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An overview of technology transfer in industry

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Abstract

The objective of this review article is to study how technology is transferred in pharmaceutical industry. This review article is to discuss the procedure for technology transfer process in pharmaceutical industry, importance of technology transfer, reasons for using technology transfer, methods of technology transfer, facets of technology transfer, list of institutes in Indian assisting in technology transfer, organization of technology transfer, function of technology transfer, steps involved in technology transfer, few case of involved in the technology transfer in the pharmaceutical industry and understand the aspects related with technology transfer.

Keywords: Technology transfer, Technology transfer dossier, Exhibit batch, Process development laboratory.

1. Introduction

In the pharmaceutical industry, "Technology Transfer" means the processes of successful progress from drug discovery to product development, clinical trials and ultimately full-scale commercialization.

There are 3 standards in the definition of technology:

- First, knowledge must be systematic. This means that it must be organized in terms of providing solutions to problems.
- Second, knowledge must exist in certain places like in someone's head or in documents, and must be able to be presented, so no matter what it means it must be able to be transferred from one person to another.
- Third, it must have purpose-orientation, so that it can be utilized for useful purposes in industry, farming, and commercial fields.

Technology transfer, also called transfer of technology (TOT), is the process of transferring skills, knowledge, technologies, methods of manufacturing, samples of manufacturing and facilities among industries, governments or universities to ensure that scientific and technological developments are accessible to a wider range of users who can then further develop and exploit the technology into new products, processes, applications, materials or services.

According to WHO, transfer of technology is defined as "a logical procedure that controls the transfer of any process together with its documentation and professional expertise between development and manufacture or between manufacture sites." It is a systematic procedure that is followed in order to pass the documented knowledge and experience gained during development and or commercialization to an appropriate, responsible and authorized party. Technology transfer embodies both the transfer of documentation and the demonstrated ability of the receiving unit to effectively perform the critical elements of the transferred technology, to the satisfaction of all parties and any applicable regulatory bodies.

There are 2 types of technology transfer vertical and horizontal. The vertical technology transfer means to transfer of the technology from basic research to the development & production respectively. The horizontal technology transfer means the movement and application of used in one place or the context to another place. It is the

process by which an original innovator of the technology makes its technology available to commercial partner that will exploit the technology. Technology transfer is very helpful to develop the dosage forms in different ways as it provides efficiency in the process, maintains the quality of the product, helps to achieve the standardized process which facilitates the cost effective production. The commercial technology transfer can be defined as the mutually agreed and goal oriented. The transfer can be said to be successful if the receiving unit and the transfer can effectively utilize the technology for the business gain. The success of any technology transfer depends upon the process understanding or the ability of predicting accurately the future performance of the process. The cost of the product development rises during the pilot scale-up and initial the production batch that is the critical path for the success is dependent on the completion of technology transfer to the production site at a cost that is affordable.

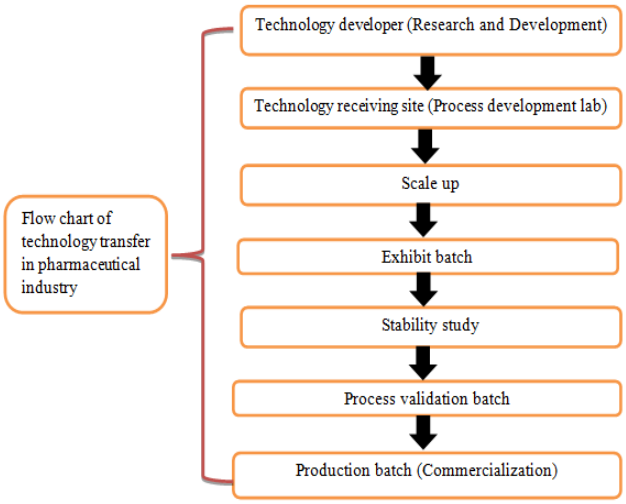

Fig. 1: Flow of stages involves after receiving the technology from R&D to PDL till commercialization of that technology in a pharmaceutical industry

1.1 Why technology transfer is required in Pharmaceutical Industry:[10-12]

In the pharmaceutical industry technology transfer refers to the processes that are needed for successful progress from drug discovery to product development, to clinical trials to full scale commercialization or it is the process by which a developer of technology makes its technology available to commercial partner that will exploit technology. In pharmaceutical industry preparation of dosage form needs scale up at several stages, such as small scale laboratory development from 0.5-2 kg batch can be scaled up to 5-10 kg and then to 20-100 kg on a pilot scale. Production scale can typically range from 200 kg to greater than 1000 kg. Technology transfer involves manufacturing drug product with increasing batch sizes on larger equipment or using continuous processing on pilot scale equipment. Generally scale up involves the transfer of technology and the transfer of knowledge that has been accumulated during the small scale development of product and processes. It is important to realize that good communication is critical for formulation and process transfer to be successful. It is essential for a researcher or developer of technology to make available this technology to another person's to exploit for the progress of development of technology and for exploitation of a technology in different fields of applications and to make is use with another organization that may have better manufacturing capability, marketing capability and commercial capability. In the pharmaceutical industry, technology transfer by collaborating with other departments and other organizations to commercialize a pharmaceutical product is a common process.

1.2 Importance of technology transfer in pharmaceutical industry [13, 3]

- Demonstration of necessary information to technology transfer from R&D to actual manufacturing.
- Demonstration of necessary information to technology transfer of existing product between various manufacturing sites.
- For the smooth manufacturing of commercialized products
- General impact of the technology transfer program.

1.3 Reasons for technology transfer [9-12]

There may be many reasons why a developer of the technology might consider making its technology available to another person to exploit, instead of exploiting the technology itself.

Forming alliances with partners that can progress the development to take it to market

The developer of the technology might have the resources to take the technology to particular state of development, such as up to animal studies and toxicology studies, but does not have the resources to take the technology through its regulatory phases and must collaborate with another organization to take it through these phases and into the market.

Forming alliances with partners with manufacturing capability

The developer of the technology may have taken the technology to a state of development so that it is near market ready but does not have the clean room manufacturing capability or resources to manufacture the product and must partner with another organization that does have the capability. The developer of technology may only have manufacturing equipment which is suitable for small scale operation, and must collaborate with another organization to do large scale manufacturing.

Forming alliances with partners with marketing and distribution capability

The developer of the technology may have fully developed the technology and even have obtained regulatory approvals and product registrations for the product to be sold but it lacks the marketing and distribution channels to give it a marking capability and must collaborate with another organization that does have that capability.

Lack of resources to launch product commercially:

The original inventor of technology may only have the resources to conduct early-stage research such as animal studies and toxicology study, but doesn't have the resources to take technology through its clinical and regulatory phases.

No commercial capability

The developer of the technology may be research institute of a University, which does not have the capability to exploit commercially at all, and need to collaborate with another organization that does have that capability. In the exploitation of pharmaceutical products, technology transfer by collaborating with this way to bring a pharmaceutical product to market is common feature of the industry.

2. Methods technology transfer:[14]

Technology Transfer can be done in various ways such as contract Research and Development, establishment of joint ventures, setting up plants, licensing patents, designs etc. Licensing is however the most common method of technology transfer that grants the right to

1. Licensing in:

In this strategy companies that are small and lack facilities to do basic research would wish to buy other's research. Also large scale and research based companies also might like to license in technology to expand its product line.

2. Licensing out:

In this, small scale companies that only have patents as their assets and cash in scarce would like to license out, whereas large companies license out technology if it is of very little knowledge for them.

2.1 Facets of technology transfer: [9]

a) Govt. laboratories to private sector.
b) Between private sectors of same country.
c) From academics to private sectors.
d) Between academy, private and govt. sectors

a. Govt. labs to private sectors:

This type of technology transfer is advantageous as the Govt. labs can get good financial support and funds from the govt. for their research work and the technology developed by them reaches the private sector.

b. Between private sectors of same country:

This type of technology transfer generally occurs due to lack of appropriate financial resources or inadequate knowledge of regulatory requirements, thus the private sector that develops the technology is paid by other sector that absorbs the technology.

c. From academics to private sectors:

Academic sectors that are actively involved in research and development the technology and make it available to private firms. By collaboration of private firms with the institutions, money can be saved.

d. Between academy, private and govt. sectors:

In this type of technology transfer govt. provides necessary funds to the academic institutions in developing technology that can be transferred to the industry.

2.3 List of institutes in India assisting in Technology Transfer: [15]

1. Asia Pacific Centre for Transfer of Technology: C2, Qutab Institutional Area, New Delhi -110016. Phone no-011 30973700
2. National Research & Development Corporation: 20-22, Zamroodhpur Community Center, Kailash colony, New Delhi-110048. Phone No-011 26489037
3. Technology Bureau for Small Enterprises: Room no-123, Udyog Bhawan, Rafi marg, New Delhi-110011. Phone no-011 23061431
4. Foundation for Innovation & technology transfer: Indian Institute of Technology Hauzkhas, New Delhi-110016. Phone no- +91 1126857762

3. Organization of technology transfer:

Since a team concept is always the best approach to accomplishing a successful technology transfer project. The core technology transfer team should be commissions immediately following the decision of executive management to pursue the drug candidate to commercialization. Typical technology transfer core team will likely be comprised individuals representive of different segments of the business.

1) Project Manager:

For overall responsibility coordination and progress communication to management. His or her role may be enhanced as necessary by additional staff & responsibility and authority delegated as appropriate.

2) Regulatory Affairs:

For coordination of the appropriate regulatory filings, advice on approval timing, content of the filing documentation and response to regulatory inquiries.

3) Engineering:

To coordinate associated capital projects and direct and control construction, equipment acquisition, installation and qualification.

4) Material management:

To include those units responsible for pure chasing, strategic planning, resource allocation and supply chain activities. This member (or members) will analyse and recommend the most favorable manufacturing strategy in consideration of internal capability, business partnership and tax advantages for the corporation.

5) Manufacturing operations:

To represent the originating site and receiving location production activities. These representatives should have sufficient authority to commit the necessary personal and plant resource to accomplish the project within the defined cost and time limitations.

6) Research and Development:

To support the technical issues and resolve problems. This groupprovides the process expertise and would be expected to train and direct the production trials atreceiving site.

3.1 Function of technology transfer team:[16]

1. **Coordinate:** Coordinating between technology users and developer between researcher and manufacturers is important element of technology transfer.
2. **Nurture:** A main ingredient for moving technology from a research laboratory to new business enterprises successfully in an environment that is supportive for entrepreneurship.
3. **Link:** Cataloging resources related to business enterprises and connecting would be entrepreneurship/ researcher and other technology developers to outside group & organization which can help in the process of starting new product, companies etc. such linkage provide referrals for individual business counseling sources of financing.

4. Steps in technology transfer process: [17]

Technology transfer is not a single way process. The development of new formulation goes through many stages. During development of a formulation, it is important to understand procedure of operations used, critical and noncritical parameters of each operation, production environment, equipment and excipient availability, which should be taken into account during the early phases of development of formulation, so that successful scale up can be carried out. Appropriate care during technology transfer is important to enhance drug quality as developed by research and development in final formulation as well as to assure quality for predetermined period of time.

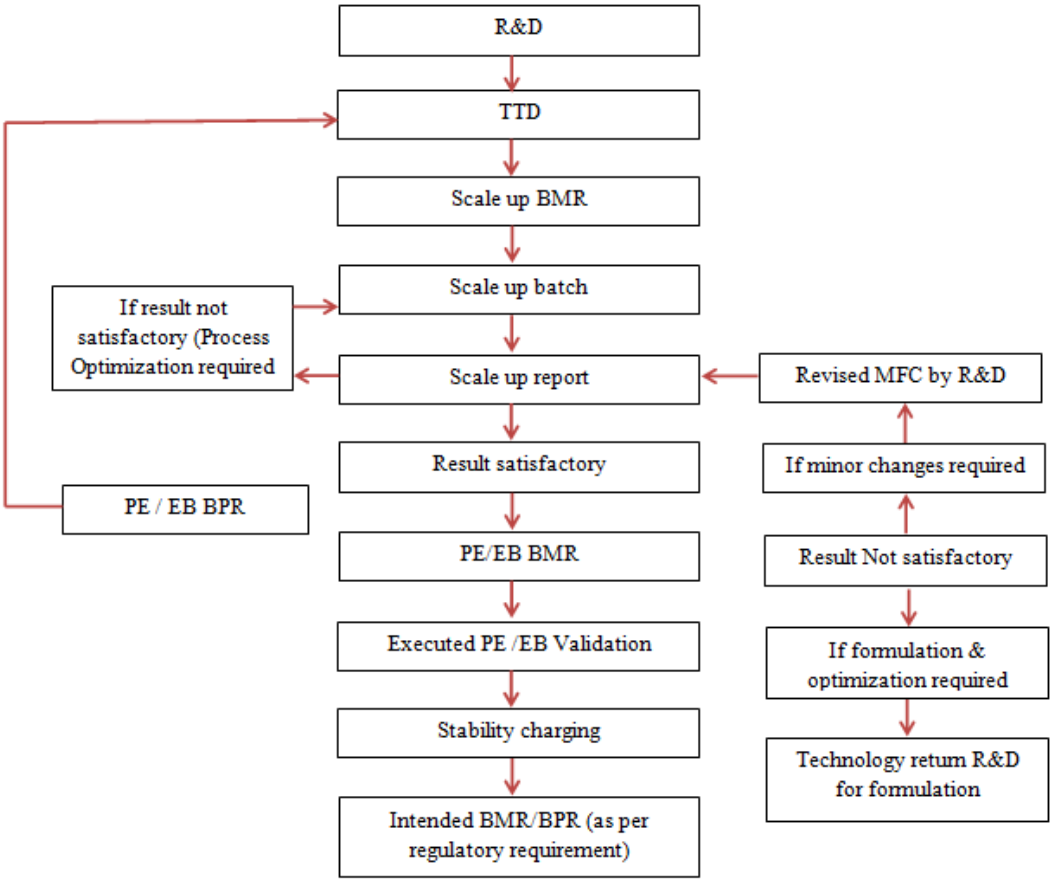

Fig. 2: Flow chart for technology transfer

TTD: Technology Transfer Dossier, MFC: Master Formula Card, PE: Pre Exhibit, EB: Exhibit Batch, BPR: Batch Packaging Record, BMR: Batch Manufacturing Record.

- Development of technology by research and development (Research phase)
- Technology transfer from research and development to production (Development phase)
- Optimization and Production (Production phase)

1) Research phase (Development of technology by research and development):

a. Quality Design:

- For drug products the quality design corresponds to pharmaceuticals design to design properties and functions such as
- Elimination of adverse reactions
- Improvement of efficacy
- Assurance of stability during distribution
- Data based on various data such as chemical and physical properties, efficacy, safety and stability obtained from preclinical studies
- For drug substance the quality design is to determine starting materials and their reaction paths and basic specification of the drug.

2) Development Phase:

a. Research for factory production:

To manufacture drugs with qualities as designed, it is required to establish appropriate quality control method and manufacturing method, after detecting variability factors to secure stable quality in the scale up (validation) that is performed to realize factory production of drug designed on the basis of result from small scale experiments.

b. Consistency between Quality and Specification:

When product specification is established on the basis of the quality of the product determined in the above, it is required to verify that the specification adequately specifies the product quality. Relations between upper and lower limits of manufacturing formula (composition and manufacturing methods) and upper and lower of control limits of the product specification should be fully understood, and the consistency between the product quality and specifications should be maintained.

In short, the consistency between quality and specification is to ensure in the products specification that the quality predetermined in the quality design is assured as the manufacture quality, and the product satisfies the quality of design.

c. Assurance of consistency through development and manufacturing:

For this purpose, the transferring party in charge of development should fully understand what kind of technical information is required by the transferred party in charge of manufacturing and should establish an appropriate evaluation method to determine whether a drug to be manufactured meets the quality of design. For stable production of consistent products, it is fundamental to fully refer to information of similar products of the past maintained by the manufacturer when research for factory production is implemented.

d. Technology Transfer from R&D to Production:[9]

R&D provides technology transfer dossier (TTD) document to process development laboratory, which contains all information of formulation and drug product as given below:

- **Master formula card (MFC):** It includes product name along with its strength, generic name, MFC number, page number, effective date, shelf life and market.
- **Master packaging card:** It gives information about packaging type, material used for packaging, stability profile of packaging and shelf life of packaging.
- **Master formula:** It describes formulation order and manufacturing instructions. Formulation order and manufacturing instructions gives idea of process order, environment conditions required and manufacturing instructions for dosage form development.
- **Specifications and standard test procedure (STPs):** It helps to know active ingredients and excipients profile, in- process parameters and specifications, product release specification and finished product details.

3) Production Phase:

a. Validation and Production:

Production is implemented after various validation studies verify that it is able to stable product based on transferred manufacturing formula. While the manufacturing facility accepting technology is responsible for validation, the research and development department transferring technology should take responsibility for validation such as performance qualification, cleaning validation, and process validation unique to subject drugs.

b. Scale up for production:

Scale up involves the transfer of technology during small scale development of the product and processes. It is essential to consider the production environment and system during development of process. Operators should concentrate on keeping these things in mind that their segment of the production process running smoothly if technology transfer is implemented thoughtfully. Effective technology transfer helps to provide process efficiency and maintain product quality.

c. Considerations of different parameters for scale-up:

Before starting scale-up, we also considered different parameters that should be optimum for successful technology transfer. These were flexibility, cost, dependability, innovation and product quality. It was important to realize that good communication was critical for formulation and process transfer to be successful.

d. Selection of method:

The method for batch fabrication was selected on the basis of data given from research and development.

Granulation, blending, compression and coating were critical parameters for technology transfer.

5. Technology Transfer Documentation: [12-18]

Generally interpreted as document indicating contents of technology transfer for transferring and transferred parties. Each step from research and development to production should be documented, task assignments and responsibilities should be clarified and acceptance criteria for completion of technology transfer concerning individual technology to be transferred. It is duty of quality assurance department to check and approve the documentation for all processes of technology transfer.

(a) Development Report:

The research and development report is a file of technical development, and research and development department is in-charge of its documentation. This report is an important file to indicate rationale for the quality design of drug substances and its specifications and test methods. The development report is not prerequisite for the application for approval it can be used at the pre-approval an inspection as valid document for quality design of new drug. The development report contains –

1) Data of pharmaceutical development of new drug substances and drug products at stages from early development phase to final application of approval.
2) Information of raw materials and components.
3) Design of manufacturing methods.
4) Change in histories of important processes and control parameters.
5) Specifications and test methods of drug substances.
6) Validity of specification range of important tests such as contents impurities and dissolution.
7) Verifications of results.

(b) Technology Transfer Plan:

The technology transfer plan is to describe items and contents of technology to be transferred and detailed procedures of individual transfer and transfer schedule, establish judgment criteria for the completion of the transfer. The transferring party should prepare the plan before the implementation of the transfer and reach an agreement on its contents with the transferred party.

(c) Technology Transfer Report:

Completion of technology transfer is to be made once data are taken accordingly to the technology plan and are evaluated to confirm that the predetermined judgment criteria are met. Both transferring and transferred parties should document the technology transfer report.

Exhibit batches: After taking scale up batches of the product, manufacturing of exhibit batches takes place. In case of exhibit, batch sizes are increased along with equipments and their processes. This is done for filling purpose in regulatory agencies. The purpose behind to run three consecutive batches are to shows process consistency reproducibility and to demonstrate that the manufacturing process is under control throughout all the stages.

5.1 Effective factors in technology transfer: [19]

"Technology transfer can be considered successful if a receiving unit can routinely reproduce the transferred product, process or method against a predefined set of specifications as agreed with a sending unit and/or a development unit". Main factors that affect the process of technology transfer in pharmaceutical industry are as follows:

1) Investment in Research and Development.
2) Establishing relationship between production and research.
3) Training of individual in relation of technology.
4) Information development in the field of technology transfer methods.
5) Organizational, equipmental and informational infrastructures.
6) Employment of international specialist in the field of technology and creation of appropriate relationship between recipient and sender technology.
7) Awareness of fundamental and important factors required for technology transfer.
8) Consideration of existing and old technologies.
9) Degree of development and improvement of technology on the basis of internal resources.

5.2 Unsuccessful technology transfer process may be due:

1) Unsuccessful or incomplete process validation.
2) High rates of batch rejections, excessive labour requirements, increased cost of product etc.
3) Incomplete documentation.
4) Product does not show specifications as intended.
5) Delayed regulatory approval and/or product launch.

6. Few cases of technology transfer: [20-25]

The process of technology transfer is actively being pursued in India through Government laboratories, Academics Institutions and Commercial entities.

1. The Bhabha Atomic Research Centre (BARC) has developed and transferred around 90 technologies in the areas such as environment and health, electronics, electrical and mechanical, chemical and metallurgy, radioisotope and applications.

2. The National Chemical Laboratory (NCL) Pune has several linkages with Universities and pharmaceutical industries to ensure successful scale up and implementation of technology.

3. Department of Biotech (DBT) has successfully transferred some techniques of forest trees through tissue culture.

4. Eli Lily has entered in technology transfer agreement with Shasun Chemicals and Drugs for the manufacturing of anti-Tuberculosis drug Cycloserine produced by Shasun to meet Eli Lily global demand.

Other pharmaceutical companies like Wockhardt Ltd, Cipla Ltd, Torrent Pharmaceutical Ltd, Dr. Reddy's Laboratories Ltd, USV Ltd have already signed in-licensing agreements with foreign drug markers.

5. Central Drug Research Institute (CDRI): has developed technologies in the areas such as Malaria and other parasitic diseases, CNS-CVS related disorder, reproductive health, diabetes and energy metabolism, cancer biology and related areas, safety and clinical development.

6. Tata Institute of Fundamental Research: has successfully transferred some techniques of mathematics, natural sciences, computer sciences, biological sciences.

7. Conclusion

Appropriate technology transfer is important to upgrade the quality of design to be the quality of product, and ensure stable and high quality of the product. A healthy communication between different countries and different organizations are the key to the success of technology transfer and development. So the knowledge and information should be transferred equally and continuously from transferring party to the transferred party, this will help in the product manufacturing process and thus the development of both the parties. Technology Transfer provides an opportunity to reduce cost on drug discovery and development thus major pharmaceutical companies look for technology transfer opportunity as it reduces risk, cost and rate of failure. The three primary considerations to be addressed during an effective technology transfer are the plan, the persons involved, and the process. Licensing is an important phenomenon of technology transfer that has gained momentum in pharmaceutical industry by which pharmaceutical companies can contribute to research and development. Technology transfer is a complex issue and should be deal with using holistic approach.

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