

## Technology Transfer: A Paradigm for Industry

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### ABSTRACT

*Technology transfer is both essential and critical to drug discovery and development process for new medicinal products. Technology transfer is a process by which technology developed in one organization, in one area, or for one purpose is applied in another organization, in another area, or for another purpose. The success of any program is highly dependent on the effectiveness of the communication which ultimately proceeds in implementation. The ultimate goal for successful technology transfer is to have documented evidence that the manufacturing processes for drug substances and drug product, respectively, are robust and effective in producing the drug substances and drug product complying with the registered specifications and Good Manufacturing Practice requirements. Productivity gains only result from the natural diffusion of innovation to the market place (technology transfer). State and local government concerns with regional economic growth also have focused attention on technology transfer as a mechanism to increase private sector innovation related activities within their jurisdiction.*

**Keywords:** *Technology Transfer, Good Manufacturing Practises, Drug Discovery.*

### INTRODUCTION

In recent years, there is a growing awareness that an appropriate transfer of manufacturing technologies (technology transfer) is important to upgrade drug quality as designed during R&D to be a final product during manufacture as well as assure stable quality transferred for many reasons between contract giver and contract acceptor during manufacture. Technology transfer is a process by which technology developed in one organization, in one area, or for one purpose is applied in another organization, in another area, or for another purpose. Technology transfer is helpful to develop dosage forms in various ways as it provides efficiency in process, maintains quality of product, helps to achieve standardized process which facilitates cost effective production. The crucial aspect in a successful transfer is the actual use of the product or process. Technology transfer is both integral and critical to drug discovery and development for new medicinal products

Technology transfer is defined as "The processes that are needed for successful progress from drug discovery to product development to clinical trials to full-scale commercialization." 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. It is the process by which an original innovator of technology makes its technology available to commercial partner that will exploit the technology.

### WHY TECHNOLOGY TRANSFER<sup>16</sup>

To development and transfer knowledge and technology has been and will continue to be critical to success in pharmaceutical industry. Technology transfer is an important in benefits of R & D and to the society especially in developing countries. Process development and commercial production are on

critical path because of compressed time-to-market expectations so there is a tremendous need of technology transfer. Insufficient Process Knowledge Results in a Poorly Scaled-up Process it results in poorly process reliability increased number of product atypical decreased production rate, not being capable of handling variations of raw materials, API, Process controls, operators, etc. Inefficient Validation.

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. The flow dig. shows basis of technology transfer in pharmaceutical development of the drug product.

**Fig.1: Stage of Technology Transfer in Drug Development**



Technology transfer provides an opportunity to reduce cost on drug discovery and development, thus major pharmaceutical companies look for technology transfer opportunities as it reduces the risk, cost and rate of failure. Technology Transfer is a vulnerable time for companies Loss of knowledge or experience, leading to “reinvention of the wheel” .Confused ownership and responsibilities Delayed approvals so to avoid all this things we are going for the technology transfer. The major thing behind Technology transfer is the international competition in market place to acquire superior position and for this they wants new techniques that results in highly desired to improve a quality assurance system of drugs at all stages through research and development (R&D), manufacturing and marketing in line with the trends by reviewing the current quality assurance system and its methods including existing Good Manufacturing Practice (GMP) to comply with the new system and adopting achievements of technological progress and international harmonization of pharmaceutical regulations.

#### **REASONS FOR COMMING OF TECHNOLOGY TRANSFER<sup>7</sup>**

- 1) **Not Accepted Manufacturing Capacity:** 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.
- 2) **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.
- 3) **Lack Of Marketing And Distribution Capability:** The developer of technology may have fully developed the technology and even have obtained regulatory approvals and product registrations, but it may not have the marketing and distribution channels.
- 4) **Exploitation In a Different Field Of Application:** Each partner may have only half of the solution i.e. the developer of the technology might be capable of exploiting the technology itself in the field of diagnostic applications and may grant exploitation right to commercial partner for the exploitation of therapeutics application.

#### **GOALS OF TECHNOLOGY TRANSFER<sup>11</sup>**

- Is a valuable step in the developmental life cycle leading to successful commercial manufacturing of drug in drug product development life cycle.
- To take all the gathered knowledge and use it as the basis for the manufacturing control strategy, the approach to process qualification and on-going continuous improvement.
- The transition of the product/process/analytical method knowledge between development and manufacturing sites.
- To ensure variability of process and parameters are controlled and sufficient in the face of the rigors of a commercial production environment to verify parameters established during development are still within the determined design space and/or adjusted at scale-up.

**TECHNOLOGY TRANSFER PROCESS<sup>9</sup>**

The quality of drug is based on the basic data concerning efficacy and safety obtained from various studies in preclinical phases and data concerning efficacy, safety and stability of drug products obtained from clinical studies. Such maintenance of Quality of drug completed in Phase II of clinical trial. At each production steps and manufacturing the standard of IPQC test is set in this flow of Production steps and Phase III of clinical trial to realize the quality of design, and the quality of design will be verified in various validation studies, and will be upgraded to be the quality of product, and the actual production will be started.

“Technology Transfer take action in this flow of Development to realize the quality as designed during the manufacture.”

Process classified in to five categories:

**1. Quality Design (Research Phase)**

The name itself shows the quality is design and performed since last preclinical and phase II of product properties and its effect. the quality design corresponds to so-called pharmaceutical design to design 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.

**2. Scale-Up And Detection Of Quality Variability Factors (Development Phase)**

- 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 drugs designed on the basis of results from small-scale experiments.

- Consistency between Quality and Specification :

In short, the consistency between quality and specification is to ensure in the product specification that the quality predetermined in the quality design is assured as the manufacturing quality, and the product satisfies the quality of design. It should be recognized that technical information of developed product are generated from data of a limited amount of batches, various standards have been established from the limited data, and quality evaluation method established in development phase is not always sufficient for factory production. 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, and this is a key to successful technology transfer.

**3. Technology Transfer From R&D To Production**

Transfer of technical information is necessary to realize manufacturing formula established in the above in the actual production facility. In past days the Research base techniques are transfer from research department to production in the same company but now days it transfer from one company to another one. In principle, how accurately transfer technical information (know-how) from transferring party to transferred party is important. When the data related with drug techniques should be transferred in the form of Research and development data format.

**4. Validation And Production (Production Phase)**

The development of the formula set by Research and Development should be validated in process before production or in the manufacturing process to get the product with predefine procedure. While the manufacturing facility accepting technology is responsible for validation, the research and development department transferring technology should take responsibility for validations such as performance qualification (PQ), cleaning validation, and process validation (PV) unique to subject drugs.

**5. Feedback**

The technology transfer results in the product formation and it totally sold to the consumers and to evaluate the market demands and to check deliberate change due to technology transfer is all possible by feedback of this all measures. For this purpose, appropriate feedback system for technical information and

documentation management of technology transfer should be established. For drugs as they have long product shelf life, documentation management should be performed assuming that the technology transfer would occur several decades after the completion of development. Although there are no significant differences between existing drugs and development drugs in terms of technology transfer, it is desirable that subject technical information of the existing drugs should be compiled in forms such as product specification.

### **Procedures and Documentation of Technology Transfer<sup>12</sup>**

To systematically transfer techniques the proper documentation should be important.

#### 1) Organisation Of Technology Transfer :

To properly transfer technology according to the above processes, documentation of technology transfer including appropriate procedures and technical documents is necessary. For successful running of any organisation there should be a plan well define organisation documentary and there precise procedure. It is desirable that this organization complies with GMP. Party to party communication should be necessary with mutual understanding and good communication.

#### 2) Research and Development Report :

The research and development report (development report) is a file of technical information necessary for drug manufacturing, which is obtained from pharmaceutical development, and the 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 drug products including information such as raw materials, components, manufacturing methods, specifications and test methods. Following points should be considered at the Research and development report file:

-Historical data of pharmaceutical drug and drug product in start from discovery to development phase of that drug sample.

-Raw materials and components.

-Rationale for dosage form and formula designs.

-Rationale for design of manufacturing methods.

-Rational and change histories of important processes and control parameters.

-Quality profiles of manufacturing batches (including stability data).

-Specifications and test methods of drug substances, intermediates, drug products, raw materials, components, and their rationale (validity of specification range of important tests such as contents, impurities and dissolution, rationale for selection of test methods, reagents, and columns.

#### 3) Technology Transfer Documentation :

It includes the documentation of efficient running of technology transfer within the parties of the group. Technology transfer documentation are generally interpreted as documents indicating contents of technology transfer for transferring and transferred parties. The raw data of the documents (such as development report) should be prepared and compiled according to purposes, and should be always readily available and traceable.

- **Product Specification :**

The manufacturing data with evaluation of the manufactured product with their specification should be mentioned in that method of product specification. The product specification file should contain the following.

- Information necessary for the start and continuation of product manufacturing.

- Information necessary for quality assurance of the product.

- Information necessary for assurance of operation safety.

- Information necessary for environmental impact assessment.

- Information of costs.

- **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, and establish judgment criteria for the completion of the transfer.

- **Technology Transfer Report :**

The technology transfer report is to report the completion of technology transfer after data of actions taken according to the technology plan is evaluated and the data is confirmed pursuant to the predetermined judgment criteria.

- **Manufacturing Related Documents Including Drug Product Standards :**

The transferred party should compile documents such as drug product standards necessary for manufacturing, various standards and validation plans/reports after the completion of technology transfer. While the transferred party is responsible for compiling these documents, the transferring party should make necessary confirmation for these documents.

- **Verification of Results of Technology Transfer :**

After the completion of technology transfer and before the start of manufacturing of the product, the transferring party should verify with appropriate methods such as product testing and audit that the product manufactured after the technology transfer meets the predetermined quality, and should maintain records of the results.

### **Technology Transfer Success Criteria<sup>5</sup>**

- To success the given technology transfer the data should be match with the flow of procedure in formulation and production department.
- All the process and control parameter should be stated at given set of procedure.
- To develop the drug the material supplier should be with their Certificate of Analysis.
  - Health, safety and environmental concerns.
  - Compliance with all registered commitments.
- Technology Transfer must also be completed :
  - Safely -The process being transferred runs as expected (yield, purity, cycle time, etc.)
  - On time (product launch) -On budget -No “CRISIS” situations.
- For the success of technology transfer the Communication should be :
  - Open communication between all team members.
  - Direct communication between the technical members
  - Effectively and timely communication with the technical and non technical members.

### **Utilization of Quality By Design Paradigm To Ensure Technology Transfer<sup>4</sup>**

Quality by Design (QbD) refers to a holistic approach towards drug development. QbD has become the answer to assist both industry and FDA to move towards a more scientific, risk based, holistic and proactive approach to pharmaceutical development. The concept promotes industry’s understanding of the product and manufacturing process starting with product development, basically building quality in, not testing it. This systematic approach to product development and manufacturing has received a great deal from traditional approach, which was extremely empirical. Implementation of QbD is enabling transformation of the chemistry, manufacturing, and controls (CMC) review of Abbreviated New Drug Applications (ANDAs) into a modern, science and risk based pharmaceutical quality assessment.

#### **Quality By Design Works For Technology Transfer like :**

- Form a diverse/skilled and collaborative development team
- Review process flow diagram for key inputs/outputs that could impact quality (QRM)
- Uni/multi variant experiments should have been completed to study relationships and gain information on potential sources of variability. (Need to know where quality could be impacted)
- Make sure you understand your measurement capability (i.e. repeatability, precision)
- Critical Process Parameters (CPPs), Critical Quality Attributes (CQAs) and other important parameters are identified
- Design space should be defined and understood consisting of a set of input ranges (CPPs) that provide high probability that CQAs will meet specification.
- A control strategy needs to be in place to assure focus on critical points.

**International Conference on Harmonisation Quality Guideline (ICH Q 10)<sup>12</sup>****A Common Thread to Technology Transfer:**

The Q10 glossary defines the Pharmaceutical Quality System (PQS) as a “management system to direct and control a pharmaceutical company with regard to quality.” The guideline introduction states that “ICH Q10 is not intended to create new expectations beyond current regulatory requirements.

**Table1: Relationship of ICH Q10 to regional GMPs**

<b>Management Responsibility</b> <ul style="list-style-type: none"> <li>• Management Commitment</li> <li>• Quality Policy &amp; Objectives</li> <li>• Quality Planning</li> <li>• Resource</li> <li>• Management Quality</li> <li>• Communication</li> <li>• Management Review</li> <li>• Quality Oversight</li> </ul>	<b>Organizational processes – quality system improvement</b>		
	Quality System Management	Risk & Knowledge Management	Human Resources Management
	<b>Support processes -product/process management &amp; improvement</b>		
	Product/Process Improvement	Change Control Assurance	Quality Management of Suppliers and Contractors
	Process Validation	CAPA Management	Documentation Management of Equipment and Facilities
	<b>Product life-cycle processes – product realization</b>		
	Pharmaceutical Development	Technology Development	Manufacturing Discontinuation Transfer

“The change management system should provide management and documentation of adjustments made to the process during technology transfer activities.” “Aspects of management review should be performed to ensure the developed product and process can be manufactured at commercial scale.”

**Management Review of Process and Product Quality**

Management review should provide assurance that process performance and product quality are managed over the life cycle. Depending on the size and complexity of the company, management review can be a series of reviews at various levels of management and should include a timely and effective communication and escalation process to raise appropriate quality issues to senior levels of management for review.

**Scope Of Technology Transfer In Various Fields<sup>6</sup>**

Department of Agriculture (USDA)

Department of Commerce (DOC)

Department of Defence (DoD)

Department of Energy (DOE)

Department of Health and Human Services (HHS)

Department of Homeland Security (DHS)

Department of the Interior (DOI)

Department of Transportation (DOT)

Department of Veterans Affairs (VA)

Environmental Protection Agency (EPA)

National Aeronautics and Space Administration (NASA)

- All this department has a application of technology transfer such as incase of Department of Health and Human Services (HHS)

**Case Study<sup>6</sup>****New Live Attenuated Vaccine Against All Four Types Of Dengue Infection (CDC)**

Vaccine discoveries at the CDC have formed the basis for a new live attenuated dengue fever vaccine. Dengue fever and dengue hemorrhagic fever are viral diseases that are among the most significant viral illnesses transmitted by mosquitoes to humans worldwide. Over 2.5 billion people, including travellers,

are at risk of contracting dengue illness in countries in tropical regions of the world. The case fatality rate for dengue infections is about 5% in most countries, with most fatal cases occurring among children and young adults. This new vaccine discovery, along with new safety assays for it, has been licensed to a small biotechnology company for manufacture and testing in humans. The license agreement was completed by the CDC Office of Technology Transfer with a goal of bringing a safe and effective tetravalent dengue vaccine to save millions of lives and decrease the economic burdens cause by dengue disease.

### CONCLUSION

Technology transfer is an active and essential mission of Research and Development Department of the Innovative Company. By leveraging our nation's innovative nature and investing in science and technology, we strengthen our economy and competitiveness in world markets. In pharmaceutical industry, technology transfer means action to transfer of information and technologies necessary to realize quality of design of drugs during manufacturing. The three primary considerations to be addressed during an effective technology transfer are the plan, the persons involved, and the process. 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. To assure the drug quality, it is desire to make sure that is what, when, and why information should be transferred to where and by whom and how to transfer, then share knowledge and information of the technology transfer each other between stake holders related to drug manufacturing .Sharing industrial new innovative techniques forms the best sharing platform which helps to avoid the deformities in the novel approaches of the industries.

### REFERENCES

1. Ali S, Pandit V, Chander S. Technology Transfer in Pharmaceuticals. *Int Res J Pharm*, **3(6)**:43-48 (2012)
2. Barton J. New Trends in Technology Transfer Implications for National and International Policy. ICTSD Programme on IPRs and Sustainable Development. **18**: 14-31 (2007)
3. Dr. John H. Technology Transfer and Local manufacturing of Pharmaceuticals: The South African case. African Dialogue on Technology Transfer for Local Manufacturing Capacity on Drugs and Vaccines Cape Town. South Africa. (2009)
4. F. Sexton, Effective and Efficient Knowledge Transfer from R&D to Manufacturing, Purdue Pharma's SMC Meeting, (2004)
5. George P. Scale Up and Technology Transfer as a Part of Pharmaceutical Quality System . Senior Director Pharmaceutical Commercialization Development .ICH Conference .Merk. (2011)
6. Gibson M. Technology Transfer Introduction and Objectives, 1-11. Cited on: (2012)
7. Gupta S , Saini S, Rana A, Chugh I. Technology Transfer in Pharmaceutical Chugh I. Technology Transfer in Pharmaceutical industry – An overview .International Pharmaceutics Scientia. **2(3)**:1-6 (2012)
8. John H. Technology Transfer and Local manufacturing of Pharmaceuticals: The South African case. African Dialogue on Technology Transfer for Local Manufacturing Capacity on Drugs and Vaccines .Cape Town, South Africa (2009)
9. M.S. Janodia, D. Sreedhar, V.S. Ligade, A. Pise, N. Udupa. Facts of Technology transfer: A perspective of Pharmaceutical industry, *J. Intellectual property rights* **13**: 28-34 (2008)
10. Ortega A, Arce N, Sequeda F, Gribenchenko I. Management of Innovation and Technology Transfer Process Between University and Industry. The Mater Res Cent Case. **2**: 7-8 (2009)
11. Patil R. Technology Transfer in Pharmaceutical industry : Objective, Issue, and Policy Approach *International Journal of Pharamceutical Research and Development*. **2(10)**: 43-48 (2010)
12. Patel DS, Nadiad. Technology Transfer an Overview of Phamaceutical Industry. *Int Biopharm Association Publ*. **2(4)**: 2-8 (2009)

13. Ruegger C, Royce A, Mollan M, Wagner R, Valazza S, Mecadon M. Scale up of Solid Dosage Forms. 2006. Cited (2012)
14. Sanyang S , Kao T , Huang W. The Impact of Agriculture Transfer to Women Vegetable Production and Marketing Groups in the Gambia. *World J Agric sci*, **5(6)**: 169-179 (2009)
15. Singh A , Aggarwal G. Technology Transfer in Pharmaceutical Industry: A discussion. *Int J Pharma Biosci*, **1(3)**: 1-5 (2010)
16. Trang le.vo, Technology Transfer Challenge in Pharamceutical industry joint CVG / Therapeutics Products Directorate International Convention and Exhibition Toronto, Canada (2006)