

WHITE PAPER

NSF's Quality Management Maturity (QMM) Assessment Model

Future-Proofing Quality and Supporting Supply Chain Robustness

Executive Summary

It is well recognized that the Quality Management System (QMS) — whether documentation, deviation and event management or CAPA — is the focus of Regulatory Inspections and indeed the cause of many findings. Given the requirements have been broadly the same for so long, why is this still an area of non-compliance?

Historically, and perhaps a harsh and simplistic assertion, is that the QMS has been managed as a function with a comprehensive set of instructions. However, more recently regulators, industry and quality professionals are looking at the QMS slightly differently. The QMS must be the heart and lungs of an organization — it needs to breathe life into the organization and must ensure that each operational part — from individuals, technology, equipment, to functions, teams and the leadership — operate in unison. This shift in mindset recognizes the need to understand the impact and risk of people and culture in the successful deployment of a mature QMS.

So, how does the QMS feed every part of the organization with oxygen and how do we ensure that those within the organization recognize the importance of the QMS? How do regulators assess the impact of these intangible elements on the effectiveness and robustness of a QMS, and therefore compliance?

The NSF QMM Assessment Model (developed and introduced in 2022, following the publication of the US FDA Drug Shortages Task Force report in 2019¹) responds



directly to this challenge. It is a disruptive innovation tool to assess organizational quality maturity across the regulated landscape. It requires a different mindset, taking a holistic view of the QMS, in parallel to the traditional considerations of compliance.

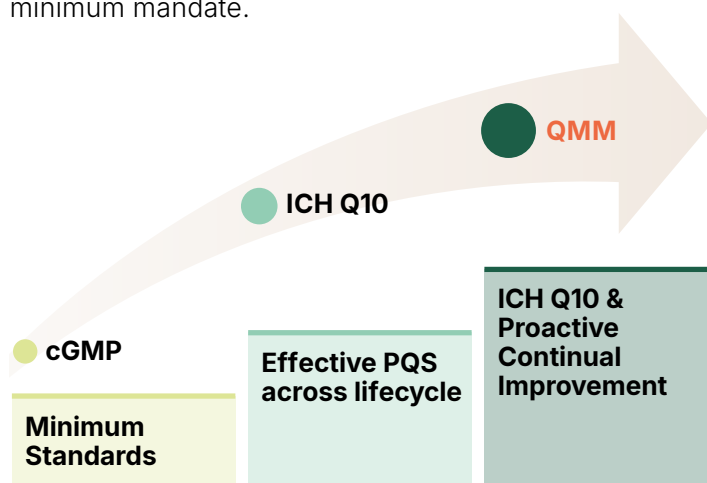
The NSF model has been designed to align and respond to the FDA's findings, to the assessment process considered by the Center for Drug Evaluation and Research (CDER), but importantly also takes into consideration other research on the impact of culture on the (quality) organization, e.g. ISPE Cultural Excellence.

The NSF QMM model has gained interest and credibility among some of the world's largest and most dynamic pharmaceutical companies who want to ensure they have a positive quality culture, and that their quality functions are both effective and robust. Ultimately, it is also recognized that proactive action on maturing a QMS, supports a more robust supply chain and minimizes supply disruption.

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History of QMM

A 2019 US Federal Drug Shortages Task Force report concluded that, 62% of shortages between 2013 and 2017 were attributed to manufacturing or product quality problems. The report concluded that manufacturers are not incentivized for enhancing the maturity of their Quality Systems beyond the bare minimum mandate.



As a result, the CDER (Center for Drug Evaluation and Research) recommended a rating system to assess Quality Management Maturity at Manufacturer's facilities. This system could potentially inform regulators, and also customers, about the robustness and effectiveness of a supplier's quality management system. The potential benefits are illustrated alongside:

FDA

FDA will benefit from QMM ratings by being more informed about the quality management practices at sites which will facilitate robust risk-based decision-making.

Industry

Transparent QMM ratings could empower manufacturers to identify ways to improve the effectiveness of their pharmaceutical quality systems, realize regulatory flexibilities described in ICH Q12.

A transparent rating system could also inform purchasers about the maturity of quality management practices at sites where they purchase drugs or drug products.

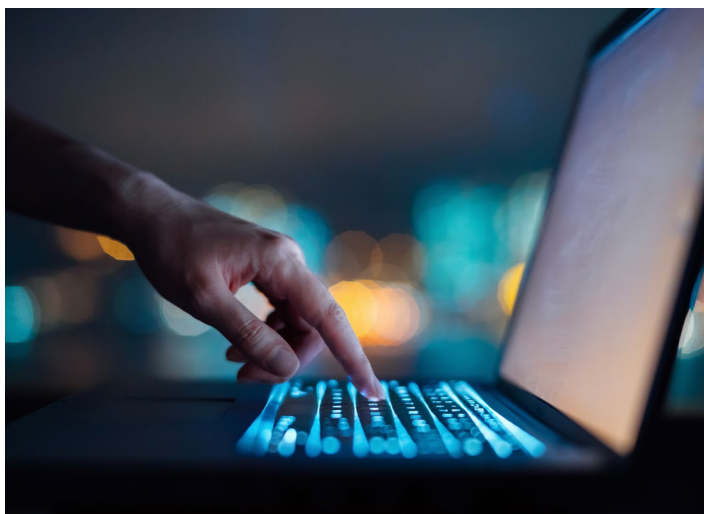
Patients

Patients and consumers will have more reliable access to drugs when industry has a stronger commitment to continual improvement.

The FDA has run two QMM pilots (Domestic and International) to assess the feasibility of implementing the QMM rating system. This pilot was followed by an Industry Stakeholder discussion on the way forward.

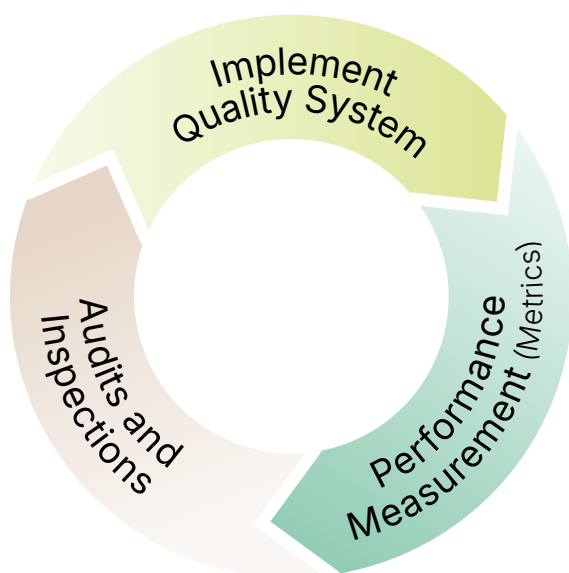
Introduction

For many years regulators have been publishing data and metrics on their inspection findings, with perhaps the hope that it informs the regulated sector of the deficiencies being identified, and also provides areas of focus for the sector to channel its efforts. Ultimately, the aim is to improve the level of regulatory compliance across the sector and hence the quality and safety of products in patients' hands.



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Traditional Approach to Assessing Quality Systems



For years however, deficiencies have been identified within organization quality systems. For example, since at least 2015² Quality Systems have been the subject of the highest number of deficiencies for the Medicines and Healthcare products Regulatory Agency (MHRA), with Documentation coming in second (for the last two years of data publication, in 2018 and 2019). Meanwhile the US Food and Drug Administration (FDA) have within their top ten Warning Letter citations³, deficiencies such as production and process controls or investigations and OOS. A significant number (525 between 2018-2022) of the citations⁴ identified the need for "responsibilities and procedures applicable to the quality control unit shall be in writing; such written procedures shall be followed".

Regulators, quality professionals, and consultants alike all speak to the need to have procedures documented and "in place" and evidence to demonstrate the procedures are "in use". Organizations spend significant time and effort training staff on procedures and monitoring training effectiveness, via supervision and audit, to confirm that the procedures are being

used appropriately and accurately followed. Yet still regulators around the globe continually identify deficiencies with what is "in place" and "in use". Perhaps when regulations, guidance or regulatory expectation changes then the reason for such findings might be understandable and perhaps due to a slowness to respond to the changing regulatory landscape or perhaps to misunderstanding or lack of awareness. However, the GxPs are not new. So why do we still see challenges with Quality Systems?

Simply put, the most likely cause is the human factor.

Indeed, many now agree that the QMS is no longer seen as a Quality Management team, distinct from the operational organization and that manage a comprehensive set of functional procedures. The QMS is now considered as a more holistic function — constituted by both the visible elements and invisible attributes.

In short, it is not just what is "in place" and "in use", but what is also happening "in reality".

It is essential to consider the QMS as the heart and lungs of the organization; the critical function that breathes life into the organization. Procedures being deployed to every inch of the organization, like oxygenated blood reaching every cell within a human body. From individuals, technology, equipment, to functions, teams, and leadership alike — operating in harmony, efficiently and robustly. When a deficiency is identified, it is investigated and resolved quickly, any impact managed and future risks mitigated — much like the treatment of a cancerous growth. Importantly, it is not hidden or ignored, but proactively and openly managed, and an assessment made to ensure that similar situations don't arise elsewhere within the organization.

Very rarely do we see this level of alignment and flow in an organization. To achieve this level of cohesion requires an enhanced state of Quality Culture which is embedded throughout the organization; driven from the top and positively managed. It requires a different approach — looking at the organization through a

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different lens, understanding the employees within, creating alignment to drive behavioral changes, motivating and incentivizing individuals toward quality deliverables, and assessing effectiveness and robustness, alongside compliance — all leading to a positive Quality Culture. At its optimal, it is a desired state of culture that requires high degree of alignment and trust, leading to higher performance, improved risk management and enhanced compliance.

Much work⁵ has been undertaken not just to consider Quality Culture, but the "Quality Climate" of an organization where dimensions such as "safety climate, innovation climate, learning climate, ethical climate and inclusion climate" are explored to determine the impact and influence of behaviors on an organization's culture. Understanding both the culture and the climate enables an organization to better shape the future culture.

However, culture change is hard and even harder to measure. It is therefore imperative that an organization pins down exactly what it needs and wants to change.

So how can an organization understand its Quality Culture and Quality Climate and determine what needs to be changed to drive high performance and ensure QMS compliance?

Quality Management Maturity (QMM) and Quality Culture

According to the US FDA⁶, "Quality management maturity (QMM) is the state attained when drug manufacturers have consistent, reliable, and robust business processes to achieve quality objectives and promote continual improvement". The US FDA has also recently⁷ alluded to the fact that QMM considers "manufacturers and those with oversight and controls over manufacturing, take ownership for quality" and this includes "the tone of commitment to quality" and that "quality systems shape culture".

Historically the dichotomy between quality and business objectives has shaped the operational activities. As a result, the performance and capability of a QMS are primarily assessed through quantitative

metrics (often derived for business performance) and audits. While effective, these often do not provide a holistic assessment. To achieve a sustained and effective quality management trajectory, one must understand their QMS' current state of maturity or capability and then plot out an action plan to achieve a desirable future state.

QMM however ensures a cohesive approach molding together a mature quality culture, technical processes, and corporate-wide business approaches. Business and quality objectives are integrated and embedded, a delivery plan or roadmap of improvements is developed, and corporate goals developed to focus on business and patient outcomes, success driven by the benefits of a mature quality management system in operation.

NSF's QMM Assessment Areas



legend: ■ Strategic ■ Tactical ■ Operational

Observing the need for integration, NSF has developed a QMM Assessment Model for a "Quality Organization" that provides a qualitative and quantitative measure of the various constituent parts of the QMS.

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The Quality Organization is assessed across three pillars — Strategic, Tactical and Operational — each containing a number of assessment areas. These can be customized to meet the needs for a specific assessment.

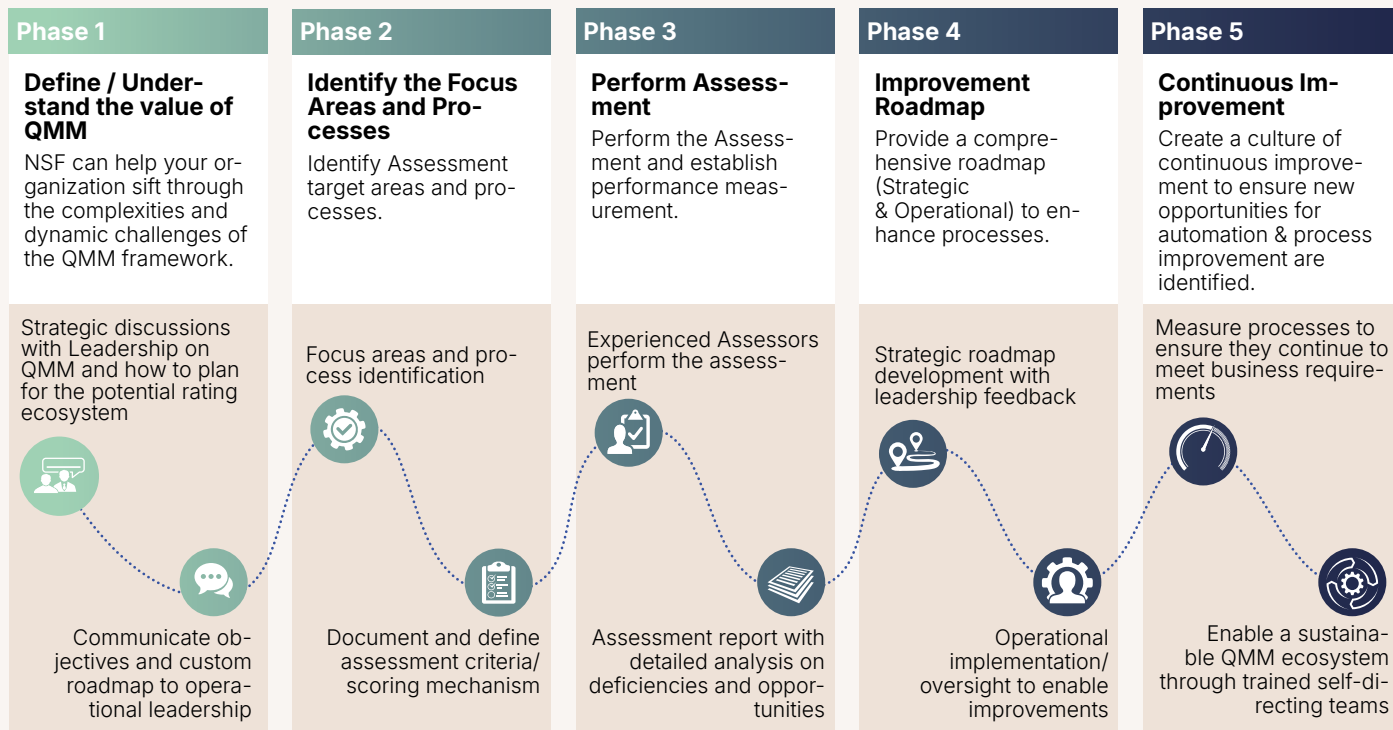
Each of the elements assessed have an associated quantitative score, which is calibrated to their respective criticality. The findings are based on information obtained through a blended assessment model of interviews and interactions, documentation review and walkthroughs. The assessment consists of obtaining information from various sources at the site and collecting and reviewing (onsite and remotely) the evidence to support the assessment ratings.

Based on the findings for each element, the maturity of each area is rated on an ascending scale — Undefined, Defined, Managed, Improved and Optimized, through a quantitative mechanism.



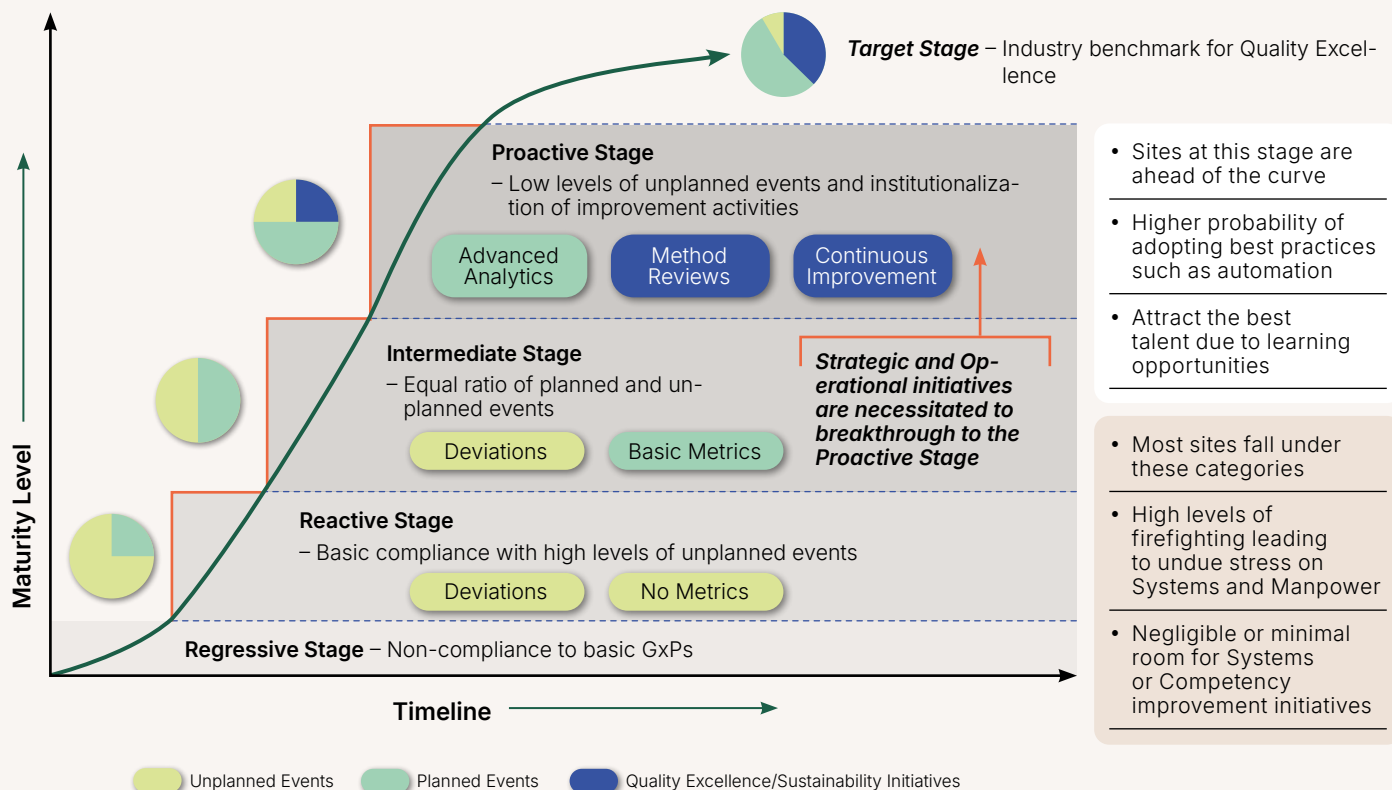
Organizations are provided with a quantitative assessment of the organization's quality maturity level and qualitative narrative for each area reviewed, along with recommendations and a mechanism to prioritize actions, in order to achieve a higher level of quality maturity.

NSF's QMM Process



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Quality Management – Maturity Evolution



Quality Management Maturity Evolution

NSF have observed that organizations with lower levels of Quality Management Maturity tend to exhibit certain traits or characteristics, such as out of date procedures, procedures not being adequately or correctly followed, little to no proactive work on continuous improvement, minimal innovation, low level of creativity and higher than average levels of unplanned work resulting from deviations and excursions. Importantly, these organizations tend also to have fragmented culture (e.g. hierarchical fractures), lower levels of staff morale and higher levels of attrition.

NSF's QMM Assessment process includes detailed analysis of the effectiveness of the systems in place, delves deeper into the root causes of these systemic

challenges and seeks out opportunities. It considers evidence across horizontal and vertical organizational systems, hierarchies, and boundaries, connecting the findings and identifying strategic level options for greater levels of system performance and proficiency. If required, operational level metrics and measurement processes can be proposed for demonstration of improvement effectiveness and maturity sustainability.

At a high level of Quality Management Maturity, organizations are operating in an optimal state. These organizations have low levels of re-work and unplanned activities, high levels of continuous improvement, application of best practice and workforce efficiency, higher levels of trust and

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autonomy leading to enhanced engagement and retention, and better risk and investment decisions. Importantly, there are clear signals of alignment. A golden thread runs through the organization from the vision and mission, through to the organization and quality strategies, into team and personal objectives. Quality and risk management feature high in the organization's objectives and values, along with financial business integrity. The Quality Climate and Culture are clear to see — trust, openness, creativity, inclusiveness, and learning are all paramount — the ethos is positive, understood, and visible.

Maintaining this state of maturity requires effort and attention. The right structures and governance must be in place and the impact of change must be carefully considered — particularly in relation to the impact on Quality Culture and Quality Climate.

The organization might also require a gap analysis to identify improvements to achieve the further advanced state of Quality Risk Management Maturity — a system where Quality Management, Quality Culture/Climate and Risk Management are all operating in harmony. Equally, further consideration might also be needed on the more recent recommendations for Outcome Based Co-operative Regulation (OBCR)⁸ where “higher levels of integrity are correlated with commercial success”, “decisions are made by empowered staff, rather than by a limited number of managers” and “the

culture of an organization has a powerful moderating (regulating) effect on behavior and outcomes”. “OBCR aims to create a framework that supports cooperation rather than conflict in regulation”. NSF's QMM Model will pave the way and lay the foundations for these advanced and optimized maturity states and further support can be provided by NSF's experts to develop and implement a plan to shape the future state of the organization.

Why QMM? What are the business benefits?

The real benefits of QMM come to the forefront when we consider business objectives in a competitive market — i.e. to maintain reliable supply of high quality, safe and compliant products and to minimize supply disruption. To achieve this, senior leaders must be open to the benefits of assessment tools such as NSF's QMM model. Recognizing the opportunity and taking the first step, could result in a cascade of benefits longer term and a more resilient organization delivering sustainable supply.

In summary, QMM:

- Is a **more mature system** — resulting in enhanced **risk management**, greater levels of resilience, and resulting in a **higher performing and sustainable organization**. This in turn could **enhance reputation and business success**.
- Considers the **organizational culture, business processes and corporate objectives** and the impact on the effectiveness of the QMS.
- Ensures and understanding of the current state of the Quality System beyond just metrics and audits. The model aligns to the **latest thinking and strategies** of global regulatory authorities. It is an important element of oversight and control.
- Future-proofs the organization — supporting **proactive continuous improvement** leading toward **sustainable compliance management** of an organization's QMS. This could also lead to quality system efficiencies, cost savings and regulatory flexibility or less frequent regulatory oversight.

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- Supports a positive culture climate that encourages **openness, trust and learning**, leading to fewer deficiencies or excursions, resulting in fewer non-compliances or recalls.
- Examines the **robustness and effectiveness of the QMS**. It looks beyond the immediate environment (i.e., what is in place/in use) and considers the wider strategic influencing factors. It can help consider the implications of change and supports best practice in execution of robust change management initiatives.
- Is flexible — The model can be used to undertake an organizational/site **health check**, or to consider QMS **maturity improvements** following a regulatory inspection, for example.
- It can be **tailored** to focus in on key areas of concern/risk. The subsequent report can provide recommendations for those highlighted areas.

Summary

NSF's QMM Assessment responds directly to the FDA's Report by the Drug Shortages Task Force in 2019¹ and provides a unique solution for organizations to get a step ahead.

It supports the evolution of the pharmaceutical manufacturing sector to be more resilient, more agile, and more open. It shifts perspectives from siloed and burdensome to cohesive and co-operative.

It encourages organizations to embrace and enhance their Quality Management Maturity and is a logical step in the evolving regulatory picture.

Only those brave enough to try will reap the rewards, and the rewards are plentiful. Don't hesitate — contact NSF today. — healthsciences@nsf.org

Why NSF?

Experienced

NSF employees have significant experience of working in/with regulatory authorities and in industry.

Strategic

We look beyond the immediate environment and consider the wider regulatory landscape to provide tailored advice.

Evidence Based

NSF have access to leading benchmarking data to support development of the NSF QMM model.

Professional

We are dedicated to providing high quality outputs that add real value to an organisation.

Flexible & Competitive

We can work onsite, hybrid or remotely, as needed. We offer best-in-class services at a market competitive rate.

Track Record

NSF have successfully used the QMM model to assess other organisations and provide recommendations for further maturity.

Learn more about NSF and how we can work with you at www.nsf.org/contact-us

For more information, please contact us at healthsciences@nsf.org.

¹ Center for Drug Evaluation and Research (2019). Report: Drug Shortages: Root Causes and Potential Solutions. [online] U.S. Food and Drug Administration. Available at: <https://www.fda.gov/drugs/drug-shortages/report-drug-shortages-root-causes-and-potential-solutions>. [Accessed 28 Feb. 2023].

² Medicines and Healthcare products Regulatory Agency (2014). Good manufacturing practice inspection deficiencies. [online] GOV.UK. Available at: <https://www.gov.uk/government/statistics/good-manufacturing-practice-inspection-deficiencies> [Accessed 24 Feb. 2023].

³ Chapman, J. (2020). Top 10 Pharma Inspection Findings from FDA, MHRA, and the Russian Drug Regulator. [online] Redica. Available at: <https://redica.com/pharma-top-10-pharma-inspection-findings-from-fda-mhra-and-the-russian-drug-regulator/> [Accessed 24 Feb. 2023].

⁴ www.thefdagroup.com. (n.d.). 2020 FDA Warning Letter & Inspection Observation Trends [Updated]. [online] Available at: <https://www.thefdagroup.com/blog/2019-fda-warning-letter-inspection-observation-trends>. [Accessed 24 Feb. 2023].

⁵ CIPD (2022). Organisational Culture and Cultural Change | Factsheets. [online] CIPD. Available at: <https://www.cipd.co.uk/knowledge/culture/working-environment/organisation-culture-change-factsheet#ref>. [Accessed 24 Feb. 2023].

⁶ Research, C. for D.E. and (2022). CDER Quality Management Maturity. FDA. [online] Available at: <https://www.fda.gov/drugs/pharmaceutical-quality-resources/cder-quality-management-maturity>. [Accessed 24 Feb. 2023].

⁷ Cder, F., Opq and Oqs (n.d.). CDER's Quality Management Maturity Program. [online] Available at: <https://www.fda.gov/media/143742/download> [Accessed 24 Feb. 2023].

⁸ INDR site. (n.d.). INDR: International Network for Delivery of Regulation. [online] Available at: <https://www.indr.org.uk/> [Accessed 28 Feb. 2023].

CASE STUDY

Quality Management Maturity

Brief/Objective

A leading fully integrated Biopharmaceutical Company contracted NSF to holistically assess their Quality Organization's functions and their effectiveness in response to repeat regulatory deficiencies. The objective of the client was to holistically assess their Quality Organization's current capability and understand risks in their QMS and the opportunities for enhancement.

Background & Scope

The scope of the assessment encompassed Quality Organizations at three different sites across two countries, with a combined employee strength of over 3000 employees, as well as the Corporate Quality Organization. The site operations were a mix of Drug Substances and Drug Products manufacturing, with multiple units within each of the sites consisting of their own captive Quality Control Laboratories. Over the past decade, the company had experienced exponential growth and had invested in expanding its manufacturing footprint. Despite operations growing organically, the Quality Organization had struggled to keep up, due to inherent challenges in scaling elements of QMS quickly. This led to huge influx of external hiring of talent in a short span of time. As a result, each site had its own organizational culture and climate, with myriad complexities. Some sites were old and had legacy equipment train prone to repeat breakdowns, while others were relatively new and had modern automated equipment train. These operations, despite their differences, were subject to the same Quality Systems and oversight. The individual sites had their own Quality organization and each of these organizations had an above site reporting structure. Supporting the site and above site quality organizations was the Corporate Quality Organization that owned the common organizational QMS.

Methodology

NSF deployed the Quality Management Maturity (QMM) Tool and tailored it to focus on four assessment areas of the Quality Organization — Strategy, Process, People and Organization. The multisite assessment was conducted across multiple geographies leveraging NSF's international network. A consultant familiar with each of the geography and culture that the sites were in, was deputed to perform the assessment onsite.

Structured assessments were carried out at each of the sites using a multimodal information gathering approach such as:

- **Documentation Reviews**

The Consultants reviewed site specific and pertinent corporate quality documentation to understand key processes and systems.

- **Key Personnel Interviews**

Based on the organogram, key personnel across all levels of hierarchy within the Quality Organization and other Cross-Functions such as Manufacturing, Engineering, Human Resources etc., were interviewed. The interviews were conducted with a questionnaire, developed based on the assessment areas. Over 100 personnel were interviewed for the assessment across all the sites over a period of 3 weeks.

- **Process Walkthroughs**

A key element of the assessment was to understand the implementation of processes and systems. Specifically, processes and systems were assessed to better understand consistency of application i.e., whether a procedure is "In Place", "In Use" or "Reality". To enable this, the consultants conducted walkthroughs and observed key processes as they happened.

Quality Management Maturity

Outcome

Each of the site assessment findings were collated and QMM tool was used to rate the maturity of each of the systems at the site. The qualitative ratings were then translated to a quantitative scale for ease of visualization and benchmarking. The assessment output illustrated a "Current State" of maturity and additionally, also described a "Future Target State" of maturity if the recommendations were to be implemented.



Risks Identified

While the primary objective of the maturity assessment is to understand the current capability state, a critical by product is the holistic appreciation of inherent risks associated with lower maturity levels. The illustration of risks across all the areas presented the senior management with a "bird's eye" view of risks and their criticality relative to each other. Unlike traditional audits or inspections, the assessment also articulates the relationship between data collected and the actual operational influences, including human factors,

holistically measuring the health of the quality system. Specifically, the correlation of documentation reviews, personnel interviews, and process walkthroughs, provides a unique yet complimentary insight into the current state of both the effectiveness and robustness of the quality systems.

Recommendations

A number of recommendations were made to achieve a target future state of maturity and the recommendations from the assessment could be grouped into two categories:

- Common recommendations were made for all the Site Quality Organizations as well as the Corporate Quality Organization.
- Site Specific Recommendations as each site had its unique set of quality maturity opportunities.

The assessment report also included a prioritization of the recommendations from a QMM perspective, to aid the client in developing an action plan for implementation. In conclusion, the assessment report provided a baseline for the client to embark on a Quality Management Maturity journey towards a proactive and self-sustaining quality ecosystem. Post implementation of the recommendations, the assessment shall be repeated to understand the progress made from the baseline state and identify laggards or actions that were not implemented effectively.

Learn more about NSF and how we can work with you at
www.nsf.org/contact-us