Pharmaceutical Technology Migration: Overview

Sakshi Subhash Bhosale[1], Gauri Mahajan[2], Swati Wakchoure[3], Diksha Shinde[4], Kaustubh Shelar[5]
[1],[4],[5]Student of Shivajirao S. Jondhle College of Pharmacy, Asangaon, Thane
[2]Assistant Professor Department of Pharmaceutics, Shivajirao S. Jondhle College of Pharmacy, Asangaon, Thane
[3]Assistant Professor Department of Pharmacognosy, Shivajirao S. Jondhle College of Pharmacy, Asangaon, Thane

Abstract— This review article delves into the concept of technology transfer within the pharmaceutical industry, as well as the legal considerations involved. Technology transfer is a structured process that requires skilled, knowledgeable personnel operating within a quality management system, with thorough documentation covering every stage of development, production, and quality control. The article specifically addresses the documentation aspect of technology transfer, offering an analysis of its key components. Successful technology transfer occurs when the receiving unit can efficiently apply the technology to achieve business objectives. The effectiveness of the transfer is heavily reliant on process understanding and the ability to predict the process's future performance accurately.

Indexed Terms- Technology Transfer, Manufacturing, Quality Assurance, Regulatory Compliance

I. INTRODUCTION

Technology transfer throughout the pharmaceutical product life cycle and the transfer of manufacturing processes from one site to another during commercial production play a critical role[1]. In the pharmaceutical industry, technology transfer encompasses the steps needed to move successfully from drug discovery to product development, clinical trials, and ultimately to full scale production[2]. This foundational knowledge shapes the manufacturing processes, control strategies, approaches to process validation, and ongoing improvements[3].

The main objective of technology transfer activities is to effectively share product and process knowledge between development and manufacturing stages, as well as among manufacturing sites, to ensure product realization. This review also aims to propose regulations to support effective technology transfer, which is essential for ensuring high-quality, consistent manufacturing of both new and existing products.

Technology transfer includes actions necessary to convey the information and techniques needed to achieve the intended quality of a drug's design in manufacturing. Some key points include:

- Effective technology transfer is essential for turning the quality of design into the quality of the final product, thereby ensuring product stability and consistency.
- It's important to recognize that drugs can impact health and life, and as they are manufactured and marketed over time, there may be changes to their raw materials, composition, and manufacturing methods.
- To uphold drug quality, it's crucial to establish what information needs to be transferred, when, why, and by whom, as well as how it should be shared between the originating and receiving parties, ensuring full communication of the product knowledge.
- Technology transfer is not a one-time event but rather a continuous exchange of information between both parties to sustain consistent product manufacturing quality.

CLASSIFICATION OF TECHNOLOGY TRANSFER

Technology transfer can be classified as following:-

- Vertical Transfer: Transitioning technology from research to manufacturing for drug production.
- Horizontal Transfer: Sharing technology between organizations at the same production stage.

- International Transfer: Moving technology between nations to enhance pharmaceutical abilities.
- Internal Transfer: Transferring processes within a company, from development to manufacturing.
- External Transfer: Delegating technology to external partners, such as contract manufacturers[4].

METHODS OF TECHNOLOGY TRANSFER:

Licensing is a widely used approach for transferring technology, with two key strategies: licensing in and licensing out.

- Licensing in: Smaller companies, or those lacking the resources for extensive research, seek to acquire research from external sources.
- Licensing out: A company grants its rights to another entity for use[5].

IMPORTANCE OF TECHNOLOGY TRANSFER IN PHARMACEUTICAL INDUSTRY:

- Speeding Up Development: Facilitates the rapid transition of drug candidates from research to large-scale production, enabling faster market introduction of new therapies.
- Maintaining Quality: Ensures that products are manufactured consistently and meet stringent quality standards, which is vital for regulatory compliance and patient safety.
- Reducing Costs: Lowers R&D expenses by enabling collaborations and access to external innovations, allowing companies to allocate resources more efficiently.
- Enabling Global Market Access: Supports expansion into international markets by licensing technologies to local manufacturers, ensuring compliance with regional regulations.
- Fostering Collaboration: Promotes partnerships between research organizations and pharmaceutical companies, driving innovation through shared knowledge and resources.
- Ensuring Regulatory Compliance: Facilitates adherence to regulatory requirements throughout drug development and production, which is crucial for securing approvals from health authorities[6].

HOW TECHNOLOGY TRANSFER IS HELPFUL ?

Academics and research institutions pursue technology transfer for several reasons, including:

- Insufficient Manufacturing Capacity: The technology's creator may only be able to produce instruments suitable for laboratory or small-scale use and may need to collaborate with another organization for large-scale production.
- Limited Resources for Commercial Launch: The original inventor may have only enough resources to complete preliminary research and early-phase clinical trials.
- Absence of Marketing and Distribution Channels: Although the technology developer might have created the technology and secured regulatory approvals and product registration, they may lack the necessary marketing and distribution networks.
- Exploration in Alternate Applications: Partners may possess only part of the solution; for instance, the technology developer might focus on diagnostic applications while granting commercial rights to a partner for therapeutic applications.
- Building Partnerships for Development: Establishing alliances with partners can help advance the technology's development for market introduction.
- Collaborating with Manufacturing Partners: Forming partnerships with organizations that have manufacturing capabilities can facilitate production.
- Fostering Local Economic Growth: Engaging in technology transfer can contribute to the economic development of the local community[7],[8].

FACETS/ASPECT OF TECHNOLOGY TRANSFER:

- From Government Labs to Private Companies: Government laboratories receive financial backing, allowing private firms to utilize their technologies.
- Between Private Companies: Companies exchange technology and compensate the creator if one lacks resources.

- From Academia to Private Companies: Academic institutions develop technologies that can lower expenses for businesses.
- Academia, Industry, and Government Collaboration: Government funding supports academic research, facilitating the transfer of technology to the industry[9].

FACTORS INFLUENCING TECHNOLOGY TRANSFER IN PHARMACEUTICAL INDUSTRY:

Here are eight crucial elements that contribute to creating favorable conditions for the transfer of medical technology:

- Local markets that are clearly visible and easily accessible.
- A stable political environment and sound financial practices.
- Well-defined development priorities.
- Efficient regulatory frameworks.
- Access to a skilled workforce.
- Sufficient capital markets.
- Robust intellectual property protections and effective enforcement mechanisms.
- A strong partnership between industry and government,

characterized by effective long-term collaboration[10].

ORGANIZATION OF TECHNOLOGY TRANSFER:

1. Project Manager: Manages the project and coordinates all activities.
2. Regulatory Affairs: Oversees regulatory submissions and approval processes.
3. Engineering: Manages construction projects and equipment acquisition.
4. Material Management: Oversees purchasing and supply chain planning.
5. Manufacturing Operations: Supervises production at both the origin and destination sites.
6. Research and Development: Addresses technical challenges and provides training for production trials[11].

STEPS INVOLVED IN THE TECHNOLOGY TRANSFER PROCESS:

During the formulation development phase, it is crucial to consider the operational procedures, critical and non-critical parameters of each operation, production environment, equipment, and availability of excipients from the beginning.

A) Development of Technology by R&D (Research Phase)

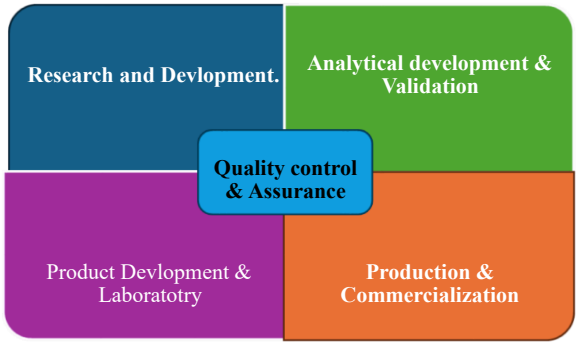

Fig.1 Steps involved in Technology Transfer

- Procedure Design and Excipient Selection: The R&D team designs the processes and selects excipients based on the characteristics of the reference product.
- Quality and Specification Identification: R&D ensures that the product's quality aligns with the specifications of the reference product[12].

B) Technology Transfer from R&D to Production (Development Phase)

The R&D department supplies a Technology Transfer Dossier (TTD) to the product development laboratory, which contains comprehensive formulation and product information, including:

1. Master Formula Card (MFC): This card details the product name, strength, generic name, MFC number, page number, effective date, shelf life, and target market.
2. Master Packing Card: This provides details about the packaging type, materials used, stability profile, and packaging shelf life.
3. Master Formula: This document outlines the formulation sequence and manufacturing instructions, including the order of processes and environmental conditions.

C) Optimization and Production (Production Phase)

Fig 2. WHO guideline for technology transfer

- Validation Studies for production: Production can commence only after validation studies confirm that the process can reliably stabilize the product according to the transferred manufacturing formula. The manufacturing department must take responsibility for validation, while R&D oversees aspects such as performance qualification, cleaning, and process validation.
- Scale-Up for Production: This step involves transferring technology during the small-scale development of the product and processes. It is vital to consider the production environment and systems during process development. Operators must focus on maintaining smooth operations within their specific segments of the production process[14].

D) Technology Transfer Documentation

This documentation serves as a record of the technology transfer contents for both the transferring and receiving parties. Each step from R&D to production should be well documented, with clear task assignments, responsibilities, and acceptance criteria for each technology being transferred. The Quality Assurance department must review and approve all documentation throughout the technology transfer processes.

1. Development Report: The R&D department is responsible for documenting the technical development in a report that outlines the rationale for the quality design of drug substances, specifications, and test methods. Although this report is not mandatory for regulatory approval, it serves as a valuable document during pre-approval and inspections. The development report should include:

- Data on pharmaceutical development from early phases to final approval application.
- Information on raw materials and components.
- Details on manufacturing methods.
- Histories of significant process changes and control parameters.
- Specifications and test methods for drug substances.
- Validity ranges for important tests such as content, impurities, and dissolution.
- Verification of results.

2. Technology Transfer Plan: This plan outlines the items and details of the technology to be transferred, including specific procedures and timelines. The transferring party should prepare this plan before the transfer occurs and reach an agreement with the receiving party on its contents.
3. Completion Report: After the technology transfer is finalized, data will be collected according to the technology transfer plan to ensure that the predetermined criteria are met. Both parties involved must document this completion reports[15].

E)Exhibit

Once scale-up batches have been completed, manufacturing of exhibit batches occurs. In this case, the batch sizes are increased, along with adjustments to equipment and processes, to prepare for regulatory submissions[16].

BARRIERS OF TECHNOLOGY TRANSFER :

a. Limited Market Share: Local manufacturers struggle to meet international quality standards, which hampers their ability to gain significant market share. A larger market share would enhance their profitability.
b. Pre-Qualification Costs: Complying with international standards is beneficial as it opens up global trading opportunities, but the costs associated with achieving pre-qualification can be substantial.

c. Labour Challenges: The pharmaceutical industry requires a skilled workforce, but high turnover rates and absenteeism—often due to unattractive working conditions—pose significant challenges.
d. Incomplete or Unsuccessful Process Validation: Failure to successfully validate processes can impede technology transfer.
e. High Batch Rejection Rates: Frequent rejections of batches, along with excessive labour demands, can lead to increased production costs.
f. Insufficient documentation: Incomplete documentation can create obstacles in the technology transfer process.
g. Non-Compliant Product Specifications: Products may not meet the intended specifications, leading to further complications.
h. Regulatory Delays: Holdups in regulatory approval or product launches can significantly hinder the transfer process[17].

Table 1- Technology Transfer Team Members And Responsibilities

Team members	Responsibilities
Process technologists	Conducts an initial evaluation of the project being transferred, assessing its feasibility and compatibility with site capabilities, and identifying resource requirements. Gathers documentation from the donor site. Acts as the central point of contact for transfer-related activities.
QA Representative	Reviews documentation to ensure it aligns with marketing authorization standards. Collaborates with the Quality Control (QC) team to evaluate analytical methods for capability and necessary equipment training. Facilitates the conversion of documentation from the donor site into the local format and systems.
Production Representative	Works with the Process Technologist to review process instructions, ensuring capacity and capability are verified. Evaluates any safety concerns related to materials used, such as solvents or sanitizing agents. Assesses the implications for local Standard Operating Procedures (SOPs) and identifies training needs for supervisors and operators.
Engineering Representative	Collaborates with the Production Representative to review equipment and requirements. Initiates necessary modifications or part purchases for engineering. Reviews preventive maintenance schedules and instrumentation needs alongside the Production Representative.
QC Representative	Assesses analytical requirements and the availability of instruments. Responsible for transferring analytical techniques for both drug substances and drug products.

INDIAN ORGANIZATION PROMOTING TECHNOLOGY TRANSFER:

A number of Indian organizations are dedicated to fostering and advancing technology transfer, such as:

- Asian and Pacific Centre for Transfer of Technology (APCTT)
- Technology Bureau for Small Enterprises (TBSE)
- National Research Development Corporation (NRDC)
- Technology Information, Forecasting and Assessment Council (TIFAC)
- Biotech Consortium India Limited (BCIL)[18].

FEW CASES OF TECHNOLOGY TRANSFER:

- Technology transfer in India is being facilitated by government labs, academic institutions, and private companies.
- The Bhabha Atomic Research Centre (BARC) has successfully transferred nearly 90 technologies in fields such as environment, health, electronics, and metallurgy[19].
- The National Chemical Laboratory (NCL) in Pune has formed collaborations with universities and the pharmaceutical sector to enable technology scale-up and implementation.
- The Department of Biotechnology (DBT) has effectively transferred tissue culture methods for forest tree propagation.
- Eli Lilly has partnered with Shasun Chemicals for technology transfer, where Shasun manufactures the anti-TB drug Cycloserine to meet Eli Lilly's international requirements[20].

CONCLUSION

Technology transfer (TT) within the pharmaceutical industry involves the process of sharing the vital information and technologies needed to ensure high standards in drug development and manufacturing. This process is not limited to a single event; instead, it entails continuous interaction and collaboration between the involved parties to facilitate ongoing product production. TT is inherently a mutual effort rather than a one-sided transaction. Successfully navigating technology transfer is a multifaceted challenge that requires a comprehensive strategy, including meticulous planning, effective communication, and teamwork among all parties to guarantee the successful manufacture of quality pharmaceuticals.

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