PHARMACEUTICAL INDUSTRY AND COMPLIANCE

Whitepaper

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Introduction

From a modest $2 million in 1948 to a healthy $26 billion in 2010, the Indian Pharmaceutical Industry has shown steady growth in the last 6 decades.[1] India currently represents $6 billion of the $550 billion global pharmaceutical industry and its share is growing at 10 percent a year, compared to 7 percent annual growth for the overall world market.[2] The Indian pharmaceutical industry is responsible for around 8% of world pharmaceutical production [3] and is expected to reach $20 billion by 2015. This will make it one of the world's top 10 pharmaceuticals markets. [4]

In the last few years, Indian pharmaceutical companies have been increasingly targeted by multinationals for both collaborative agreements and acquisition. India's largest export destination for pharmaceuticals is USA, followed by the UK, Germany, South Africa and Russia. Pharmaceutical exports are booming at $13.9 billion, with formulation exports at $5.8 billion and APIs at $8.1 billion. [5]

This growing opportunity has brought with it fresh challenges in the form of international business requirements, faster time to market and compliance. Compliance is the most critical, as non-conformance can lead to huge fines, plant shut down, and even imprisonment. Mergers and acquisitions (M&A) further complicate business operations. The M&A activity creates broken and inefficient processes as companies struggle to integrate new operations while maintaining a regulatory environment.

Due to the stringent regulatory environment, higher business complexity and increased accountability, organizations now are taking steps towards pursing compliance. US Federal regulations require companies to maintain a secure audit trail of information for every phase of drug development, from invention to even distribution.

Compliance: A Critical Consideration

Pharmaceutical companies nowadays are located across various geographies and are subject to local laws. Compliance varies from state to state and is subject to frequent and unpredictable changes. To run a successful manufacturing unit, the company has to comply with all national and local standards. Adhering to compliance becomes very important and requires full time monitoring and expertise to mitigate risks.

Non-compliance leads to large fines, delay in product approval, product recalls, plant shut downs, and even imprisonment. In addition the adverse publicity generated directly impacts sales and customer confidence.

Recently, the Chennai manufacturing facility of Orchid Chemicals & Pharmaceuticals Ltd was issued a closure notice by the Tamil Nadu Pollution Control Board (TNPCB). [6] This facility makes active pharmaceutical ingredients (APIs). The **closure notice** to the facility by TNPCB was issued due to non-compliance of regulations related to the disposal of solid waste.

Non-compliance of good manufacturing practices (GMP) in Mexico has led to the US Food and Drug Administration (FDA) banning Dr Reddy's Laboratories products manufactured at their plant in Mexico. As a result of this **import ban,** Dr Reddy's Laboratories stands to lose up to $30 million. [7]

The FDA issued a **warning** to Cadila Healthcare for the violation of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals at its facility in Gujarat. Sanand plant of Cadila was inspected by the FDA again and the failure to implement sufficient corrective actions may result in the FDA refusing admission of articles manufactured at the Sanand facility into the US. [8]

Rosenberg Pharmaceutical Company was **prohibited** from manufacturing and distributing drugs by the federal government due to a *"history of significant violations"* of manufacturing requirements.[9] It failed to obtain required FDA approval for its prescription drug products. It also failed to comply with FDA regulations governing OTC drug products and current good manufacturing practice requirements.

Highly Regulated Environment

Today firms need to strictly adhere to regulation to prevent shutdowns in manufacturing operations, product withdrawals, fines, lawsuits, revenue loss, and tarnished reputations. Regulations apply across the entire product cycle - from invention to testing, manufacturing, and even marketing.

Governmental agencies regularly track various records to check compliance. These include history records that have manufacturing dates, manufactured and released quantity, components consumed and acceptance records that indicate if the product was manufactured in accordance with the approved process. Records may also include operator data such as, operator training, compliance with standard operating procedures (SOP) and existence of electronic signatures at different steps in the manufacturing process.

Effective compliance requires a combination of industry regulations knowledge, accurate real time information, and risk focused indicators to establish a program that not only identifies potential compliance issues but adds insight to business process improvement.

Achieving regulatory compliance is crucial for pharmaceutical companies and needs to be built in as part of the manufacturing infrastructure. Compliance helps the organization develop processes and internal controls to meet the requirements imposed by governmental bodies, regulators, industry mandates or internal policies. It also helps build product that meets and exceeds customer expectations.

Manufacturers can achieve compliance using a manual or an automated approach. Manual process of compliance is subject to human error and increased risk in quality checks, and having an automated system in place helps reduce risks of disordered practices. Manufacturers are undergoing a transition from manual to automated process to minimize human errors, reduce production cost, improve product quality and time to market.

Manufacturers that have plants spread across several continents and various product lines get nearly 100% benefits from automation of compliance. [10] Smaller manufacturers that are partially involved in research can reduce laboratory labor content by 40-50% compared with the equivalent paper-based operations by using automated compliance. [11]

Manufacturing Execution Systems (MES)

A Manufacturing Execution System (MES) is an electronic interface between personnel, equipment automation, orders, logistics, equipment and processing instructions and helps provides control over each part of production process.

MES helps bridge the gap between regulatory control and operational control. Regulatory affairs are focused on compliance and manufacturing operations are focused on manufacturing and quality issues. By bringing these groups together, MES helps pharmaceutical companies reduce time-to-market; improve manufacturing efficiency and product quality, while at the same time lowering manufacturing costs and developing products that meet regulations. It also enables review by exception for batch records.

Benefits

Pharmaceutical manufacturers can garner many benefits by switching from paper recordkeeping systems to automated data-collection systems. MES helps manufacturers ensure that operators follow the process as it was designed by engineering and allows management to accurately map the physical plant. It also allows the management to deploy current instructions and specifications to the plant floor to ensure that any changes to the process are incorporated as quickly as possible, with an appropriate and approved process validation.

- **Reduces cost of compliance** by automating quality assurance functions and reporting features, thus reducing the effort required to research product deviations.
- **Increases productivity** by electronic documentation of batch records.
- **Reduces error in documentation** by regular data entry in sequence and also eliminates calculation errors.
- **Provides quick and easy access** to product and process data.

- **Increases throughput** and reduces cycle time by minimizing paper work, rework and unnecessary checks.
- Enables pharmaceutical manufacturers to **synchronize business processes** across multiple plants, while allowing for plant-specific variations.
- **Improves the visibility of Work in Progress (WIP) Inventory**, helping reducing the excess stock.

- Helps plant personnel **uncover rework loops** that reduce manufacturing efficiency and increase the risk of product failure.
- **Improves efficiency** by eliminating redundant verifications like material checks, weight verification and product checks.
- **Enforces adherence to manufacturing process**, ensuring all tasks are completed, carried in proper sequence & performed by properly trained operators.
- **Replaces scattered file cabinets** with a computerized database.
- MES has the ability to **detect & react to production problems early** in the process.
- **Reduces time to market** by enabling review by exception for batch records. MES helps in tracking stock and work procedure throughout the manufacturing process by using WIP tools. This aids in saving time and costs by reducing cycle time, thus contributes in reducing time to market.

MESTECH Services Private Limited

MESTECH Services Private Limited is a Manufacturing IT consulting firm headquartered in Pune, India with operations spread across India and US.

We focus on Technology Consulting and Software Implementation for managing Manufacturing Operations. We have been successfully delivering technology consulting services to Automotive and Life Sciences majors with focus around implementing Manufacturing Execution Systems. We execute projects from concept to completion, wherein we start with requirements gathering and end with commissioning the system onsite, followed by support. Furthermore, we specialize in Rockwell Automation's MES solutions (PMX, FTPC, FTPS) that are based on their FactoryTalk platform. We are strategic partners with Rockwell Automation (RA) and Cognizant Technology Solutions (CTS).

List of Acronyms

MES: Manufacturing Execution Systems

FDA: Food and Drug Administration

TNPCB: Tamil Nadu Pollution Control Board

API: Active Pharmaceutical Ingredients

OTC: Over The Counter

ERP: Enterprise Resource Planning

WIP: Work in Progress

M&A: Mergers and Acquisitions

GMP: Good Manufacturing Practices

CGMP: Current Good Manufacturing Practice

SOP: Standard Operating Procedures

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