

Key Considerations in QTL Monitoring Tool Design



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Monitoring Clinical Trials

Standard KRIs

- Portfolio, TA, Program and Study level
- Identify systemic issues with overall/general quality
- Thresholds determined based on historical data, industry standards and agreed on governance level

Example

Time to Data Entry, Adverse Event rate, Protocol Deviation (PD) under/over reporting, PD category trend analysis

KRI

- Trial, country, site level, subject level to drive day-to-day actions and mitigations
- Impact on subject safety and/or data integrity varies low/medium/high
- Operational focus providing indication of risk
- Thresholds can be TA, compound or study specific

Example

Number of missing imaging assessments

QTL

- Trial level
- Breaching a QTL indicates **High impact** on subject safety and/or data integrity
- Linked to Scientific question of the study and Estimand / Statistical Analysis Plan
- Study specific thresholds

Example

% annual drop out rate

Critical to Quality Factor
Study Specific Monitoring

QTL Monitoring Tool Development

Define Parameter

- Identified by QTL Study Team
- Parameter is the leading variable in the development of the monitoring tool

Define Thresholds

- Simulate data to investigate impact
- Benchmark against similar studies/ historical data
- Apply different assumptions to the sample size calculation

Impact

- Verify what the study circumstances related to defined parameter are

Select Variables

- Variables from eCRF or Vendor database that identifies QTL

Collaboration between the Central Monitor, Monitoring Tool Programmer, Statistician and Clinician

QTL Monitoring Tool Calculation

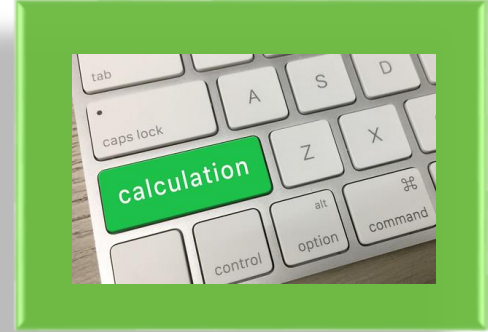
$$\frac{x}{y} = \% \text{ or Rate}$$

number of subjects who
discontinued study
treatment early

number of subjects
randomized to date

=

Percentage of
subjects that
discontinued
treatment early



QTL study team identifies which CTQs will have an impact on the **scientific question and the statistical analysis** of the study and determine the associated QTL parameter

Key Considerations for QTL Monitoring Tools



$$\frac{x}{y} =$$

Percentage of subjects for whom questionnaire assessment was not evaluable at Day XX.

What are circumstances and possible scenarios?

Subject completed 5 from 10 questions of the questionnaire

Subject completed questionnaire at Day XX

Subject discontinued from the trial before Day XX

Subject didn't complete questionnaire at Day XX

Subject is randomized

What are variables describing identified circumstances?

Questionnaire actual completion score

Randomization date

Questionnaire/Day XX date

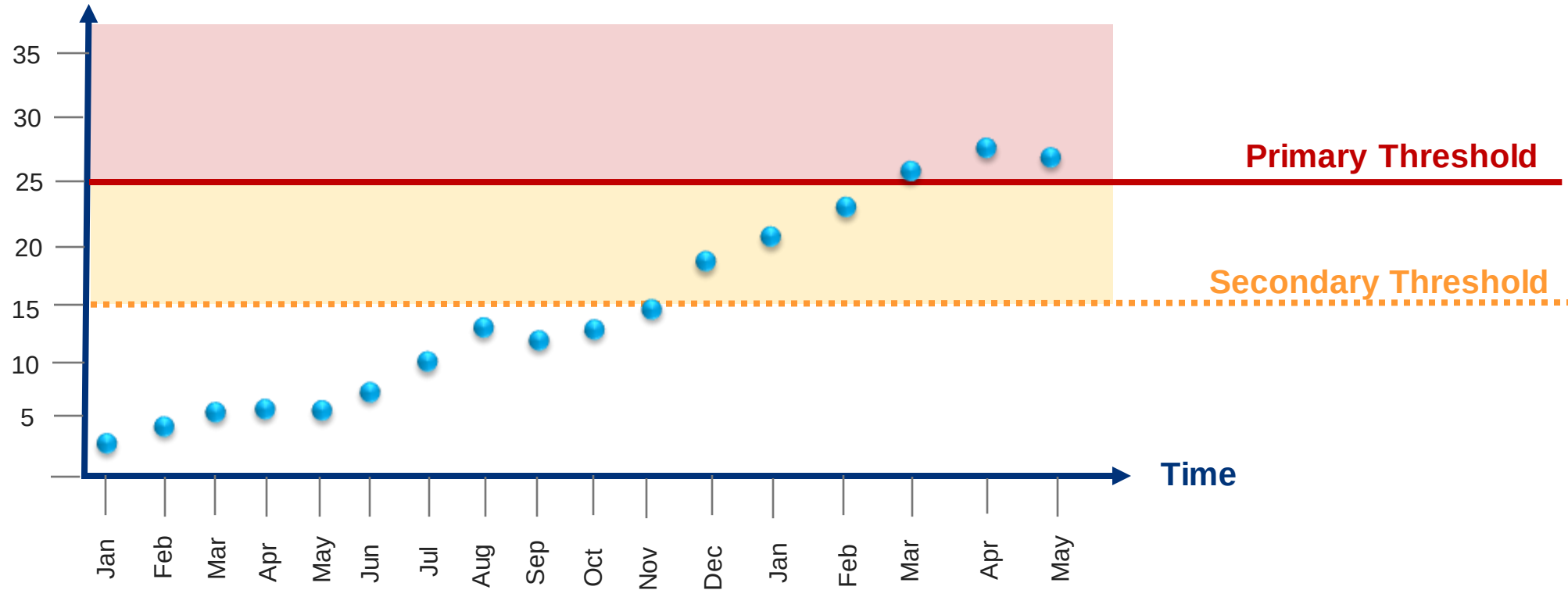
Expected Day XX date

Trial discontinuation date

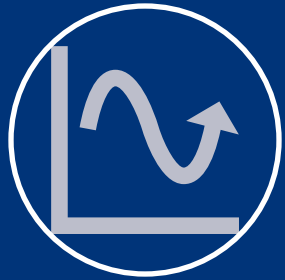
QTL Monitoring Tool in Practice



Parameter



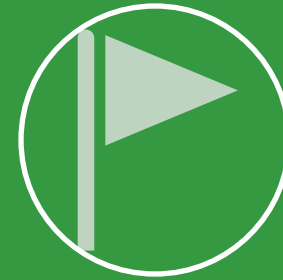
QTL Monitoring Tools Key Takeaways



Study specific
set up



Close
collaboration and
communication



Early signal
detection enables
real time action

Successful QTL Monitoring

Thank you for your attention



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