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Review Article

Technology Transfer in Pharmaceutical Manufacturing - A Review

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ABSTRACT
Technology Transfer (TT) is vital action from drug development in Research & Development (R&D) Department to commercial manufacturing till the product discontinuation. This review is an attempt to give an insight about the transfer of pharmaceutical product from R&D to production including necessary documents required to review the supporting documents and execution procedures in production shop floor. TT is considered effective, if there is a documented evidence that the process and its parameters, repeatedly results in desired product quality which was established upon during TT between the transferee and transferor. For the execution of TT process, expertise from different department such as Engineering, R&D, QA, process analyst and production are teamed. the transmission comprises of arrangements procured in these flows of improvement to achieve the quality as planned throughout manufacture.

KEY WORDS: Technology Transfer, Transferor, Transferee.

INTRODUCTION

Technology transfer is defined as "a systematic procedure that influences the transfer of any process in conjunction with its documentation and professional expertise between development and manufacture or between manufacture intra- and inter-sites". In Medicinal manufacturing, success of "Technology Transfer" begins from discovery of the drug to product growth and finally full scale commercialization. Both the transferor and the transferee should consider Regulatory requirements of their countries and translate invariably in every part of technology transfer process. Documented evidence is essential for the successful technology transfer project to produce results within the predetermined set of specifications. The Transferee should communicate back to the transferor if, there is any problems with the process during transfer and it should be documented. (WHO)

Why/ Causes of Technology transfer

Shortage of production space

The manufacturer of product comprises the equipment which is used for small scale production and essential to cooperate with contract manufacturing firms to produce in large scale production.

Shortage of sources to introduce manufactured goods to market

The Developer consist facility to operate preliminary phase research such as animal examination and toxicology study, but doesn't have the facility to exhibit outcomes.

Shortage of marketing and suppling capacity

Manufacturer consist the advance technologies and received the regulatory approvals and product registrations, but it may not have the marketing and supplying passage.

Technology transfer team

The Technology process is classifieds into:

Research Phase

Production method starts with the selection of the New Chemical Entity (NCE), its form and formulation. It should combine discovery, preliminary development process scale up and manufacturing.

Improve systems to upgrade;
Molecule Selection.
Form Selection & Formulation design.
Process development & Optimization.
Process control.
Scale up & technology transfer.
Process validation.
Process monitoring & Continuous improvement.

These parameters illustrate the reduced risk to regulatory agencies.

Development Phase

In this phase the F&D start designing of the product. Raw materials innovative characteristics like Critical Quality Attributes(CQA) (Chemical, Physical, Biological & Microbiological) this can be defined, measured and Continually monitored to ensure final product outputs remain within acceptable quality limits, Critical Process parameters(CPP) in pharmaceutical manufacturing are key variables affecting the product process. CPPs are attributes that are monitored to detect deviations in standardized production operations and product output quality or changes in CQA and Critical equipment are validated as per requirements. Develop the analytical method validation for raw materials, excipients and packaging materials with standard test procedure and specifications.

Subsequent to completion in developmental phase the execution of small scale from 0.5 to 2 kg batch can be scaled up to 5-10kg and three validation batches should

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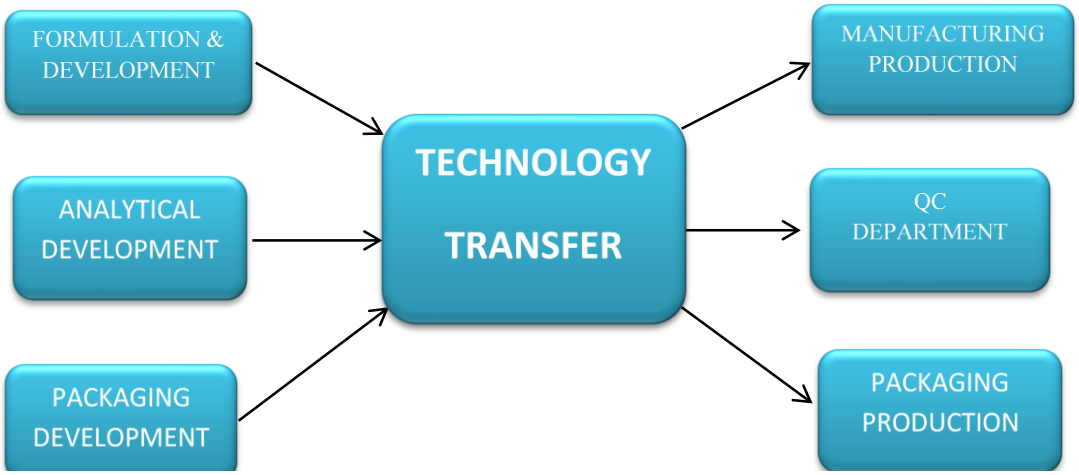
Table 1: List departments with their responsibility in Technology Transfer team.

Technology Transfer Members	Responsibilities
Research & Development Department	R&D shall initiate technology transfer of products and documentation. R&D should review product development report including critical control points like storage conditions, shelf life, equipment based on available facilities, applicable tests with method validation, analytical method, regulatory requirements, safety and label claims.
Quality Assurance Department	Responsible to review adequacy of documents as per requirements. Shall prepare the process validation documents. To review analytical validation method with quality control to regulate proficiency.
Production Department	Responsible to review suitability of manufacturing & packaging process, equipment's, facilities. To ensure availability of required resources to execute process.
Quality Control Department	• Reviews Analytical method requirements and accessible with instruments. • Organize the Analytical method transfer for drug substance and drug product.

Technology Transfer Process:



meet predetermined quality limits and then it is proceed to 20-100kg on a pilot scale.

Technology Transfer from R&D to Production

After verification of three validation batches of pilot scale and it is scaled up to production of 200kg to greater than 1000kg.Prior to commercial production, R&D should send supporting data should be shared to Quality Assurance department for review of the product. The supporting data are as follows;

Master Formula Record

It contains the product name, MFR No, Mfg. lic.NO, Batch size, Shelf Life, Effective date, General do's and don'ts, CCP's Equipment list and expected, theoretical and percentage yield range etc.

Stability data of Lab and Pilot scale validation batches

Stability report of at least 6month Real time study (30°C& 70% RH/30°C & 75% RH/30°C &65% RH and 25°C &60% RH), accelerated study(40°C ± 2°C/75% ± 5% RH), Photo stability, Cold condition (2°C to 8°C).

Specification and STP's

Raw material specification, Bulk Specification, Finished Product Specification, Packaging Specification and Standard Test Procedure should perform.

Production Phase (Validation and Production)

R&D shall provide the protocol for cleaning validation of equipment's involved in manufacturing and state that the existing cleaning procedure is adequate. Before starting the production manufacturing facilities, equipment's and process should be validated against standard protocol.

Quality Assurance should jointly review the supporting documents with production, Quality control and other relevant departments for the adequacy of all documents prior to the technology transfer and Quality Assurance should share the observations with R&D. Quality Assurance shall review response to observation and corrected documents provided by R&D. Based on approved Master formula record by Quality Assurance should prepare process validation protocol, Batch manufacturing formula and batch packaging record to execute in commercial production facilities.

Technology Transfer Documentation

By documenting the data in every step of transmission that can be considered as successful, has to be designed and specified in a technology transfer summary report, the report should give an outline of the scope of transfer. Potential deviations should be recorded and suitable

decisions are discussed, it is desirable to sort them before/during the process.

Data are documented from the beginning till the completion of the process. The documents are;

Critical process parameters.
Critical quality attributes.
Standard operating procedure (SOP).
Lab Batch Manufacturing Record (BMR).
Stability data of Lab scale validation batches.(at least 6 months real time study)
Pilot Batch Manufacturing Record (BMR).
Batch packaging record.
Drug Master File (DMF).
Raw Material Certificate of analysis.
Analysis of excipients
Analytical method validation.
Process validation report.
Cleaning Validation report.
Standard test procedure.
Specifications.
Facilities & Equipment validation report.
Change control form.
Deviation reports.
Complaints.
Training Documentation.
Technology Transfer summary report.

Product Specification (Product Specification File)

The product specification is to gather data which allows the manufacture of the product and to describe specification, manufacturing and assessment methods of the product and its quality and the transferring party is responsible for documenting the file. The development report for new products can be used as a part of product specification file. The product specification file should be examined at regular intervals, and integrate various information obtained after the start of production of the product, and be reassess as appropriate. The product specification file should contain the following;

To commence the manufacturing of the product.
Quality assurance of the product.
To pledge the operation safety.
Environmental effect evaluation.
Instruction on price.
Other specific information of the product.

Technology Transfer Plan

To illustrate components and contents of technology to be transmitted and complete plan of individual transfer and transfer programme, and organize the conclusion of the transfer. The transferor should prepare the plan before the execution of the transfer, and reach an agreement on its contents with the transferred party.

Technology Transfer Report.

Is to report the accomplishment of technology transfer after execution of the process according to the technology plan is analysed and the data is persistent in accordance to the pre-agreed judgment criteria. Both transferor and transferee can document the technology transfer report; however, they should reach an agreement on its contents.

Check and Approval by Quality Assurance Department.

It is preferable that the quality assurance department should initiate confirmation process for all form of technology transfer documentation and to execute together with production as per the Batch Manufacturing Process, should check and approve the documentation.

Enforcement of Technology Transfer

By assisting the technology transfer documentation is not sufficient to implement process. It is suggested that the both parties should collaborate to enforce technical education, training and validations at facilities where the transferred technology is actually used.

Confirmation of Conclusions of Technology Transfer

Before and subsequent execution of technology transfer process, transferring party should confirm the suitable procedure for the evaluation of the manufactured products reach the pre-agreed quality limits and it should be documented.

Analyse Post-Marketing Technology Transfer

During the routine inspection we may find some marketed products do not have progressive report, those products are reported as raw data, so that for these products newly documented as a reference file.

Execution

After the successful execution in the lab and pilot scale subsequently executed in the commercial scale with the extended batch size, equipment's and processes.

#Case Study-Blend Uniformity problem during Process Validation.

Condition

Blending is a recognised unit operation in manufacturing process; problems are not occurred during the risk assessment and even the drug load is not low but resulted in delay so to blending process is revalidated to evaluate the root cause for the blend uniformity problems upon the material transfer.

Output

By optimizing the blending capacity and drop heights of material from blender to receiver. By understanding downstream effect on material separation. During the technology transfer required to recognize possible complications. In Process or Formulation risk assessment equipment & material management should examined.

CONCLUSION

Proper technology transfer provides extreme transmission between technical members. Feasibility test are performed before the execution in the commercial scale and carried out as per the protocol provided by transferor to meet the quality limits as decided during development of the product and it is necessary to document the every steps performed during the processes for the favourable result of the technology transfer. Approachable interaction between all team members and timely communication with regulators provides the effectives transmission.

REFERENCES

1. WHO guidelines on transfer of technology in pharmaceutical manufacturing World Health Organization WHO Technical Report Series, No. 961, 201.
2. George P. Millili, Ph.D. Senior Director Pharmaceutical Commercialization Development - Scale-up & Technology Transfer as a Part of Pharmaceutical Quality Systems.
3. ICH Q10 Pharmaceutical Quality System (PQS)
4. Shaik.Naseeb Basha, Asst.Professor, Dept of Pharmaceutics, G.Pulla Reddy College of Pharmacy Hyderabad-Technology Transfer Process in Pharmaceutical Industries.ppt.
5. Guideline for Technology Transfer (Draft), Cited 2009 December 12. Available from: URL: http://www.nihs.go.jp/drug/GMP/04BDH014 9-1post.pdf.
6. Regulatory Education for Industry (REdI): Focus on CGMPs & FDA Inspections Sheraton | Silver Spring, MD | July 15-16, 2015- Facilities & Equipment: CGMP Requirements.
7. Tever cook-Journal of Intellectual Property Rights May 2014-The EU guidelines for Technology Transfer Agreements.
8. PIC/S January 2017-GUIDE TO GOOD MANUFACTURING PRACTICE FOR MEDICINAL PRODUCTS PART –I.
9. Dr. Bhanuben Nanavati College of Pharmacy-Technology Transfer and Scale-up in Pharmaceutical Industry.
10. Gibson M., Technology Transfer Introduction and Objectives, 2012. Available from: URL: https://store.pda.org/bookstore// Tech_Transfer_Ch01.pdf.
11. George P. Scale Up and Technology Transfer as a Part of Pharmaceutical Quality System. Senior Director Pharmaceutical Commercialization Development. ICH Conference .Merck. (2011).
12. Seema S, Surbhi G et al. Technology transfer in Pharmaceutical Industry-An Overview, Internationale Pharmaceutica Sciencia, 2012, Vol. 2 (3), Pg. 1-6.
13. Technology Transfer from R&D to Production, cited 2010 February 6. URL:http://www.bioqc.org/workshopdata/1Technology.pdf.
14. Technology Transfer in pharmaceutical contract manufacturing- https://www.interphex.com/RNA/RNA_Interphex_V2/2016/.../Fong-Norman.pdf
15. Bradley, S.R. Hayter, C.S. Link, A.N. Models & Methods of University Technology Transfer, Department of Economics Working Paper Series, The University of North America Grecensboro, June-2013, pg no- 6-9.
16. Pazzi M.G.,Revised Technology Transfer block exemption rules.
17. http://ec.europa.eu?competition/consultations/2013_technology-transfer/index_en.html16
18. Swapnil Nivrutti Misar-Technology Transfer: A Paradigm for Industry, International Journal of Pure and Applied Bioscience.
19. Manu C, Review on Technology Transfer in Pharmaceutical Industry International Journal of Pharmaceutical Quality Assurance 2016; 7(1); 7-14.