

EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Robust Technology Transfer

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## Definition

A Technology Transfer consists of planned and controlled actions that are based on well-defined acceptance criteria to convey a manufacturing process, analytical method, packaging or any other step or process along the pharmaceutical drug lifecycle from an originator site known as a sending unit (SU) to a new site, the receiving site (RU).

A technology transfer take place when a product must be transferred:

- from the process development teams to the manufacturing teams of the same Company;
- from one site to another site of the same Company;
- from one company to a contract manufacturing organization (CMO);

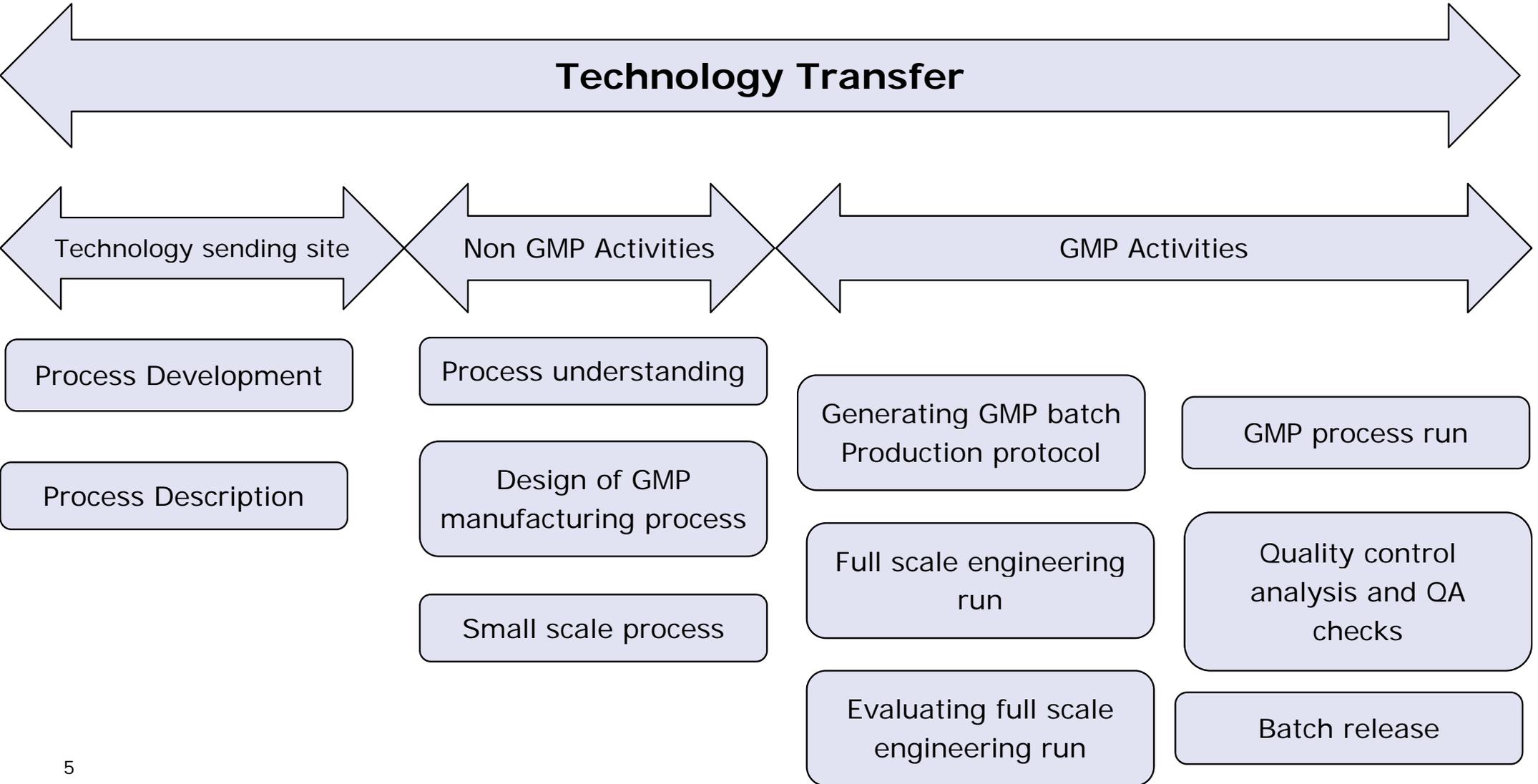


The main goal of the tech transfer is to minimize as much as possible any changes from a sending company to a receiving company.

## **Challenges:**

- Difficult to scale-up the process
- Differences in the type and capabilities of equipment
- Poor documentation
- Lack of clear and open communication
- Time pressure combined with limited budget

- Quality Assurance (QA)
- Quality Control (QC)
- Manufacturing
- Engineering
- Maintenance
- Regulatory Affairs
- Legal Department





The technology transfer activities often start with the transfer of documents from the technology sending site to the receiving site.

In this phase the communication between both parties must be clear and open.

The information provided from the sending site should have sufficient details for the best understanding of the process.

A GMP process should be designed by a small-scale prototype process and/or engineering full scale run.

## Quality Agreement

Before transferring the documents a quality agreement between the sending site and the receiving site should be signed.

All the responsibilities between the two entities should be clearly outlined in the QA.

There are also legal and economic implications:

- Royalties
- Pricing
- Conflict of interest
- Confidentiality

## **Documentation package**

A typical technology transfer package includes the following documents:

- Transfer protocol
- Risk assessment
- Change Control
- Process Production protocols and reports

The SU and the RU should jointly develop a protocol for the transfer.

The transfer protocol should list the intended sequential stages of the transfer:

- objective and scope;
- key personnel and their responsibilities;
- a parallel comparison of materials, methods and equipment;
- the transfer stages;
- identification of critical control points;
- experimental design and acceptance criteria for analytical methods;



- information on engineering runs, qualification batches and process validation;
- change control and deviations encountered;
- assessment of final product;
- arrangements for keeping retention samples;
- conclusion and approval.

The TTP team must identify and mitigate the impact of the technology transfer.

ICH Q9 and Q10 provide examples of tool and principles to achieve this objective.

QRM should cover the potential risk to the patient regarding the quality the safety and efficacy of the medicinal product being transferred from the SU to the RU.

Specifically, the QRM applied to a TTP should evaluate:

- The source of the process variability
- The appropriate risk mitigation strategies and controls
- All the quality and critical parameter that must be controlled

QRM should at least address:

- Processing operations and parameters
- Impact of new equipment, facilities and utilities
- Potential cross contamination with internal and external sources



Any changes and adaptations made during the course of the technology transfer should be fully documented.

The RU should manage the transfer via its change control procedure to evaluate the impact of the new process on the affected departments.

In the course of scale up process parameters and equipment may be subjected to change.

Procedure should be in place in order to manage any changes and maintain traceability.



During the transfer process, the RU should identify any differences in facilities, systems and capabilities and communicate with the SU about these differences to understand the potential impact on ability to run the process to deliver good product quality.

Critical raw materials, that define the performance of the process, should not be changed at the receiving site.



The process validation provide scientific evidence that a process is capable of consistently delivering a high quality product.

Successful process validation allows for regulatory approval submission and subsequent commercial manufacturing.

A process validation protocol should provide at least:

- Definition of critical product attributes
- Controlled parameters (Critical control points, in process control critical in process control)
- A process flow diagram
- Process parameter reports
- Review of the potential hazards

An important part of the TTP implementation is the cleaning of the equipment train and facility used for the manufacturing process.

Adequate cleaning procedures are essential to minimize the risk of contamination and cross contamination, operator exposure and environmental effects.

SU should provide information on cleaning at the RU, including:

- Solubility information
- Minimum therapeutic doses
- Toxicological assessment
- Existing validated cleaning procedures
- Cleaning validation reports
- Cleaning agents used
- Recovery studies



Engineering runs are normally produced to confirm process capability before initiating formal validation.

At a minimum, all critical processing parameters and finished product specifications should be assessed.

Once process capability has been established at the RU, process validation and cleaning validation can be carried out.

Any significant discrepancy in yield or quality must still fall within the limit for desired application of the drug substance, whereas the technical reason behind the discrepancy must be well understood and under control

The analytical control methods should be transferred before the manufacturing process to ensure proper testing of the products. (small-scale or engineering batches).

The analytical method transfer should accommodate all the analytical testing required to demonstrate compliance of the product to be transferred with the registered specification.

Analytical methods used to test pharmaceutical samples should be implemented at the testing laboratory before testing of samples for process validation studies is performed by the RU.

Appropriate training should be provided and all training activities and outcomes should be documented.

Possible experimental designs and acceptance criteria for the main analytical testing methods are shown in Table 1 of WHO TTP guideline.

A protocol defining the steps should be prepared for transfer of analytical methods.

There are a number of ways in which the transfer may be carried out:

- Comparative Testing
- Co-validation between two or more laboratories
- Revalidation
- Transfer waiver



The SU should provide information to the RU on the layout, construction and finish of buildings and services which have an impact on the product, process or method to be transferred.

The SU should provide information on relevant health, safety and environmental issues.

The RU should review the information of all equipment provided by the SU and perform a comparison at the two sites in terms of their functionality and qualification status (Comparability report).

The RU should perform a gap analysis to identify requirements for adaptation of existing equipment, or acquisition of new equipment, or a change in the process, to enable the RU to reproduce the process being transferred.

GMP requirements should be satisfied and intended production volumes and batch sizes (e.g. same, scaled-up or campaign) should be considered.

The equipment selected or designed for executing the process must be compatible with the desired raw materials and must ensure the performance at the desired process conditions and parameters.

Technology transfer starts with the transfer of the document package and ends with the successful engineering run.

Technology transfer ensures the success of GMP production, although the GMP manufacturing operation itself is not a part of technology transfer.



Pharmaceutical companies should pay more attention to optimizing their technology transfer process to ensure the rapid and successful introduction of new medicinal products to market.

Technology transfer can be considered successful if a RU can routinely reproduce the transferred product, process or method against a predefined set of specifications as agreed with a SU.

To achieve this end, it is recommended that a company should adopt a rigorous process to select its contract manufacturing partners to prevent any kind of issues.



## Any Questions?

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