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Good Distribution Practices for Pharmaceutical Products

Setting the Context

Innovations driven by new science and technology have transformed human healthcare beyond recognition in the last 50 years. The healthcare industry has evolved with our deepening understanding of the human body and disease. New products and services in Pharmaceuticals, Biotech, MedTech, Diagnostics, and Patient support have transformed medical care. With technological and scientific advancement, our understanding of product quality and its determinants have significantly improved, and in parallel, customer expectations around product quality have tremendously increased. Our ability to manage product manufacturing, product quality, and quality deviations has undergone significant transformation too. Consequently, the entire management of product design (with quality built into the design), raw material and input quality, manufacturing quality (infrastructure, process control, etc.), and supply chain quality are today required to meet standards that are far more rigorous and controlled than ever before.

The Indian pharmaceutical industry is a mature industry that has witnessed remarkable growth over the last few decades. India is a key player in the world Pharmaceuticals market today and is known as the "Pharmacy of the world," supplying a very significant share of the global demand, especially of generic pharmaceuticals and vaccines. The domestic pharmaceutical market in India has similarly witnessed tremendous growth and development.

Our vision for the Indian Pharmaceutical industry needs to be to maintain and improve on this leadership position and make India a preeminent global hub for pharma. This will involve strengthening our standards across the entire supply chain, including manufacturing and distribution. Our goal should be to ensure global standards for manufacturing plants and product quality, both for domestic and international markets.

This needs to be supported by the required regulatory standards, administration, and implementation.

The finished product distribution component of the supply chain of pharmaceuticals in India needs immediate focus and attention from all stakeholders in the system. Today, distribution in India is still fragmented, unorganized, and characterized by wide variation in infrastructure quality, processes and systems, and technical capability. This could put product integrity, quality, and patient safety at risk. Pharmaceutical distribution in all developed markets is governed by regulations/guidelines known as Good Distribution Practices (GDP). WHO also has published GDP guidelines for pharmaceuticals, and it is essential that

India defines and adopts her GDP without further delay. The Indian regulator - the Central Drugs Standard Control Organization (CDSCO), has developed and issued draft guidelines for Good Distribution Practices (GDP) for pharmaceuticals in 2018 for comments. We believe that it is imperative to finalize and implement these guidelines as soon as possible.

The implementation of pharmaceutical GDP guidelines will ensure that India keeps pace with peer countries in ensuring optimal product quality, reduce counterfeit drugs and product contamination in the system, and also importantly help in managing product recalls in case of adverse events/quality deviations. The GDP guidelines will ensure that adequate distribution standards are followed in our domestic market and not just in export markets.

In line with the industry vision and patient safety requirements, the Organization of Pharmaceutical Producers of India (OPPI) aims to bring up this important discussion around GDP guidelines with this whitepaper. It is essential that quality is embedded in our supply chain in keeping with global best practices

Sharad Tyagi

President, OPPI
Managing Director, Boehringer Ingelheim India Pvt. Ltd.

K G Ananthakrishnan

Director General, OPPI

Foreword

While COVID-19 has brought global and national healthcare under scrutiny, the world continues to depend on Indian pharmaceutical and vaccine manufacturers substantially for their supply of medications. The Indian pharmaceutical industry has an important role in promoting local and global health goals. Rightly hailed as the 'Pharmacy to the World,' Indian pharma is home to over 3,000 manufacturers and ~10,500 manufacturing units, with domestic annual revenue of USD 20 billion as of 2019. The world's 3rd largest manufacturer by volume, India's role in manufacturing affordable medicines, particularly generics, makes the industry critical in the global landscape.

An industry with strong continuing growth prospects, Indian pharma still has considerable room to improve in the area of quality standards for domestic distribution practices. With experts suggesting that the pharmaceutical industry could grow to ~USD 100 billion in size by 2025, there is a clear need for strengthening domestic and global supply standards to unlock such potential.

Good Distribution Practices or 'GDP' aim to establish standards to help maintain the quality and integrity of pharma products across the supply chain. As GDP would cater to a wide range of products with different storage requirements and shelf lives, this challenging initiative requires close collaboration between policymakers and the industry. India's complex Supply Chain, which has limited traceability and a highly localized and fragmented last-mile delivery network, further compounds the challenge.

Effective management of product distribution is globally recognized as a critical issue and receives continuing focus and attention from major stakeholders and regulators. Global regulators have identified and addressed it, with the USFDA, WHO, EU, and PIC/S issuing GDP guidelines in their respective jurisdictions. Overall, these guidelines focus on critical areas like quality management, warehouse management and storage standards, product transportation and tracing, and training and manpower development, among others. India's pharmaceutical GDP initiative was initiated by the Central Drugs Standard Control Organization (CDSCO) in 2018, with the release of draft guidelines. These now need to be rapidly reviewed and finalized, followed by quick well-governed implementation.

Establishing and abiding by detailed and well-structured GDP would go a long way in solidifying the global aspirations of Indian pharma. Not only can GDP help improve patient health outcomes, but it can also help address reputational, litigation, and financial risks for pharma manufacturers. This includes managing product recalls, reducing counterfeiting, or ensuring compliance with local permissions, among others. The supply chain needs an overhaul and a regulatory impetus can certainly catalyze the change.

As India moves to achieve the goal of 'One Nation, One Drug,' the quality gap between export and domestic markets needs to be eliminated. While the initiative requires significant monetary and policy investment, the clear and tangible benefits to stakeholders in the medium to long run certainly justify it.

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- MSD Pharmaceuticals Pvt. Ltd.
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- Novo Nordisk India Pvt. Ltd.
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- Pfizer Ltd.
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- Sanofi India Ltd.
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- Takeda Pharmaceuticals India Pvt. Ltd.
- UCB India Pvt. Ltd.

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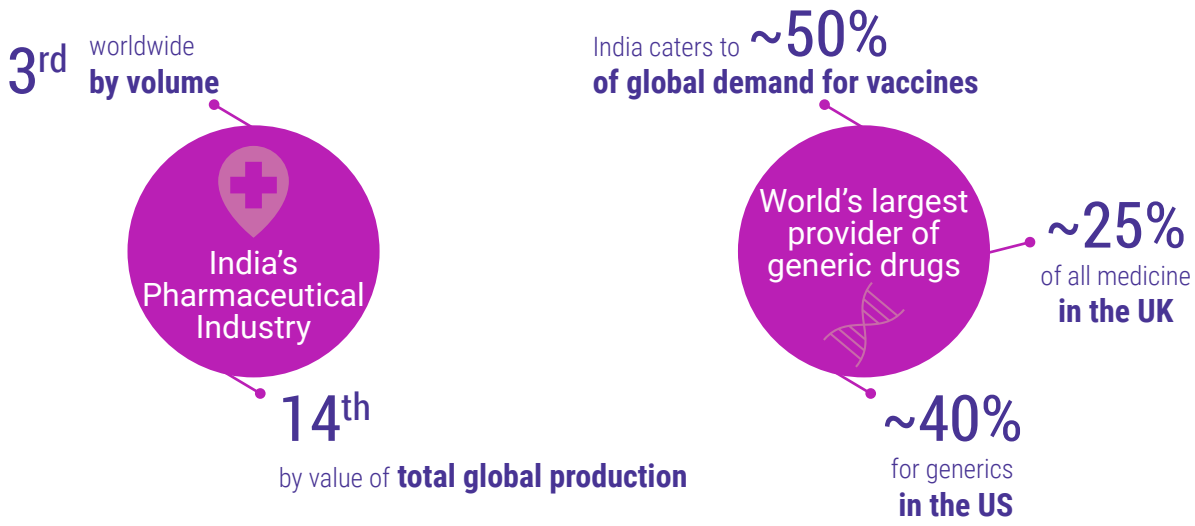
India's Role in the Global Marketplace



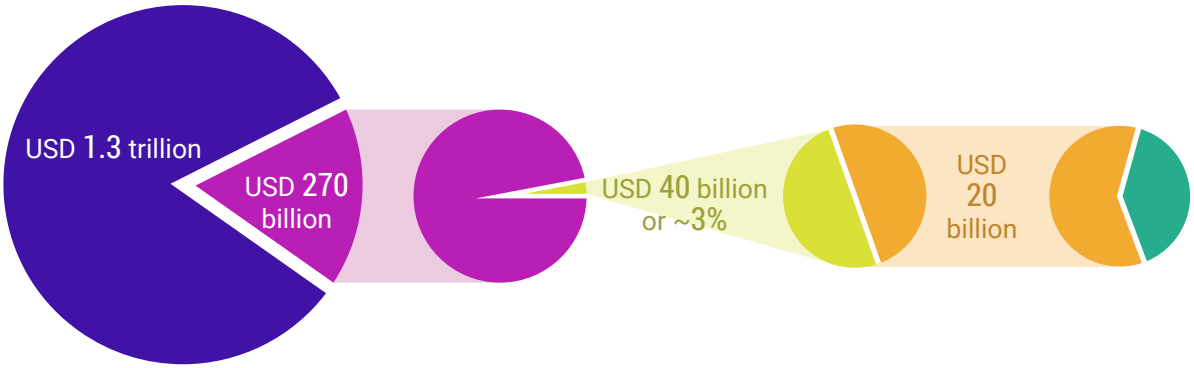
This makes India a critical player in the global pharmaceuticals industry. Further, with an existing talent pool of highly qualified scientists and engineers, India has the capability to strengthen and consolidate the position as the

'pharmacy to the world'.

Overview of India's Domestic Manufacturing Capacity

India is currently home to the highest number of US-FDA compliant Pharma plants (more than 262 including Active Pharmaceutical Ingredients or 'APIs') outside of the USA, more than 2000 WHO-GMP approved sites, and 253 European Directorate of Quality Medicines (EDQM) approved sites. Domestic production spans nearly 60,000 generic brands across 60 therapeutic categories and around 500 different APIs. The market size of India's API manufacturing in 2019 was valued at USD 9.8 billion, accounting for 57% of the APIs on the WHO's pre-qualified list.

Size and Growth Rate



40% of that export is predominantly to the US, with the UK, alongside major exports to African countries.

Global pharma industry | **Global generic pharma industry** | Indian pharma industry | Indian exports

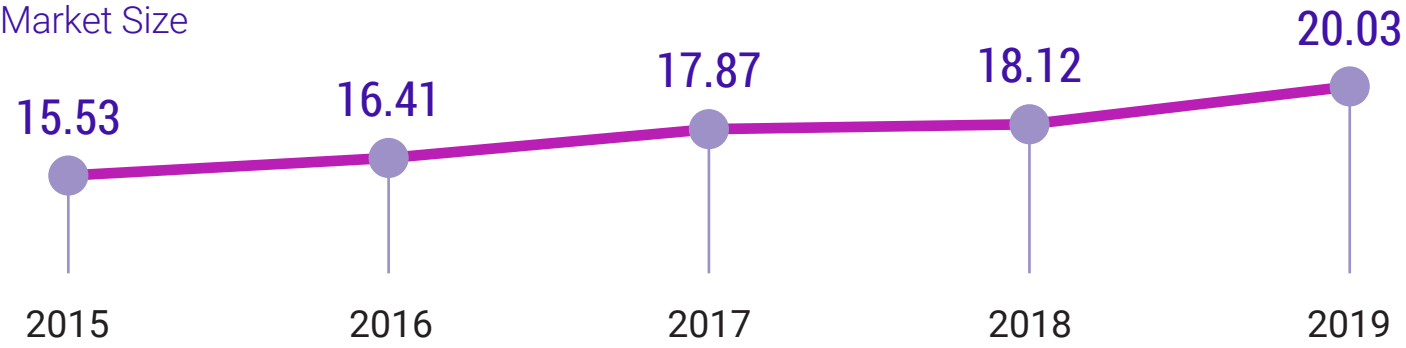
In the next 4-5 years, patents valued at ~USD 200bn are expected to expire.

India's generics industry can greatly benefit from this opportunity, potentially reaching

~USD 100 billion in size by 2025.

Revenue of Domestic Pharmaceutical Sector (USD billion)

Market Size



The Indian Pharmaceutical Landscape

Ensuring uniform product availability across India's large and diversified geography is a herculean task for manufacturers. The plethora of stakeholders involved, each with unique challenges and systems, further adds to this complexity. End consumers access drugs in a variety of ways, through traditional retail chemists, e-pharmacies, or even hospitals. Hence, drugs both literally and figuratively travels a great distance before reaching the end consumer, posing concerns on **quality and efficacy.**

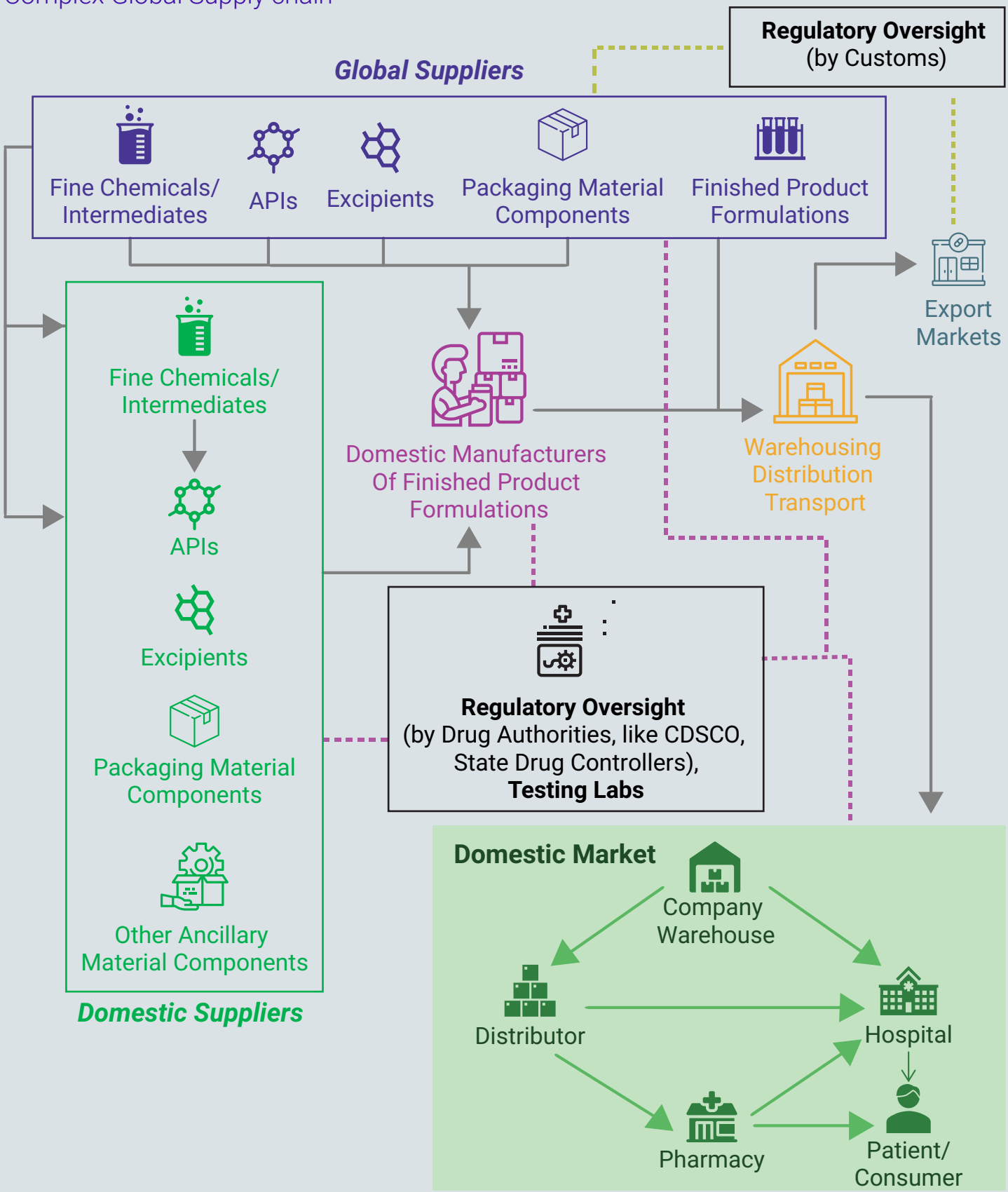
Equitable access to drugs and healthcare services is still a challenge in India. Accessibility is far greater in urban areas than in the rural parts of the country, which not only leads to information asymmetry but also a lack of awareness about available treatments.

With a variety of challenges across the length and breadth of the country, the pharma industry is stretched on multiple fronts, including the number of therapies, price points, striking an urban-rural balance, etc. A deeper analysis of the supply chain, roles of stakeholders, and regulatory constraints can help represent the scale and complexity of operations within the industry.

The Pharmaceutical Supply Chain

The Indian pharmaceutical industry has a unique supply chain structure, and a large number of participants makes integration or streamlining difficult. The complexity and fragmentation raise a variety of concerns around storage and transportation procedures, product quality and safety, and traceability, among others. These issues have repercussions at multiple levels that can affect health outcomes.

Complex Global Supply chain



E-pharmacies

Compared to traditional trade, e-pharmacies present another modality of distribution, adding to the complexity of the supply chain. The industry is expected to witness steep growth and an increase in vendors, compounding the complexity problem. Hence, it is important to bring about standardization in terms of supply chain and quality management. To achieve this, the role of various stakeholders in this value chain becomes critical.

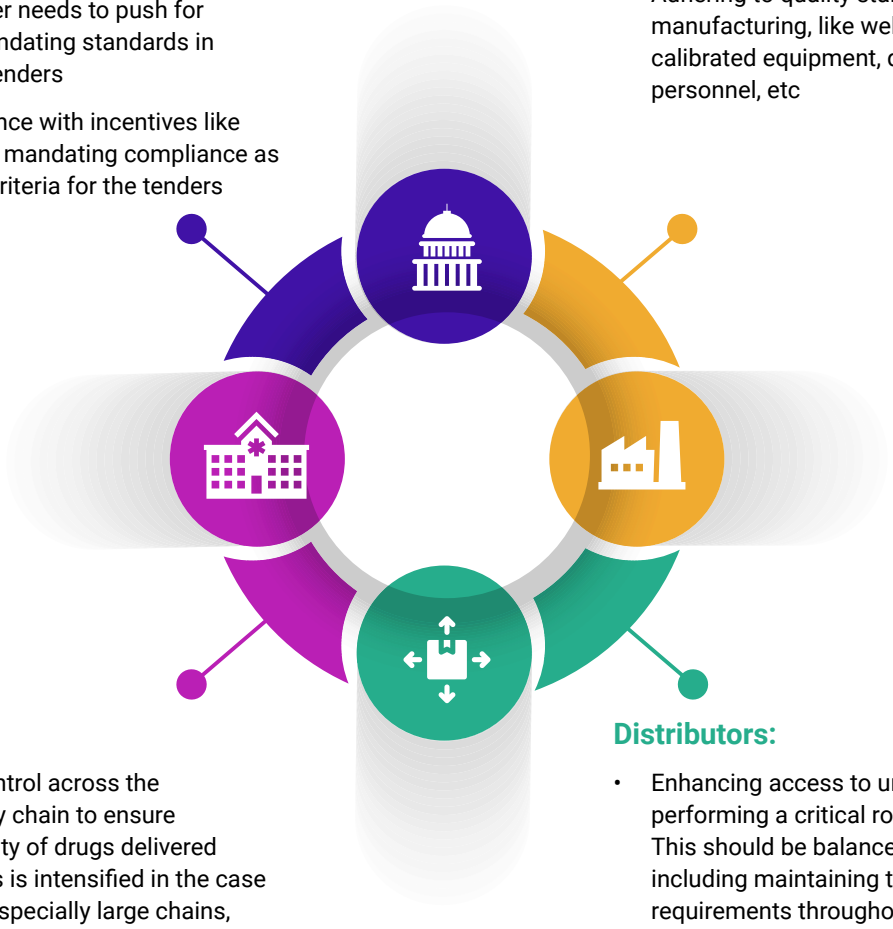
Role of Stakeholders in Quality Management

Government/Regulator:

- Developing a strong regulatory environment with best-in-class regulations and strict enforcement, which is essential to sustaining India's market leadership position and ensuring patient safety
- As one of the largest consumers/buyer of drugs, this stakeholder needs to push for higher quality by mandating standards in public procurement tenders
- Encouraging compliance with incentives like preferential pricing or mandating compliance as part of the eligibility criteria for the tenders

Manufacturers:

- Recognizing the critical and irreparable nature of patient trust and focusing on maintaining it
- Ensuring that all vendors and partners adhere to temperature and storage requirements for each product
- Adhering to quality standards during manufacturing, like well-maintained facilities, calibrated equipment, qualified and trained personnel, etc



Hospitals:

- Mandating quality control across the manufacturer's supply chain to ensure uniformity in the quality of drugs delivered across locations. This is intensified in the case of private hospitals, especially large chains, that procure drugs in bulk through central procurement contracts
- Enforcing quality measures in purchase contracts, since this channel is an important source of revenue for the manufacturers
- Maintaining temperature and storage requirements for drugs at their premises until the medication is dispensed, with proper documentation

Distributors:

- Enhancing access to underserved areas by performing a critical role in last-mile access. This should be balanced with quality control, including maintaining temperature and storage requirements throughout the transportation journey
- Distributors have to educate and inculcate a culture of compliance across sub-distributors and retailers to ensure that drug efficacy remains unchanged

The way to ensure that the quality of the product is maintained across the supply chain is to mandate regulations and guidelines which direct how drugs are transported and stored across the supply chain. While it is a massive effort, which would increase both – supplier costs and supervisory effort to trace quality control at various stages, it is critical to improving health outcomes. In other words, it is well worth the effort and cost!

Varying Regulatory Requirements:

- Currently, Indian pharma manufacturers export drugs to over 150 countries, each with a different set of regulations and guidelines. Moreover, India is the largest supplier of vaccines that need WHO approval, necessitating compliance with the body's regulations
- The country-specific regulations for drugs are different not only for formulations but also for labeling, packaging, etc. Product specifications have to be customized for each country, which leads to increased production runs, more SKU's, and documentation
- There are often different storage and temperature control regulations for a variety of drugs that have to be adhered to, from the factory to the end consumer
- Essentially, in the last two decades, quality standards across the globe have been evolving and becoming more stringent
- It is crucial to bring the local Indian standards to a minimum base for all manufacturers so that we eliminate quality differences between India and global markets. This is the only way to achieve the goal of 'One Nation, One Drug'

Introduction to GDP Requirements

Why are GDPs needed?

- Pharmaceutical Labels
- Distribution
- Exploring the need: GDPs in India

Pharmaceutical Labels

A pharmaceutical product label is a critical part of the product's packaging. It conveys necessary information about the drug from a manufacturer, distributor, physician, and patient perspective, including the conditions required to maintain product efficacy. With this perspective, a label is crucial for both the distributors and consumers. Some of the key information aspects the label covers is as follows:

Shelf Life

This includes the manufacturing date and the use by date, indicating the period in which the drug can be consumed.

Dosage Information

For OTC products, it can indicate how much of the drug can be consumed by the patient and when. For others, it could also say that the dosage should be prescribed by physicians basis the patient's treatment needs

Storage Information

Advises where or how the drug has to be stored, for example, 'store away from direct sunlight' or 'store at 15 to 30 degrees centigrate'

Batch Number

An identifier for a particular package unit of drug indicating the manufacturing lot/batch number. This helps investigation and further actions in case of complaints or reported adverse reaction.

Warnings

This indicates the possible side effects of the drug or adverse effects of exceeding the prescribed intake

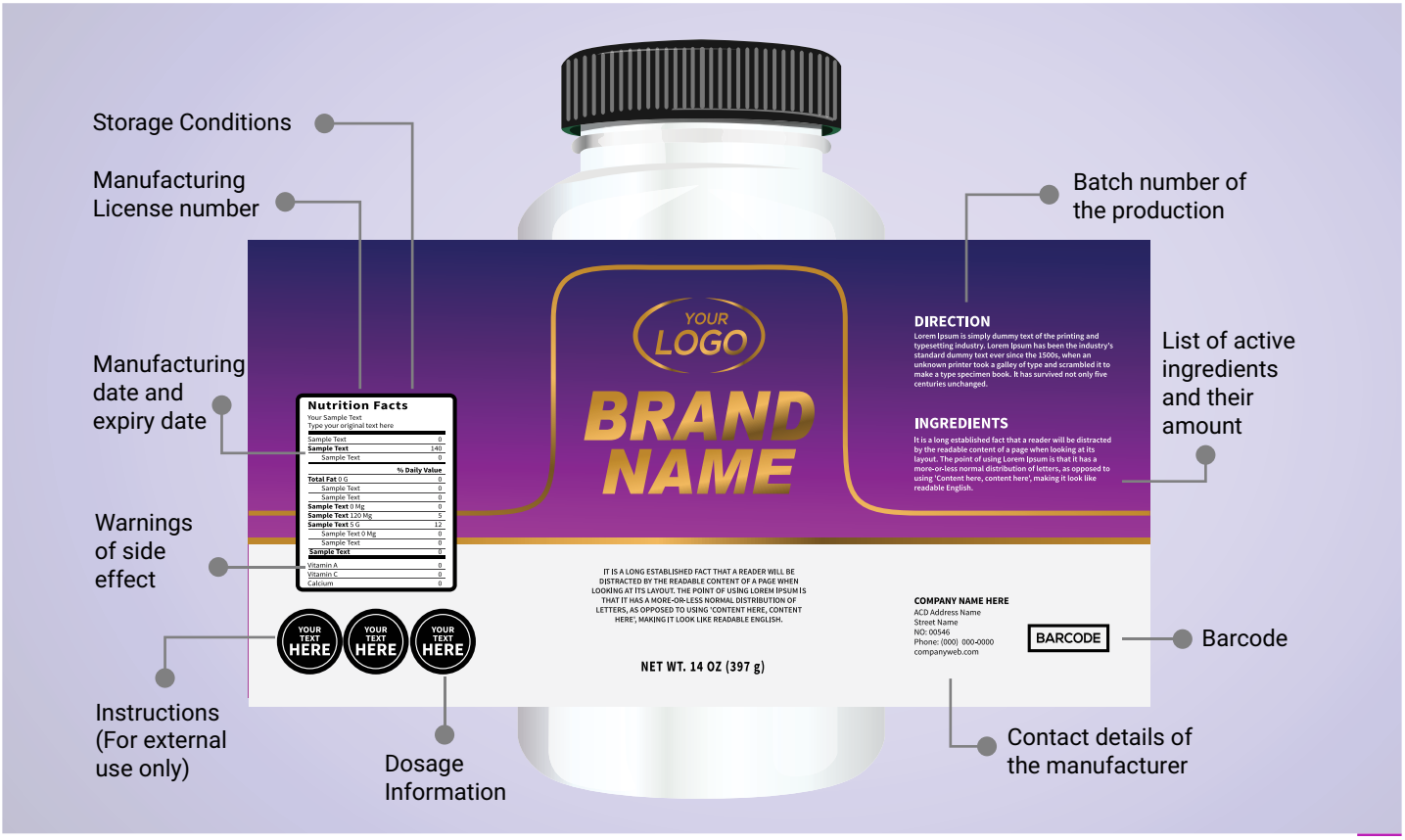
Instructions

Outline how to consume the drug, where they need to be stored, and other necessary information

Barcode

These act as identifiers but could contain more information than the 'batch number,' including the supply chain stakeholders, i.e., distributor, stockist, and retailer involved in relaying the package to the patient. This helps identify counterfeit drugs and track recalls, and product returns. In India, barcodes are mandatory on exported products but voluntary for domestic distribution.

Hence, a label is a critical element of the product, and regulators worldwide emphasize getting it right. It acts as a guide from the manufacturer to all other stakeholders in the supply chain.



Distribution

Distribution plays a pivotal role in the integrated supply chain of pharmaceutical products. The distribution network is becoming increasingly complex, with several stakeholders handling products during the journey from manufacturer to patient. With product labels indicating different storage requirements, pharma supply chains need to adapt processes, facilities, and infrastructure to adhere to them.

- The specified shelf life and storage conditions (temperature/ humidity/light etc.) as per the label of different products is an important consideration in the supply chain, including transportation
- Excursions of the products outside prescribed storage conditions need to be minimized and monitored
- Product segregation, including a clear separation of saleable and unsaleable stocks, quarantine stocks, etc., is critical
- Counterfeit or tampered products pose a threat to the supply chain. Unauthorized access or product tampering needs to be prevented. Strict tracking is required to ensure that only genuine products reach consumers

Given the complex requirements governing the distribution of pharmaceutical products and the number of stakeholders in the supply chain, it requires strong control and supervision. Last-mile distribution is critical to keeping the quality, identity, and integrity of products intact.

In order to minimize quality deviations and risks during product handling in the distribution chain, clear guidelines governing the distribution of pharmaceutical products are needed. To meet these objectives, regulatory bodies and agencies all over the world have issued guidance on 'Good Distribution Practices (GDP) for pharmaceutical products,' which are:

- Essential to ensure product integrity, quality, efficacy, and traceability from the time of manufacture to final usage
- Developed based on regulatory requirements, supply chain risk assessment and mitigation strategies, good storage warehouse, transportation management, and global best practices
- Outline a framework for quality systems in pharma supply chain management to ensure that products, local or imported, reach the end consumer in good condition
- Applicable to all nodes of the pharma supply chain. These practices involve a close interplay of people, processes, and technology. Hence, strong accountability, oversight, controls, and verification is needed to ensure that these guidelines are understood and practiced across the supply chain.
- Mandated by regulators across the globe since the product's integrity and quality affects a patient's well being

Exploring the need: GDPs in India

Effective supply chain management can be a competitive strength and a differentiator and requires the focus of an organization's senior leadership. Currently, India's supply chain costs are higher than in many developed nations. This can be attributed to the complex, fragmented supply chain and is compounded by the diverse geography and population spread, and infrastructure problems. The pharma industry faces numerous challenges, especially in distribution, with a clear need to significantly improve the quality and governance of distribution practices.

It is important to formulate guidelines for Good Distribution Practices of pharmaceutical products in India and ensure their rigorous implementation. In the current scenario, CDSCO has published draft guidelines on "Good Distribution Practices" in 2018 for the pharmaceutical supply chain, but they are yet to be notified by the government. This section highlights why GDPs are essential for the pharmaceutical industry.

Quality Standards

The Indian pharma industry is a mature and significant global player. This position was achieved through technology, innovation, and effort and should be maintained. The industry needs to:

- Focus on quality to maintain the status of the 'Pharmacy of the World'
- Build the brand of 'Pharmaceuticals Made in India' by ensuring world-class products, approved by regulatory agencies across the globe
- Establish robust manufacturing and distribution standards to build this brand and capitalize on the existing market leadership position
- While Schedule M of Drugs and Cosmetic Act, 1940 outlines the quality requirements in manufacturing, implementing GDP practices will ensure adequate strong quality standards in distribution

Last Mile Integrity

Research indicates that pharma companies normally have visibility and good control over the supply chain, from manufacturing to Carrying and Forwarding Agents (CFAs) and Third-Party Logistics (3PL) warehouses. However, the later part of the distribution chain, particularly last-mile logistics, is an area of concern.

- The downstream part of the supply chain has a large number of individual distributors, stockists, and retailers, and unorganized operations result in increased risk to product quality and integrity
- Several incidents of quality deterioration occur due to poor transportation, storage, and handling practices
- Counterfeiting is a major problem due to a lack of traceability of the downstream supply chain. Enforcing GDPs for all stakeholders across the supply chain can help maintain visibility and control, improve traceability, and enable quick recalls of defective or suspected products.

Cold Chain requirements and Cold Chain Integrity

The label conditions for storage and transportation can vary for different products. Several pharma products need to be stored and transported in cold/refrigerated conditions, specified in the product label.

Given India's size and diversity, ensuring reliable infrastructure for cold storage and refrigerated transport is a serious challenge that needs to be addressed. Pharma product quality is a function of storage and temperature conditions, and any deviation could result in loss of product efficacy.

The integrity of the cold chain of pharmaceutical products during the distribution, storage, and transportation requires reliable monitoring of temperature controls through the distribution chain.

- Excursions need to be tracked and reviewed for possible actions
- In addition to temperatures, humidity/light levels also may have to be maintained and monitored
- An important concern is maintaining the required storage temperatures, especially in the hot summer months. In cases where distributor warehouses are not temperature controlled, there are instances where drugs have lost their original efficacy due to heat exposure
- The distribution ecosystem needs to be mindful of temperature and humidity control for all pharma products, not just high-value drugs
- Cold chain warehouse availability and supply issues are well documented in the country and are often more intense in some regions
- Distributors and retailers in the downstream supply chain need to calibrate instruments (like thermistors, IR thermometers, RTDs, etc.) required to monitor and record temperature changes or fluctuations and need proper training, vigilance, and control.

Fragmented and Unorganized Distribution Network

With over 10,000 manufacturing facilities, Indian's pharma industry is highly fragmented and unorganized. Most pharmaceutical companies have a network dependency on 20 to 25 Carrying and Forwarding Agents (CFAs). The downstream supply chain consists of nearly 65,000 distributors and 5.5 lakh pharmacists. Diversity and variations in the workforce and operational and infrastructural capabilities of small-to-medium distributors in last-mile delivery result in huge challenges in managing product quality over shelf life.

Shelf Life

- Shelf life is a function of various factors like temperature, humidity, light, the reaction of APIs with excipients, and exposure contaminants.
- A product's shelf life is determined by conducting stability studies in standard conditions prescribed by regulators. These studies are carried out both under accelerated conditions as well as long duration real-time studies.
- Hence, if the product storage conditions are not met, it is not uncommon for the product to fall out of its specifications and hence may need to be recalled or returned.
- With the unorganized and fragmented distribution set-up in India, it is crucial to ensure that the product's efficacy conditions are met at all times.

Track and Trace

In cases of loss of efficacy, it is important that the product can be recalled or returned, mandating a track and trace mechanism. One of the biggest issues with track and trace is documenting the batch numbers combined with the distributor and retailer names. Moreover, illegal practices, such as the use of a pharmacist's license at multiple retail pharmacies against a fixed monthly payment (or commission) or selling drugs by breaking up the retail pack and dispensing smaller quantities without proper labeling, can result in loss of traceability.

Difference in Procurement Standards - Public vs. Private

Public procurement of pharmaceutical products is a very complex process, involving specialized stakeholders like agencies, ministries, and different manufacturers. Pre-existing procurement policies are frequently inadequate, and at times, hinder the efficiency in responding to the modern pharmaceutical market.

- In most countries, health professionals have limited experience in developing and designing an optimal procurement system. Therefore, many countries are moving away from a fully centralized public sector procurement and distribution and encouraging private sector participation to improve public health programs
- Another issue in public procurement is that both central and state governments have different procurement policies, leading to no consolidated procurement at a state or national level
- There is a need for well-defined quality standards in public procurement that match the private market expectations while also also following strict guidelines for vendor qualification.
- GDP guidelines are required to be maintained in the public procurement system.

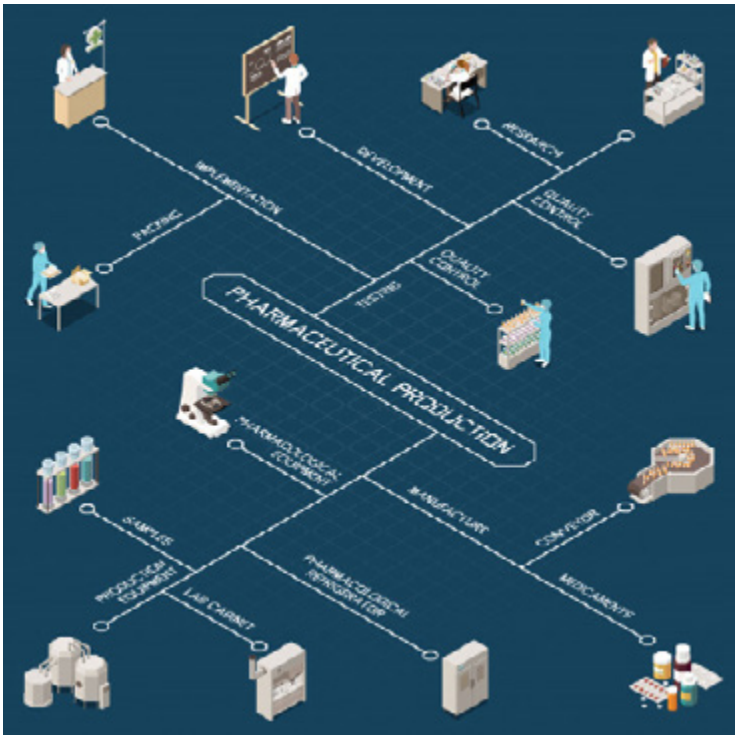
Mishandling Causes Product Integrity Defects

Product integrity in terms of size, shape, and form is important to achieve the intended pharmacological action. The product's shape and packaging are designed as per the required biological action, which is why the product label outlines how it should be handled during distribution. Due to surface abrasion, at times, a capsule or tablet may be damaged and lose efficacy. Thus, standard procedures for handling different products is important to keep the product integrity intact

Maintaining Product Packaging

Deliberate or accidental incidents during product storage, distribution, or transportation may alter the product information printed/coded on primary and secondary packages. The information containing product strength, batch number, manufacturing, and expiry date may be affected due to to damage to packs during transit, rough handling at replenishment time, or smudging of coding information due to contact with moisture or solvents. The loss of information also affects the manufacturer's ability to track and trace the product in the event of a recall.

Governance of distribution practices, which are critical in a high-volume market like India, needs improvement. GDP guidelines can ensure quality management across the distribution chain by detailing standards of infrastructure, processes, and systems and capabilities to be built across the distribution system. They will also promote traceability, allowing for better tracking to ultimately improve health outcomes.



GDP Guidelines

Global Practices

- WHO Guidelines
- EU-GDP guidelines
- Pharmaceutical Inspection Co-operation Scheme (PIC/S)
- GDPs in India
- The Scope of GDPs

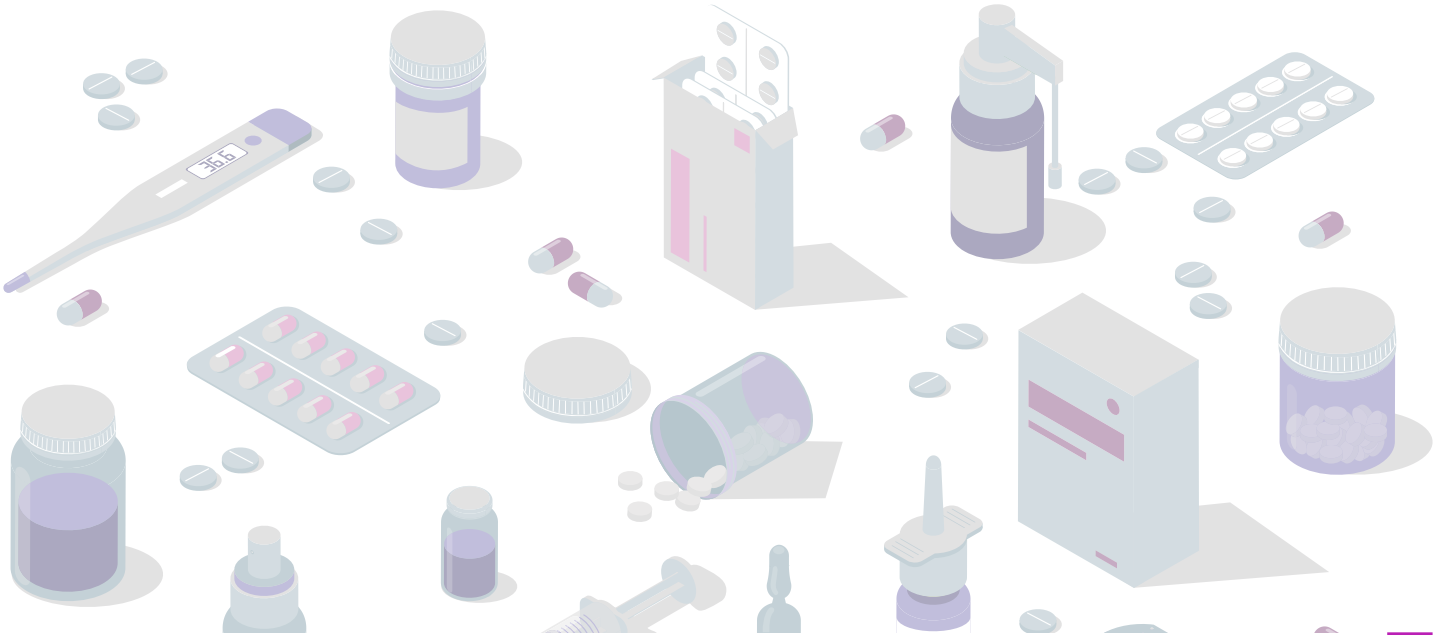
Maintaining product quality and integrity requires a coordinated effort by stakeholders involved across the supply chain. It requires clear communication of risk mitigation guidelines. GDP guidelines are needed to monitor and control pharmaceutical products from manufacturers to end consumers. Major pharmaceutical regulators like US-FDA, WHO, European Union, and PIC/S have issued GDP guidelines in their respective jurisdictions.

WHO Guidelines

WHO issued GDP guidelines related to the distribution and storage of pharmaceuticals back in 2005. Recently, WHO revised its GDP guidelines during the 53rd meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations held in October 2018. The committee recommended the consolidation of the GDPs and the elements of Good Distribution Channels for pharma products into one document, which was released in 202011. The guidelines apply to all businesses involved in distribution, storage, and trade, including manufacturers, suppliers, distributors, brokers, traders, logistic providers, transport companies, and forwarding agents.

EU-GDP guidelines

EU-GDP guidelines were published in 1994 for the first time by the European Commission and were revised in March 2013 to take into account recent advances in the storage and distribution of pharmaceutical products in the European Union. These guidelines contain appropriate tools to help wholesale distributors carry out operations and prevent falsified or counterfeit pharmaceuticals from entering the supply chain. Compliance with these guidelines ensures a check over the supply chain, maintaining the identity, quality, and integrity of pharmaceutical products. The guidelines cover major aspects of quality management, risk mitigation, premise, and warehouse layout, recalls, complaints, traceability, etc. They also cover the storage of Active Pharmaceutical Ingredients (APIs) and other ingredients used for manufacturing pharmaceuticals.



Pharmaceutical Inspection Co-operation Scheme (PIC/S)

The Pharmaceutical Inspection Co-operation Scheme (PIC/S) is a nonbinding, informal cooperative agreement between 53 global regulatory authorities in the field of GMP and GDP practices of pharma and medical products for human use. The PIC/S GDP guidelines are based on the EU-GDP guidelines. These guidelines are a guidance document for participating authorities. The PIC/S guidelines cover various aspects of the supply chain and lay down rules and regulations related to quality risk management, personnel handling operations, documentation, and recall of counterfeit/tampered products.

GDPs in India

In India, the idea of GDP came into the picture in 54th Drug Consultative Meeting held on July 7, 2018, and recommendations were provided to take necessary steps to impart legal sanctity to GDP guidelines as a schedule to the Drugs & Cosmetics Rules 1945.

According to a recent WHO report, it is estimated that one out of ten pharmaceutical products sold in middle and low-income countries like India is either falsified, counterfeited, or substandard. These medicines not only fail to prevent or treat diseases but also lead to serious illness or death. Thus, on September 25, 2018, CDSCO published the draft guidelines on 'Good Distribution Practices' (GDP) to ensure and monitor the quality of pharmaceutical products, including biological products in general, across the full supply chain. These guidelines aim to ensure that product identity and quality are protected. The areas covered under these guidelines include, but are not limited to, purchase, storage, distribution, procurement, documentation transportation, and record-keeping practices. These are expected to apply to all businesses or agents involved in the pharma supply chain. However, the guidelines have not been notified yet.

The Scope of GDPs

The guidelines issued by various regulatory bodies across the globe are similar in their fundamental approach. They outline the practices to be followed in the key areas of distribution, processes, infrastructure, and workforce. These areas are highlighted below:

Personnel

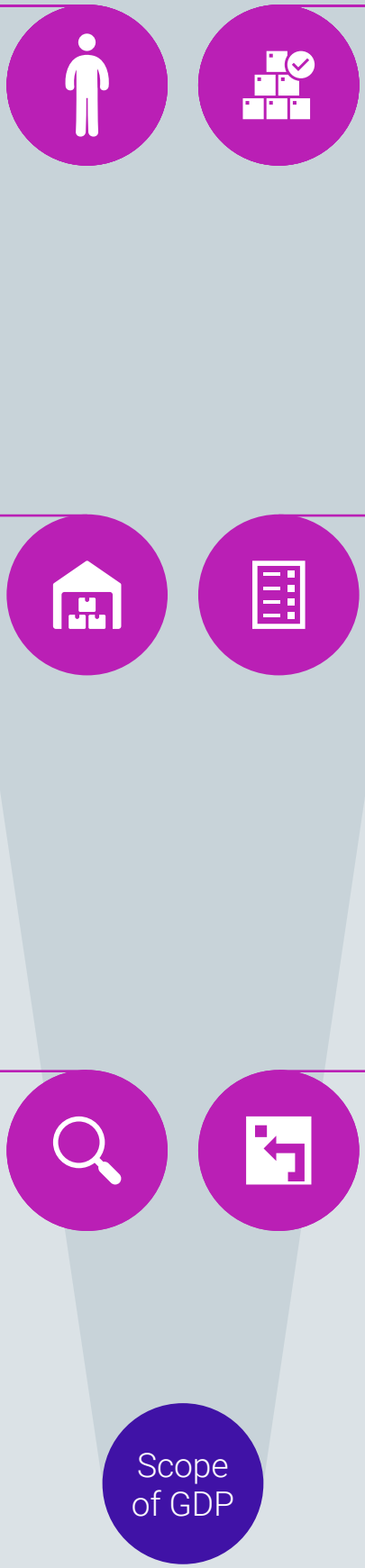
- Designate people responsible for GDP compliance. Personnel should be competent, experienced, trained, and qualified.
- Training and maintenance of training records based on documented SOPs
- Adopt appropriate procedures related to personnel hygiene, health, and clothing
- Establish an organizational structure with clearly defined responsibilities and interrelationships
- Get a code of practice and punitive procedures in place to address counterfeiting or contamination issues.

Premises and Warehouse

- Ensure good storage practices
- Enforce precautions and policies to prevent unauthorized access
- Dedicate storage area for hazardous, quarantine and counterfeit products
- Follow First Expiry, First Out (FEFO) during distribution
- Ensure adequate lighting and HVAC system

Traceability

- Prepare procedures and documents to ensure traceability of products distributed, to facilitate recalls
- Identify and map all stakeholders involved in the supply chain, depending on the type of product and national policies and legislation
- Develop internationally compatible product coding and identification system in collaboration with involved parties



Quality System

- Document a Quality Policy with defined procedures and that are periodically reviewed
- Appoint designated personnel to ensure a quality system with specified authority
- Authorize procurement and release procedures
- Inspect, audit, and attain a certificate of compliance with ISO quality standards
- Conduct periodic risk assessments

Documentation

- Maintain appropriate documentation with written/ electronic records of all activities
- Ensure that documents are completed, approved and signed by the authorized personnel
- Prepare documents that are sufficiently comprehensive, with clear and unambiguous language
- Retain documents for the specific periods stated in national legislation

Complaints and Returns

- Systematically record and review complaints
- Make early communication to concerned entity in case of counterfeit or substandard product
- Investigate and identify the reason of complaints thoroughly
- Prepare written procedures for handling and acceptance of returned products
- Ensure physical segregation and storage of returned stock from saleable stock

Recommendations

- Quality Management
- Premises, Warehouse, and Equipment
- Traceability
- Personnel
- Documentation
- Transportation

The distribution and storage of pharmaceutical products require scientific processes, infrastructure, and controls that are diligently executed and carefully monitored. The finished products are critical for restoring patient health. However, deteriorated, spurious, or damaged products can go beyond being ineffectual – they can also do immense harm to a consumer.

There have been numerous instances where such problems have arisen due to flaws/lacunae in the distribution system, causing both health and reputational damage.

Product traceability for pharma products is as critical as it is challenging. The lack of adherence to proper guidelines is responsible for counterfeit drugs and loss of revenue and market share for Indian pharma. Complying with the stringent US Drug Supply Chain Security Act (DSCSC) has been challenging for domestic players.

Good distribution standards and guidelines for pharmaceutical products in our country are likely to have other advantages, like enhancing product recall resulting in better patient safety. Pharma suppliers across the world need to be able to handle product recalls quickly and efficiently when triggered. We see numerous examples where Indian pharmaceutical firms have had to recall batches of products in international markets across a variety of categories like diabetes, gastritis/excess stomach acid, analgesics, and psychiatric medications. Thus, it is necessary for the Indian government to implement and enforce strict GDP guidelines similar to international standards like WHO, PIC/S, etc., to ensure that product recalls are well handled with minimal risk to patients.

Drugs banned for sale or withdrawn by the Drugs Controller General of India (DCGI) should not be available in the market, but lapses are often noticed. While no system is foolproof and risk-free, it is essential that robust processes and rules are in place and constantly improved whenever market failures occur. Appropriate GDP guidelines are required to ensure that distribution practices are of a high standard and complied with by all stakeholders in the pharma distribution chain to ensure patient safety and health outcomes. Some of the recommendations for critical areas to be covered under GDP guidelines are outlined in this section.

Quality Management

GDP Guideline coverage

- Documented Quality Policy on
  - Requirements of the distributor authorized by management
  - Authorized procurement and release procedures to source products from authorized suppliers
  - Ensure the integrity of pharmaceutical products in case of counterfeiting or tampering
- Quality Management System
  - Quality management system laying down the structure, procedure, and processes for adherence
  - Inspection, auditing, and certification of compliance with ISO quality system by external bodies
  - Periodic risks assessments of Quality System to identify new risks

Recommendations

- Active participation by an organization's management and leadership, supported by staff commitment
- Periodic reviews of the size, structure, and complexity of distributor activities
- Establish provisions to ensure immediate communication to authorized distributors or any relevant authority in case of product counterfeiting
- In the case of the e-pharmacy distribution model, define procedures and adequate systems to ensure traceability and patient confidence

The management needs to establish a formal process for periodic reviews of the quality system, which should include:

- Monitoring achievement of the quality system's objectives
- Performance assessment tracking indicators that can be used to monitor process effectiveness, including recalls, returns, complaints, deviations, CAPA, process changes, feedback on outsourced activities, self-assessments (including risk reviews and audits), and external assessments, such as inspections, findings, and customer audits
- Emerging regulations/ quality issues that potentially impact or change the quality management system
- Innovations that might enhance the quality system
- Changes in the business environment and objectives

Quality systems should extend to control and review any outsourced activities for pharma products, including procurement, holding, supply, import, or export. These processes should drive quality management and include:

- Suitability and competence assessment of the Contract Acceptor to carry out the activity, preserving the integrity and security of the medicinal products, and requesting, preserving documentation, and checking authorization or marketing status, as required
- Defining the responsibilities and communication processes for the quality management activities of the stakeholders involved
- Regular performance monitoring and reviews of the Contract Acceptor to identify and implement the required improvements

Premises, Warehouse, and Equipment

GDP Guideline coverage

- Precautions and policies in place to prevent unauthorized access to storage areas
- SOPs for cleaning, especially for pest control to prevent the risk of contamination
- Designated storage capacity to store various categories (commercial, non-commercial, quarantine, counterfeit, radioactive/rejected, etc.)
- Better design of storage areas to ensure conditions suited to product specifications
- FEFO (First Expiry/First Out) should be followed during distribution
- Records of temperature, lighting, and HVAC monitoring data of storage area must be maintained throughout shelf life
- Calibration of equipment required for monitoring storage conditions at regular intervals

Recommendations

- Storage conditions should comply with the manufacturer's recommendations
- Visitors should be accompanied by authorized personnel
- Employee rest and refreshment areas should be adequately separated from storage areas
- Storage areas need to be clean and free from accumulated waste and vermin to lower the risk of contamination
- Preventive maintenance should be planned for critical equipment
- Where a 'quarantine status' is managed by storage in separate areas, those areas must be marked and restricted to authorized personnel
- An initial temperature mapping exercise needs to be carried out on the storage area to understand temperature conditions and deviations
- Temperature monitoring equipment should be placed according to the results of the mapping exercise, ensuring their placement in areas that are more likely to experience fluctuations

Traceability

GDP Guideline coverage

- Procedures in place to ensure document traceability of products received and distributed to facilitate product recalls
- All parties involved in SCM must be identifiable, depending on the type of product and on national policies and legislation
- Procedure in place for creation and maintenance of a pedigree along with records including expiry and batch numbers of pharmaceutical products
- Internationally compatible product codes and identification system to be developed in collaboration with involved parties

Recommendations

- Retailers should record patient details before dispatching prescription medicines, and these records should be kept for at least two years from the date of sale
- Products should be handled appropriately during transport and storage so as to ensure batch numbers and other details are not smudged or rubbed off

Personnel

GDP Guideline coverage

- All personnel involved in distribution activities should be trained about the requirements of the GDP guidelines, as applicable
- Training should cover documented standard operating procedures (SOPs) for GDPs, including roles, responsibilities, and accountability. Introductory and continued training for personnel, which are assessed periodically according to a well-defined and monitored training program, should be instituted
- The key personnel involved in pharma distribution should have the relevant knowledge, capability, and experience to ensure well-managed distribution process.

Recommendations

- Stakeholders need to ensure the availability of a well trained workforce to carrying out distribution processes. The Government and industry bodies will need to make long-term investments to develop skill and capability building initiatives to ensure the availability of such workers
- Personnel dealing with medicinal products requiring more stringent handling such as hazardous products, radioactive materials, products presenting special risks of abuse (such as narcotic or psychotropic drugs), or temperature sensitive products should be given specific training
- Personnel who can be contacted outside of regular office hours for emergencies/exigencies need to be clearly identified. These designated personnel should be allowed to delegate duties but not responsibility
- National regulations relating to the qualifications and experience of personnel should be adhered to

Documentation

GDP Guideline coverage

- Define ‘good documentation’ to be:
  - Written/electronic and records all distribution activities
  - Completed, approved, and signed off by an authorized person
  - Sufficiently comprehensive with clear and unambiguous language
- State requirements in the national legislation for the retention of documents for a specific period
- Highlight the minimum information that records must include, like the date, product name, quantity received and supplied, supplier name and address, customer or consignee details as appropriate, and batch number, expiry date.

Recommendations

- Maintain sufficient and comprehensive documentation capturing the scope of the wholesale distributor's activities in a language that is easily understood by personnel
- Ensure ready access to documentation for each employee for the executed tasks
- Prepare records at the time of each operation in a way that can trace all significant activities or events
- Encourage distributors to have a 'Business Continuity Plan' that is updated regularly
- Mechanisms to facilitate the transfer of information should be developed, including quality or regulatory information between manufacturers and customers, as well as the transfer of information to relevant regulatory authorities where required

Transportation

GDP Guideline coverage

- To ensure the quality,
  - Vehicles must be dry and free from insects, rodents, etc. to prevent pilferage, contamination, or adulteration
  - Where special storage conditions (e.g., temperature and relative humidity) need to be maintained, these should be provided, checked, monitored, and recorded
  - The individuals responsible should be informed about all relevant conditions for storage and transportation
- To ensure product safety,
  - Technology such as Global Positioning System (GPS) enabled electronic tracking devices, and engine-kill buttons to vehicles should be used
  - Dedicated vehicles must be used for transportation
  - In case of the use of third-party carriers, distributors should maintain a written contract as per the national legislation

Recommendations

- In the case of deviations in the route or schedule of delivery, the distributor and recipient must be made aware immediately
- During transportation, wherever possible, mechanisms for the segregation and storage during the movement of recalled, rejected, and returned pharmaceutical products should be established
- Suitable transportation means (air, land, or sea) and routes must be utilized for the transportation of pharma products as per storage and transportation requirements
- Optimization of Truck Loads to FTL (Full Truck Loads) must be ensured, which improves space utilization and cuts down costs and the risk of damage

Pharmaceutical products should be stored and transported following procedures to:

- Protect the product's identity
- Ensure that the product does not contaminate and is not contaminated by other products
- Take adequate precautions against product spillage, breakage, misappropriation, and theft. Spillage during transport needs to be handled as per the type of product according to the manufacturer's SOPs
- Maintain appropriate environmental conditions, e.g., using cold chain distribution for thermolabile products

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About OPPI

The Organisation of Pharmaceutical Producers of India (OPPI) established in 1965, represents the research-based pharmaceutical companies in India. OPPI remains committed to supporting the nation's healthcare objectives and collaborating with all stakeholders to find sustainable solutions. OPPI believes the need for innovation must be balanced with the necessity for more accessible medicines, within a robust IP environment.

For more information, please visit https://www.indiaoppi.com/

About Nexdigm (SKP)

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