Best Practices, Metrics and Symbolic Action
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Sun Pharmaceutical Industries Limited
Metrics: How Healthy is your Organization?
Quality metrics are used throughout the pharmaceutical industry to monitor quality systems, processes and drive continuous improvement efforts in drug manufacturing. Quality Metrics (QM) are the refined and systematic representation of Quality manufacturing operation.
The IPA Quality forum was setup 3 years back, by a group of 6 founding member companies, and supported by McKinsey & Company as their knowledge partner.

IPA QF Mission

- Be the conduit of change through thought leadership, knowledge development, and best practice sharing
- Measure, benchmark, and publicise the achievements of the Indian Pharma Industry in Quality
- Expand the size and base of Quality talent in India
- Deepen, and strengthen the industry’s relationship with key stakeholders – both within and outside India
- Provide platforms for members and other stakeholders to interact and network
• Measure current performance to enable continuous improvement
• Bring cost efficiencies
• It is an expectation from Regulator Agencies
• Would enhance risk-based surveillance inspection
• Predicts future failures for prevention
• Reduce recalls
• Revert Quality related drug shortages
Parameters used to measure quality, performance and analyze trends
- Assigned a weightage based on criticality
- Quality score for each parameter in percentage
- Overall Site Quality Index is cumulative score of individual parameters
- Targets set for Site Quality Index
  - >95 : Green
  - 85-94 : Yellow
  - ≥85 : Red

<table>
<thead>
<tr>
<th>Scoring Parameters</th>
<th>Monitoring Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change Control (CC)</td>
<td>Lot(s) Pending for Disposition &gt; 30 Days</td>
</tr>
<tr>
<td>Unplanned Deviation (UPD)</td>
<td>Lot(s) Reprocessing Rate</td>
</tr>
<tr>
<td>Out of Specification (OOS)</td>
<td>Out of Trend (OOT) and Laboratory Event</td>
</tr>
<tr>
<td>Corrective and Preventive Action (CAPA)</td>
<td>Environment Monitoring and Media Fills</td>
</tr>
<tr>
<td>Product Quality Complaint (PQC)</td>
<td>QC Productivity</td>
</tr>
<tr>
<td>Lot Rejection Rate / Lot Failure Rate</td>
<td>Service Level – Testing turnaround time</td>
</tr>
<tr>
<td>Stability</td>
<td>Instrument Utilization</td>
</tr>
<tr>
<td>Regulatory Inspections</td>
<td>Adherence of Preventive Maintenance / Calibration / Qualification schedule</td>
</tr>
<tr>
<td>Field Alert Report</td>
<td>Scale-up / Pre-validation issues</td>
</tr>
<tr>
<td>Product Recall / Sales Return</td>
<td>Internal Audit observation closure</td>
</tr>
<tr>
<td>Right First Time</td>
<td>Quality cost and Manpower Ratio</td>
</tr>
</tbody>
</table>
Harmonized Definition is a Must

• Each one will measure based on what they wants

• Align on the purpose and requirement and measure uniformly, assure your data is accurate
Tools as enablers for Data Analysis and Trending globally in a reliable manners

**TW Workflows for:**
- Change control
- Investigations
- OOS
- CAPA
- Deviations
- Complaints
- Global Assessments
- Recall Management

**Quality Management Systems**
- Approved Test Procedures and Specification for raw material, packaging material and finished product on LIMS
- Sample management and results in LIMS
- Chromatography instrument on Empower 3

**QC Laboratory**
- **Business Process Procurement-to-Release**
- **Document Control & Management**
- **Training & Learning**
  - Policy, Standards and Procedures on EDMS
  - Learning Management
  - Curriculum based on Roles
  - Training Material
  - Employee Database
# Example – Global Quality Index Dashboard

<table>
<thead>
<tr>
<th>Sites Name</th>
<th>Quality Index</th>
<th>Parameter</th>
<th>Target</th>
<th>85-94</th>
<th>&lt; 85</th>
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<tbody>
<tr>
<td>Site 1</td>
<td>99</td>
<td>10.0</td>
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<tr>
<td>Site 2</td>
<td>76</td>
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<td>Site 3</td>
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<tr>
<td>Site 4</td>
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<td>10.0</td>
<td>10.0</td>
<td>2.0</td>
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<tr>
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<td>10.0</td>
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<td>Site 6</td>
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<td>10.0</td>
<td>10.0</td>
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<tr>
<td>Site 7</td>
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<td>2.0</td>
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<tr>
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<td>10.0</td>
<td>10.0</td>
<td>2.0</td>
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<tr>
<td>Site 9</td>
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<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>2.0</td>
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<tr>
<td>Site 10</td>
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<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>2.0</td>
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<tr>
<td>Site 11</td>
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<td>10.0</td>
<td>10.0</td>
<td>2.0</td>
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<tr>
<td>Site 12</td>
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<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>2.0</td>
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<tr>
<td>Site 13</td>
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<td>2.0</td>
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<tr>
<td>Site 14</td>
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<td>Site 17</td>
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<td>10.0</td>
<td>10.0</td>
<td>2.0</td>
</tr>
</tbody>
</table>
Metrics: How to look at Data?
Who should look at the Data?

- Why we want to measure?
- What should be measured?
- How do we measure?
- What do we want to achieve?
- Analytics for actions and solutions
Metrics Governance and Review Structure

Cross functional involving Quality, Operation, R&D

MD-Managing Director-Quality Review Board
Global Quality Review Board
Regional Quality Review Board
Drug Formulation
API Mfg.
Site Quality Review
Site 1  Site 2  Site 3  Site 4  Site 5  Site 6  Site 7  Site 8  Site 9  Site 10  Site 11  Site 12

The management of QRBS shall be executed as a four tier process.
Shop Floor: Knowing how the Products are doing?
Training

- Trainer/Coach Qualification Program
- Integrated Site Training Calendar
- Corporate GMP/GxP Training Programs
  - GxP Training Library available 24x7
  - On-going GMP Training
  - On-Boarding GMP Training
- Technical Functional Training Programs
  - Operations Program
  - Sun Pharma Quality Control Program (SPQC)
  - Six Sigma Training for Product Performance and Statistical Analysis
  - Corporate Quality Certification programs: Auditor, Investigator/Approver and Microbiologist
- Behavioral Training and Development Programs
  - Leadership Capability
  - Managerial Capability
  - Supervisor Skills
  - Operator Level
Example 1 – Lot Rejection

- Assessment of individual rejection to understand whether it is product issue or operational failure
- Statistical trend analysis to understand process capability index and understand the repetitive nature
- Analyze the root cause and fix the problem by correcting the process/analytical method/material/equipment
- Example – dissolution failure due to method change
Example 2 – Product Complaints

**Product 1 - Nasal Spray**

<table>
<thead>
<tr>
<th>Year</th>
<th>Complaint</th>
<th>Root Cause</th>
<th>Corrective actions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>Non-operation of device</td>
<td>Complex device operating instructions</td>
<td>Design of the device changed for easy operation by end user</td>
</tr>
<tr>
<td>2017</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Product 2 - Tablets (Bottle Pack)**

<table>
<thead>
<tr>
<th>Year</th>
<th>Complaint</th>
<th>Root Cause</th>
<th>Corrective actions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>Broken Desiccant</td>
<td>Silica/Carbon particles coming out of desiccant canister</td>
<td>Canister replaced with Sachet</td>
</tr>
<tr>
<td>2017</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Example 3 – Product Complaints

Product 3 – Tablets (Bottle Pack)

<table>
<thead>
<tr>
<th>Year</th>
<th>Broken Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>16</td>
</tr>
<tr>
<td>2017</td>
<td>6</td>
</tr>
<tr>
<td>2018</td>
<td>5</td>
</tr>
</tbody>
</table>

Complaint: Broken Tablets
Root Cause: Shape and size of the desiccant container
Corrective actions: Shape of desiccant container changed

<table>
<thead>
<tr>
<th>Year</th>
<th>Change Implemented</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>16</td>
</tr>
<tr>
<td>2017</td>
<td>2</td>
</tr>
<tr>
<td>2018</td>
<td>0</td>
</tr>
</tbody>
</table>

Product 4 – Tablets (Strip Pack)

<table>
<thead>
<tr>
<th>Year</th>
<th>Bad Smell and Taste</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>77</td>
</tr>
<tr>
<td>2017</td>
<td>10</td>
</tr>
<tr>
<td>2018</td>
<td>0</td>
</tr>
</tbody>
</table>

Complaint: Bad Smell and Taste
Root Cause: Primary packing material (Al foil) containing ethyl acetate in ink used for printing
Corrective actions: Change to solvent free ink for printing on Al foil
Example 4 – Invalidated OOS due to Human Error

- Establish investigation teams to help identify correct root cause
- Revise test procedures to include clear instructions for chemist
- Providing test kits to the chemist which includes all glassware required for testing
- Feedback from chemist converted into solution themes for improvement
Sun - Quality Metrics Journey

Started this journey in 2015

- Harmonized Quality Metrics parameters
- Parameters redefined with targets
- Data Analytics; actions derived for improvement
- Predictive GMPs with Risk Assessment Tool

Currently aiming in 2019

Expanding, beyond metrics for Quality Management System, into Product performance (improving sigma levels)
Risk and escalation

Visibility
- Management review
- Cost of quality analysis
- Recall committee

Action
- Material review board
- Process improvement
- Efficiencies

Trending
- Management review
- Stability trending
- Annual product review

Monitoring
- Product complaints
- Deviations
- OOS
- QA self inspection

Risk visibility

Quantity
Overview of Site Risk Assessment Model

- **Initiate Quality Risk Management Process**
  - Risk Assessment
    - Risk Identification
    - Risk Analysis
    - Risk Evaluation
  - Risk Control
    - Risk Reduction
    - Risk Acceptance
  - Risk Review
    - Review Events

- **Risk Communication**
- **Site Action – Mitigation Control, Corrective Action**
- **Risk Assessment Dashboard**
- **Management Review**
Risk Assessment Tool covers
- GMP Compliance: Processes & Procedures and Product Performance
- Business: Service Levels and Quality Cost Element
Product Quality – True Root Cause Analysis

- 21st Century Quality Initiative for supplying robust products to patients
- An initiative on the lines of ICH Q10 for Product Lifecycle Management including post approval changes
  - Process Understanding
  - Product, Process & Analytical Assessment
  - DMAIC approach for improvement
  - Filing changes with Regulatory agency

• 21st Century Quality Initiative for supplying robust products to patients
• An initiative on the lines of ICH Q10 for Product Lifecycle Management including post approval changes
  • Process Understanding
  • Product, Process & Analytical Assessment
  • DMAIC approach for improvement
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![Diagram showing Process Capability with Six Sigma levels: 1 sigma, 2 sigma, 3 sigma, 4 sigma, 5 sigma, 6 sigma. The diagram illustrates the transition from "Here" to "There" with strategic and tactical leverage.](image-url)
Product Quality – PUR and PAR

- **Product Understanding Report (PUR)**
  - Process Map
  - Product & Process details
  - Specifications
  - Fish Bone – mapping the CQAs to the process steps
  - Control Strategy for materials and process steps
  - Heat map & FMEA for process parameters and its variable versus impact on CQAs
  - Heat map & FMEA for analytical method and its variable versus impact on CQAs
  - Risk Assessment for input material attributes versus CQAs
  - Risk Assessment for CPPs versus CQAs

- **Product Assessment Report (PAR)**
  - Statistical evaluation of historical data
    - Critical Process Parameters
    - Critical Process Attributes
    - Stability Data and Trends
  - External Quality Assessment
    - Confirmed Market Complaint
    - FAR
    - Recall
  - Internal Quality Assessment
    - Confirmed OOS (In-process, Finished product, Stability)
    - Major Changes
  - Define Sigma Level for the Product
DILBERT TEACHES ELBONIA “TOTAL QUALITY” METHODS.

YOU START BY IDENTIFYING PROBLEM AREAS.

HMM... SOMETIMES OUR MITTENS GET STUCK TO OUR NOSES AND WE CAN’T BREATHE.

YORGI! TRY TO BREATHE WITH YOUR MOUTH!

PEOPLE! LET’S TALK METRICS, PLEASE!
Utilizing Data to Drive a Culture Change towards Patient Care

Caring for Patients
Together with One Quality Voice
Thank you