TMF Quality Reviews using Risk-Based Approaches Up-taking an ISO / ANSI method

Dr. Katharina Weisrock
Global Clinical Development & Operations
Boehringer Ingelheim Pharma GmbH & Co. KG

Meet the Speaker

Dr. Katharina Weisrock

Title: Principal Process Capability Manager

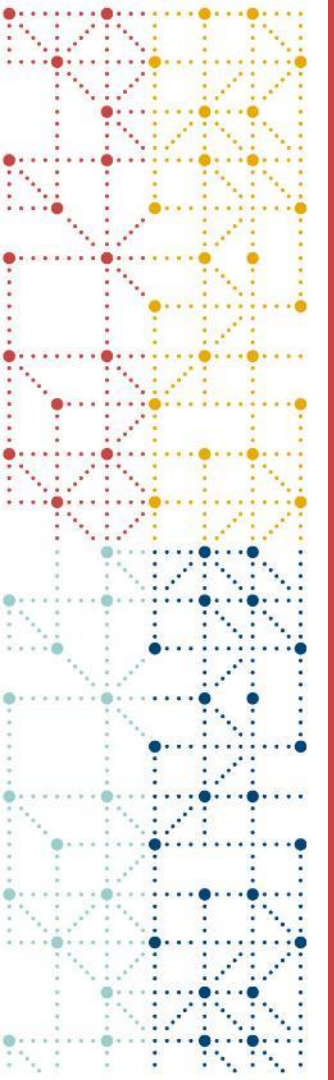
Organization: Boehringer Ingelheim Pharma GmbH & Co. KG

Dr. Katharina Weisrock is an experienced driver of global clinical quality initiatives and is currently leading an Initiative on TMF Oversight at Boehringer Ingelheim Pharma GmbH & Co. KG. In addition to her primary job function she is highly interested in brining industry-standards and digital innovation together to embrace quality by design in clinical settings. She has wide range of experience in academic research, animal health, pharmacovigilance, mergers and digital implementation.

Disclaimer and Disclosures

- *The views and opinions expressed in this presentation are those of the author(s) and do not necessarily reflect the official policy or position of CDISC.*

- *The author(s) have no real or apparent conflicts of interest to report.*
- *Intended Audiences Notice*
  - *For presentation at CDISC 2024 Europe Interchange*
  - *Any unauthorized review, use, disclosure, copying or distribution is strictly prohibited.*



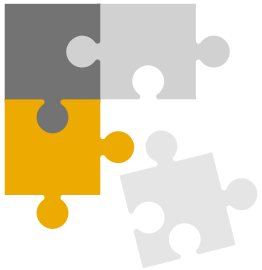
Agenda

1. Challenge
2. Method
3. Attributes
4. Feedback

Challenge

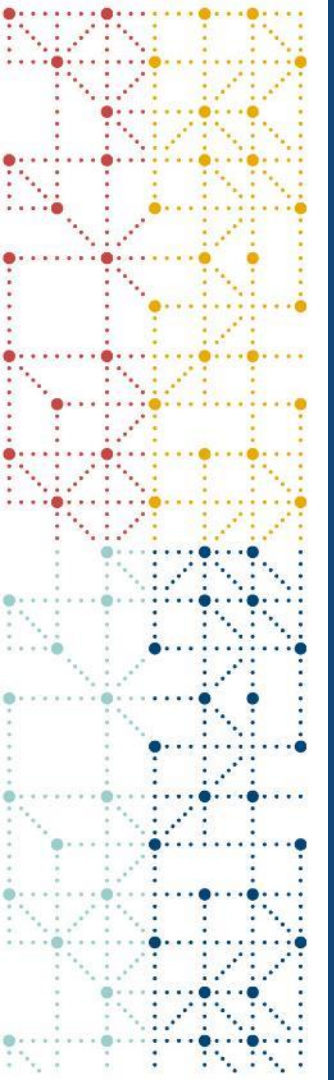
- Lack of industry-wide standards & guidance
- What do you need QC checks for: archiving, TMF transfer, routines?
- How to determine the appropriate proportion of trial documentation to consider for QC ?
- What is the rationale for risk-based approach?
- How to justify the selection of e.g., 15% or 50% of records for QC?
- Can your company adapt its approach based on trial design and status, or is a baseline approach required for trending?

Could we use a Method?



Adopting ISO 2859-1 / ANSI ASQ Z1.4

- establish sampling plans for risk-based QCs by using pre-defined parameters (AQLs & Inspection Levels)
- control continuous record filing series based on pre-defined attributes
- count numbers of nonconformities in a series of records, with respect to a given requirement or set of requirements.



Let´s try this!

What do you want to know?

Attributes and Inspection Level

What is your question or hypothesis to test?

What are your critical to quality factors?

Level of insights?

Critical to Quality Factors

ANSI method is highly adaptable to any settings used in a clinical trial, any process reviews or can be used as a baseline oversight approach leading to signals.

In Practice

ISO 2859-1 / ANSI ASQ Z1.4

Example
General Inspection Level (Normal) and 4 % AQL Limit:

Lot	Sample	Acceptance Quality Limit (AQL)
1500	125	10 accept / 11 reject
9000	200	14 / 15
36000	315	21 / 22

Lot	Sample	Acceptance Quality Level (%)
A Lot or Unit is a set of continuous and comparable records for review.	Based on pre-defined Inspection Level and Acceptance Quality Level, the sample is randomly derived from the lot.	Percentages of conformities or nonconformities are derived from ANSI parameters. 97% passed review and there was no signal. Switching rules are based on the trend over time.

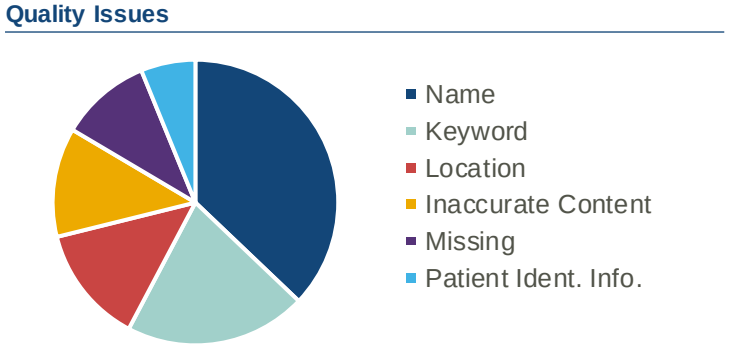
Quality Tolerance & Acceptance Levels

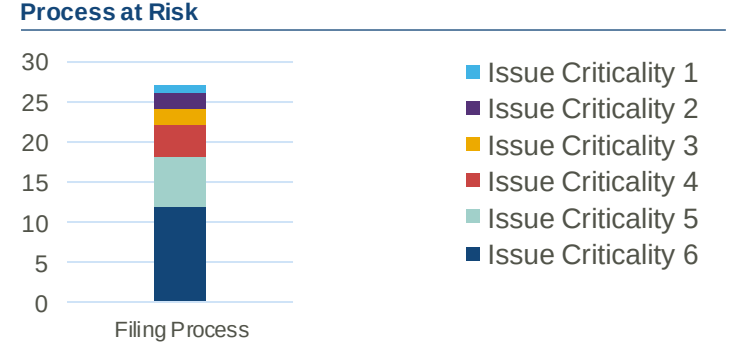
Assessment

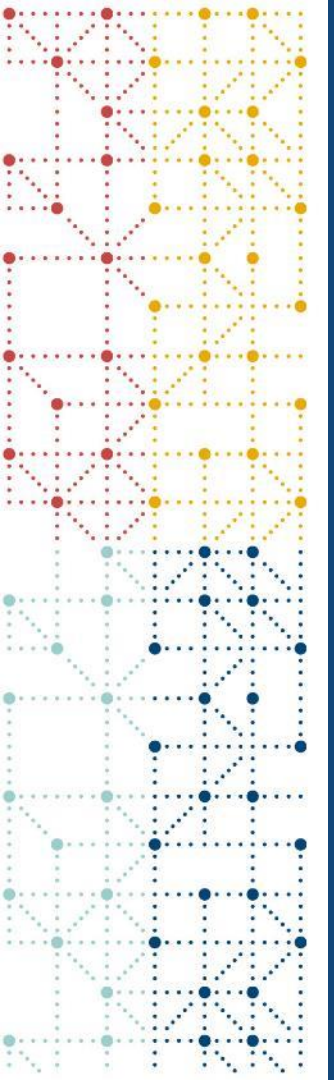
Based on Critical to Quality Factors and Inspection Level & AQL used it is assessed if sample quality meets the expectation

- Signal Management
- Meaningful Trends
  - Switching rules
  - AQL adaptation
  - Hypothesis review

Example:
Continuous positive Trend after e.g., 5 reviews.
Switch rule to reduced general inspection level







Feedback

Did you find out what you wanted to know?

Benefits

ISO 2859-1 / ANSI ASQ Z1.4 :

- Easy to use sampling plans and tables.
- Considerations
  - Attributes
  - Critical to Quality Factors
  - Unit(s)
  - Acceptance Quality Level(s)
- Highly adaptable to needs

Thank You!

Dr. Katharina Weisrock

Global Clinical Development & Operations

Boehringer Ingelheim Pharma GmbH & Co. KG

Binger Str. 173 | 55216 Ingelheim am Rhein

T +49 (6132) 77-142357

M +49 (151) 15021681

E katharina.weisrock@boehringer-ingelheim.com

ICH E8 (R1) §3 Designing Quality into Clinical Studies