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Review Article

Review on Technology Transfer as a Regulatory Aspect with Inclusion of ICH Guidelines

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ABSTRACT

Technology transfer in simple terms transfer of the technology in the form of idea, innovation and process etc. for successful technology transfer there is an involvement of the two sites together with its documentation. Here this review paper describes various models proposed for the technology transfer such as qualitative model and quantitative models and there requirements, and it also includes basic principle and goals for the technology transfer.

Key-words: Technology Transfer, ICH guidelines, regulatory aspects

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Introduction. [1][2]

Technology transfer is the expression of couple of words 'The Technology' and 'The Transfer'. First of all the term "Technology" itself is hard to interpret, observe or assess, it is simply define as the accumulation of strategies, abilities, techniques and procedures utilized as a part of the creation of products or administrations or in the achievement of objectives, for example, logical examination, scientific research. Technology (Innovation) can be the information of methods, procedures, and so on. And the "Transfer" means to convey or to move something from one place to another.

"Technology Transfer is define as it is the way toward exchanging (spreading) technology or the innovation from the places and in groups of its origination to wider distribution among more individuals and places. It happens along different axes: among universities, from universities to organizations, from large organizations to smaller ones, from governments to organizations, across borders, both formally and casually, and both transparently and surreptitiously. Regularly it happens by purposeful push to share abilities, learning, innovations, strategies for manufacturing, tests of manufacturing, and offices among governments or universities and different establishments to guarantee that technological and scientific advancements are available to a more extensive scope of clients who can then further create and adventure the innovation into new processes, materials, applications, products, or services." So in simple term the Technology Transfer or the Transfer of Technology means to convey or to move the technology in the form of procedure or method or anything else from one place to another.

World Intellectual property organization (*WIPO*) Defines-"A series of processes for sharing ideas, knowledge, technology and skills with another individual or institution (e.g.: a company, a university or a governmental body) and of acquisition by the others such ideas, knowledge, technologies and skill".

Here by with regards to the pharmaceutical industries the term technology transfer is defined as "a consistent procedure that controls the exchange of any procedure together with its documentation and expert aptitude between improvement and manufacture or between manufacturing sites "The process of technology transfer having widened application in the pharmaceutical industry which covers the all fields or the branches of the pharmaceutical industries which includes the manufacturing, formulation and development, analytical method development, packaging and risk management as well as the full commercialization of the pharmaceutical product, in the same plant or to the another plant of the same organization or the industry or in to the different industries too. Technology transfer is both fundamental and basic to the drug discovery and advancement process for new therapeutic products. Technology Transfer is useful to create dosage forms in different courses as it gives productivity in procedure, maintains or upgrades quality of product, accomplishes standardized procedure which encourages cost effective production. It is the procedure by which an original inventor of technology makes its innovation accessible to partner that will exploit the technology. Technology transfer is both necessary and basic to drug discovery and advancement for new therapeutic product. In pharmaceutical industry, "Technology Transfer" refers to the procedures of effective advancement from drug discovery to commercialization of the drug, clinical trials and ultimately full-scale commercialization. "Technology transfer" refers to the procedures that are required for effective advancement from drug discovery to product development to clinical trials to full-scale commercialization or it is the procedure by which a developer of technology makes its technology accessible to partner that will exploit the innovation. technology transfer is essential for such research to appear on a large scale for commercialization particularly on account of manufacturing .Technology transfer includes not only the patentable parts of production as well as it does also includes the business processes, for example, information and skills.[1][2]

Technology transfer models: . [1][3]

Since the early 1970s, considering the challenges and complexities confronted by directors of technology projects, scientists, specialists, and experts of technology transfer have been proposing models of technology transfer that could encourage the effective planning and usage of technology transfer projects. Both qualitative and quantitative models have been proposed. Jagoda (2007) points out that, "Qualitative models often have as their objective the delineation of activities involved in managing Technology Transfer

and the elicitation of factors and issues that can influence the success and/or effectiveness of Technology Transfer. Quantitative models, on the other hand, aim at quantifying parameters of significance in Technology Transfer and analyzing them with a view towards minimizing goal incompatibility between the transferors and transferees of technology."[8]In this review, emphasis will be on the qualitative models. The mathematics involved in the quantitative models will not be elaborated upon and only their major findings will be presented.

Followings are some qualitative models Technology transfer models:

i. The Bar-Zakay Model: Bar-Zakay (1971)
ii. The Behrman and Wallender Model Behrman and Wallender (1976)
iii. The Dahlman and Westphal Model Dahlman and Westphal (1981)
iv. The Schlie, Radnor, and Wad Model Schlie (1987)
v. The Chantramonklasri Model(1990)

i. The Bar-Zakay Model (1971):

Bar-Zakay built up or maybe extensive TT model based on a project management approach. He separated the TT procedure into the Search, Adaptation, Implementation, and Maintenance stages. He illustrated the practices, activities, points of reference, milestones and choice focuses (go or no-go) in each of these phases as appeared in Figure 1. The upper portion of the figure depicts the exercises and requirements of the transferor (alluded to as the "giver" or "donor" by Bar-Zakay) and the lower half portion of that of the transferee or the "recipient."

The activities to be done are indicated in point of interest in this model and the significance of both the transferor and transferee securing abilities to attempt technology forecasting, long-range planning, and gathering of project-related intelligence is emphasized. The model uses the term "donor" for the transferor giving the impression that the proprietor of technology is giving without end an important resource out of un-selfish reasons! This terms may be evaded. The Bar-Zakay model also suffers from another disadvantage: "The model has limited importance today since a large number of the activitis, terms, and thoughts communicated reflected, when purchasers of technology were mainly passive recipients who depended greatly on aid programs for the purchase of technology. It was additionally a time when government controls were instrumental in deciding the rate, direction, and scope of technology flows."

The lessons that can be learnt from the Bar-Zakay model are the accompanying:

There is a requirement for an extensive examination of the whole TT process from "search" right through to "post implementation" activities. A process approach must be received in arranging and executing TT projects It is important to have turning points and choice focuses with the goal that activities can be strengthened, mistakes corrected, or even the project terminated at any point in time.

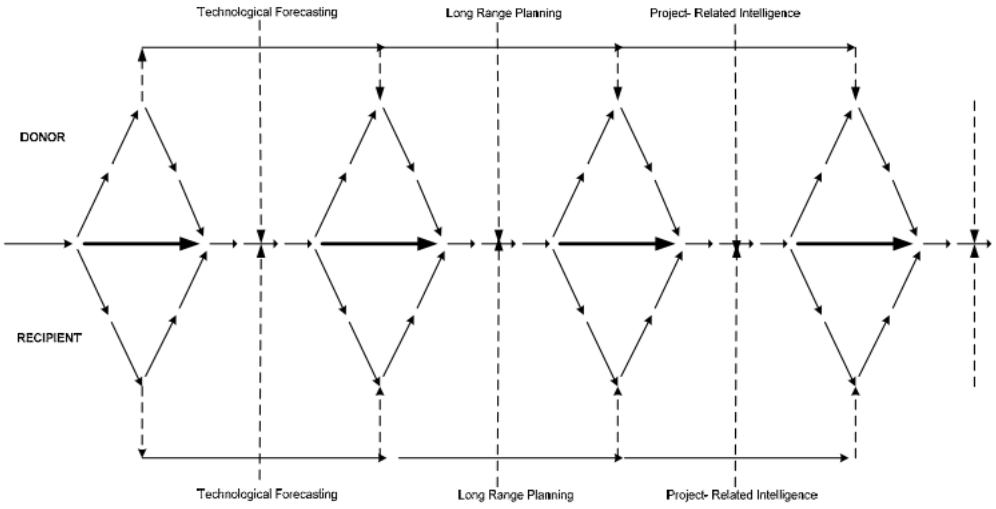


Fig.-1: Bar zakay model

ii. *The Behrman and Wallender Model(1976):*

Behrman and Wallender have proposed a seven phase process for universal technology transfer that might be more relevant to multinational companies. The seven stages are:

1. Manufacturing proposal and wanting to touch base at choices in regards to location and setting up a business case including good resource assessments.
2. Taking decision about the product design technologies to be transferred.
3. Specifying elements of the plant to be designed to produce the product and different aspects identified with infrastructure and construction.
4. Plant development and production start-up.
5. Adjusting the procedure and product if necessary and reinforcing production frameworks to suit local conditions.
6. Enhancing the product technology transferred utilizing local skills.
7. Providing external support to fortify the relationship between the transferee and transferor.

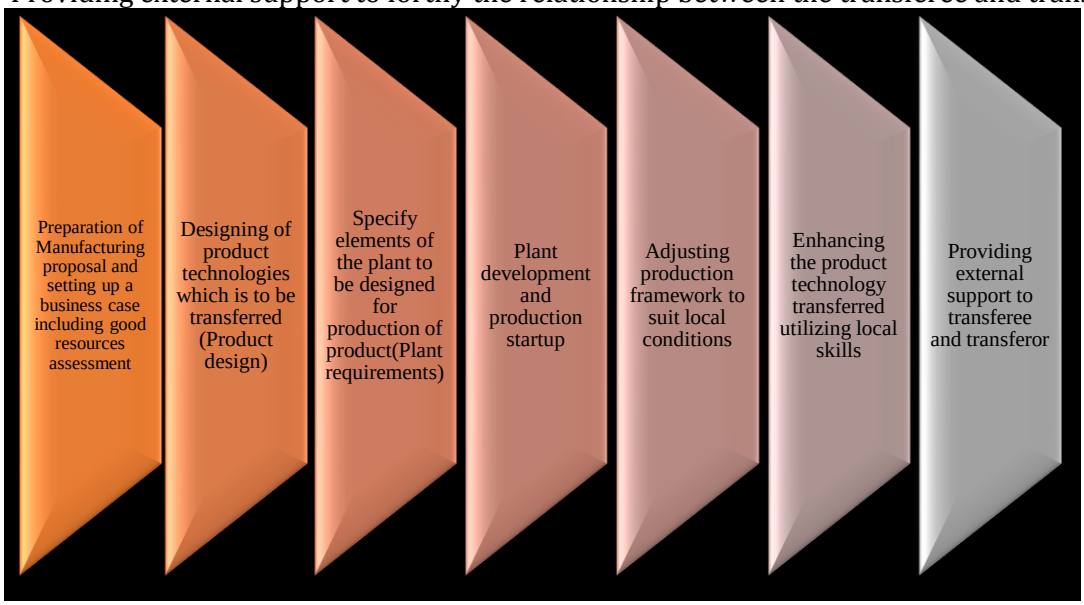


Fig.-2: The Behrman and Wallender Model

One of the deficiency of this model is that, during the initial three phases, the transferor builds up the technology transfer project with minimal involvement of the transferee in this manner fortifying dependency. However, in the 5th and 6th stages there is significant scope for the transferee to acclimatize and enhance both product and process technology. This serves to underline the way that technology transfer does not stop with beginning of production and unless there is a mechanism to cultivate assimilation the project can't be considered to have delivered.

iii. *The Chantramonklasri Model (1990):* Behrman and Wallender model has been further upgraded by Chantramonklasri.

The five phases of the chantramonklasri model.

- Carrying out a pre-investment and feasibility study.
- Developing engineering specifications and design based on the feasibility study.

- Commence capital goods production based on the engineering specifications and designs that have been developed.
- Commissioning and start-up including comprehensive of the workforce.
- Commence commercial production.

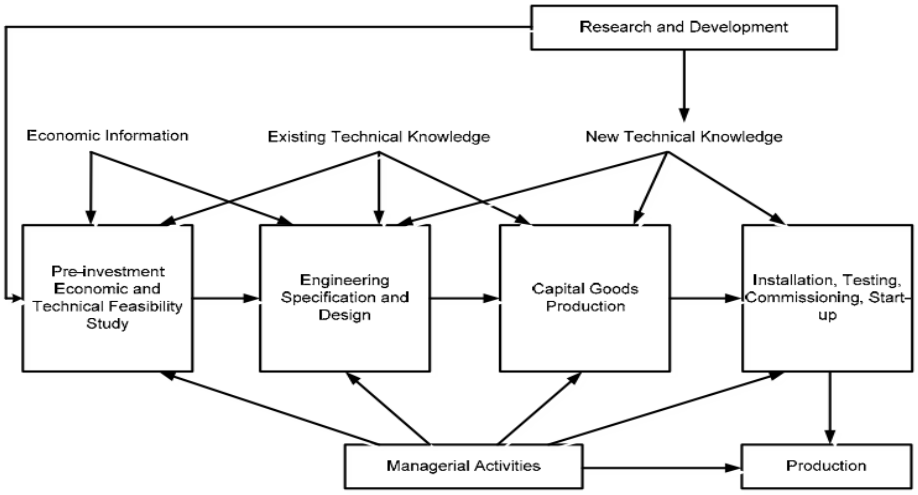


Fig.-3: The Chantramonklasri Model.

GOALS OF TECHNOLOGY TRANSFER. [4]

1. It is a significant step in the formative life cycle leading to successful commercial manufacturing of the pharmaceuticals.
2. It is to transfer product and process knowledge between and manufacturing, and within or between manufacturing sites to accomplish product realization. This knowledge forms the basis for the manufacturing process, control strategy, process validation approach, and ongoing continual improvement.
3. To take all the gathered knowledge and utilize it as the premise for the assembling control procedure, the way to deal with process qualification and on-going consistent improvement.
4. The transition of the analytical method/process/product's knowledge between development and manufacturing sites.
5. To ensure variability of parameters and process are controlled and sufficient even with the rigors for environment of commercial production, to ensure parameters built up during development are still inside the determined design space and/or adjusted at scale-up.

Wings of technology transfer. [5]

The process of technology transfer is divided in three parts.

1) Production.
2) Quality control.
3) Documentations.

The technology transfer process is critical from research and development to manufacturing site because of the scale up of the formulation to the large scale commercial batch from pilot batch. The process of transfer of technology is divided in to the three parts in the pharmaceutical industries.

1) Production Technology Transfer :

Preparation of product transfer protocol jointly by the sending unit and receiving unit to transfer the information related to the product which is to be manufactured. Whole information regarding the product is conveyed according to the technical expertness of the staff and the manufacturing site capabilities to run the whole process smoothly.

i. Raw material: The properties of the raw material those can alter the quality of the product should be identified and materials which are used for the production on sending unit and the receiving unit should have consistency.

a. **Active pharmaceutical Ingredients:**
Drug master file (DMF) is provided by the sending unit and other related information of the API, these includes the followings.
- Production flow chart of the product.
- Physical of the materials likewise bulk density and tap density.
- Water activity including moisture content.
- Sterility, bio burden and endotoxins as required.
- Dissolution profile
- Particle size, solubility and pH of the solution.
- Supply chain of the materials.
- Other information such as light, heat & etc.

b. **Excipients:** Excipients also have the significant effect on the final product so their detailed information should be provided to the receiving unit by the sending unit. It may include the following information:

- Viscosity of material
- Flow chart of the production of the drug material
- Physical properties like bulk density and tap density.
- Moisture content range
- Melting range
- Bio burden, endotoxin and sterility as per requirements
- Ion strength
- pH of solution
- Solubility, particle size distribution & Specific gravity
- Dissolution profile
- Manufacturer and the supply chain of the material
- Compliance for BSE and TSE requirements
- MSDS and light, heat and moisture sensitivity.

ii. **In-process Materials:**
Receiving unit should have the detailed information of the manufacturing process, physical description, in-process controls & specification

iii. **Finished Production:** History of the advancement of the product should be provided for the further improvement or development or process optimization after the effective transfer of technology.
Information regarding the environment, health, safety & wellbeing should be given to the accepting unit. It should also be provided to the receiving unit. It should also include the information on product quality review, stability, validation, and environment condition for manufacturing. Trial batches are taken at the accepting (receiving) unit to test the capability as well as manufacturing parameters of the manufacturing process before taking the validation batch.

iv. **Packing Process:** All the information regards to the packing should be transferred as the manufacturing process. It includes the specific details of foils or containers and closures, and other related information as design labelling, drawings and drawing.

v. **Cleaning Process:** To prevent the contamination in the pharmaceutical products, it is essential the follow the adequate cleaning procedure. It can minimize the risk of Cross Contamination during manufacturing. Receiving unit should validate the cleaning procedure and sending unit should provide the required information such as existing cleaning procedure, solubility of all materials, therapeutic dose, toxicity of the API, cleaning agents and recovery study.

vi. **Manufacturing Facility :** Sending unit should provide the information related to the facility design

a. **Premises:** It should include the layout of facility, buildings, utility services, fire risk, health and safety requirements for operators and environmental issues.

b. **Equipment:** A list of required equipments with their make and models should be provided by the sending unto. It should include the manuals, drawings and cleaning, operating and maintenance procedures. IQ, OQ and PQ of the equipments should be done by the receiving unit.

2) **Quality control: Analytical Method Transfer:** Analytical method has its own importance because the manufactured product shall be tested by the developed analytical method and accuracy in analytical method can save time. Receiving unit should implement the method of analysis for finished product, raw materials, packing materials and cleaning residues before the starting of the process validation Analytical method transfer protocol should be prepared including responsibilities of both sending unit and receiving unit, specification of product, acceptance criteria, interpretation of results, report formats, reference standards and deviations during analysis. Training should be provided to the analysts and should be documented in training record.
3) **Documentation:** Every step followed during the technology transfer process should be documented and a summary report should be prepared containing the conclusion of the technology transfer. Discrepancies found during the process should be listed and should be resolved by taking the appropriate action. Following documents should be prepared during the successful tech transfer.
   - Technology transfer protocol
   - Facility qualification protocol and report
   - Equipment qualification protocol and report
   - Process validation protocol and report
   - Cleaning validation protocol and report

Principles of Technology transfer: [6]

To make the technology transfer successful following principles cannot be omitted.

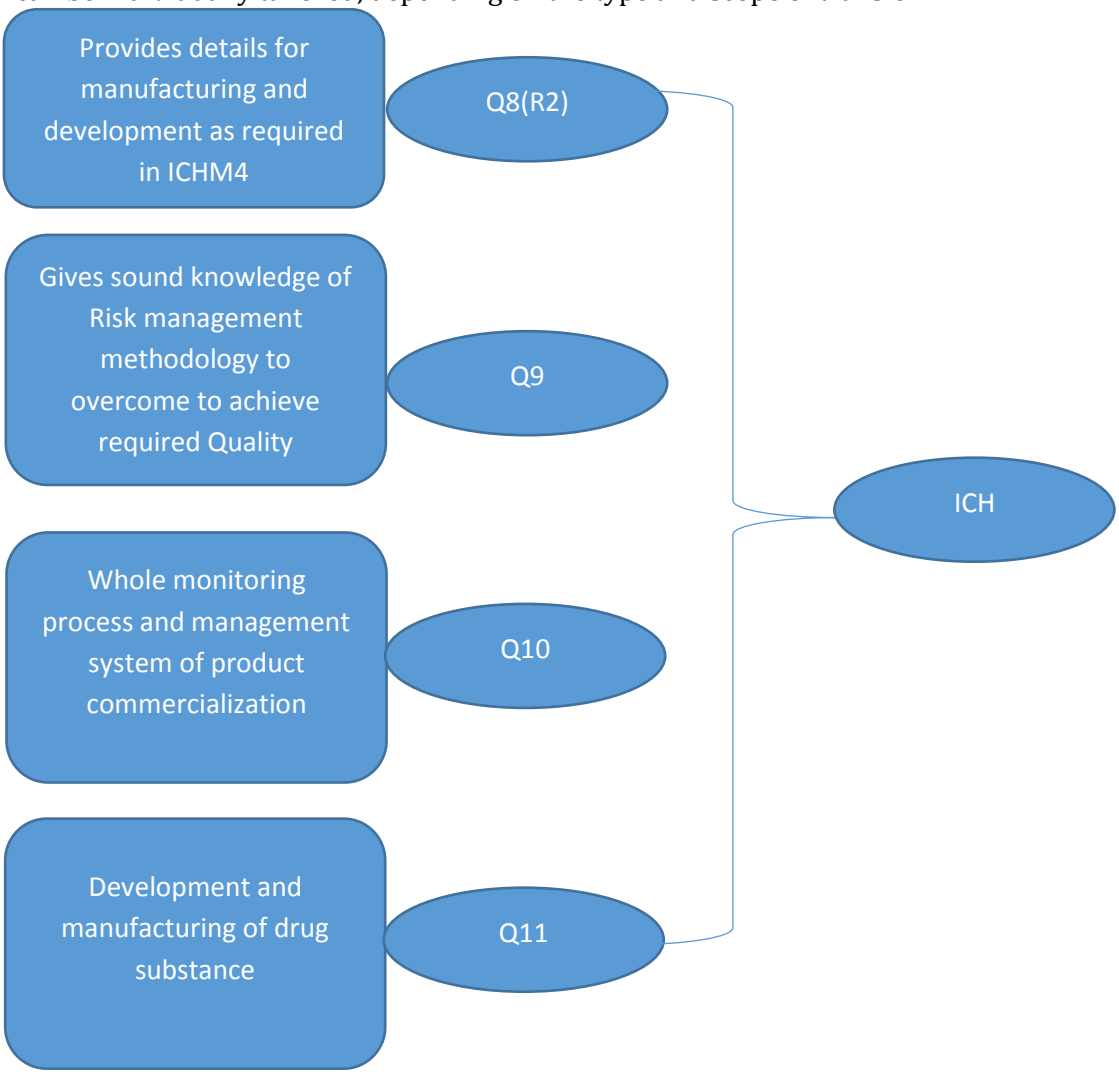
- Robust information exchange, providing the receiving party with all data as well as whole information that is applicable to the procedure, associated assay and process.
- Project management with Careful front-end planning and with the designation of point people for specific portions of the project.
- Ensuring that analytical assays are transferred in front of the process or parallel with the process.
- Performing small-scale verification at the receiving site. This gives conformation that the information exchange was successful and permits the receiving party to be more independent going forward.
- Perform pre-GMP engineering runs.
- GMP runs are the last objective. Put your tech transfer project in setting by characterizing GMP success and failure and don't dismantle your team until success here has been confirmed.

None of these steps can be discarded without serious consequences.

To avoid a strategic distance from project creep, it is important to build up limits amongst development and technology transfer at the beginning of a project. Technology transfer demands some process modification or adjustment, however when things go beyond negligible tweaking, the process needs to go back to development. An extreme example would change the cell line specified for an expression system as a major aspect of the technology transfer.

Role of ICH guidelines in Technology transfer. [24][25] [26][27]

- Technology transfer (TT) includes knowledge transfer, science and risk-based principles including ICH Q8, Q9, Q10, Q11 and efficient processes to meet evolving business needs.
- These identifies criteria for successful Technology Transfer and provides 'how to' conduct technology transfer, which can be individually tailored, depending on the type and scope of transfer.



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