Best practices in Quality Metrics

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Management reviews & quality metrics have existed for a while

Management review should provide assurance that process performance and product quality are managed over the lifecycle. …management review can be a series of reviews at various levels of management and should include a timely and effective communication and escalation process…

— ICH Q10 Pharmaceutical Quality System —

Management with executive responsibility shall review the suitability and effectiveness of the quality system at defined intervals and with sufficient frequency according to established procedures to ensure that the quality system satisfies the requirements of this part and the manufacturer’s established quality policy and objectives

— 21 CFR, Part 820.20 (c) —
Quality metrics have become increasingly important for the pharmaceutical industry.

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<th>What are Quality metrics?</th>
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<td>▪ Important component of an effective quality management system; enables thorough oversight of drug quality</td>
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<td>▪ <strong>Objective measurements</strong> of quality performance and maturity of a site or the entire manufacturing network</td>
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<td>▪ Critical tool to ensure robust manufacturing process and operational reliability; enables continuous improvement of process performance and product quality</td>
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<td>▪ Tool to <strong>baseline &amp; benchmarking</strong> quality across sites/organizations</td>
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<th>Why are KPIs / metrics becoming increasingly important?</th>
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<td>▪ Increasing focus on customer safety &amp; regulatory compliance</td>
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<td>▪ Increasing cost of non-conformance</td>
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<td>▪ Need to drive continuous improvement</td>
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We have studied quality metrics for years through several industry-wide efforts.
7 key learnings from our quality metrics research

1. Good sustainable quality outcomes are driven by three foundational blocks.

2. There is significant variability in performance across pharma companies in India & across different sites.

3. Unbalance observed towards lagging metrics vis-à-vis leading metrics which limits prediction and prevention.

4. Advanced companies use leading metrics to predict & correct quality outcomes proactively.

5. Metrics need to be cascaded down to the shop floor level and linked to performance KPIs.

6. Effective cross-functional review forums are critical for root cause assessment & decision making.


SOURCE: McKinsey analysis
Good sustainable quality outcomes are driven by three foundational blocks:

1. **Quality outcomes**
   - **Quality performance**
     - Patient safety, efficacy, compliance, availability etc.
   - **Total cost of quality**
     - Direct and indirect financial impact

2. **Foundational blocks**
   - **Operational maturity** (process & product robustness)
     - Right first time (or lot acceptance)
     - Reject rate
     - Deviations rate
   - **Quality systems maturity**
     - CAPA effectiveness
     - Recurring (repeat) deviations
     - Supplier certification
   - **Quality Culture maturity**
     - Preventive maintenance
     - CAPA with preventive actions
     - Non-conformities without confirmed root causes

SOURCE: McKinsey Analysis
We observe significant variability in performance across Indian pharmacos/sites. Select example.

**Quality outcomes**
- **Recall events**
  - Top Q: [Bar Graph]
  - Bottom Q: [Bar Graph]
  - ~67% difference

- **Confirmed complaints**
  - Top Q: [Bar Graph]
  - Bottom Q: [Bar Graph]
  - ~11x difference

**Total cost of quality**
- **QC productivity**
  - Top Q: [Bar Graph]
  - Bottom Q: [Bar Graph]
  - +60% difference

- **QA productivity**
  - Top Q: [Bar Graph]
  - Bottom Q: [Bar Graph]
  - +189% difference

**Operational maturity**
- **Right-first-time**
  - Top Q: [Bar Graph]
  - Bottom Q: [Bar Graph]
  - +6% difference

- **Deviation rate**
  - Top Q: [Bar Graph]
  - Bottom Q: [Bar Graph]
  - -60% difference

**Quality maturity**
- **Recurring deviations**
  - Top Q: [Bar Graph]
  - Bottom Q: [Bar Graph]
  - -68% difference

- **Investigations over 30 days**
  - Top Q: [Bar Graph]
  - Bottom Q: [Bar Graph]
  - -73% difference

SOURCE: POBOS Quality, POBOS Manufacturing
Typically, we observe an unbalance in Quality KPIs towards lagging metrics, limiting prediction and prevention.

1 KPIs that show past performance; 2 Indicators that give an indication of future outcome

SOURCE: Interviews with Quality experts and companies
We have shown a link to quality performance (lagging) indicators for certain operational and quality system maturity (leading) indicators.

**Quality performance**
- Complaints
- Recalls
- Regulatory observations
- Adverse events

**Quality system maturity**
- Deviations recurrence
- Supplier certification
- Investigations and CAPA cycle time

**Operational maturity**
- Deviations rate
- Right first time
- Reject rate

P-value is probability that correlation between X and Y is zero, value below 0.05 indicates statistically significant results.

SOURCE: POBOS Pharma Quality; POBOS Medical Device Quality; ISPE Quality Metrics initiative
We have shown how quality culture indicators influence quality maturity and performance.

Correlations with p-value <0.05

- Quality system maturity
  - Lab errors
  - Deviations recurrence
  - Deviations without assigned root cause
  - Planned maintenance rate
  - CAPA with preventive actions
  - Culture survey scores

- Quality performance
  - Complaints
  - Recalls
  - Right first time
  - Reject rate
  - Rework rate

- Operational maturity
  - Prevention focus
  - Employee turnover rate
  - Embeddedness

P-value is probability that correlation between X and Y is zero, value below 0.05 indicates statistically significant results.

1 Operations FTEs engaged in quality work out of total FTEs engaged in quality work (Quality or Operations personnel)

SOURCE: POBOS Pharma Quality; POBOS Medical Device Quality; ISPE Quality Metrics initiative
Examples of these correlations

**Total recalls with Recurring deviation rates**

**Total Recall Events, # of annual recalls**

![Graph showing correlation between Total Recall Events and Recurring Deviation rate.](image)

- **R² = 48%**
- **P = 0.00**

**Confirmed complaints with Investigation quality**

**Confirmed complaints with Investigation quality**

![Graph showing correlation between Investigation quality and Confirmed complaints.](image)

- **R² = 0.27, p = 0.001**

**Total complaints with Planned maintenance rate**

**Total complaints rate (including LOE)**

![Graph showing correlation between Total complaints rate and Planned maintenance.](image)

- **R² = 46%**
- **P-value = 0.00**

**Lot acceptance rate with Quality culture scores**

**Lot acceptance rate, % of lots dispositioned (not rejected)**

![Graph showing correlation between Lot acceptance rate and Quality culture scores.](image)

- **R² = 0.29**
- **P-value = 0.001**

**Note:** Images include correlation plots for the variables mentioned. Each graph illustrates the correlation between two variables, with **R²** indicating the proportion of variance explained and **P-value** indicating statistical significance. The plots demonstrate the relationship between Total recalls with Recurring deviation rates, Confirmed complaints with Investigation quality, Total complaints with Planned maintenance rate, and Lot acceptance rate with Quality culture scores, highlighting the importance of quality metrics in healthcare.
Advanced companies use leading metrics to predict & correct quality outcomes – Case Example

High degrees of KQI correlations found along pyramid of incidents...

Correlation coefficients between Quality metrics (perfect correlation = 1.00)

- Total cost of recalls: 0.43
- Number of recalls: 0.56
- Complaints rate: 0.71
- Rejects rate: 0.91
- Deviations rate: 0.96
- Right first time rate: 

Example of Quality metrics correlation at a selected site

- Deviations: % of batches produced
- Rejects: % of batches produced
- Complaints: Absolute no of complaints received

- Rising deviation rates provide early warning
- 4 months time shift (correlation 0.83)
- Reject rates typically rise 4 months later
- Issues iwere detectable ~ 6 months prior to crisis
- 6 months time shift (correlation 0.86)

SOURCE: McKinsey Analysis
Metrics need to be cascaded down to the shop floor level and linked to performance KPIs - Pharma plant example
Effective cross-functional review forums are critical for root cause assessment & decision making.
Digital & Advanced Analytics approaches significantly reduce manual effort required and improve quality of insights & decision making - Deviation reduction example

Exploratory advanced analytics models to reduce deviations

Root cause suggestion through predictive algorithms

Product mastery to increase process/product capability

Advanced analytics platform: real time data from local and global systems keeps teaching and improving the model

Data lake
Collection and easy retrieval of data sources

Natural Language Processing

New deviation
Root cause
Probability
Drivers
RC A
70%
Driver 1
Driver 2
RC B
30%
Driver 1
Driver 2

Root cause A
Root cause B

Driver 1
Root cause A
70%

Driver 1
Root cause B
30%

Root cause B

Past examples

# deviations/1000 batches

CAPA1
<XX>

CAPA2
<XX>

Production data

Deviations

CAPAs

SOURCE: McKinsey Analysis
THANK YOU

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