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Responding to the FDA Federal Notice on Quality Metrics

There is an argument to be made – and some industry insiders make one – that pharmaceutical manufacturers are willing and capable of self-regulating process and product quality. Additionally, those insiders say that, beyond the obvious desire to produce safe and effective drugs, application of continual improvement makes good business sense. Application of continual improvement may require changes to manufacturing processes and in turn this may require changes to manufacturing process and control procedures documented in drug applications.

“We’d like to see a shift to more industry self-regulation and self-driven continual improvement,” said Mairead Goetz, head of compliance at Novartis and chair of the ISPE Quality Metrics Core Team. “I believe the FDA sees this as a step in the journey to provide more latitude, flexibility and agility within the industry.”

How does introduction of FDA’s Quality Metrics program¹¹ fit with this vision?

There are many quality issues that continue to concern the FDA. For example, it issued 36 warning letters to prescription drug manufacturers in 2015.¹ As of December, there were shortages of more than 60 drugs,² including 5 oncology products and 14 anti-infectives, and 40 Class I drug recalls.³

With the expansion of overseas operations and the increasing number of drug applications and post approval supplements, the inspection burden has become a problem for the agency.^{5,6} For example, all eight warning letters issued to API manufacturers were to API makers based outside the United States, underscoring the inspection challenges the FDA faces with the globalization of the industry’s supply chain.⁵

“I get questions all the time, like ‘What about manufacturing in India? What is the level of quality?’” said Janet Woodcock, the director of the Center for Drug Evaluation and Research (CDER) at the FDA, in her keynote address at the ISPE quality metrics meeting held in Baltimore, MD in April 2015. “Well, I don’t know. All I know is the result of some different observations that are made. I know there is a lot of variability, but there is in the U.S. as well, and all around the world.”^{14,15}

Last year there were many cited data integrity issues, which are red flags for the FDA, particularly regarding a company’s quality culture.⁷ One facility was testing drugs in a lab that was unknown to the agency and had shipped products that had failed tests.^{8,9}

To address these problems, the FDA is leveraging a risk-based approach to inspection as provided under the Food and Drug Administration Safety and Innovation Act (FDASIA) rather than to inspect manufacturing facilities biannually to ensure they comply with GMPs.⁴ Part of the requirements of FDASIA is that information could be provided in advance or in lieu of an inspection. Some of this information are quality metrics data. In February 2013, the agency announced its Quality Metrics Program via a *Federal Register* notice¹⁰ and over the past two years, the agency sought feedback from industry on choosing standardized data and metrics that would be reported. In July 2015 FDA released its *Request for Quality Metrics: Draft Guidance*.¹¹

In their draft guidance FDA indicates how they expect their Quality Metrics Program can help FDA and industry:

Quality metrics are used throughout the pharmaceutical industry to monitor quality control systems and processes and drive continuous improvement efforts in drug manufacturing. These metrics can also be used by FDA: to help develop compliance and inspection policies and practices, such as risk-based inspection scheduling of drug manufacturers; to improve the Agency’s ability to predict, and therefore, possibly mitigate, future drug shortages; and to encourage the pharmaceutical industry to implement state-of-the-art, innovative quality management systems for pharmaceutical manufacturing.

The draft guidance explains what facilities are covered by the guidance, the required data and data provider and which quality metrics the FDA intends to calculate.

“[W]e at FDA do not know or have a good handle on where the industry is,” Woodcock said. “I have said this before. Quality metrics, in fact, are part of our effort to ascertain in a quantitative manner, what the status of quality is in pharmaceutical manufacturing. We do not know that right now.”¹⁴ She also pointed out that the industry has failed to embrace continual improvement.^{14,15}

Preliminary responses from ISPE and other industry groups to the Request for Quality Metrics were presented initially to the FDA in a public meeting with industry in August 2015.^{12,13}

Formal responses were provided before the end of November. The agency has said it will publish its Quality Metrics Program, complete with selected metrics soon.

Some of the data the FDA proposes collecting – which it believes is already collected by companies following cGMPs – is the number of lots attempted, specification-related rejected lots, attempted lots pending disposition for more than 30 days, out-of-specification (OOS) results, product quality complaints and annual product reviews (APRs) and product quality reviews (PQRs) for the product.¹³

The agency would then use these data to calculate metrics such as lot acceptance rates, product quality complaint rate, invalidated OOS rate and APR or PQR on time rate. It also asked for comments on optional metrics, such as quality culture measured by engagement of senior management and CAPA effectiveness, and process capability/performance.¹¹

Does the industry need a standardized quality metrics program?

There is no doubt that there are quality issues and that some regulatory oversight is necessary. But is collecting industry-wide standardized metrics the way to meet the FDA's stated goals?

"A large segment of the pharmaceutical industry has quality systems that are robust and reliable said Goetz. "We have many of our own metrics. The selection that the FDA is considering is a small piece of that and, generally, a variant of those that companies already will have. But we realize that we don't represent the whole industry and it's the diversity of the industry that makes regulation challenging from a burden/benefit perspective."

Chris Potter, ISPE advisor, agrees that ISPE works in a world of quality converts that may not be indicative of the entire landscape that the FDA is regulating.

"The quality of most of the industry is acceptable," Potter said. "The number of major crises is low. The generics and OTC companies are big players in volume terms and their quality standards are in most cases at least as good, if not better, than the major Rx firms. It's the outliers of cavalier companies or sites, and some products within some companies that pose problems. A potential criticism of the FDA's quality metrics program is that they are imposing a big program to hunt a relatively small part of the industry."

Potter believes the large companies will buy in if they can see the benefits: reduced inspection frequency, risk-based inspections and a reduction in post-approval change processes. The latter are currently often necessary to support implementation of continual improvement opportunities, however, submission and approval is bureaucratic and difficult to manage because of different procedures and time scales between countries around the world.

Prospective submission of quality metric data could be considered a step in the direction of the industry vision where provision of information may increase regulator's confidence that industry's quality systems are performing to a high standard.

ISPE's response to the FDA draft guidance

ISPE's response to the FDA draft guidance, Request for Quality Metrics, was based on the society's data findings from its Quality Metrics Pilot Program Waves 1 and 2.¹⁶ Wave 1 sought to determine whether industry could practically collect and report standardized quality metrics and concluded this objective could be achieved. ISPE is continuing its research, canvassing participants in Wave 2 to determine the amount of effort and burden involved in gathering product-based data with Wave 2 including the quality metrics proposed by the FDA. Wave 2 results will be published by the ISPE in the spring of 2016.

"We at ISPE appreciate the opportunity to provide input to the FDA and support the agency's effort to implement a quality metrics program," Goetz said. "Our comments are based on our experiences and are genuinely designed to assist FDA with successful implementation of their program. We look forward to maintaining this objective data-driven dialogue with the FDA."

In its response to the FDA, ISPE is largely silent on the relationship of standardized quality metrics to drug shortages.

"Standardized metrics across the industry are likely not the solution to predict drug shortages," Goetz said. "Metrics need to be relevant to the situation to monitor and be predictive of a drug shortage. They need to be pertinent to the risk, to the situation, to the lifecycle of the product."

"There's no doubt that some metrics help alleviate drug shortages," said Goetz, who wrote the chapter on metrics in *ISPE Drug Shortages Prevention Plan*,¹⁷ which includes a suggested list of performance indicators that could be used to assess a quality metrics program. "But the metrics we highlight are not necessarily the standardized metrics that are in the FDA's draft guidance and are not advocated for consistent cross-industry implementation. Rather the key message there is selection of the KPIs that are pertinent to the risk at hand. There is potential for confusion."

"FDA proposed standardized metrics might well help predict the potential for drug shortages, but from ISPE's perspective, we're not sure how," Potter said. "We haven't seen any published or public information showing that they will alleviate drug shortages."

In addition to supporting the FDA's overall effort to implement the QM program, ISPE responded with six other points with clear rationale justified based on the findings of its Quality Metrics Pilot Program:

1. ISPE believes the program needs to start with a small, targeted approach, so both industry and the FDA can learn and evolve the program over time.
2. ISPE recommends a phased introduction that will maximize learning, minimize burden on both the industry and FDA and enhance the chances of a successful implementation such as allowing clear benefits to be evident. ISPE suggests voluntary reporting for firms that are not participating during the initial period with a possible incentive of reduced inspection frequency.

In their responses to the draft guidance, a number of organizations also want the FDA to take a phased approach to implementation, including the Pharmaceutical Research and Manufacturers of America (PhRMA), the Biotechnology Industry Organization (BIO) and the Generic Pharmaceutical Association (GPhA).^{18, 19, 20, 21}

3. ISPE advocates starting with only three of the proposed metrics:

- Lot Acceptance Rate (report by site differentiated by product, evolving to product differentiated by site)
- Product Quality Complaint Rate (report by product only)
- Invalidated Out-of-Specification Rate (report by site)

Additional clarity is requested on definitions

It is very important that definitions are clear and have the most appropriate denominator.

ISPE also addressed the issue of collecting metrics from contract manufacturing organizations (CMOs). Currently, the quality data the FDA wants to collect is not routinely gathered or shared between CMOs and license holders. This will add an additional burden on firms and CMOs because the license holder prior to its submission should verify the data. Thus, ISPE recommends that data be reported by the CMO after agreement of the data with the license holder.

4. ISPE recommends deferring some metrics and data points, including APR or PQR on Time Rate, optional metrics related to quality culture and process capability and the complementary data point of “lots pending disposition for over 30 days”, given the relatively high burden for collection.
5. ISPE is concerned that the burden to the industry is underestimated, based on the industry’s experience, both in terms of upfront investment and ongoing cost. The burden estimate should include the additional time required to collect the proposed metrics, the anticipated costs to establish routine governance practices, adjust internal IT systems and incorporate additional review and retention of data to support verification during inspection.

ISPE considers that the recommendations given above will contribute to reducing the burden with the additional recommendation that data are reported annually rather than quarterly.

6. ISPE requests greater transparency in the manner in which data will be assessed, and outcome and conclusions determined and communicated.

ISPE was engaged in in the Cross-Industry Quality Metrics Collaboration Group, which represents interested parties across the pharmaceutical industry, including PhRMA, BIO, GPhA and others.¹⁶ This group proposes that quality metrics should be part of a continual improvement program, not used as a punitive measure; and requested that the FDA adopt a phased-in approach to its quality metrics program. The Collaboration Group also recommended that:

- The reporting period begin at least six months after the FDA issues its final guidance
- Reporting be done annually with specific submission dates determined by each firm to balance workload and align with existing quality system procedures
- Trending should be incorporated into the analysis model
- The FDA provide time to make adjustments and provide clear guidance about who is accountable for reporting which metrics
- The FDA clarify if and under what circumstances API manufacturers should report their own data and how that date should be reported

“The feedback we got from our colleagues who participated in Wave 1 suggested that the logistics of implementing a program like this are enormous, which is a challenge for both the FDA and industry,” Potter said. “It involves getting the definitions right, then having the industry and the agency know how to collect and manage the data. For us, the \$64,000 question is, once the FDA has all this information, what is it going to do with it? Analyzing the information to get some benefits will be a huge challenge and hence small, carefully managed steps are appropriate.”

Toward a more self-regulating industry

“For ISPE, the short-term perceived benefits of this program include reduced inspection frequency, say from annual for some to every two years for others,” Goetz said.

The FDA has suggested that recognition of a company’s robust quality system program would offer a perceived benefit among one’s peers. A company might, for example, list its ranking in an FDA classification system, say

as a Tier 1 or Tier 2 manufacturer. “ISPE doesn’t necessarily see it this way,” Goetz said, “but you will see that in the discussion.”

“It’s possible that, with classification, you could assess your partners – CMOs or joint venture partners – more robustly than you can now,” said Potter. “It might help with your selection criteria.”

Goetz suggested that the biggest benefit from an industry perspective could be to improve the post-approval change process. “This could lead to less agency reporting, which will facilitate navigating the global regulatory post-approval change process and the complicating differences that exist in this landscape,” she said. “There’s a deliberateness around making changes today because of the complexity of the process. So some changes are not made because of the burden of the process.”

Goetz reflected that having standardized quality metrics could provide assurance to agencies about the level of compliance. This should, in the long term, give them confidence in the ability of industry to self-regulate.

“This may be a step in the journey to provide more flexibility and agility within the industry,” Goetz said. “The upside for us is we’d have more latitude to be self-controlling. Janet Woodcock says the industry needs to lead continual improvement ourselves. If we realize the benefit of, for example, post-approval changes, it is getting closer to the vision of industry being in control of its own destiny. The FDA believes that these metrics could indicate the system’s health and the likelihood we can be self-controlling, with less regulatory oversight. Time will tell.”

There’s an aspect to Potter’s vision of a successful future that is also longer-term, though he considers it “a bit of blue sky.”

“If industry could report information including quality metrics that is understood and trusted globally by regulators, then there is a potential to reduce the burden of multiple inspections by various inspectorates,” said Potter. “There would be more reliance on companies to provide information than on inspectors turning up. It’s not a stated goal of the FDA, but it could be at the back of the minds of senior quality leaders in the industry.”

In keeping with that same longer term vision, Goetz believes the FDA’s quality metrics program could, as a side effect, drive a lot more collaboration and benchmarking between firms. They might be willing to share metric structure and best practices about metric performance. For example, what is the difference between the quality system at a Tier 1 and a Tier 2 manufacturer?

“The conversations I see happening in executive boardrooms around quality system performance and continual improvement are compelling,” Goetz said. “The needle has moved in the quality metrics dialogue.” ■

By James Hale and Scott Fotheringham, PhD

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Looking at quality metrics in the auto industry

No matter how robust a quality metrics program is, it can't prevent cheating, as Volkswagen has shown. Since the carmaker was caught programming its diesel vehicles to evade emissions controls except during testing, it has been forced to recall 482,000 vehicles.¹ Given this, it may seem counterintuitive to look to the auto industry as a model for comparisons to the current discussions about quality metrics in pharma manufacturing. However, automotive manufacturing, like pharmaceuticals, is a must-not-fail enterprise that demands adherence to a complex combination of government regulation and internal quality control.

"This is a wonderful time for the auto industry to really forge forward in terms of quality," said Danica Kelso who teaches in the Automotive Business program at Georgian College in Barrie, Ontario. "As a result, technologies and practices will continue to change and evolve with the end result of a better product, better sales and content consumers."

As in drug making, automakers have dozens of quality metrics, measuring such things as parts-per-million defects, supplier improvement, customer satisfaction and severity incidents per billion.

"European, Asian and North American manufacturers share and use these metrics to improve their products and productivity," Kelso said. "It also allows manufacturers to better measure themselves, not only against their fellow competitors, but also to assess a manufacturer for possible future acquisitions or mergers."

A notable difference in the auto industry is that a supplier, with its own internal quality management system, may be producing dozens of different parts, for many automakers, each of which has its own quality and process standards. This contrasts with Big Pharma's outsourcing of drug production to suppliers that make one or, at most, a few different products for them.

To deal with this, the IATF, an ad hoc group of automakers and trade associations, developed

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a technical spec that functions industry wide. ISO/TS 16949 includes requirements such as the development of a supplier quality management system, specs for processes such as heat treating, plating, coating and soldering and measurement system analysis.² Certification is almost always a requirement of supplying parts or services to an original equipment manufacturer.³

Kelso noted that these standardized specs mean that manufacturers "can easily compare themselves not only to other manufacturers belonging to TS 16949, but can also compare plants and products within individual companies. This type of data could be used to determine which plant has the best quality to produce specific products."

In addition to the technical standard, suppliers of production materials, service parts and finishing services must refer to each automaker's customer-specific requirements (CSRs).⁴ Although automakers strive to align these internal requirements to the technical specification,⁵ the non-standardized nature of individual CSRs can result in a burden on the whole supply chain, adding a level of complexity without necessarily improving quality.⁶

A recent article comparing the current state of drug manufacturing to that of the US auto industry prior to the 2008 economic collapse, points to drugmakers' lack of attention on quality and quality metrics. Prabir Basu argues that this could be remediated if government and industry copied the auto industry and "encourage investment in fundamental science and engineering to design and manufacture pharmaceutical prod-

ucts. Greater savings can be easily achieved with innovative science and technology.⁷⁷ This, at a time when Big Pharma actually spends far more on marketing than it does on R&D.⁸

“The recent quality metrics guidance will not ultimately make a particularly large impact, as the metrics does not have any teeth, it does not reflect the quality culture,” Basu wrote. “Manufacturing the metrics to look good is easy.”

At times, too easy, as the scandal at Volkswagen shows. According to Lynne Frances Baxter, a researcher and senior lecturer in management systems at the University of York, manipulating metrics is a common problem. “There has long been a culture of gaming metrics in the automotive industry and other sectors do it too,” she says.⁹

Despite the errors and deceit that does go on, the mix of external and internal regulation in automotive production provides useful insight for the current discussion of quality metrics in drug making. ■

By James Hale And Scott Fotheringham, PhD

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Look outside, not just inside

Quality benchmarking is vital to provide a stimulus for improving quality. However, benchmarks have often been scarce or hardly comparable. **Now that benchmarking is becoming ubiquitous and also supported by industry-standard Quality Metrics, knowing where you stand is becoming the new standard.** Furthermore, benchmarking reveals the large gaps that exist in process and product maturity between different sites and firms.



In the pharmaceutical industry, KPIs typically showcase large differences in quality performance between sites and between firms.

The pharmaceutical industry has long been and still is a bastion of science and science-based operations. Clearly, there is a desire to learn from the best scientific information. But in practice the learning is often limited. The first question that is often asked is whether quality is actually measurable and comparable? The work in quality benchmarking but also in ISPE Quality Metrics answers that question: most firms do measure quality. With effort, it is even possible to standardize definitions and to find reasonably comparable information. Enough to draw interesting learnings.

Secondly, regulation in the industry has grown around securing patient safety after incidents have happened. Therefore, much documentation in the industry is batch-based, incident-based or product-based. Useful learning actually comes from opening the aperture far wider. Interesting benchmarks can be found across value chains, not just along value chains. Many of the KPIs we have are lagging, rather than leading. Regulators have seen this and have been asking firms more and more for systematic root causes and systematic learning - but metrics have not caught up. Cross-company learning mechanisms are far and few between. Cross-company learning is actually much more common and even institutionalized in some other highly regulated industries, like nuclear power or aviation.

Benchmarking can play a useful role to stimulate that learning. In the pharmaceutical industry, KPIs typically showcase large differences in quality performance between sites and between firms. We see this whether we compare KPIs like first-time-right, the number of deviations per batch, yields, cost of quality or speed and productivity of the quality system. Differences of performance between sites from the median in the industry to best-of-best can be as large as a factor 4-10. The pharmaceutical quality system is set-up to correct any errors before they reach the market - but it is still an uncomfortable fact that there is so much room for improvement.

If the pharmaceutical industry were a commodity industry producing widgets, this kind of disparity in performance would be quite detrimental to lower-performing firms. Quality of pharmaceutical products however is

not transparent to customers - and even only partially to regulators. Hence, we see the primary audience of this information as the pharmaceutical firms themselves, since they have the ability to understand this information and to act upon it.

What would best-of-best quality look like?

To get an idea of what a best-of-best site would look like in terms of quality performance, we consider some of today's benchmark sites out of McKinsey's POBOS Quality benchmark and combine their best-of-best performance across various dimensions (Exhibit 1). That hypothetical site would demonstrate quality performance unlike anything seen yet. Consider these possibilities:

- The site has zero recalls, no adverse events, and close to zero confirmed complaints.
- Shop-floor processes are incredibly reliable, with a right-first-time, end-to-end record of at least 99%.
- The site's quality systems operate effectively and fast, leading to less than 1 percent recurrence of deviations.
- This future site has only one quality assurance (QA) full-time equivalent (FTE) per 1,000 batches instead of the approximately ten common today.

In sum, the performance of this best-of-best site would be an order of magnitude closer to flawless performance compared with today's above-average performing sites—simultaneously hitting new heights not only with quality but also with productivity and speed.

So what would it be like to visit this “perfect” pharma site? We believe that if you spoke with any operator there, you would quickly sense that everyone considers quality his or her responsibility. You would realize that people shoulder this responsibility without expecting to depend on a large,

dedicated quality function focused on checks and controls. You would also see that the site's quality system runs less on detailed operating procedures and more on deep process knowledge, a strong quality culture, and clear values.

Moreover, your visit would show you that the paper burden on operators is very light. That's because the majority of critical-to-quality (CTQ) parameters are captured automatically, requiring little manual verification. This best-of-best site is also making extensive use of advanced analytics systems to make processes more reliable; its analytics tools have vastly improved the availability of data on true root causes of typical quality problems. It would also be apparent that the site's operators truly understand the science behind their products. Thanks to simplification, the processes they use are inherently robust. Operators can therefore devote the bulk of their time and energy to preventing future quality issues rather than having to deal with past problems.

Clearly, if we believe that we can achieve benchmark performance, pharmaceutical quality could look fundamentally different in 2030. Companies that could achieve the levels of performance described above could even gain strong competitive advantage. The ability to produce at much higher quality translates into significant cost savings, a stronger reputation, and better profit margins and thus could even alleviate pricing pressures as more products become generic.

The way forward

We think benchmarks also point to a different role that the Quality function should be playing, and how quality is perceived. Quality employees are frequently perceived as "police officers" who check and control adherence to standards and enforce bureaucratic requirements, or as "firefighters" who arrive on the scene to prevent issues from growing into catastrophic events. Quality procedures are seen as overly bureaucratic and too complex, perhaps better suited to meet regulators' increasing expectations but not to achieve the ultimate goal of improving patients' lives. These perceptions are a source of frustration for the entire industry because they place quality in a no-win situation.

Most executives are aware of quality's "inspiration gap" and acknowledge that closing it will require significant effort—but yield great benefits. As a first step to closing the gap, they will need to convince their organizations that inspiration and quality improvement are inextricably linked.

Inspiration is the starting point for each change a business organization seeks to make, whether to catch up to the industry average or to improve from "good" to "great." At companies that are lagging behind their industry peers, inspiring stories of success can open employees' eyes to the gap between their current performance and best practice and motivate them to start the journey toward greatness. For companies that are on par with their industry peers, inspiration is particularly important for dispelling employees' complacent beliefs that "everything is good" or "we are doing fine." Examples of what superior performance looks like can provide a case for action that motivates employees to overcome their complacency and pursue new avenues to success.

Externally, managers can first look to competitors within the pharma industry for inspiration. Understanding how these competitors advance quality can be best experienced through site visits. Engaging in real discussions with colleagues, consultants, and academics can help. Participation in in-

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dustry benchmarking exercises can help to start to understand what best in class means. A benchmarking study will provide relevant insights into a company or site's quality performance relative to its competitors and highlight the corresponding best practices.

External inspiration can also be found beyond pharma, from other industries that have faced similar challenges or are strong in certain functional or technical areas. For example, some automotive plants have used innovative approaches to foster quality awareness. Executives at one injection-molding plant, for instance, put defective parts on display in the plant's cafeteria. The "parade of ugly parts" raised awareness of the issues and motivated employees to discuss how to improve quality. Another automotive company sent all employees a package bearing the message, "See who's responsible for quality." Employees found a mirror when they opened the package. Other companies post this message next to the restroom mirrors. As another example, nuclear power companies have a mind-set of reporting and addressing every near miss—not only incidents that actually occur. They are also very adept at detecting low-likelihood but high-impact events - a much more leading rather than reactive way of managing quality. Subsequently, they share these issues in global forums so that their lessons.

We believe that there is a bright future for operations and quality leaders who know how to turn benchmarking into a true source of inspiration and learning. There is a world of performance improvement out there, starting with the first step of believing that you yourself can never be perfect - but that permanently striving for perfection is a worthy struggle. ■

About the authors

Paul Rutten is an Expert Principal at McKinsey & Company in Amsterdam. He joined McKinsey in 1998 and is leading the Quality, Compliance and Remediation practice of McKinsey with a focus on Europe. He is the sponsor of McKinsey's POBOS Quality benchmark and of McKinsey's involvement in the ISPE Quality Metrics initiative.

Vanya Telpis is a Director of Knowledge at McKinsey in New Jersey. She joined McKinsey in 2002 and is the Practice manager of the Quality, Compliance and Remediation Practice of McKinsey. She is the founder of McKinsey's POBOS Quality benchmark and is a team member of the ISPE Quality Metrics team.

Note: this article contains excerpts from "Flawless: From Measuring Failure to Building Quality Robustness in Pharma", McKinsey & Company, July 2014, edited by Paul Rutten, Vanya Telpis et al. The book contains further reading on Quality metrics, inspiration for quality and using site visits as a journey of inspiration. The book can be ordered via the McKinsey.com website.



Cultural Excellence: Ensuring that “Culture of Quality” is more than just a slogan



The ISPE Quality Culture team, operating under the auspices of the current ISPE Quality Metrics Initiative, launched their “Six Dimensions of Cultural Excellence” framework at the Quality Metrics Summit held in Baltimore in April 2015. **In this article, Nuala Calnan, team co-lead, shares some insight on the subject of quality culture and outlines the work the team is undertaking to develop a series of practical tools, templates, and training for use by the industry to support the implementation of the cultural-excellence framework.**

Since the February 2013 publication of the *US Food and Drug Administration [FDA] Drug Shortages Task Force and Strategic Plan; Request for Comments*, announcing the FDA’s intention to explore the use of manufacturing quality metrics to assist in the evaluation of product quality, there has been much talk about the role that culture plays in an organization’s manufacturing quality performance.

The FDA’s recent draft guidance *Request for Quality Metrics Guidance for Industry* brought with it an acknowledgment of its ongoing quality concerns, noting that it has “not fully realized [its] 21st-century vision for manufacturing and quality—there continue to be indicators of serious product quality defects.”

Culture remains on the agenda as a potential means to resolve these challenges with its inclusion as one of the topics singled out for “specific request for comments and information” by the FDA in the draft guidance. The FDA invited input on its proposed “optional” metrics related to quality culture and the extended commenting period closed on 27 November 2015. The dialogue with the industry continues, and the ISPE Quality Culture team has responded to the call.

Much of the talk about culture has emphasized the need for the pharmaceutical industry to engender a “culture of quality,” but what does this mean, and what are we actually talking about when we talk about culture?

What are we talk about when we talk about culture?

“The way we do things around here...” – Marvin Bower (Bower, 1966)

The concept of corporate culture has been the subject of much debate over the past 50 years. Marvin Bower’s well-used phrase, quoted above, so simple in construction and sentiment, belies the underlying complexities of culture. Edgar H. Schein, another noted expert on organizational culture, identifies culture as an abstract concept—difficult to describe and comprehend—yet the forces that derive from it are powerful, and he cautions that “if we don’t understand the operation of these forces, we become victim to them.” (Schein, 2004)

Schein’s simple definition of culture, similar to Bower’s, is “how we perceive, think about, and feel about things”; it formally links behavior and culture by indicating that behavior is a *derivative* of culture. It is this link to behavior that provides a concrete means to understand and interpret the operation of the powerful forces he warns of and offers a focus for action for those in the pharmaceutical industry seeking to improve their quality culture.

Schein formally links behavior to culture by indicating that behavior is a derivative of culture.

Transforming the cultural DNA of the pharmaceutical industry

Schein also proposes that the prevailing cultural paradigm can be thought of as critical “genes” in the cultural “DNA” of an organization. To map these links between culture and behavior, he extends the analogy: If the total set of shared basic assumptions of a given organization’s culture can be thought of as its DNA, then individual genes can be examined in terms of their potency in forcing growth in certain kinds of (desired) behaviors while other genes inhibit or prevent specific (undesired) behaviors.

This concept lends itself to envisioning a genetic reengineering of the cultural DNA of the pharmaceutical industry from a *compliance-led* culture to an *excellence-led* culture of quality. The author holds that the traditional culture of compliance is a fatal flaw ingrained in the DNA of the pharmaceutical industry. The evolution toward a culture of quality will require a reordering of the sequence to build a double helix, strengthened by a combination of *patient focus* and *excellence*. This concept is depicted in Figure 1:



Figure 1: Transforming the cultural DNA of the pharmaceutical industry (Calnan, 2015b)

(Image reproduced with permission of the author)

This transformation of the genetic building blocks facilitates the identification and selection of the “desired” behaviors in order for them to be “hardwired into new habits so that employees can become assets to, and champions of, the transformation effort.” (Morse, South, and Gideon, 2013)

Compliance versus quality: the transformation towards excellence

Let us imagine that a compliance-led approach to quality provides quality with a small “q,” narrowly focused and limited in scope. Whereas, an excellence-led approach to quality provides quality with a big “Q,” enabling protection for the patient and offering an integrated, holistic business excellence strategy.

In her plenary address at the September 2014 PDA/FDA Joint Regulatory Conference, Janet Woodcock, Director, Center for Drug Evaluation and Research, addressed this culture of compliance versus culture of quality head-on. She stated that in order for the industry to *own* quality, everyone from the “shop floor to the CEO must be fanatically committed to high quality—not to compliance.” (Woodcock, 2014)

Explaining that a culture of compliance requires that you meet someone else’s expectations, whereas a culture of quality means that you are trying to meet your own expectations, Woodcock acknowledged that it is a journey. She proposed that the FDA cannot mandate for this—it can only foster a culture of quality. Realistically, this desired state can only be achieved through the inclusive interaction between the pharmaceutical industry and the regulators, working together to deliver this outcome for the patient.

Leadership's role in delivering behavior-based quality

Critical to this transformation are *enabled leaders* who build a case for change and whose own behaviors accelerate the adoption of the new way at all stages of the transformation through an *engaged workforce* that is motivated and mobilized in the change effort. In order for employees to become passionate about eliminating mistakes, leadership and credibility of vision must be evident to motivate and sustain a culture of quality, and there is a growing awareness within the pharmaceutical industry about its impact. (Friedman, 2014; IPQ, 2014; ISPE, 2014; Paulson, 2013; Skibo, 2013)

Indeed, Woodcock has persistently provided both leadership and vision over the past decade as one of the most outspoken international regulators on the subject of product quality and, more specifically, manufacturing quality. She reminds us of how high the stakes are “because the consequences of quality problems such as sub-potency, lack of sterility, or product mix-ups can be so devastating.” (Woodcock, 2012) The role of leadership in fostering and developing a vision for quality formed the starting point of the Six Dimensions of Cultural Excellence framework. (Calnan, 2015a)

The six dimensions of cultural excellence

The ISPE Quality Culture team, operating within the ISPE Quality Metrics Initiative, came together in July 2014 to develop a response to the question of whether it was possible to measure or quantify the impact of culture on the quality outcomes that matter to the patient.

The team, involving collaboration between industry and academia, shared insights gained from their experiences, programs, practices, and research. It soon became clear that no single tool or practice provided either a quantitative or qualitative “silver bullet” as a means to establish the current health of the quality culture within an organization.

This work led directly to the development of a cultural-excellence framework encompassing six different yet integrated dimensions of cultural excellence. (See Figure 2.) Taken together, these dimensions provide a pathway for an organization to foster and develop, monitor and measure, and learn and improve key areas that influence both culture and the underlying behaviors.

Work has now commenced on the development of tools, templates, and training resource materials within each of the individual dimensions.



Figure 2 : The Six Dimensions of Cultural Excellence

Context is crucial

A key tenet of ISPE's position on quality culture lies in the acknowledgment that each organization will have a different context within which its quality culture exists. This may be based on an amalgamation of influences, including organizational ownership and history, supply-chain configuration, maturity, product mix, and regional influences. At an individual site level, this can be further impacted by ready access to qualified staff, language, and the influence and maturity of the local regulatory authority.

Knowledge of this context and its impacts is crucial when assessing, or planning to develop, the health of the culture at a given facility. The Six Dimensions of Cultural Excellence framework incorporates elements that enable the capture of this context, such as in its use of Gemba walks to enable open dialogue, coaching, and active listening.

An outline of the holistic framework

The cultural-excellence framework opens with the “Leadership and Vision” dimension, which focuses on establishing and engendering the quality vision through leader-led behavior. Resources in this area will incorporate the 5V concept (Visibility, Vigilance, Vision, Voice, and Values):

- Visibility: Leader's presence, Gemba, what he or she gives priority to/ reacts to
- Vigilance: Leader's ability to drive accountability, grit, focus, follow-through
- Vision: Leader's strategy, game plan, unifying goals, mantra
- Voice: Leader's passion, credibility, authenticity, clarity, motivational ability
- Values: Leader's guiding principles, ethics, behavior, humility, empathy

The second dimension is understanding and influencing the “Attitudes and Mindsets” of the employees within the organization. This examines the relationship between the prevailing employee attitudes and mindsets and the actual behaviors practised in the day-to-day execution of tasks. Employee-engagement surveys, focus groups, and other mechanisms used to inform management of the current status of culture within their firm are under development, including best practices in closing the loop following the receipt of feedback from employees.

The third dimension is pivotal to the framework and involves assessing the behaviors through the use of “Gemba Walks.” This is closely linked to the leadership elements described above and is a key engagement and communication tool. When used effectively, Gemba walks provide an opportunity to unify and motivate and facilitate accountability and recognition. They are a powerful operational excellence tool, and their role in cultural-excellence development is key.

The framework then moves to those elements related to the monitoring and surveillance of key “Triggers and Leading Indicators of Quality (LQI).” In acknowledgment of the Peter Drucker truism “What gets measured gets managed,” the role of measurement in driving the desired behaviors is included in the model. These triggers and LQIs will not reflect the traditional quality performance metrics. Rather, they will focus on the selection of meaningful measures that target specific behaviors to promote prevention rather than a cure.

In closing the loop on the variety of surveys of attitudes, assessments of behaviors, and surveillance of targets and results, the fifth dimension explores tools to facilitate the proactive “Oversight, Reporting and Reviews by Leaders.” This dimension focuses on how best to integrate and convey the outputs of the various assessments and measurement tools in order to provide “heat maps” of where the current strengths and weaknesses lie to facilitate action by leaders.

Finally, the framework is completed through reflection on the “Cultural Enablers” required to build competencies in areas such as:

- Learning organization development and the development of learning teams
- Influencing and recognizing change
- Proactive problem solving and getting to the true root cause

In summary, this cultural-excellence framework seeks to provide a comprehensive set of practical tools and principles to enable organizations to move beyond sloganeering and deliver real and sustainable improvements in the behaviors that matter to their patients.

I would like to acknowledge the commitment and dedication of the many volunteer team members who persist and inspire this work. We look forward to sharing the outputs with you in the coming year. ■

By Nuala Calnan, PhD, Dublin Institute of Technology, Ireland

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