21st Century Regulatory Surveillance:
Measuring the Effectiveness of Quality Management Systems

Ramona Wildgoose
Johns Hopkins Center of Excellence in Regulatory Science and Innovation (JHCERSI)
2022 Writing Competition
Word Count: 2,952 words
INTRODUCTION

The U.S. Food and Drug Administration (FDA) conducts three types of inspections: 1) for-cause, 2) pre-approval, and 3) routine surveillance inspections. At its most basic level, the purpose of routine surveillance inspections is to monitor the compliance of FDA-regulated establishments to U.S. law. The ultimate objective however, is to ensure that FDA-regulated products are safe, effective, and of high quality when they reach American consumers and that there is an adequate supply of critical-to-life products.

In fiscal year 2019, the FDA completed 94% of its 18,000 planned surveillance inspections.\(^1\) Despite the number of inspections completed, there were 373 recalls in 2019 and 531 recalls in 2020.\(^2\) Surveillance inspections are a review of quality systems, processes, and procedures at a specific point in time. As a standalone tool, they could be proactive if conducted more frequently (i.e., yearly or more) but this is impossible given the number of FDA-regulated establishments versus the number of FDA inspectors available. Therefore, surveillance inspections tend to be more reactive (responding to negative outcomes) than proactive (preventing negative outcomes). To improve their ability to prevent unsafe, low quality, or ineffective FDA-regulated products from reaching American consumers, the FDA must develop additional measures.

The FDA published two draft guidance documents in 2015 and 2016 for the pharmaceutical industry to implement a Quality Metrics Reporting program.\(^3\) Quality metrics reporting is expected to provide predictive signals alerting the agency to establishments at high risk of releasing unsafe, ineffective, or low-quality pharmaceutical products. The data would enable the FDA to take a data-driven, risk-based approach for allocating resources to surveillance inspections. The aim of the program is also to reward mature quality management systems using incentives such as reduced surveillance inspections.
Industry response to the 2015 draft guidance, which presented a mandatory reporting program, was resistant. Concerns included the FDA exceeding its statutory authority and the industry resource burden such a program would introduce (i.e., having to generate the proposed metrics on a regular basis). The 2016 revised guidance was toned down, presenting a voluntary program that allowed the FDA to trial quality metrics reporting with a small subset of companies. In 2022, the FDA presented findings from these programs which included learning how companies create and utilize internally reported quality metrics, differences between the industry’s metrics and FDA-proposed metrics, and how different metrics are reported differently among different sectors of the industry.

**PURPOSE**

The 2022 FDA Quality Metrics Reporting publication sought feedback from industry stakeholders on topics including but not limited to, frequency of reporting, other metrics that should be considered, and measurement of “Quality Culture”. This paper will assess the usual elements of quality management systems and identify the most important factors that affect quality management system maturity. Once identified, they will be compared to the FDA-proposed metrics to determine if additional factors should be included for measuring Quality Management Maturity (QMM).

**THE QUALITY MANAGEMENT SYSTEM**

**FOUNDATIONAL ELEMENTS OF THE QUALITY MANAGEMENT SYSTEM**

The International Organization for Standardization (ISO) introduced the widely adopted ISO 9001\textsuperscript{iv} international standard to specify the requirements of a quality management system
for any organization (i.e., irrespective of industry, size, or the types of products or services provided). The quality management system elements defined in ISO 9001 are as follows:

1. **Leadership** – Leadership and Commitment, Customer Focus, Quality Policy, Organizational Roles, Responsibilities, and Authorities
2. **Planning** – Addressing risks and opportunities, Quality objectives, and Changes to the QMS
3. **Support** – Communication, Awareness, Competence, Resources
4. **Operation** – Process planning and control, Product design and development, Supplier management, Production controls, Identification and traceability, Product release, Nonconforming product control
5. **Performance evaluation** – Internal audits, Management review, Customer satisfaction, Monitoring, measuring, analysis and evaluation of organizational data
6. **Improvement** – Nonconformities and CAPA, Continual improvement

The central elements of ISO 9001 are also very similar to the Total Quality Management (TQM) model. TQM as defined by the American Society for Quality (ASQ) is “a management approach to long-term success through customer satisfaction”. The 8 primary elements of TQM are:

1. Customer Focus
2. Total employee involvement
3. Process thinking
4. Integrated system
5. Strategic planning/management
6. Continual improvement
7. Fact-based decision making
8. Effective communication
Building on ISO 9001, the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) established the ICH Q10 guideline as a model for an effective Pharmaceutical Quality System. Common elements are shared between ISO 9001 and ICH Q10. According to ICH Q10, elements of an effective pharmaceutical quality management system include:

i) Process performance and product quality monitoring system

ii) Corrective action and preventive action (CAPA) system

iii) Change management system

iv) Management review of process performance and product quality

The University of St. Gallen (Switzerland), with FDA support, conducted a 3-year study of performance metrics from over 300 pharmaceutical manufacturing sites worldwide. The purpose was to develop a model to assess the state of pharmaceutical organizations’ quality systems. The St. Gallen Pharmaceutical Production System Model (PPSM) defines Pharmaceutical Quality System (PQS) Excellence as a combination of PQS Effectiveness and PQS Efficiency. In this model, Operational Stability has a significant impact on PQS Effectiveness and Supplier Reliability has a significant impact on PQS Efficiency. There are two foundations of this model – Cultural Excellence is the first, and CAPA Effectiveness is the second.

The above sources all describe abstract attributes that form the framework of quality management systems, but to develop metrics that predict risk of quality system failures, it is important to identify the critical factors affecting QMS effectiveness.
MEASUREMENTS OF QMS EFFECTIVENESS

CRITICAL ATTRIBUTES OF EFFECTIVE QUALITY MANAGEMENT SYSTEMS – STUDY REVIEWS

Mohammadi et al. (2021) performed a review of scientific literature related to Quality Management Systems (QMSs), Quality Management (QM), and ISO quality standards ISO 9001, IATF 16949, ISO 13485 and ISO/ TS 29001. This review was of quality systems from the medical devices, automotive, oil, gas, and petrochemical industries. From this study, 15 critical success factors (CSFs) and 7 critical failure factors (CFFs) were identified for quality management systems. These factors are illustrated in Figure 1.

![Critical Factors Diagram]

**Figure 1. QMS Critical Factors - Literature Review**

Sun et al. (2019) reviewed previous studies on ISO 9001 effectiveness to identify the most frequently mentioned factors affecting QMS effectiveness. The industries represented were manufacturing, service, and construction. The factors described in Table 1 were determined to be critical to the success/effectiveness of quality management systems.
Mohammad Mosadeghrad (2014) performed a literature review of 54 TQM empirical studies to identify the major reasons TQM programs fail. The most frequently mentioned reasons for failure were (in order of highest to lowest frequency):

1. Insufficient education and training
2. Lack of employee involvement
3. Lack of top management support

---

**Table 1. Critical Factors Affecting the Effectiveness of the QMS**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Examples/Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Motivation</strong></td>
<td>CSF: Internal motivation (e.g., Company seeks ISO9001 certification to improve quality and overall performance.)</td>
</tr>
<tr>
<td></td>
<td>CFF: External motivation (e.g., Company seeks ISO9001 certification to improve corporate image or in response to customer pressure.)</td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td>CSF: Commitment and participation (e.g., Management ensures adequate resources are allocated and promotes employees’ active participation.)</td>
</tr>
<tr>
<td></td>
<td>CFF: Lack of commitment and participation (e.g., Without top management commitment and participation, staff put a low priority on quality and adequate resources aren’t supplied.)</td>
</tr>
<tr>
<td><strong>Employees</strong></td>
<td>CSF: Well-trained employees, employee acceptance of required changes, the know-how of employees, employee involvement and commitment.</td>
</tr>
<tr>
<td></td>
<td>CFF: Insufficient employee training and education, lack of employee involvement and commitment, negative attitude towards quality, employees’ resistance to change, lack of communication.</td>
</tr>
<tr>
<td><strong>Resources</strong></td>
<td>CSF: Adequate human and financial resources</td>
</tr>
<tr>
<td></td>
<td>CFF: Lack of human resources, financial constraints</td>
</tr>
<tr>
<td><strong>Certification Organization (Auditors)</strong></td>
<td>CSF: Auditors knowledgeable in the industry and processes, consistency in interpreting the standard between auditors and certification organizations, value-added auditing</td>
</tr>
<tr>
<td></td>
<td>CFF: Nit-picking auditors, documentation-driven auditors, variation between certification organization standards, lack of auditor capacity, concern with paperwork that does not add value to the QMS</td>
</tr>
</tbody>
</table>
4. Inadequate resources
5. Deficient leadership and poor management
6. Lack of a quality-oriented culture
7. Poor communication
8. Lack of a plan for change
9. Employees’ resistance
10. Short-term thinking
11. Lack of a monitoring and measurement system
12. Lack of customer focus

The critical success and failure factors presented from the three studies above were passed through an online text analyzer to identify which words are mentioned most frequently. After removal of common words such as ‘of’, ‘and’, ‘to’, ‘the’, ‘a’, the words mentioned 3 times or more, along with their frequencies, are illustrated in Table 2.

**Table 2. Critical Factors - Text Analysis Results**

<table>
<thead>
<tr>
<th>Order</th>
<th>Unfiltered word count</th>
<th>Occurrences</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>lack</td>
<td>14</td>
</tr>
<tr>
<td>2.</td>
<td>employee¹</td>
<td>12</td>
</tr>
<tr>
<td>3.</td>
<td>commitment</td>
<td>6</td>
</tr>
<tr>
<td>4.</td>
<td>management</td>
<td>6</td>
</tr>
<tr>
<td>5.</td>
<td>involvement</td>
<td>4</td>
</tr>
<tr>
<td>6.</td>
<td>resources</td>
<td>4</td>
</tr>
<tr>
<td>7.</td>
<td>auditors</td>
<td>4</td>
</tr>
<tr>
<td>8.</td>
<td>motivation</td>
<td>3</td>
</tr>
<tr>
<td>9.</td>
<td>quality</td>
<td>3</td>
</tr>
<tr>
<td>10.</td>
<td>customer</td>
<td>3</td>
</tr>
<tr>
<td>11.</td>
<td>procedures</td>
<td>3</td>
</tr>
<tr>
<td>12.</td>
<td>financial</td>
<td>3</td>
</tr>
</tbody>
</table>

¹ In Table 2, the occurrences for ‘employee’ includes the words ‘employees’ and ‘staff’ because they have the same meaning.
There are consistent themes/factors that are critical to QMS success or failure. Based on Table 2, these themes are illustrated in Figure 2 in order of decreasing frequency. The associations to each theme are also included in the illustration. Please note that ‘auditors’ is represented separately since auditors are typically external to the organization and exist primarily to evaluate the quality management system.

**Figure 2. Critical Factors for an Effective Quality Management System**

**CURRENT PROPOSED METRICS**

The 2015 FDA draft guidance for Quality Metrics reporting included four mandatory metrics and three optional metrics as follows:

1) **Mandatory**
   a) Lot Acceptance Rate
   b) Product Quality Complaint Rate
c) Invalidated Out-Of-Specification Rate  
d) Annual Product Review (APR) On Time Rate  

2) Optional  
a) Senior Management Engagement  
b) CAPA Effectiveness  
c) Process Capability/Performance  

The comments received for the 2015 guidance led to the guidance being replaced with a 2016 revision, which included only three voluntarily submitted metrics. The three metrics defined were: 1) Lot Acceptance Rate; 2) Product Quality Complaint Rate; 3) Invalidated Out-Of-Specification Rate.  

The FDA Quality Metrics Research performed by the University of St. Gallen utilized numerous metrics to support its model of PQS Excellence. In the St. Gallen Pharmaceutical Production System Model (PPSM), PQS Excellence is a score built from PQS Effectiveness and PQS Efficiency. The Level A foundation is Cultural Excellence which is based on Employee Engagement, Quality Behavior, and Quality Maturity. The Level B foundation is CAPA Effectiveness. The third level (Level C) is a combination of Operational Stability, Supplier Reliability, and Lab Robustness. The metrics that form the scores for these different elements are illustrated in Figure 3 and Figure 4. Please note, the yellow boxes in Figure 3 are metrics that are also in the 2016 FDA draft guidance.
In 2022, the FDA published findings from its work with organizations that voluntarily submitted quality metrics per the 2016 guidance. One key finding was that different industry sectors use different quality metrics. The FDA had been focused on standardizing the quality
metrics reported, but this finding led them to re-evaluate. The 2022 publication proposes that regulated establishments choose the metric(s) most meaningful to their organization as long as they adequately reflect the identified practice area. The 2022 publication identified the following four practice areas and example metrics:

1) **Manufacturing Process Performance** – Process Capability/Performance, Lot Acceptance Rate, Right-First-time Rate, Lot Release Cycle Time

2) **PQS Effectiveness** – CAPA Effectiveness, Recurring Deviation Rate, Change Control Effectiveness, Overall Equipment Effectiveness, Unplanned Maintenance

3) **Laboratory Performance** – Adherence to schedule, Right-First-Time Rate, Invalidated Out-Of-Specification Rate, Calibration Timeliness

4) **Supply Chain Robustness** – On-Time In-Full Delivery Rate, Fill Rate, Disposition On-Time, Days of Inventory on Hand

**METRICS FOR CRITICAL FACTORS**

The Office of Pharmaceutical Quality published a whitepaper on Quality Management Maturity (QMM) that states: “A quality culture is necessary to achieve high levels of QMM”. The St. Gallen model defines Cultural Excellence as the Level A (base) foundation for pharmaceutical quality system excellence. Merriam-Webster defines culture as “the set of shared attitudes, values, goals, and practices that characterizes an institution or organization”. This definition along with the previous mentions of the importance of ‘culture’ to QMS effectiveness corroborate the model in Figure 2.

It makes sense that the employees and management are most critical to the success of the QMS because they create, define, and contribute to the quality culture. They also create the outcomes that affect other performance indicators.

For a true measure of QMS effectiveness, it is important to measure the quality culture. The practice areas presented in the 2022 FDA publication are good indicators of the current
state of a quality management system. However, none of the practice areas or example metrics provide a measure of the Quality Culture. Based on Figure 2, important questions that a quality management rating system should be able to answer are the following:

1) Are strategic quality objectives defined?
2) How engaged and committed are employees?
3) How engaged and committed are managers?
4) Are resources adequate?
5) Are employees adequately trained?
6) What is the level of conformance to procedures?
7) Are customer needs being met?

The example metrics presented in the 2022 FDA publication answer a few of the above questions but to answer questions about Quality Culture, the practice areas should be redefined. Figure 5 illustrates an alternative QMM measurement model that includes both quality culture indicators and technical/performance indicators. This alternative model includes five practice areas and example metrics for each practice area. Please note, the red boxes are metrics that are also included in the 2022 FDA publication and wherever the word ‘ratio’ is mentioned, the company should be allowed to define what the ratio will be in relation to, as long as the ratio remains meaningful.
With this alternative model, pharmaceutical organizations can select from the list of example metrics or propose alternate metrics that adequately reflect the state of each of the five practice areas. This approach provides companies the flexibility to report on metrics that are most meaningful to their business. The FDA could then develop an internal rating scale for each of the five practice areas that company-provided metrics can be calibrated to.

**CONCLUSION**

Many studies have been completed to determine critical factors affecting the effectiveness of Quality Management Systems. A crude analysis of these factors was performed and the most important of them were determined to be employees, management, resources, (strategic) quality, and customer. Quality culture by definition is most impacted by
employees and management, and quality culture is known to have a significant effect on the maturity of a quality management system. Quality management metrics should therefore include measures of quality culture.

Five practice areas were defined for an alternative QMM measurement model – Customer Satisfaction, Management Commitment, Employee Engagement, Process Performance (including Lab Performance), and Adequate Resources. Regulated establishments could select from a list of example metrics (or propose new metrics) to report on the state of these five areas. The more metrics reported for each practice area, the stronger the indicator is. The FDA could develop an internal rating scale that company-reported results can be calibrated against or converted to. The internal FDA ratings for these five measures can then be used to judge risks to product quality and drug supply.


3 Food and Drug Administration Quality Metrics Reporting Program. 87 Fed. Reg. 13297 (March 9, 2022)


