



Technology Transfer: A New Buzz Word in Pharmaceutical Industry

Amrita K^{1*}, Pullam Raju K¹, Shrikhande S², Prudhvi R P¹, Biswas U. K¹, Bajaj A³

¹K.G.R.L college of Pharmacy, Bhimavaram (A.P)

²C. U .Shah college of Pharmacy, Santacruz (W), Mumbai

³Shri Ville Parle Kelavani Mandal, B.N.C.P, Ville Parle Mumbai,

*Corresponding author: amrita.sndt@gmail.com

ABSTRACT

With fast globalization of competition, the pharmaceutical industries with a trust for achieving enhanced operating performance and commercialization of products opt for transferring their owned technology to another unit which possess all the necessary requirements. There is a sturdy increase in the demand of medical services due to ever increasing population and diseases, so the global pharmaceutical industry needs to maintain the pace with the demand. The pharmaceutical industry is under regulatory and patent protection; its ethical and religious issues are the focus of attention. Hence, the main focus is how the idea or process is further carried from a research program towards commercialization. The success depends on the effectiveness of the communication preceding its implementation. This review gives a brief knowledge about the knowhow of technology transfer, its barriers, various agreements and the process for it.

Keywords: Technology transfer, transfer process, contractual agreements, methods of technology transfer

1. INTRODUCTION

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 (RU) to effectively perform the critical elements of the transferred technology, to the satisfaction of all parties and any applicable regulatory bodies [1].

“Technology transfer” in pharmaceutical industry 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 the technology [2].

Technology transfer (TT) is defined as “the transfer of the manufacturing process for a new pharmaceutical Drug Substance (DS) and Drug Product (DP), respectively, from the transferring site (in this case R&D) to the receiving site or designated commercial manufacturing site.” This includes all

the associated knowledge, information and skills to be able to manufacture the DS and DP at the receiving site [3].

The development and transfer of knowledge and technology has been and will continue to be critical to success in pharmaceutical industry. The transfer of technology is considered as both fundamental and significant to the drug discovery and development process for any new medicinal entity. This process is important for to elucidate necessary information for technology transfer from R & D (Research & Development) to PDL (product development laboratory). This review gives a brief description about the importance, objective, steps in technology transfer, various issues and main contractual agreements by which technology transfer takes place.

2. REVIEW

2.1. Importance and need for technology transfer to pharmaceutical industry

Development of pharmaceutical process in R& D labs and conversion to commercial production are on crucial path because of condensed time-to-market expectations. The need of hour for pharmaceutical companies is to speed up delivery of new drug products to the market to maintain competitive effectiveness. New drug discoveries and formulations must be rapidly brought to market. In recent years launching of new chemical entities has slowed down because it has become more

complicated to meet all the requirements of safety, clinical and regulatory in areas of unmet medical needs. Statistics from the pharmaceutical industry also shows that there is a high risk of failure in drug discovery and development, with only one in five to one in ten new candidate drugs nominated from research to development actually achieving registration and reaching the market [4].

The transfer of technology for Drug Substance and Drug Product between R&D and the respective Production sites is critical to successful and timely development. The aim is to get to market quickly with the development of a drug and product of the appropriate quality and to do it "right first time, every time. In a pharmaceutical industry drugs or drug products are manufactured with large batch sizes on pilot scale equipment. This pilot scaling up involves the transfer of technology and the transfer of knowledge from labs that are acquired during the small scale development of product and processes. It is essential for a developer of particular technology to make it available to exploit for the progress of development of technology, for better manufacturing capability, marketing capability and commercial capability [5].

2.2. Various Procedures for technology transfer [6]

The specific procedures of technology transfer process are

(a) Post management - Monitor compliance to the conditions of the contract and actual inspection & report

(b) Negotiations & contract - Propose of transfer conditions

Establish negotiation strategy

Negotiate on technology transfer conditions & details

Draw-up & analyze draft contract

Different for each depending on the type & form of technology

(c) Marketing activities - Prepare marketing materials for technology transfer

Conduct activities such as the participation in Techno mart

Analyze methods to expect maximum effect with minimum cost

Discovery and contact of potential demanding parties

Research & analysis of demanding party (party seeking implement)

Prior-proposal of technology transfer conditions to the parties seeking to receive the technology transfer

(d) Packaging - Draw-up technology information document for the smooth execution of technology marketing

If possible include prototype

(e) Technology valuation & demand selection

Qualitative/quantitative value valuation of the secured technology

Analyze possibility of clash with a 3rd party owned technology

Establish transfer strategy in accordance with the technology type & form

Preliminary matching of technology demand/supply

Pre-analysis of whether the transferred technology can secure competitiveness if seeking to transfer overseas

(f) Discovery of technology - Discovery of competitive technology

Transfer request or arranging & securing technology that is possible to transfer but is not possessed in-house

2.3. (A) Technology transfer process in pharmaceutical industry

Transnational corporations designated as TNC^s are the world's most widely accepted experts at applying science and technology to production and marketing. The transfer of technology takes place through investment contracts with these corporations headquartered in developing countries. It has been estimated that only 12 % of the R & D projects results in commercial success. The financially secure corporations endure the risk of conducting R & D to support various projects [7].

In the first process for a drug substance, the quality design is prepared to determine starting materials and their reaction paths, and basic specification of the drug along with properties and functions such as elimination of adverse reactions, improvement of efficacy, assurance of stability during distribution, and adding usefulness based on various data such as chemical and physical properties, efficacy, safety and stability obtained from preclinical studies [8]. The process of technology transfer is shown in Fig.1.

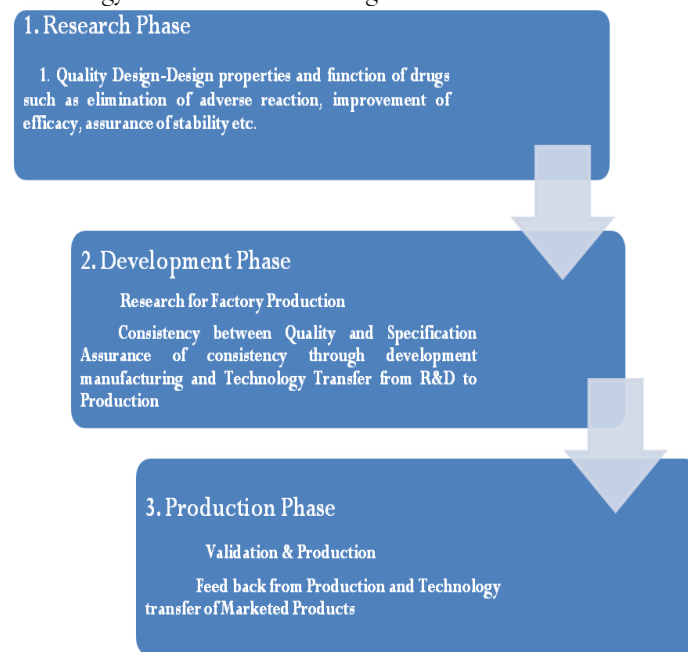


Fig 1: Technology transfer process in pharmaceutical industry

The second phase is the development phase which includes scale up detection and quality variability factors. Appropriate quality control method and manufacturing method are

established for manufacturing the drugs of required qualities. Different variability is detected from small scale experiments conducted on lab scale for which validation is carried out for production on large scale. So, this process is also called as the research for factory production. R and D provides the technology transfer dossier (TTD) document to product development laboratory, which contains all information of formulation and drug product as Master Formula Card, Master Packing Card, Master Formula and standard test procedures. The next step is to verify the consistency between the quality and specifications of the product that was established earlier so that the product satisfies the quality of design. The technical information of product is generated from limited amount of batches for which various standards and quality evaluation method should be established for factor production. Here assurance of the fact that the product developed in small scale will produce similar product during factory production.

Transfer of technology of new products from research and development department to production department is carried out with all the technical complied as research and development report.

In the production phase all the validation parameters are implemented by the manufacturing facility personnel to verify the consistency and accuracy of the data transferred from research and development phase [9].

Technology Transfer Documentation –It includes the document of the technology transferred to the receiving parties. Each and every step from R&D to production is documented including the task assignments and responsibilities. Quality Assurance department is responsible to check and approve the documentation for all processes of technology transfer [10].

(B) Forms of Technology Transfer

Technology transfer promotion law established on January 28, 2000 defines technology as patents registered in accordance with relevant laws such as the patent law, utility models, designs, and semiconductor allocation design, capital assets based on technology, software and intellectual assets technology as well as design, whereby these are deemed to be the objects of technology transfer. The technology to be transferred is included under intangible technology which means manufacturing site, manufacturing method, confidential skill, and know how constituting the entire intellectual property having economic value. The success of business and technology transfer depends upon understanding the various characteristics of intellectual property [11].

(C) Different methods of technology transfer

(i) By sale or Transfer of technology

When the transfer of rights is carried out in agreement with a contract is called the sale of technology. By this inclusive control and management is handed over to the buyer who pays the price (sales price). The owner demands a high and fixed price for full transfer of rights to the buyer but the buyer will not easily agree unless the buyer is convinced of the economic value & potentiality of utilization of the patent.

The reasons for sale or transfer of technology arises where

1. The owner of patent does not have the capability to execute and there are problems in licensing to a 3rd party.
2. There is a problem in developing a basic patent into a commercial product.
3. It is difficult to produce the finished goods, based on partial patent
4. Sales by specialized technology development and sales companies are in the ordinary course of their business.
5. An individual inventor raises research & invention funds.

A contractual agreement between the two parties is required for this kind of technology transfer but it is only possible when the patent is registered with Intellectual Property Rights Organisation.

(ii) By licensing of technology

Licensing covers the broad spectrum of permissions that are granted for the use of patents, technology, and trademarks. Of the various methods of transferring technology internationally, licensing is the most versatile. It offers flexibility in technology choice and an opportunity for the source and the receiving institution to negotiate. Technology license agreements also enables a foreign licensor to reap profits from the transfer of technology without risking capital in a sometimes volatile foreign market [12].

Internationally, amongst the various forms of transferring the technology, licensing method is the most versatile and offers flexibility in choice of technology. Licensing means permissions that are granted for the execution of patents, technology and trademarks. Both the parties that give and take the execution & usage of the rights enter into a licensing contract under specified conditions including payment of technical fees for a specified period etc. After the period is over, execution and usage becomes invalid. The most commonly used methods in technology transfer are the sales and licensing method. Technology transfer is mainly conducted in the sales method as the licensing method of technology transfer is not properly recognized. So, there is a need for the spread of recognition as well as the development & propagation of transfer techniques [13].

(iii) By combination of capital, management and know-how

In case of highly advanced and improved technology, the success of commercialization is not guaranteed, so the technology is transferred together with the capital, management know how and core components.

(iv) By sale of technology data such as plans, microfilms etc

Aims at using a part of technology information for solving simple technological problems in case of small scale projects.

(v) By using technical personnel as the medium

Here the technical personnel are directly involved in the technology transfer through invitation and deployment of technical personnel, resolution of technological issues through the employment.

2.4. Preventive factors of technology transfer process

1. Must be conscious of the fundamental and important factors in technology transfer process
2. Failure factors of technology transfer process
3. An effort must be added in acquisition of suitable technology for achieving appropriate organizational position.
4. Deliberation of existing, active and old technologies [14]

2.5. Factors for effective technology transfer process

In technology transfer process, technological evaluation, requirements, capacities recognition and selection of technology methods are of utmost importance [15]. The effective factors of technology transfer process are

- a. Proper development of managerial and organizing skills in organizations with a long-run strategic planning in technology development, Investment in R&D.
- b. A proper relationship has to be establishment between production and research and training of individual related to technology must be provided alongwith interaction with different international centres in technology cooperation areas.
- c. Information development in the field of technology transfer methods; Modification of cultural value systems in organizations; and Diffusion of scientific attitude in organizations.
- d. Employment of entrepreneur managers and Creation of standards and capabilities in companies
- e. Infrastructure related to organization, equipment, information and human.
- f. Training in international companies and employment of international specialist in the field of technology

- g. Technological factors such as degree of achieving the technology, its price, simplicity and complicity of technology and development of technology [16].

2.6. Issues in the Technology Transfer Process

There is increasing competition among the pharmaceutical industry as they are outsourcing the production, manufacturing networks and in-licensing activities to less costly contract research organisations. These premeditated initiatives involve effective technology transfer. Technology transfer also affects companies' ongoing operations-from research through commercial production. It underlies all key development and manufacturing activities needed to successfully bring a product to market. The main issues with technology transfer process are

(a) Pharmaceutical industries transfers the process in the form of documents or in other words it can be said as procedural exchange of process documents between sending and receiving parties. If the technology developed in the laboratory is not scaled up then the companies are again forced to reinvent the scalable processes. This process leads to various inefficiencies, such as suboptimal allotment of resources, unmitigated cycle times, higher development costs, quality and compliance issues.

(b) As more and more big pharmaceutical companies are outsourcing early research and scale-up activities to contract manufacturing organizations, a process to manage information exchange with contract manufacturing organisation in the remote locations becomes even more critical. Due to time difference and language barriers, many companies their initial expectations of significant cost reduction often fall short [17].

2.7. Keys and Ways of successful technology transfer

The key to successful technology transfer is:

- (a) Amalgamate strategy, organization and processes both within and across organizations which should be customer-focused. Customer focussed strategy helps ensure configuration of regulatory requirements and filing strategies. To augment the competence of technology transfers and minimize the risk of late-stage site changes, the companies must strategically select sites to match their product's technology, process, and capacity requirements early in the development process.
- (b) The next job is meticulous selection process of contract manufacture organisation. Looking at the objectives one must adopt a very rigorous process in the selection and based on the requirements on business, technical, quality and regulatory aspects. The companies which are selected go for establishment of non-disclosure agreement with

- companies they are interested to allow for more comprehensive discussions.
- (c) Establishment of timeline and cost-savings objectives for the transfer.
 - (d) Highly skilled, dedicated technology transfer teams with excellent managerial skills.
 - (e) Technology transfer takes place during one of the stages in the product's lifecycle: early discovery, toxicological evaluation, clinical development, scale-up and commercial manufacturing, and in-line production. At every stage it requires different type of transfer, rationale, and key participants. So a road map is required to translate the transfer strategy into unambiguous activities, to define the timing, sequence, and dependencies among these activities, and to identify the stakeholder responsibilities and deliverables.
 - (f) In spite of having excellent strategy and road map, successful technology transfer demands that the organization to which the technology is transferred must ensure that the technology is successfully implemented the technology keeping in mind all the variables [17].

A legal relationship is created by which the possessor of technology, or the proprietor of licensed rights exploit the technology which grants new rights of exploitation to the technology transfer partner which are contractual in nature. Legal agreements are entered into by which:

1. The right to exploit the technology is granted by the technology owner or rights holder, to the technology transfer partner that will exploit the technology

2. The technology owner or rights holder is compensated, usually financially, for the grant of those rights,
3. The respective rights duties and obligations of the parties that will govern their legal relationship are set out.

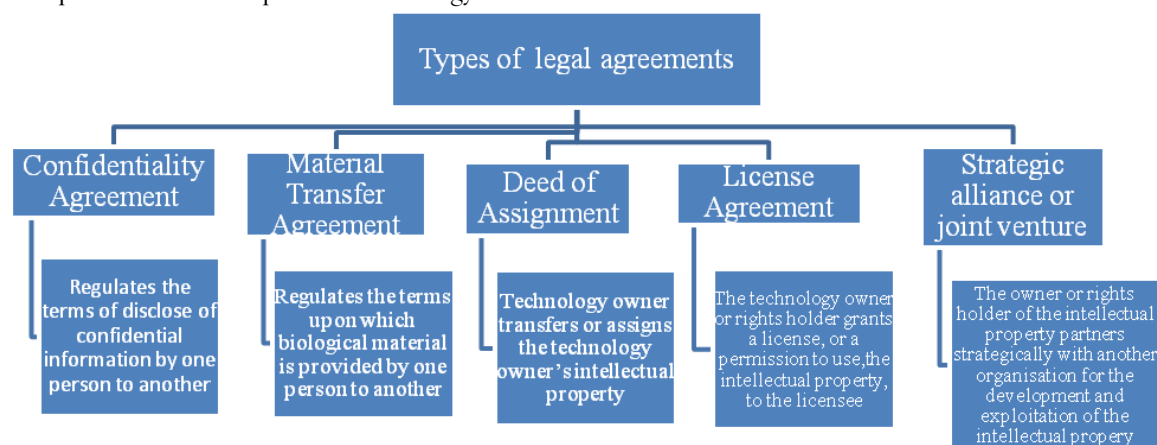
2.8. Main contractual agreements by which technology transfer takes place [18]

The principal mechanisms by which technology transfer takes place in the pharmaceutical industry and the types of legal agreements are:

2.8.1. WHO guidelines on transfer of technology

The business strategy of most of the pharmaceutical companies involves intra and intercompany transfer of technology. The main reason for such transfers is the need for additional capacity, repositioning of operations and mergers. The development of product in a laboratory scale faces problem of scale up, manufacturing and production.

It involves a sending unit and receiving unit and a unit managing the process. It requires documented and planned approach involving well trained and skilled persons working with quality system. Documentation of all the works was done covering the areas of production, development and quality control [19].



The WHO Expert Committee on Specifications for Pharmaceutical Preparations recommended in its forty second report that:

Based on the principles of quality risk management and covering the quality aspects of the project, the plan should be made. Technical risk assessment and potential regulatory requirements of the countries of sending unit and receiving unit should be performed as needed. Sufficiently trained staff should be trained at the receiving unit.

1. The process is considered to be successful if the receiving unit sufficiently produces documented evidence that the receiving unit can routinely reproduce the transferred product, process or method against a predefined set of specifications as agreed with the SU.
2. In case of any problem with the receiving unit during the transfer, it should converse back to the sending unit to ensure continuing knowledge management
3. If transfer of projects is in between two companies, then the legal and economic implications must be resolved. Issues

pertaining to intellectual property rights, royalties, pricing, conflict of interest and confidentiality should be addressed before and during planning and execution of the transfer.

4. Any lack of transparency may lead to ineffective transfer of technology [20].

Organisation involved in technology transfer

World Intellectual Property Organisation

National Institutes of Health

Technology Transfer Desk Reference

Biotechnology Industry Organisation

3. CONCLUSION

The pharmaceutical industries in most of the developed and newly industrialized countries transfer modern and suitable technologies to the industries to increase its efficiency for rapid development and fast commercialisation. The transfer of technology from research and development, to the commercial production site is a critical process in the development and launch of a new medicinal product. For this reason, the pharmaceutical companies must place more attention to reorganize and optimise the technology transfer process for rapid and successful introduction of product to market.

It is suggested the organization should implement a meticulous process for selection of contract manufacturing partners to prevent issues in the future collaboration process. Along with it the organization establishes a formal feedback mechanism for continuous improvement and increases the efficiency of subsequent transfers. A strong support is required in the area of scientific research to the academic institutions so that the barrier between the industry and academic is removed for the free flow of science and technology. The platform must remain open for the exchange of new ideas and knowledge. Therefore, the technology transfer process could be streamlined in a better and successful way.

Accordingly, pharmaceutical companies should be more accurate in the technology transfer process. Since the process is a complex issue, so the pharmaceutical companies should strive to build up scalable process for technology transfer. Consequently, it is required that accurate process must be applied for selecting the receiving unit for collaboration.

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