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Flawless

From Measuring Failure to Building Quality Robustness in Pharma

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For many years health care professionals in the US took drug quality for granted. Now, shortages, recalls, counterfeits, and contaminations seem to be in the news every other day, and Congress has passed legislation to secure the drug supply chain and better oversee imported medicines. But the real story, of course, is about drug manufacturing, and the path to consistent quality coupled to high efficiency. With all the challenges currently facing the pharmaceutical industry, it would seem that quality manufacturing might take a back seat. And traditionally, this has been the case. But crises have a great way of focusing the mind on what is important. For the industry to continue to be successful, drug manufacturing must become agile, rapidly scalable, efficient, reliable—and less costly. FDA has embarked on a new chapter of our "Pharmaceutical Manufacturing for the 21st Century Initiative." We hope to move closer to our vision of a pharmaceutical manufacturing sector that reliably produces high quality drugs without extensive regulatory oversight. This book reflects expert thought and experience on how the industry can get there.

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Making a case for change

Flawless: From measuring failure to building quality robustness in pharma

Andrew Gonce, Lorenzo Positano, Paul Rutten, Vanya Telpis

Having zero errors—being flawless—should be the one overriding objective for quality in the pharmaceutical industry. However, many pharmacos today continue to work on resolving issues and process deviations rather than emphasizing what it takes to build products and processes that are robust. How can we build better products and processes from the very start?

Over the past seven decades, the pharmaceutical industry has grown tremendously and developed a complex system to ensure that patients receive high-quality products. Yet as the levels of complexity have risen, so have the numbers of quality incidents—far faster than the rate of growth. Something more is needed.

This book provides some answers to the big question of what else the industry can do. In the pages that follow, McKinsey recognizes and applauds the industry's enormous efforts to strengthen quality performance. We also ask another pivotal question: whether, given stakeholders' rising expectations and the industry's soaring complexity, eternal vigilance must be the destiny of the quality function.

We believe there is a better way.

Probing for root causes

The hard truth is that there have been big increases in the number of incidents reported by the US Food & Drug Administration (FDA) and in the severity of those incidents. Many of the most acute drug shortages

can be traced to quality problems. And most regrettably, there are still instances where lives are lost or health is damaged as a consequence of bad product quality, as happened during the heparin scandal of 2008, or during the drug supply shortage for patients with Gaucher and Fabry diseases in 2009 to 2010.[1]

Pharmaceutical companies are attuned to the challenges, of course. They have been working overtime—and spending plenty—to ensure that quality issues are detected and reported in order to comply with regulators' quality standards. They have been all too aware of the risk of site closures for noncompliance—and of the enormous damage to reputation that several industry leaders have already incurred. At the same time, the public's expectations are rising. Now, the expectation for the industry is straightforward: zero lives lost, zero incidents, zero recalls, and zero defects.

So why is quality still such an issue, despite decades of vigilance and in spite of so many advances and innovations in production methods and in pharma science and technology overall? In part, the rise in the number of incidents can be explained by steadily increasing product volumes—up by 6 percent per year in the past decade alone. The risk of errors has also risen with the increasing complexity of the pharma supply chain (for example, the number of SKUs on an average packaging line is increasing by 8 to 10 percent every year) and with the fragmentation of the market—from more industry players to more nodes on the supply chain. Moreover, new product introductions are more complicated, featuring everything from advanced coating materials to drug-device combinations to far more diverse patterns of usage by patients. Those factors alone add up to a fundamental challenge: simply to keep quality incidents at the same levels as today, the industry needs to improve control of its processes tremendously.

A more fundamental challenge is that the pharma industry does not readily share learnings, particularly when those learnings stem from quality failures. Information that is shared tends to be focused on the failure incidents themselves, such as observations and warning letters. The industry bias toward punitive measures for noncompliance motivates pharmaceutical manufacturers to focus on tracking failures when they should be encouraged to investigate how to prevent failures in the first place.

Interestingly, pharma does much less to learn from its failures than is typical of the nuclear, petroleum, and aviation industries, for instance. The nuclear incidents

1 FDA briefing, March 19, 2008; "Drug tied to China had contaminant, FDA says," *New York Times*, March 6, 2008. Andrew Pollack, "Enzyme Drug Is in Short Supply", *New York Times*, September 15, 2011.

at Chernobyl and at Fukushima, as well as BP's Deepwater Horizon oil rig disaster, led to publicly accessible and easy-to-grasp explanations that delivered new ways of designing facilities, procedures, and processes. The nuclear industry has a history of producing well-written reports that are easy for the general public to understand and are based on clear root-cause analyses that highlight technical, management and cultural failures. The nuclear industry also uses easily searchable databases that contain a wealth of quantitative information on issues such as frequency of failure modes. But there are no comparable levels of reporting and no similar analyses or forums for the biggest pharma incidents.

Additionally, McKinsey's longtime experience in the industry has shown that many pharmacos are struggling to increase their process capabilities in line with rising expectations and ever-present cost pressures. Too often, these upgrades of the underlying processes and facility investments drop down the list of priorities.

There's also the challenge of shifting mind-sets across an industry that has focused predominantly on compliance rather than on truly knowing the root causes and effects of quality issues. Too frequently, we see failures attributed to individuals rather than being traced back to process or systems issues, fixes focused on retraining instead of permanent corrective actions, inspection responses focused on the warning letter rather than the spirit or intent of the observation. Many letters reference inadequate investigations and preventive actions. If it is tough to tackle the underlying processes and systems, it is markedly more difficult to shift the mind-sets of the quality group, not to mention those of the operations department.

There are other root causes. The industry is saddled with a set of products whose process design has been geared for speed to market, not for quality in mass production; there are few incentives to reformulate and retest products that were proven effective decades ago. Very few pharmaceutical manufacturers have found ways to make low-cost updates to existing processes and face expensive change controls or regulatory filings, which means that known quality issues or underperforming processes can linger for years. Additionally, there is a persistent sentiment that "if we dig too deeply into quality issues, we may learn something we're better off not knowing." Indeed, the risk and costs of these counter-incentives slow the progress that pharmaco executives want.

The same is true for the compliance bureaucracy created by the interplay of regulators and pharmacos. Quite a few companies have upward of 30,000

standard operating procedures (SOPs). One organization found that collectively, operators in its factory were applying 10 million signatures a year to batch records, deviation records, and so on. Think about it: if you were an operator with 90 or so SOPs against your name, could you be absolutely certain that you were always doing the right thing, every day and with every batch? More importantly, with so many SOPs to work with, how could you know which SOPs matter most to quality?

Similarly, change controls sometimes need dozens of signatures, a requirement that prevents fast turnarounds from the moment a quality issue is signaled to the point at which the pertinent process is fixed. The desire to eliminate risks has led to filing ever more variables and locking down specifications to levels that in some cases are literally impossible to maintain.

Perhaps most serious of all is the fact that quality is still too often seen as "something that the quality function does to us." Full support for quality requires active daily support by senior leadership, not to mention constant attention on the shop floor from shift supervisors. It also requires employees and managers to be trained and capable of making judgments about risk.

Overall, a pharmaco quality leader today who wants to drive change faces multiple impediments and challenges.

Resigned to eternal vigilance?

The upshot? It is not fun to work in a company that faces quality issues. Apart from the emotional burden of possibly harming patients, there is the extra bureaucracy of dealing with the aftermath of a crisis. Unfortunately, the converse is not necessarily true: a pharmaco without quality issues can still have inefficient and frustrating practices. Too often, quality expectations tend toward a kind of "eternal vigilance," with the quality organization in a gatekeeper role, keeping a watchful eye across the organization to minimize risks and suppress changes.

We believe this does not have to be the case. Quality improvement can be as rewarding as operational excellence. Best-practice processes alleviate bureaucracy and give employees the time to focus on what's truly important—that is, on reducing risks to patients. Building robustness in processes and products means that problems are prevented in the first place, leading to less rather than more need for quality oversight. The good news is that best practice in quality does not

have to be derived from scratch. There is substantial overlap with safety, health, and environmental best practices, and even with operational excellence and continuous improvement initiatives. The upshot: pharmacos can learn not just from the quality best practices of others in their industry but from a wide range of practices and industries.

A best-practice quality system has quality leaders who not only help to set standards but also are teachers and coaches who help the rest of the organization become stronger. As such, they can strive to build better systems, better culture, and more-robust practices that directly reduce the risks of quality shortfalls.

Putting such systems and cultural norms in place never happens by accident. McKinsey contends that pharmacos should be deliberate in benchmarking where they stand versus the relevant regulatory requirements, versus other companies, and even versus themselves on their best days. They should explicitly target clearly defined improvements and set up the right lean production and quality systems. After that, they need to seek out specific opportunities, projects, and cases where they can deploy their new quality practices. They have to look systemically for opportunities to scale best practices across their operating networks. Last but by no means least: they must look for ways to make continuous improvements, everywhere and every day.

Quality, then, is not about eternal vigilance. It is about building a system and culture of preparedness and robustness that can preempt many of the biggest risks.

The many returns on good quality

Today, most pharmaco executives understand the returns on good quality, but in a world that puts a great premium on measures such as net present value, they struggle to justify those returns. In general, investments in quality are considered "compulsory due to compliance" and typically are outside of the routine investment approval process. McKinsey's argument is that this stance fails to account for risk mitigation and undervalues the business impact of quality. Given the significance of the costs of noncompliance and the size of the opportunities to improve operations outcomes, quality must be managed not only with attention but with intention.

Considered in their broadest sense, the benefits of high quality are underestimated. Worldwide, pharma remains one of the most innovative industries

in terms of research. So why can't it have the same reputation in quality? An impeccable quality record and sterling quality processes would be—can be—an inspiration to patients, doctors, regulators, and employees alike.

At the same time, quality should be a source of renewal for the industry. It should be the reason for new research into better clinical trials, clearer product characterization, improved production methods, and more effective shop-floor operations—plus the inspiration for making products at much lower cost than ever before. It should enable pharma to stand tall as the industry with an outstanding quality record, with the ability to produce products that epitomize trust in corporations.

Put simply, pharmacos, together with their employees and investors, could reap rewards on many levels if their quality systems enabled results that are as close as possible to flawless.

No more merely measuring failure

So what would it take to attain such levels? The short answer is that it takes considerably more than most pharmacos are doing or even aiming to do today. The mark of the true leaders in quality will be visionary step-change approaches, not incremental evolution.

This book is designed to show such approaches in action. It offers ideas on how to think boldly, to set aspirational goals, to build the fundamentals, and to put the transformation into play.

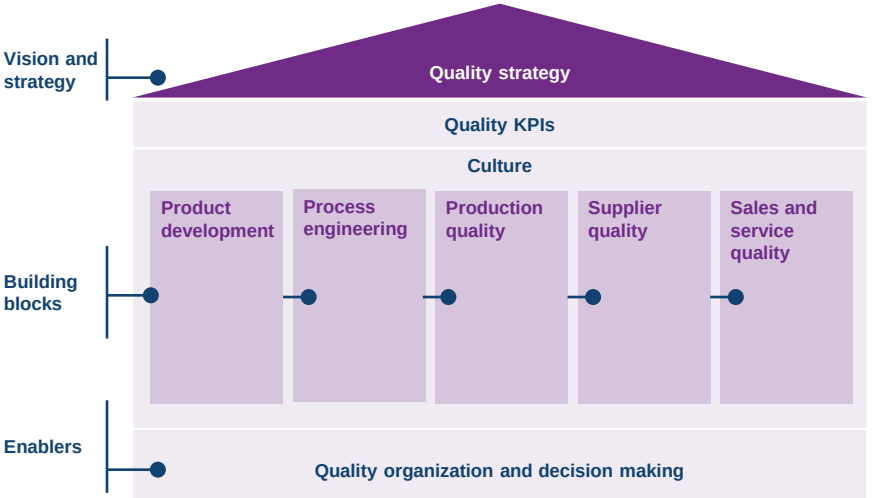
The book's perspectives are organized around five main themes. Three are tied to what McKinsey believes are the components of a comprehensive approach to quality—what we call the "House of Quality" (Exhibit 1):

- The vision and strategy
- The building blocks: functional quality processes
- The enablers: organization, governance, metrics, and culture

The other two themes address more holistically how a company with quality concerns should manage risk and remediation, and how it can go from good to great in terms of its quality performance.

Exhibit 1

A comprehensive approach to a quality system has 3 components



Source: McKinsey Quality Service Line

Here are snapshots of those five themes:

Quality vision and strategy

Recent years have seen significant industry shifts: more rigorous, more capable, and more sophisticated regulators; evolving thinking in quality systems; big data that provide transparency for regulators and payers. Individually and collectively, these factors create challenges and opportunities for pharmacos.

McKinsey contends that it is important for companies to set out a clear vision for quality improvement, using powerful examples to show why it is meaningful for all employees. How can a pharmaco move beyond compliance and short-term issue fixes to a step change in quality using new technologies, new science, and new management techniques? What is the right design for a quality system if it is to meet regulatory requirements but also be lean, simple, and agile? What best practices can pharma adopt from mature industries such as automotive,

aerospace, and semiconductors? How can they design their operating models, organizations, and culture so that they sustain quality best practices?

Building blocks of quality

Many pharmacos focus their quality improvements on manufacturing. However, those efforts should span the full value chain. Quality excellence starts with product and process development, where it's critical to have a scientifically sound review and quality assurance process that creates clear, measurable, and objective quality standards and accounts for risk-benefit trade-offs of a particular product or treatment. Quality excellence should also extend to external suppliers—increasingly important given the global span of today's supply chains. Proactive collaboration with suppliers and external manufacturers will help companies address and prevent significant issues. In manufacturing, quality improvement efforts should address operations fundamentals—increasing process capabilities and robustness and underscoring process execution with a robust quality presence on the shop floor. Good shop-floor process maturity can simultaneously deliver high quality, operational excellence, and short lead times.

Quality enablers

Winning in quality relies on good execution and on a robust culture of quality. Quality organization design may often be a top-of-mind concern, but we find it doesn't influence performance as much as execution and governance do. Culture is the fundamental ingredient in achieving good quality performance and enabling further improvement and change. Transparency of cost and performance is also essential, yet few pharmacos measure quality performance with leading indicators that cover fundamental operations. And fewer still gauge how quality is upheld on the shop floor.

Quality risk and remediation

The pharma industry is struggling with a big uptick in quality problems and much more regulatory scrutiny—challenges that can lead to significant short-term expenses and costly strategic consequences. If not handled properly, remediation efforts may fall well short of stakeholders' expectations. For companies that face regulatory challenges, the total cost of remediation is often far greater than realized—knowing the total cost upfront can help quality executives make better choices earlier in the remediation programs—before making major commitments.

Quality remediation can be done successfully without creating overhead that has to be "leaned out" later. Leading pharmacos apply proactive systematic approaches to identify and mitigate the top quality risks and ensure that business functions coordinate their activities.

Transforming quality from good to great

Overhauling quality activities is not only for companies in crisis; every pharmaco can and should do so. Companies that can currently claim good quality should not become complacent but push for higher levels of performance and greater risk preparedness. They should seek out compelling change stories that motivate and inspire employees to strive for continuous improvement. With that in mind, we share how one site made the transition from firefighting to prevention of quality risks, implementing a mini-transformation that addresses the entirety of how a production line operates. In a second example, we describe a US-based biopharmaceutical site whose quality-led transformation delivered enormous gains: a threefold improvement in productivity, with deviations cut in half.

Even after a major quality overhaul is under way, it can be a challenge to sustain the momentum; many efforts fizzle out once the initial goals are achieved or the most pressing issues are corrected. Transformations are by no means one-shot efforts, and they don't need to happen all at once. Scaling good practices across the organization can be done in a variety of ways, and this book gives specific examples of best practices, like designing and implementing mini-transformations that address one unit a time.

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We hope you find these topics relevant, important, and, of course, interesting.

Ideally, this book will spark new ideas or spur fresh initiatives that allow you to further improve quality in your organization. We hope that the industry can indeed shift its emphasis from "eternal vigilance" to "production system design," which will help to achieve a performance that is close to flawless.