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Quality Excellence: The next frontier for the Indian pharmaceutical industry

Quality Excellence: The next frontier for the Indian pharmaceutical industry

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Page 4

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Page 5

Contents

1. Indian pharmaceutical industry – the journey so far	4
2. Distinctive capabilities across the value chain	8
3. Indian pharmaceutical industry’s commitment to quality	12
4. Six areas for improvement in quality for Indian pharmaceutical companies	16
5. Holistic quality transformation through operating, management and people systems	20
6. Quality excellence examples from other industries	22
7. Potential steps to build quality excellence	26
8. IPA’s aspirations and commitment for future	32

Quality Excellence: The next frontier for the Indian pharmaceutical industry

1

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Chapter 1

Indian pharmaceutical

industry – the journey so far

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Page 9

1. Indian pharmaceutical industry – the journey so far

The Indian pharmaceutical industry makes a unique contribution towards ensuring the supply of affordable and quality medicines to the developed and developing world. India accounts for 60 percent of global vaccine production, contributing 40 to 70 percent of the WHO demand for DPT (Diphtheria, Pertussis and Tetanus) and BCG (Bacillus Calmette–Guérin) vaccines, and 90 percent of the WHO demand for measles vaccine (Exhibit 1). Today, India is a leading provider of drugs

for international public health institutions, such as the US President’s Emergency Plan for AIDS Relief (PEPFAR), Clinton Foundation, and Doctors without Borders (MSF). It provides more than 30 percent of annual UNICEF supplies globally.

Exhibit 1

Indian industry’s contribution to global drug access



SOURCE: Press Information Bureau; "Affordable Efficacious Medicines – All Roads Leads to India" report by IDMA; BrandindiaPharma.in

Through its position in the generics market, the Indian pharmaceutical industry helps to substantially reduce healthcare costs across the world. Generic drugs were responsible for health-related savings of USD 254 billion¹ in the year 2014 in the US. According to latest Indian Pharmaceutical Alliance (IPA) estimates, the share of products of Indian origin in US pharmaceutical sales increased from 18 percent in 2009 to 33 percent in 2014. In the UK, approximately 25 percent of the medicines used are made in India². In Africa, the availability of affordable Indian drugs contributed to greater access to treatment for AIDS with 37 percent of AIDS patients receiving treatment in 2009 compared to just 2 percent in 2003³.

Within India, the industry continues to supply drugs, including essential drugs, at highly affordable prices. While first-generation HIV medicines came with a price tag of USD 10,000 nearly a

1 Generic drug savings in the US Report 2015, GPhA

2 UK and India regulators agree deal for closer collaboration to improve public safety, Press Release, Government of UK, 5 October, 2015

3 Pharmaceuticals: India’s generics flow into Africa, African Businesses Magazine, 19 January 2012

Quality Excellence: The next frontier for the Indian pharmaceutical industry

Exhibit 2

Indian pharma industry’s contribution to affordable healthcare



drugs approved by
US FDA for PEPFAR¹

of all medicines
dispensed in US²

health system savings in US³
by generic, generic
contribution by India
USD 254 bn

***Millions will die if India
cannot produce new HIV/AIDS
medicines in the future – it is a
matter of life and death⁴***

– UNAIDS

***Generic medicines
have saved the US health
system USD 1.7 trillion
from 2005 to 2014⁵***

– CDER, FDA

¹ US FDA website's International Programs section
² IFA estimate, 2014
³ Generic drug savings in the US Report 2015, GPhA

⁴ 'UN welcomes India's decision to continue making generic HIV/AIDS drugs',
July 6, 2011, UN News Center
⁵ Congressional Testimony, Director CDER, US FDA, February 4, 2016

decade ago, multiple generic manufacturers in India provide these medicines at roughly USD 100, today, a reduction of more than 99 percent. Similarly, treatment costs of life-threatening diseases such as chronic myeloid leukemia and hepatitis C were reduced to less than 5 percent of the original costs. The industry has supplemented this with effective initiatives to drive access and awareness across the country, leading to around 50 percent higher drug penetration in rural India.

The Indian pharmaceutical industry creates a large number of jobs—estimates suggest that India's pharma industry directly and indirectly employs nearly 2.5 million people⁶. More than a million new jobs were created in the pharmaceutical industry in the last five years, mostly in high-skilled areas like R&D and manufacturing. India's domestic economy has also gained immensely from the pharmaceutical industry. The industry generates around USD 10 billion⁸ of trade surplus every year and is the third-largest contributor to reducing India's trade deficit.

The industry is striving to continue its remarkable contribution to public health across developed and developing countries. According to the US FDA, India accounted for 33 percent of ANDA filings in 2015, second only to the US at 44 percent. Similarly, more than 40 percent of DMFs filed in 2014⁹ were from India. Indian companies accounted for 1,200+ UK MHRA (Medicines and Healthcare products Regulatory Agency) market authorizations by May 2014¹⁰. Recent developments such as the indigenous manufacturing of new vaccines and the India–US oncology agreement are expected to further strengthen India's global position.

⁴ amFAR, Foundation for AIDS research, Doctors Beyond Borders (MSF)

⁵ *Access to Costly New Hepatitis C Drugs: Medicine, Money, and Advocacy*, Oxford Journals, Vol 61, Issue 12; Changing the cost of care for chronic myeloid leukemia, PMC, October 2015

⁶ OPPI Annual Report 2013–14, Census of India

⁷ *Indian life sciences: Vision 2030*, FICCI June 2015

⁸ Export Import Bank of India; Reserve Bank of India

⁹ US FDA website

¹⁰ ¹¹ Annual Report 2014-15, Pharmaceutical Export Promotion Council of India (Pharmexcil), Set-up by ministry of commerce and industry, Government of India

Chapter 2

Distinctive capabilities across the value chain

© Getty images

2. Distinctive capabilities across the value chain

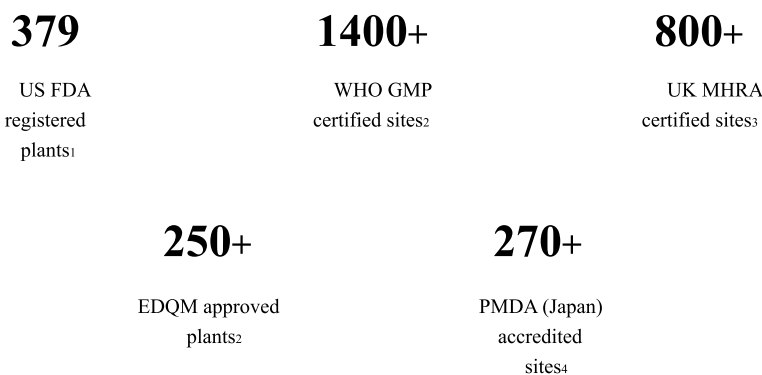
The Indian pharmaceutical industry’s success is built on a foundation of distinctive capabilities in key areas of the value chain. In particular strong manufacturing, product development and process innovation capabilities have enabled Indian companies drive significant efficiencies.

Over the past two decades, the industry has invested heavily in upgrading its manufacturing plants to match international standards. Approximately 1,400 manufacturing units in India are WHO GMP¹¹ (Good Manufacturing Practices)–certified, and over 800 are UK MHRA¹¹ approved. India continues to have the highest number of US FDA-registered¹² manufacturing facilities outside the US (Exhibit 3). The industry can boast of indigenously producing almost all pharmaceutical formulations and bulk drugs. Driven by strong process innovation capabilities, it is considered as one of the world leaders in efficient and cost-competitive manufacture of API.

The industry also has strong capabilities in product development (Exhibit 4). Indian pharmaceutical companies have the largest share of DMFs and ANDAs outside the US. Between 2011 and 2014, India received 37 percent of the total ANDA approvals in generics, 22 percent of global ANDA approvals in speciality generics and 14 percent of 505(b) two approvals in new therapeutic entities¹³.

Exhibit 3

The Indian pharmaceutical industry has one of the largest number of manufacturing plants of international standards



¹ US FDA website, API and formulations manufacturing plants only

² 11th Annual Report 2014-15, Pharmaceutical Export Promotion Council of India (Pharmexcil), set-up by ministry of commerce and industry, Government of India

³ Pharmexcil Report 2012

⁴ Pharmaceuticals and Medical Devices Agency (PMDA), Japan website

¹¹ Pharmexcil data 2012

¹² Manufacturing sites with a unique Facility Establishment Identifier (FEI) number assigned by FDA to monitor and track inspections of regulated firms

¹³ Evaluate (2013), US FDA website

More than 1100 Certificates of Suitability (CEPs) by European Directorate for the Quality of Medicines and Healthcare (EDQM) were received by Indian manufacturers as of 2015¹⁴.

Indian companies are increasingly focused on innovation — the Indian pharma industry’s share in the number of complex products approved by US FDA increased from 15 percent in 2011 to 34 percent in 2013¹⁵. Over 60 biosimilars¹⁶ (30 active substances¹⁷) are already approved for marketing in India. Two new medical entities (NMEs) developed by Indian companies—Synriam and Lipaglyn—have also been launched in India.

Exhibit 4

Evolution of the Indian pharmaceutical industry



¹ Includes active Type II DMF filings

SOURCE: US FDA (for number of DMF filings)

¹⁴ Pharmexcil 11th Annual Report 2014–15

¹⁵ US FDA Orange Book

16 FirstWord Pharma biosimilar Index, McKinsey Biosimilar Interest Group
17 CDSCO data listed by GaBi Online

10

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Chapter 3

Indian pharmaceutical industry's commitment to quality

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3. Indian pharmaceutical industry’s commitment to quality

The global pharmaceutical industry faces the challenge of upgrading quality systems and delivering life-saving medicines simultaneously. India is no exception. On one hand, the industry is moving towards complex products, driving automation and integrating new technologies. On the other hand, current good manufacturing standards (cGMP) are evolving rapidly across the globe. While companies realize the importance of building stronger quality and operations systems across their manufacturing facilities, quality systems have unfortunately not seen upgrades at a proportionate pace.

The global pharmaceutical industry has seen a rise in quality sanctions in recent years. Between 2008 and 2014, the number of product recalls and warning letters received by pharma companies globally tripled¹⁸. On average, one pharma facility across the world entered into a consent decree every year since 2008. Many major pharma companies received warning letters or multiple 483s across multiple sites in the last few years.

In India, too, pharmaceutical companies have had mixed success in upgrading their quality systems. The number of warning letters from US FDA to Indian manufacturing sites has increased in the last five years. While the proportion of OAI and VAI decisions in US FDA inspections has remained the same (around 65 percent), the number of inspections increased by 30 percent in 2015 (Exhibit 5).

Exhibit 5

Inspections of Indian Pharma manufacturing sites by US FDA



102

OAI + VAI 65% 63%

	Avg. 2011–14	2015	Avg. 2011–14	2015
Share of global total	6%	11%		

¹ CDER inspections for Drug Quality Assurance
² Data available up to September 2015 extrapolated for whole year
 SOURCE: US FDA inspections database

18 Gold Sheet multiple issues

Quality Excellence: The next frontier for the Indian pharmaceutical industry

13

Page 18

Four GMP non-compliance reports were issued to Indian companies in 2015 compared to an average of around eight in 2011–14¹. In the last five years, ~30 percent of quality related warning letters, ~10 percent of OAI inspections and less than 5 percent drug recalls were attributed to Indian companies (Exhibit 6).

As the industry continues to grow and expand in scale and complexity, it is crucial to pursue quality excellence relentlessly.

Exhibit 6

Regulatory actions on Indian pharma manufacturing sites by US FDA

	102 ¹	296 ²	6,604 ³
Rest of world			
India	~30%	~10%	~4%
	Warning letters	OAI inspections	Drug recalls

¹ For 2011–2015 as of January 2016 on FDA website
² CDER OAI inspections in 'Drug Quality Assurance' project area from 2011 to September 2015
³ For 2011–2015, excludes single incident in 2011 in which Aidapak Services realized that penicillin could have cross-contaminated numerous products
 SOURCE: US FDA website; FDA inspection database; FDA enforcement sheets

19 EduraGMDP database

14

Quality Excellence: The next frontier for the Indian pharmaceutical industry

Chapter 4

Six areas for improvement in quality for Indian pharmaceutical companies

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Page 21

4. Six areas for improvement in quality for Indian pharmaceutical companies

The IPA, working jointly with McKinsey & Company as the knowledge partner, has formed a Quality Forum to identify and focus on six areas for improvement in quality. The Group recognizes that quality issues have the potential to affect patients adversely. We are committed to addressing these quality challenges comprehensively and upgrading quality management systems to deliver world-class outcomes.

4.1. Establishing robust and seamless data management and documentation

Data reliability has emerged as an important area globally. Of the 19 quality-related warning letters issued globally in 2014, 10 had data reliability issues. Similarly, in 2015, 9 out of 10 quality related warning letters issued globally (up to August 2015), cited data reliability concerns. Reflecting these concerns, the UK MHRA, WHO and Parenteral Drug Association (PDA) released fresh guidance documents in 2015 emphasizing data integrity and good record management.

Some of the improvement areas highlighted by the IPA Quality Forum include accurate and contemporaneous data recording, access controls for sensitive data (e.g., eliminating common user logins and password information for multiple users), audit trails and data storage and maintenance practices.

In addition to directly addressing these issues, it is important to improve underlying processes and capabilities that can impact data reliability. These enablers include upgrading documentation systems (e.g., from manual to electronic data), improving employees' understanding of critical parameters, simplifying processes (e.g., change control) and their documentation (e.g., manufacturing records) and increasing awareness and capabilities. It is also critical to establish management oversight (e.g., governance and metrics) simultaneously or ahead of time.

4.2. Ensuring effective and robust quality investigations

According to UK MHRA, 'Investigation of anomalies' is one of the most frequent defect categories observed in its inspections worldwide²⁰. A direct consequence of weak investigation systems is that companies often face recurring deviations²¹ impacting product quality. A global pharmaceutical industry benchmark²² reveals that top quartile companies face only 5 percent recurring deviations while for median companies, the rate is 13 percent. Improvement areas include problem definition, root-cause analysis and comprehensive risk management processes.

As the industry grows, it is important to build best practices across the six stages of quality investigations and the corrective and preventive actions (CAPA) process—identification of deviation or incident, investigation and root-cause analysis, corrective and preventive action, implementation, verification and effectiveness monitoring. These include developing the right tools, defining the right success metrics and identifying the right team.

²⁰ Review of GMP Inspections Deficiencies, UK MHRA, 2013

²¹ "Recurring deviations" can be defined as deviations that recur within two years from the first instance

²² McKinsey's POBOS benchmarking which covers 600+ plants across the globe

4.3. Aligning management systems with increasing operational complexity

As the industry scales up, it is crucial to build effective management systems. These include metrics to help managers understand quality performance and risks to quality and forums to enable decision making and tracking until effective implementation. Regulations require pharmaceutical companies to regularly conduct quality management reviews and are increasingly emphasizing standardized metrics.

Appropriate metrics can build in leading quality indicators, incorporate measures of culture and capture total risk from quality. Leading indicators help anticipate quality issues. Measuring and baselining quality culture are initial steps in driving a culture transformation. Incorporating risk from poor quality in addition to the direct cost of quality is critical to drive optimal decisions. These could be implemented through a balanced scorecard that captures quality holistically.

To measure parameters correctly, it is important to define metrics in detail and without ambiguity, define calculation methodology with linkage to raw data and apply metrics consistently across sites. The definitions and calculation methodology should be in line with emerging regulatory

requirements. Further, the cadence of forums should enable every level (from shop floor to top management) to solve problems, review, make decisions and escalate when required.

4.4. Building a culture of quality across the organization

Extensive research on the topic of organizational health and performance shows that companies with a stronger quality culture ultimately have better operational outcomes overall²³. A global pharmaceutical industry survey²⁴ shows a positive link between quality culture and performance as well as quality productivity (Exhibit 7).

It is true that the understanding of a ‘culture of quality’ varies across organizations. Arguments abound over the meaning of a culture of quality and how it could be defined or measured. Many companies and leaders believe that measuring quality is an elusive goal. However, a study²⁵ conducted across 100+ plants globally including many in India shows it is feasible to measure quality through a combination of an employee level survey, focus group discussions and deep structured interviews. The same study also found 3–5 major mindsets and behaviours related to the ‘culture of quality’ and how they differ between geographies (India and the world).

International Society for Pharmaceutical Engineering (ISPE) and McKinsey have come together to pilot the demonstration of the feasibility and value of tracking standard quality metrics in the pharma industry²⁵. The goal of ISPE is to enable better understanding of performance of sites and hence allow participants to gain better insights into the implications for setting up internal processes and facilitating change management dialogues with internal stakeholders.

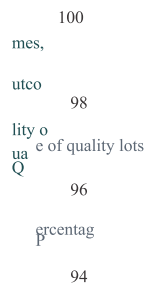
4.5. Expanding and upskilling the talent pool

With increase in scale and complexity of operations, there is a need for both higher numbers of professionals as well as broader skill-sets of quality and operations. The recent increase in remediation

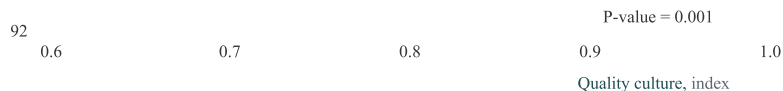
23 Flawless; “The invisible but essential foundation: Fostering a culture of quality in pharma”, by Alessandro Delfino, Paul Rutten, Vanya Telpis, McKinsey & Company
24 McKinsey’s POBOS benchmarking which covers 600+ plants across the globe
25 <http://www.ispe.org/quality-metrics-initiative/ispe-concludes-successful-quality-metrics-pilot-wave-1>

Exhibit 7

Quality culture is empirically linked to quality outcome: Stronger culture scores lead to higher quality outcomes



R₂ = 0.29



R² measures how well variability of a given metric X explains variability of metric Y. It ranges from 0 (no relationship) to 1 (perfect linear relationship)
 P-value is probability that correlation is zero, value below 0.05 indicates significant results
 SOURCE: POBOS Quality Survey; ISPE Quality Metrics pilot July 2014 to March 2015

activity is adding further to the demand. At the same time, fresh graduates need months of additional training before they are industry-ready. Even professionals with experience in domestic manufacturing often need significant retraining before they can be deployed at quality manufacturing sites. This supply-demand mismatch is reflected in high attrition rates at multiple Indian sites, contributing to a vicious cycle of heavy workload, high attrition and resource challenges in quality functions.

In addition, as the industry’s product portfolio shifts towards more complex products, the demand for operations and quality personnel for the manufacture of these products is also increasing. There is a limited supply of experienced talent for such operations. Some players have recognized this talent crunch and have initiated internal training programs to systematically train employees. There is a need to set up and operationalize industry-wide ‘at scale’ capability building programs that go beyond just training people.

4.6. Embedding quality into product development and technology transfer

A product lifecycle view to quality emphasizes building robustness into our products and processes at the early stages (e.g., design and development or technology transfer). This is a fundamental yet hard-to-address challenge in pharmaceutical manufacturing. The industry currently operates at approximately three-sigma level globally with an average Process Capability Index (CpK) of 1.2 for solids and 1.0 for steriles²⁶. This often leads to compliance risk, unnecessary costs, supply disruptions and wasted efforts.

There are several ways to improve quality performance, ranging from an increased understanding of the critical parameters in the manufacturing process to end-to-end knowledge management from filing to commercialization. Companies have to move towards a structured approach that incorporates quality processes at every stage of the product life cycle.

²⁶ McKinsey’s POBOS benchmarking which covers 600+ plants across the globe

Chapter.5 Holistic quality transformation through operating, management and people systems

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5. Holistic quality transformation through operating, management

and people systems

Addressing quality issues requires a combination of interventions across systems — operating, management and people (Exhibit 8).

Exhibit 8

Outstanding quality involves building quality into operating, management and people systems



SOURCE: McKinsey Quality, Compliance and Remediation service line

5.1. Quality in the operating system: Product development and operations

Operating systems ensure that the technical solution is in place and the SOPs required to follow the solution are established. This requires upgrading SOPs and protocols in line with guidelines and best practices (e.g., validation of SOPs in line with ICH Q8). In the long-term, this means building quality into product development and transfer processes, supported by a deep understanding of critical quality attributes, process parameters and material attributes.

5.2. Quality in the management system: Power of predictive metrics and effective governance

Strong management systems help management to rapidly identify issues, design solutions and ensure effective implementation of solutions. A best-in-class management system anticipates and proactively resolves quality issues through predictive metrics. It also plays a critical role in ensuring that learnings are effectively transferred across sites and functions.

5.3. Quality in the people systems: Embedding a culture of quality and robust training infrastructure

We need to strengthen our people systems to develop a culture of quality across organizations. This calls for capability building, resourcing, work-planning and setting the right quality aspiration.

Chapter 6

Quality excellence examples from other industries

6. Quality excellence examples from other industries

Multiple Indian companies across industries, such as airports, airlines, hospitality, automotive, steel and information technology (IT) have been able to build a culture of outstanding discipline and quality. The common theme across these companies is a holistic approach towards quality. As we embark on this journey and develop our roadmap, we can draw on the experiences of these institutions. In particular, we feature case studies of these sectors as well as industry bodies (e.g., NASSCOM) which played an instrumental role in driving an industry-wide quality agenda.

Indian airports are at the forefront of delivering world class customer service quality at scale. Delhi and Mumbai airports are among the busiest airports globally with annual passenger traffic between 25 to 40 million²⁷. Both these airports have been recognized among the global top five Airport Service Quality (ASQ) airports in the second highest annual passenger traffic category four years in a row²⁸. Moreover, the Delhi's Indira Gandhi International Airport is the top ranked ASQ airport in the Asia-Pacific region today²⁹, and has consistently been in the top five since 2012³⁰.

Similarly, airlines from India have a strong track record of safety comparable to other large economies like the US, the UK and France³¹. India's largest low cost carrier—Indigo Airlines—has built a reputation for discipline. It is ranked among the top 10 players globally with an average on-time performance of 81 percent³². In terms of customer service quality, Indigo is in the top 10 globally and top three in Asia, according to Skytrax's customer satisfaction survey³³. Indigo Airlines won the Airbus "Best Operational Excellence Worldwide" award in 2014³⁴ among 300+ large fleet operators globally. The award recognized its disciplined operations among a number of technical and efficiency-related parameters³⁵.

There are a number of other such examples. Indian organizations are leading from the front in the luxury hospitality sector. Hotels from the Oberoi Group along with the Taj Group rank among the top 10 hotels globally³⁶. Toyota India, which has zero defects per vehicle, is among the top units in the global Toyota network. Tata Steel, India's third largest and the world's 11th largest steel company^{37,38}, is the first integrated steel company outside Japan to win the Deming Grand Prize in 2012³⁹ for TQM excellence.

27 Airports Council International Airport Service Quality (ASQ) Survey

28 Airports Council International ASQ rankings 2011–2015

29 Airports Council International ASQ rankings 2015

30 Airports Council International ASQ rankings 2012–2015

31 Aviation Safety Network; Cumulative accidents data from 1945 to January 2016

32 Average Ranking and OTP data over 4 quarters on the basis of FlightStats database (July 14 – July 15)

33 Skytrax World Airline Awards, 2015

34 Achievements; website of Indigo – <https://content.goindigo.in/Information/Awards#2014>

35 Indigo wins Airbus award, Business Standard, 21 May, 2014

36 Travel and Living Magazine, World Top 100 Rankings 2014

37 JSW Steel catching up fast with Tata Steel, Business Standard, 24 November, 2014

38 Statistics; World Steel Association

39 Union of Japanese Scientists and Engineers (JUSE)

Exhibit 9

Indian players have been able to build a culture of quality and discipline

#1 ranked airport worldwide: Delhi International Airport; in the top 3 for 4 years in a row

Mumbai and Delhi airports are among the **Top 5** airports in Asia-Pacific in terms of Airport Service Quality (ASQ)

10th best in cumulative air accidents record; ahead of US, UK, and France

Top 3 in Asia³ with a customer satisfaction score of 8/10

Indigo Airline **won** the Best Operational Excellence Award among 311 airlines⁴; **Top 10** in on-time performance in Asia-Pacific⁵

Leaders in hospitality globally: Oberoi Group and Taj Hotels

Have properties ranked in **Top 10** by Travel and Leisure magazine

¹ ACI Airport Service Quality ranking for 25 to 40 million passengers per annum, 2014
² ACI, 2014

³ Skytrax database
⁴ Achievements, website of Indigo, Airbus A320 award
⁵ FlightStats database over July 2014 to July 2015

While these organizations have been able to demonstrate a culture of discipline, industry associations like NASSCOM have also been able to facilitate quality-at-scale in their respective sectors. NASSCOM's concerted efforts over the last two decades have helped the Indian IT industry emerge as a reliable and high quality service provider and in the process, have contributed immensely to global economy.

The IPA is already taking inspiration from NASSCOM's approach as it aims to achieve industry-wide product and process robustness. We are optimistic about achieving this through a holistic approach along with industry action at scale that engages stakeholders like governments, regulators and customers.

Case study

How did NASSCOM establish quality-at-scale in the IT industry?

In the early 1990s, the Indian IT industry was facing challenges in establishing its reputation as a reliable and high-quality service provider. The National Association of Software and Services Companies (NASSCOM) was instrumental in bringing together and galvanizing the IT industry around a common standard for quality and establishing robust quality processes industry-wide.

NASSCOM was able to achieve these outcomes by tackling the quality problem through interventions at multiple levels⁵⁰:

- Driving adoption of globally accepted quality standards such as Carnegie Mellon University's Capability Maturity Model Integration (CMMI) for process and delivery excellence, Project Management Professional certifications for project management expertise and ISO 27001 for data security expertise. These were further complemented by individual company-level certifications, e.g., CISCO, .Net, Oracle, Java.
- Initiating industry-level dialogue with experts to build capabilities to support uniform and effective implementation of standards. This created an ecosystem of accreditors and auditors.
- Comprehensively engaging external stakeholders such as customers, industry analysts, consultants, regulators and business media through industry events and publications in India and abroad.

NASSCOM also encouraged its members to learn from best-in-class companies and focus on identifying and eliminating any process gaps to build robustness.

Through NASSCOM's continuous efforts, the Indian IT industry was able to become a crucial part of the global IT industry providing economic value add to over 90 percent of Fortune 500 firms⁵¹. The industry is now recognized for helping corporations transform and become globally more competitive.

40 Interview with Som Mittal, ex-President of NASSCOM

41 Contribution of India's Tech Industry to the US Economy; NASSCOM, 2015

Quality Excellence: The next frontier for the Indian pharmaceutical industry

25

Page 30

Chapter 7

Potential steps to build quality excellence

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Page 31

7. Potential steps to build quality excellence

Achieving our quality goals requires concerted action from individual companies, IPA, regulators and government.

- Pharmaceutical companies need to diagnose and identify challenges and design and implement solutions. Initiatives typically span operating, management and people systems. Many of these initiatives may draw heavily from industry wide collaborative efforts driven by the IPA.
- IPA will facilitate industry-wide collaboration, like creating best practices, creating guidelines, developing training content and building industry-wide institutional mechanisms.
- Government and regulators, both Indian and foreign, can support industry by providing inputs and feedback on initiatives by industry bodies to ensure quality, and engage constantly on any changes in regulations.

7.1. Potential steps for pharmaceutical companies

7.1.1. Operating system

- **Evaluate and upgrade Quality Management Systems (QMS):** Quality management systems require constant upgradation as companies evolve. For this purpose, companies could comprehensively evaluate their existing systems against the latest guidelines and evolving current good manufacturing practices (cGMP). As they identify and address gaps, a risk-based prioritization approach will help ensure that each solution gets adequate resources and management attention.

Typical areas of improvement include validation and technology transfer processes, data reliability, risk management including robust internal audit systems, investigation and CAPA management, sterility assurance, IT and project management processes. Several pharma companies have already moved to action. While most companies are upgrading these processes, many have also launched multi-year quality transformations to fundamentally upgrade their QMS.

As a part of QMS upgradation, pharmaceutical companies could extend quality discipline to suppliers and contractors by guiding and helping them with their quality system.

Finally, as organizations become larger and distributed across various geographical locations, formal continuous improvement processes help ensure that the QMS remains agile, harmonized and lean. This implies continually scanning the external world for evolving global best practices and regulatory guidance. It also includes rapidly sharing internal CAPAs and lessons learnt across the network. Many pharma companies are establishing regulatory surveillance groups and cascaded CAPA management systems such as control towers to address this. As the QMS improves continuously, a formal well-defined document hierarchy helps ensure harmonization across the organization.

Page 32

- **Embed quality into the product lifecycle:** Factors affecting patient safety and commercial product quality can be addressed at every stage of the product lifecycle. During product development, companies need to incorporate a stage-gated Quality by Design (QbD) process with clear quality related milestones at each stage.

Technology transfer processes aim to build capability in the operations team to ensure quality on a commercial scale factoring the operational constraints at the site. This may require sustained cross-functional engagement beyond just three validation batches.

Further, during commercial production, continuous process verification help ensure processes to remain in a state of control and build better process understanding. Companies may also make one time effort to enhance understanding of Critical Process Parameters (CPPs) and Critical Material Attributes (CMAs) of legacy products.

Perhaps even more importantly, strong quality feedback loops across stages to ensure information sharing could be established. These could include formal involvement of operations from the early stages of the stage-gated development process, cross-functional risk management forums e.g., FMEA workshops, and robust knowledge management especially between filing and launch.

7.1.2. Management system

- **Harmonize metrics driving accountability and collaboration:** Cascaded quality metrics from the CEO to the shop-floor help drive accountability for quality outcomes at every level of the organization. For instance, while unconfirmed OOS is a metric often measured at a site or product level, it is also critical for each lab cell or lab group to measure and review this based on their contribution to this overall metrics. Similarly, shared metrics could help drive effective collaboration across functions. Harmonization is a key enabler for effectiveness of these metrics. Over the past year, several Indian companies have seen the advantage in proactively ensuring a shared understanding of metrics across sites, common calculation methodology and accountability. Companies should detail out the definitions of metrics for common understanding, link them to raw data and create a standardized reporting template.

Initiatives to implement quality metrics are already underway in the industry. For example, ISPE in cooperation with McKinsey, established the Quality Metrics Pilot Project in 2013.

This program compiled selected metrics for 44 sites across 18 companies allowing participants to gain insights into the relationship between various metrics as well as practical challenges in implementing harmonized metrics across sites and companies.

- **Adopt predictive metrics over and above output metrics:** Predictive metrics help identify and resolve quality issues in time. Industry benchmarks like POBOS commonly track predictive metrics such as right-first-time rate, yield, CAPA implementation time, investigation cycle time and recurring deviations. There is a high degree of correlation between these predictive metrics and eventual quality outcomes. Measuring and acting on these indicators could potentially help pre-empt quality issues.

42 <http://www.ispe.org/news/2014/metrics-pilot-launched>

28

Quality Excellence: The next frontier for the Indian pharmaceutical industry

Page 33

- **Improve governance mechanisms:** Companies could further strengthen cascaded review mechanisms through regular forums from the shop floor to the CEO. Multiple Indian pharmaceutical companies already have senior management forums. This cascading needs to be enforced consistently and formalized as part of the company's governance mechanism. These mechanisms could be linked to shop-floor review discussions through a set of common metrics.

Finally, it is important to emphasize, the role of strong top management support and engagement in adopting and driving quality initiatives.

7.1.3. People system

- **Embed a culture of quality:** This requires companies to develop and implement a holistic plan across four blocks of culture change methodology. These include (a) extensive and multi-layered communication (b) role modelling by senior leaders (e.g., senior leaders' engagement in site walk, Gemba, and coaching and problem solving) (c) building skill set (see next section) and (d) adopting changes in the way we measure performance (balancing productivity and quality) and rewarding employees (e.g., for systematic approaches to solving problems rather than one-time fixes).
- **Develop robust capability building infrastructure:** Large-scale quality transformations often require companies to build capability across the organization. Capability building goes beyond mere classroom training, and requires using learning principles that thoughtfully combine classroom training and field work.

Capability building should include front-line (e.g., operators, QC and QA analyst) as well as middle and senior managers and address both mass and at scale capabilities as well as targeted specialized topics (e.g., data reliability, sterility assurance in injectables).

An objective, metric-driven approach to measure training effectiveness is also an important element in capability building. This requires close alignment between the QMS element and the

quality training management process.

- **Strengthen the organization:** As the complexity and scale of operations evolve, companies may need to strengthen the organization by creating new specialist roles and upgrading competencies in existing roles.

For example, embedding quality across the product life cycle (e.g., validation and continuous process verification), driving excellence in investigation and building robust data reliability systems all require a specialized and cross-functional skill set. Companies may build these specialist roles gradually based on criticality of the function to their organization.

7.2. Potential steps for IPA

IPA intends to support companies in the quality excellence journey through the following actions

- **Create guidelines on key elements of quality:** IPA intends to focus on creating a targeted set of guidelines to help the industry as a whole. For example, IPA has initiated creating a data reliability guideline that is being built in consultation with IPA companies and external experts. It also invites inputs from regulatory authorities on the guideline document.

Quality Excellence: The next frontier for the Indian pharmaceutical industry

29

- **Facilitate creation of best practices:** As individual companies upgrade their QMS, the IPA intends to support creation of best practices for the industry as a whole. It will also attempt to also bring together pharmaceutical companies to define and measure key benchmark metrics for quality.
- **Evolve a strong pool of pharma talent:** IPA intends to work closely with academia to ensure that the curriculum addresses changing quality challenges in the industry by inclusion of courses like SCADA and IT in quality. IPA will, in future, consider the feasibility of facilitating large-scale interventions and coordinate with pharmaceutical companies to develop learning modules to deliver practical learning in these institutes.

7.3. Potential steps for regulators and the government

Regulators can potentially support Indian pharmaceutical companies by being part of various industry-wide initiatives on quality—guiding companies and industry bodies by providing feedback on guidelines, best practices, benchmarks and training modules under development. Regulators could also help through periodic dialogue to clarify our understanding of guidelines, clauses and metrics.

Chapter 8

IPA's aspirations and commitment for future

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Page 37

8. IPA's aspirations and commitment for future

We have begun the journey of quality excellence by setting up the IPA Quality Forum dedicated to helping support improvement in quality systems across the industry. The IPA Quality Forum has initiated focused actions in three areas.

- **Data reliability:** The IPA Quality Forum has developed a version of detailed implementation oriented data reliability guidelines. These draw from published guidelines from various regulators and translate them into tactical guidance on designing operating, management and people

systems for data reliability. The guidelines directly address six elements critical for data reliability — technology systems, process design, risk management, governance, culture and capability.

In addition, the IPA Quality Forum members have initiated knowledge sharing for creation of best practices for targeted areas like process validation, investigation, vendor qualifications and good documentation practices

- **Capability building and culture:** The IPA Quality Forum plans to conduct a quality culture survey across 6 major Indian pharmaceutical companies to baseline culture and identify industry wide shifts required. The forum also plans to develop industry standard capability building modules on topics such as data reliability, investigations and sterility assurance. The aim is to develop a consistent industry-wide terminology on these topics, use experiential learning techniques to drive true capability building and facilitate at scale deployment by using technology.

Pilot Quality Change Leaders Forum for middle managers conducted on 16, and 17, February 2016

Quality Excellence: The next frontier for the Indian pharmaceutical industry

33

Page 38

- **Defining and measuring key Quality metrics:** The IPA Quality Forum aspires to define and measure key quality metrics. This will be useful to create a baseline for the companies to define and achieve progress. As a first step, the IPA Quality Forum has identified the following metrics — Lot acceptance rate, Product quality complaint rate, Invalidated OOS rate, Annual product review time rate and CAPA effectiveness rate. The IPA Quality Forum is in the process of streamlining the data collection and starting a pilot.

IPA acknowledges that these are early steps in the long journey of quality excellence. Over the next five years IPA will work to:

- Measure and benchmark Indian pharma quality with the rest of the world and track progress.
- Create targeted guidelines and best practices.
- Expand the skill and capability of quality talent for Indian pharmaceutical companies.

To facilitate measurement and reporting of the progress towards quality, IPA will develop a five-year action plan with clear intermediate milestones over the next 12 months. IPA will also review the progress annually and further refine the plan.

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It is the stated aspiration of IPA to help Indian pharmaceutical industry in its journey to be the global benchmark on quality. We, at IPA, intend to deepen and strengthen the industry's relationship with key stakeholders — Indian and global. IPA commits to being the conduit for change in the industry through thought leadership, knowledge development and member engagement.

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