:09 PM)
 - Entry outside normal operating hours.

POSSIBILITIES????????????

- ✓ ePRO completed after clinic visit, not in real time.
- ✓ ePRO was completed remotely.
- ✓ Delayed data entry.
- ✓ Inadequate site training on ePRO completion requirements.

Scenario 2: ePRO Assessments to be completed during onsite visits



Central Monitoring observation:

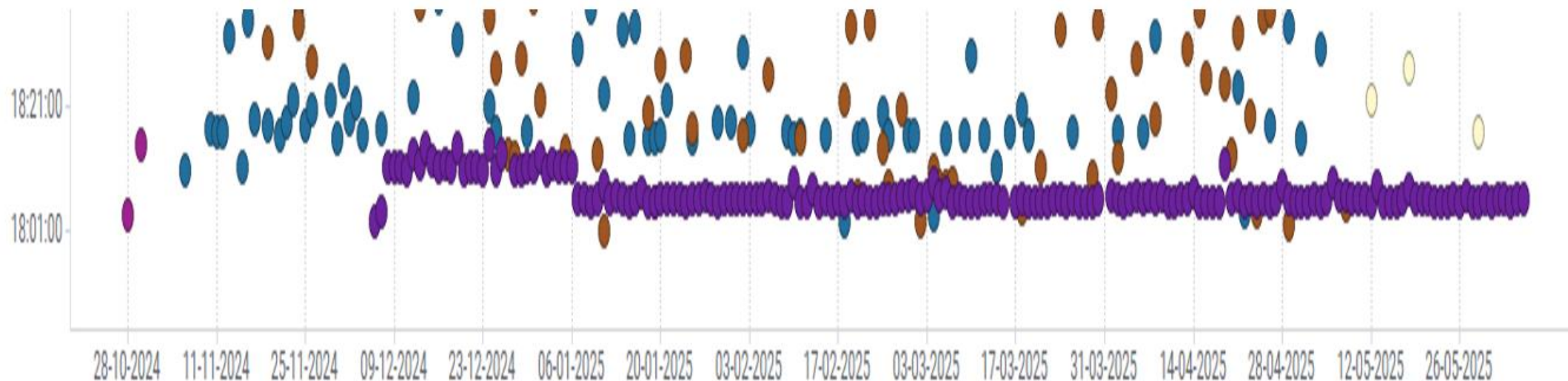
- ✓ Visit date: 10 March 2025
- ✓ ePRO completion timestamps showed two distinct clusters: 12:00 PM and 19:52 PM (approx. 08 hours gap).
- ✓ All entries recorded on the same visit date.

Why this triggered review?

- ✓ On-site visit assessments are expected to be completed within a narrow visit window.
- ✓ Wide time separation suggests non-uniform assessment execution.

What is your finding for the given data set?

Case Study 2 - Daily Dosing Diary



Data Signal Observed:

- Data Reviewed-
 - IPF daily dosing diary completion timestamps.
 - Study period: October 2024 – March 2025
- Observed pattern-
 - Majority of diary entries completed between 6:05 PM and 6:11 PM.
 - Pattern persists across multiple weeks.

POSSIBILITIES??????
???????

Investigational Product (IP) - Compliance & Safety

Aim: Ensuring correct investigational product administration, compliance (Missed/Overdose) and patient safety.

CM Approach:

- CM triggers alerts when compliance falls below acceptable thresholds.
- Triggers alerts when potential overdoses may have occurred.
- Assesses factors that could lead to missed doses (e.g., medication complexity, patient forgetfulness, lack of understanding).
- Assesses factors that could lead to overdoses (e.g., dosage errors, miscommunication).

Benefits:

- Reduces the risk of trial disruption due to non-compliance.
- Enhances data quality related to IP administration.

Case Study 1 - IP Compliance

A genetic disorder study using IP in the form of Ointment (to be applied topically)



The Challenges:

Confusion over correct amount of ointment application (ointment/gel based IP).
Potential for IP sharing with non-participating family members (genetic disorder context).



Mitigation:

Training: Site & Subjects trained on IP usage guidelines.

Dosing Cards: Provided to patients for uniform IP application.

IP Weighing: Tubes weighed before dispensing and upon return. Visualizations identify non-compliance trends.

ePRO Dosing Diaries: Subjects record doses daily, allowing central identification of missed doses.

Benefit: Ensures consistent IP exposure and accurate efficacy assessment

Case Study 2 – Out Of Window IP Compliance

OOW outlier:



After CM mitigation strategies:



Central Monitoring observation:

- Site ID: XXX
- Higher proportion of OOW IP administration compared to study baseline.
- Signal strength:
 - Site – 27.5% OOW
 - All centers – 5.1% OOW

Outcome after CM intervention:

- Reduction in OOW IP administrations.
- Signal strength:
 - Site – 7.0% OOW
 - All centers – 5.1% OOW
- Improved protocol adherence without on-site escalation.

The Power of Centralized Monitoring in RBQM

Central Monitoring (CM) enhances clinical trial oversight by utilizing sophisticated tools, such as statistical detection, cross-site and cross-subject comparisons and Key Risk Indicator (KRI) trends, to identify critical outliers in data reliability, safety, efficacy and subject retention.

Through real-time monitoring, CM swiftly detects anomalies and potential risks, allowing for immediate interventions that maintain trial integrity and safeguard participant safety. These proactive measures facilitate rapid responses to unexpected issues, fostering trust among stakeholders and improving overall trial outcomes.

By ensuring transparency, optimizing data quality and adhering to regulatory standards, CM supports adaptive trial designs and enhances participant engagement, ultimately contributing to the successful completion and credibility of clinical research endeavors.

**THANK YOU
FOR
YOUR ATTENTION**



GSK