TECHNOLOGY TRANSFER IN PHARMACEUTICAL INDUSTRY - A REVIEW ARTICLE
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ABSTRACT
This review article is to discuss the procedure for technology transfer process in pharmaceutical industry. Technology transfer is both integral and critical to drug discovery and development process for new medicinal products. This process gives necessary information for technology transfer from R&D (research and development) to PDL (process development laboratory) and for development of existing product to the production for commercialization. The technology transfer is not only the transferring of the product but also the use of knowledge and its application. R&D place a vital role in creating these technologies, but not always benefits are being transferred to needy people and so need of technology transfer arises. Generally the cost of product development rises dramatically during the pilot scale –up and initial production batch efforts. The ultimate goal for successful technology transfer is to have documented evidence that the manufacturing process for drug substance and drug products.
1. INTRODUCTION:
Importance of technology transfer

Technology transfer is an important in extended benefits of R&D to the society especially in developing countries. 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 5/10kgs and then to 20/100kg on a pilot scale. Production scale can typically range from 200kg to greater than 1000kg. 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. Research is carried out in laboratories on an experimental scale (small batches) before it could be produced for commercial use (large batches). Technology transfer is important for such research to materialize on a larger scale for commercialization especially in the case of developing product. Technology transfer includes not only the patentable aspect of production but also includes the business of processes, such as knowledge and skills. 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. The technology transfer can be happen any ways like government labs to private sectors, between private sectors of the same country, from academic to private sectors, between academy, government and private sectors of different country.

REASON FOR TECHNOLOGY TRANSFER:

Forming alliances with partners that can progress the development of the technology 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 clinical and regulatory phase 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 have the clean room manufacturing capability or resources to manufacture the product, and must partner with another organization that does have that capability.
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

Exploitation in a different field of application: 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 applications. By transferring the technology for the use in another field of application to another person, the developer of the technology creates another income stream from the exploitation that takes place on that takes place in that other field.

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.

Steps in technology transfer:

The quality of design will be almost completed in phase II clinical study. Various standards for manufacturing and test will be established in process of reviewing factory production and phase III study to realize the quality of design, if design will be verified in various validation studies will be upgraded to be the quality of product and the actual production will be started. Technology transfer consists to action taken in these flows of development to realize through the quality as designed during the manufacture. Even if the production starts, the technology transfer will take place in process such as changes in manufacturing places. The processes are classified into the three categories:

i. Research Phase
ii. Development Phase
iii. Production Phase

Design of procedure and selection of excipients by R&D: Selection of materials and design of procedures is developed by R&D on the basis of innovator product characteristics. For this different test and compatibility studies are done.
Drug products 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, & adding usefulness based on various data such as chemical and physical properties, efficacy, safety, and stability obtained from preclinical studies. For drug substance quality design in to determine starting materials and their reaction paths and basic specification of the drug.

**Identification of specification and quality by R&D:** Quality of product should meet the specification of an innovator product for this different stability studies are carried out for innovator product and for product which is to be manufactured.

ii. **Development Phase (Technology transfer from R&D to production):** R&D provides technology transfer dossier (TTD) document to product development laboratory which contains all information of formulation and drug product as given below.

**Technology Transfer Dossier (TTD):** TTD contained all the information of drug product as given below:

- Master formula card (MFC)
- Master Packaging Card (MPC)
- Master formula
- Standard Test Procedures
- Specifications
- Development report
- Packaging development report

**Master formula card (MFC):** MFC included Product name along with its Strength, Generic name, MFC number, Page number, Effective date, shelf life, market, packaging details, storage conditions, precautions for personnel safety as well as for the product safety. Ingredients details with pharmacopoeial status along with the specifications numbers, brand names / grades along with approved vendors label claim and a brief manufacturing detail

**Masters packaging card:** It gives information about packaging type, material use for packaging, stability profile of packaging and shelf life of packaging.

**Master formula:** It describes formulation order and manufacturing instruction. Formulation order and manufacturing instruction gives idea of process order, environment condition required and manufacturing instruction for dosage form development.

**Specification and standard test procedure (STPs):** It helps to know active ingredients and excipients profiles, in process parameter and specification, product release specification and finished product detail.

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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.

Consistency between quality and specification: When product specification is established on the basis of the quality of product determined in the above, it is required to verify that the specification adequately specifies the product quality. 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 manufacture quality and the product satisfies the quality of design.

Assurance of consistency through development and manufacturing: To make developed product have indications as predetermined in clinical phases, quality of design should be reproducible as the quality of product (assurance of consistency). For this purpose 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 [8].

Technology transfer from R&D to Production: Transfer of the technical information is necessary to realize manufacturing formula and actual production facility. Technical information to be transfer should be compiled as R&D report.

i. Production Phase

Validation studies: Production is implemented after various validation studies verify that, it is able to consistently manufacture product based on transferred manufacturing formula with a higher degree of stability. Research and development department transferring technology should take responsibility for validation such as performance qualification, cleaning validation and process validation unique to subject drugs.

SCALE-UP: Scale up followed after getting all information from R&D. It involved the transfer of technology and the transfer of knowledge. From sifting to film coating each process had its own set of challenges. The development of robust formulation and process through the use of Design of Experiments (DoE) as well as understanding the critical v/s non-critical parameters for each operation were be major determining factors for success v/s failure on scale-up.
The following chapter focused on the same of the scale-up issues and considerations for several unit operations that may be utilized during the manufacture of solid dosage forms. Full scale commercialization includes: Active Pharmaceutical Ingredient (API), Drug product (dosage form or delivery system), analytical methods.

**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.

**Selection of method:** The method for batch fabrication was selected on the basis of data given from R&D. Granulation, blending, compression and coating were critical parameters for technology transfer.

**Feedback from Production and Technology Transfer of Marketed Products:**
Technical information of developed products is obtained 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. It is highly desired to feed back and accumulate technical information obtained from repeated production. In addition, it is important to appropriately modify various standards established before based on this information. Accountability and responsibility for design and manufacturing should be executed.

**Technology transfer documentation:** technology transfer documentation is generally considered as document indicating content of technology transfer for transferring and transferred parties. Each step from R & D 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 the duty of quality assurance department to check and approve the documentation for all processes of technology transfer.

1. **Development Report:** The ultimate goal for successful technology transfer is to have documented evidences. The development report contains data of pharmaceutical development of new drug substances and drug product at stages from early development phase o finale application of approval, information of raw materials and components, rational for dosage form and formula designs and design of manufacturing methods, change in histories of important processes and control parameters, stability profile, specification and test methods
of drug substances, intermediates, drug products, raw materials, which also includes validity of specification range of important tests such as contents impurities and dissolution, rational for selection of test methods, reagents and columns, and traceability of raw data of those information. This report contained the method of development as well as process development. Process development and commercial production were on critical path because of compressed time-to market expectations.

i. Packaging development report: This information provided details about packaging development to the concerned technology transfer person for executing the function.

ii. Technology transfer plan: The technology transfer plan is to describe items and content of technology to be transferred and detailed procedure of individual transfer and transfer schedule, and to establish judgement 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.

Exhibit: After taking scale up batch of the product, manufacturing of exhibit batches take place. In case of exhibit, batch sizes are increased along with equipment and their process is involved. They are done for filing purposes in different regulatory agencies.

CONCLUSION:
In pharmaceutical industry, technology transfer is important to upgrade the quality of design to be the quality of product and to ensure stable and high quality of product. The technology transfer means action to transfer of information and necessary technology for the quality 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 processes. Technology transfer does not mean one time action taken by the transferring party toward the transferred party, but continuous information exchange between the both parties to maintain the product manufacturing. Technology transfer can be considered successful if a receiving unit routinely reproduce the transferred product, process or method against a predefined set of specifications agreed with a sending unit and 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.

REFERENCES:

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TTD: Technology Transfer Dossier

MFC: Master Formula Card

PE: Pre Exhibit

EB: Exhibit Batch

BPR: Batch Packaging Record

BMR: Batch Manufacturing Record.