Taking a Leap Toward Global Supply Chain Efficiency

IFPMA

INTRODUCTION

Pharmaceutical manufacturers face a number of challenges to **produce and deliver** medicines and vaccines to patients around the world. The purpose of this brochure is to create awareness of the importance of global supply chain integrity and to highlight challenges that manufacturers, distributors, wholesalers and National Regulatory Authorities (NRAs) need to overcome to ensure that medicines and vaccines are delivered safely, reliably and efficiently to patients.

PROBLEM STATEMENT

The complexity concerning the production and supply of medicines and vaccines, particularly for products that utilize a multinational manufacturing process, must be better communicated to regulatory authorities and other stakeholders.

A CALL TO ACTION

IFPMA advocates for regulatory system strengthening and convergence worldwide to allow timely and reliable access to medicines and vaccines. In this brochure, IFPMA provides insight into the challenges faced by manufacturers to maintain supply chain assurance. It is important that regulatory processes are constantly updated and improved to ensure that they facilitate the reliable supply of high quality medicines and that they do not become the rate limiting step in medicines or vaccine availability. To this end, risk-based review, fixed review timelines, reduced redundant reviews/testing/inspections through cooperative country NRA recognition, guideline convergence and shared expertise and training must be adapted to improve regulatory capacity and efficiency in assuring access to safe, efficacious, life-saving medicines to patients worldwide.

EXECUTIVE SUMMARY

1. Globalization has resulted in increasingly **complex pharmaceutical supply chains;** encompassing multiple geographical manufacturing, testing and distribution sites often needed to maximize production capacity to meet global demand;

PAGE 4

2. Supply chain **integrity and resilience** are important components of patient access to medicines and vaccines, as disruptions can quickly lead to drug shortages or introduction of falsified products;

PAGE 5

3. **Flexibility** is needed in supply chain manufacturing and distribution in order to respond to dynamic supply needs and to comply with evolving regulatory requirements;

PAGE 8

4. Manufacturers need to make **timely changes** to implement new technologies that improve the availability, stability and/or the quality of medicines and vaccines;

PAGE 8

5. **Implementation** of changes in medicines and vaccines is complicated by both the globalization of the supply chain and the divergence and occasional unpredictability of requirements and review timelines applied by each NRA; and

PAGE 9

6. **Fragmentation** is increasing in the supply of medicines and vaccines because of the more frequent occurrence of “pending regulatory approvals” (e.g., approval delayed with undefined timelines in some countries, and/or not granted at all in other countries).

PAGE 10

1. GLOBALIZATION OF SUPPLY CHAINS

A supply chain is a complex network that links together manufacturers, wholesalers, and distributors, all contributing to the goal of providing a product to the end user[1]. Multiple manufacturing and distribution sites and raw material suppliers are often needed to maximize production capacity and flexibility to ensure medicines and vaccines are available to patients.

At the time of first commercial approval of a medicinal product, manufacturers typically launch the product using centralized single production sites for intermediates, drug substance (DS) and finished drug product (FP). However, despite the logistical simplicity of a single site approach, associated risks and disadvantages can arise quickly in the post-approval lifecycle of a globally distributed product – driving companies to implement differentiated business models that include more flexible multi-sourcing. In this scenario, the FP and/or its components are produced at more than one manufacturing site, and often in multiple different countries. There can be several reasons contributing to the decentralization of the manufacturing chain, including:

1. Moving from locations of centralized expertise and resources during clinical development and initial commercial launch to local manufacturing sites to enable faster distribution and better patient access;
2. Improving the security of supply by reducing the risk of wide-spread stock-out;
3. Addressing country-specific expectations to manufacture locally for the local market;
4. More efficient use of the company-owned and/or outsourced (contractor) manufacturing facility network and ability to respond to unforeseen events such as pandemic diseases and natural disasters; and
5. Increasing supply chain resilience in light of unforeseen events (e.g., pandemics, natural disasters) impacting single manufacturing /distributions sites or suppliers.

Even under ideal circumstances, the path from raw materials to medicinal product manufacture, followed by distribution and finally the arrival in the hands of the physician or patient may take in excess of 300 days[2].

1 ICHQ10 : Pharmaceutical Quality
2 Shah, N. (2004) Pharmaceutical Supply Chains: Key Issues and Strategies for Optimization. Computers & Chemical Engineering; p. 28, 929-941.

Credit: kadmy

2. SUPPLY CHAIN INTEGRITY

A secure and reliable supply chain is an important component of patient access to medicinal products, as disruptions can quickly lead to drug shortages or introduction of falsified products. Pharmaceutical manufacturers together with wholesalers and logistics providers strive to develop robust supply chains to ensure that the medicines and vaccines delivered to patients are safe and effective. However, these supply chains are complex and replacing any one component requires quality oversight. Shortages or issues anywhere in this supply chain can interrupt the supply to patients. Manufacturers may need to act quickly to replace a material, but this replacement may be delayed or complicated due to regulatory oversight including review timelines and policies.

6 ways to Getting the Supply Chain in Sync

GLOBAL COMPLEXITY

CHALLENGES

Multi-sites:
- Manufacturing
- Distribution
- Testing

ENABLERS

- Allow Flexible Multi-site Activities

INTEGRITY

CHALLENGES

- Counterfeit
- Theft

ENABLERS

- Anti-Counterfeit
- Secure Supply Chain

REQUIREMENTS GUIDELINES

CHALLENGES

Divergent:
- Guidelines
- Data Requirements

ENABLERS

Convergent:
- Guidelines
- Data Requirements

RESOURCES

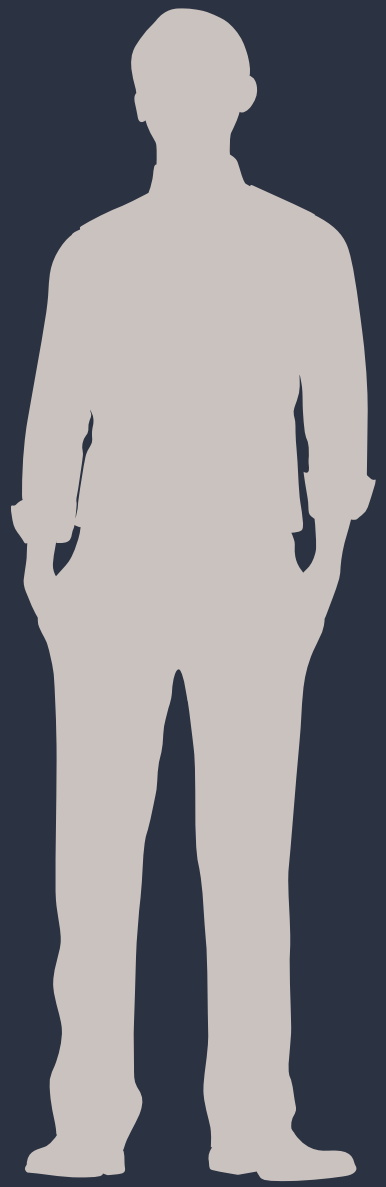
Capacity Issues:
- Backlog
- Reviews
- Inspections
- Training to Strengthen Expertise

FRAGMENTATION

Mandatory:
- Minimum Inventory
- Product Specific Monograph (PSM) Adherence
- Release Testing

IMPLEMENTATION OF CHANGES

Divergent:
- Submission Categories
- Review Times



Mutual Recognition:
- Reviews
- Inspections
- WHO Training and Workshops

- Inventory to Meet Needs
- PSM not Applicable for Biotech Products
- Reduce Redundant Release Testing

- Standard Submission Categories
- Standard Defined Review Times

3. SUPPLY CHAIN FLEXIBILITY

The ability of both manufacturers and NRAs to adapt to and find new solutions to manage this increased complexity will be critical to assure the best possible and uninterrupted access of patients to the medicines they need. Global convergence of regulations, scientific data requirements and interpretation will be essential to achieve this goal. In this effort, the WHO and International Council on Harmonization (ICH) are key partners for NRAs, industry, patients and other stakeholders.

4. SUPPLY CHAIN MANAGEMENT OF CHANGES

Medicinal products are manufactured by a diversity of techniques and processing steps, which depend on the unique molecular characteristics of the product. During the life-cycle of a product, manufacturing process changes or other changes to the approved medicinal product may be needed for several reasons, including:

a. To make the production process more efficient;
b. To increase manufacturing capacity (scale-up);
c. To move the production into a new or different facility;
d. To incorporate technical or scientific progress (e.g., improved analytical methods);
e. To implement changes that are consequential to changes made by suppliers of active substances, excipients, raw materials or packaging materials;
f. To comply with new regulatory requirements; and
g. To supply the medicinal product in a new dosage strength or under a new formulation (e.g., from a tablet form to a syrup).

5. IMPLEMENTATION

Once a product has been approved, regulatory oversight does not stop. Market Authorization Holders (MAHs) have an obligation to ensure that the product continues to be manufactured in accordance with the rules set forth by the NRAs. Implementing post-approval changes in cooperation with local regulations helps ensure consistent availability of high quality, safe and effective medicines; this strict compliance must be conducted at every single step in the process, from the production and procurement of raw materials up to the final shipping of the medicine to the country of destination. As a result, the implementation of any changes to the individual components or to the manufacturing process of a medicinal product are monitored by each NRA. Although in principle this oversight is absolutely essential and supportive of public health, in practice the individualized country-by-country execution of the review and approval process is lengthy and complex. This delay in review can have a negative impact on public health and the timely access of patients to the medicines they need. In addition, some health authorities require approval of the change by a reference health authority before they will begin their review of the very same change, further delaying the implementation of these key manufacturing changes. Finally, implementing necessary changes is far more complicated when multiple manufacturing sites are involved.


Credit: Avatar_023

6. FRAGMENTATION

Many intended changes to manufacturing inputs and control parameters must first be reviewed and approved by global health authorities prior to implementation and distribution of the post-change product. This review is important to minimize the risks associated with loss of integrity in the supply chain for medicines and vaccines. Unfortunately, the variation in review time required by each NRA can often lead to a global divergence of pending regulatory approvals. The net result is fragmented implementation of these manufacturing changes between various regions and countries. As more changes are needed and overlap, a product process version may be years apart between countries causing supply chain inventory problems until all countries catch up.

Supply chain post-approval change:

Global Complexity Contributing to Delayed Patient Benefit

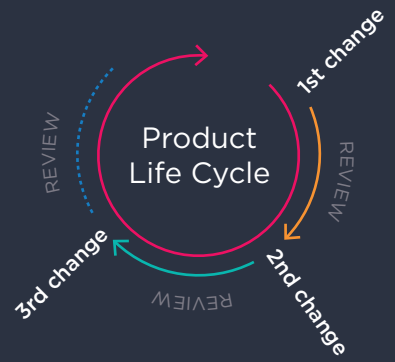
When it comes to licensing a **Medicinal Product** at country level, it will be subject to changes

Hard to step up to the challenge as:

1 change could trigger 0.5-2 year delay

2 changes could trigger 1-4 year delay

3 changes could trigger 1.5-6 year delay



⚠

CHALLENGES:
Unsustainable inventory fragmentation

18m => Fastest timeline for licensure +1 post-approval change

5.5y => Longest timeline for licensure + 1 post approval change

+years => Multiple changes will lead to different product versions

✓

SOLUTIONS:
Important for countries to reach convergence on:

1. Data license requirements
2. Timelines for review
3. Inspection requirements
4. Product testing requirements

International Federation
of Pharmaceutical
Manufacturers & Associations

Chemin Des Mines 9
P.O. Box 195
1211 Geneva 20
Switzerland
Tel: +41 22 338 32 00
Fax: +41 22 338 32 99
www.ifpma.org

IFPMA

ABOUT IFPMA

IFPMA represents the research-based pharmaceutical companies and associations across the globe. The research-based pharmaceutical industry's 2 million employees research, develop and provide medicines and vaccines that improve the life of patients worldwide.

Based in Geneva, IFPMA has official relations with the United Nations and contributes industry expertise to help the global health community find solutions that improve global health.

Acknowledgment
The production of this publication is the fruit of the labors of a working group representative of member companies and the secretariat of the International Federation of Pharmaceutical Manufacturers and Associations. This publication was managed by Cristina Arnes, in coordination with Sadia Kaenzig.