Topic –
Granularity of Technology Transfer Process

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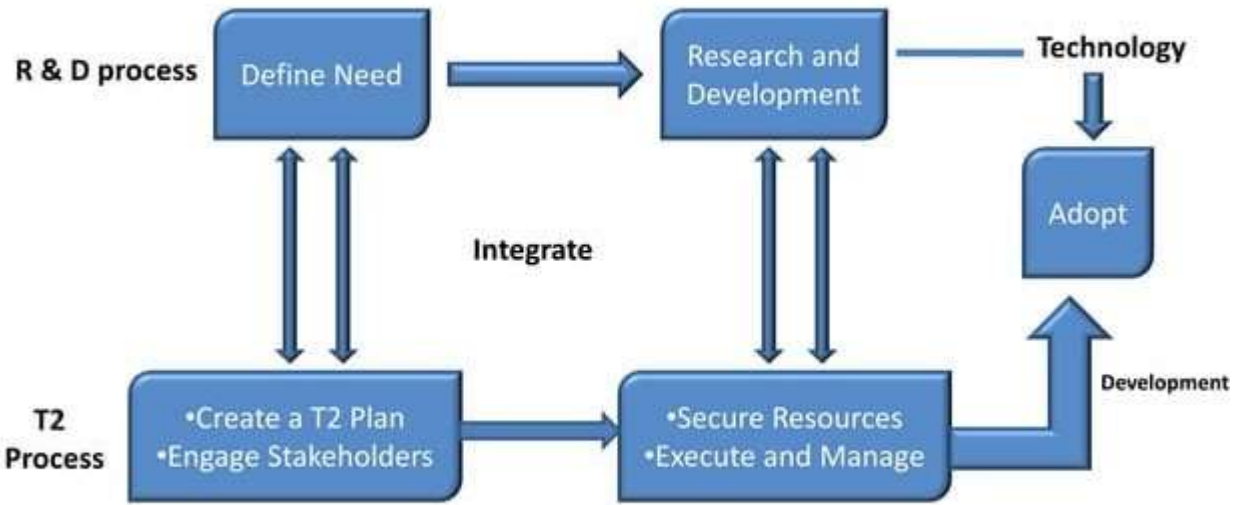
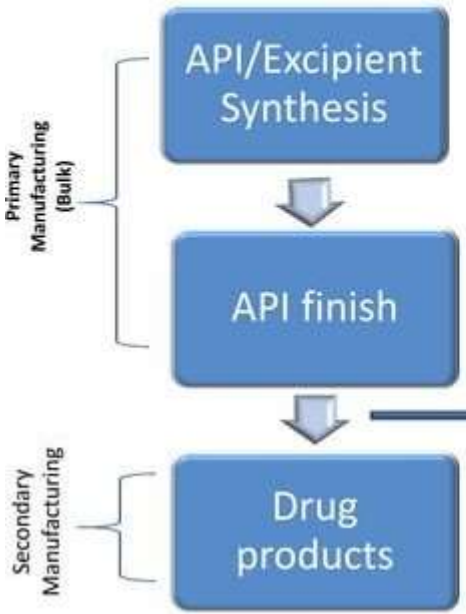
Granularity of Technology Transfer Process

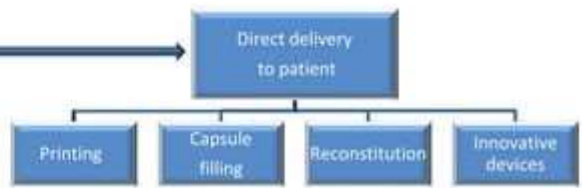


Granularity: The scale or level of detail in a set of data.

Active Pharmaceutical Ingredient



The sending Unit (SU) should offer the Receiving Unit (RU) with the open (applicant's) part of the API master file (APIMF) or Drug Master File (DMF) or Active Substance Master File (ASMF) and any important supplement data on an API suitable for manufacturing pharmaceutical products.



Examples of data which may be provided

- Manufacturer and related supply chain.
- Stage of the API to be transferred
- Flow chart of synthesis pathway, including entry point for raw materials, important steps, process control and intermediates.
- Definitive physical form of API and polymorphic and solvate form.
- Solubility profile
- pH in solution
- Partition coefficient and its determination procedure
- Intrinsic dissolution rate and its determination procedure
- Partition coefficient and its determination procedure
- Water content and determination of hygroscopicity
- Microbial consideration
- Specifications and validations

Excipients

- The excipients to be use influence the final product.
- Their specifications and important functional features should be made available by the Sending Unit (SU) for transfer to the Receiving Unit (RU)
- **Ideal excipient properties:**

1. Stable and reproducible.
2. No unwished interaction with drug.
3. Pharmacologically inert.
4. Desired functionality.
5. Coast effective.

Example of data which may be provided are:

- Manufacturer and related supply chain.
- Explanation of functionality, with validation for addition of any antioxidant, preservative or any excipient.
- Solubility profile.
- Intrinsic dissolution rate and its determination procedure.
- Partition coefficient and its determination procedure.
- Bulk physical characteristic.
- Compaction properties.
- Melting point and pH range.
- Particle size and distribution and its determination procedure.
- Specific density.
- Ionic strength.

Finished products

- The Sending Unit (SU) should give a through description of the product, its qualitative and quantitative composition, physical description, manufacturing method, in-process quality control, control procedure and specifications, packaging constituents and configurations and safety and handling requirements.
- The sending Unit (SU) should offer data on the history of process development that may be needed to all the receiving unit (RU) to make any additional development or process enhancement after transfer.

Packing materials

- The transfer of packing materials should comply with the same procedure pattern as those of the production transfer.
- The data of packing to be transferred from SU to RU includes specification for an appropriate container or closure systems and also any important supplementary data on design, packing, processing or labeling requirements, tamper –proof required by the packing components to qualify at RU.
- Depending on data the RU should conduct a suitable study for initial qualification of the packing components.
- Packing is thought to be appropriate if it offers sufficient protection, safety, compatibility and performance.

Cleaning

- During the manufacturing process, pharmaceutical products and APIs can be contaminated by other pharmaceutical products or APIs if the plant is processing different products.
- To minimize the risk of contamination and cross-contamination, operator exposure and environmental effects, adequate cleaning procedures are essential.
- Cleaning procedures and their validation are site-specific.

- In order for the RU to define its cleaning strategy the SU should provide information on cleaning at the SU to minimize cross-contamination due to residues from previous manufacturing steps, operator exposure and environmental impact, including:

- Information on solubility of active ingredients, excipients and vehicles;
- Minimum therapeutic doses of active ingredients;
- Therapeutic category and toxicological assessment;
- Existing cleaning procedures.

- Additional information should be provided, as appropriate and where available, e.g.:

- Cleaning validation reports (chemical and microbiological);
- Information on cleaning agents used (efficacy, evidence that they do not interfere with analytical testing for residues of APIs, removal of residual cleaning agents);
- Recovery studies to validate the sampling methodology.

Documentation

- Most essential part of TT process.
- Important document listed in WHO guidelines
- Amendments should be done depending upon the time

Essential document for Technology Transfer:

- TOT protocol
- Training protocol
- SOPs
- Process validation protocol and report
- Cleaning validation protocol
- Qualification protocol
- Analytical method transfer protocol

Premises and equipments

- Two major requirements needed for the manufacturing of pharmaceutical product are:

1. Premises
2. Equipments

1. Premises:

SU provide information to RU on:

- Design
- Layout
- Construction
- Services (temperature, water, power etc)

SU provides information related safety, health and related environmental issues including:

- Risk inherited in manufacturing process
- Major health and safety essentialities
- Emergency plan
- Waste management plans

2. Equipment:

- SU responsibilities
- RU responsibilities
- Gap analysis: identification of critical elements

Points considered for gap analysis:

- The facilities and building specific location of all equipments at the RU should be consider.
- The impact of manufacturing new product on products currently manufactured with the same equipment should be determined.
- Any modification of existing equipment that need to be adapted to became capable of reproducing the process being transferred should be documented in the transfer project plan.

Quality control: Analytical Method Transfer

- Transfer of analytical methods 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 products, starting materials, packaging components and cleaning (residue) samples, if applicable, should be implemented at the testing laboratory before testing of samples for process validation studies is performed by the RU.
- Process validation samples may be tested at the RU, the SU or a third laboratory.

- **The SU's responsibilities for the transfer of analytical methods are to:**

✓ Provide method-specific training for analysts and other quality control staff, if required;

✓ Assist in analysis of QC testing results;

✓ Define all methods to be transferred for testing a given product, starting material or cleaning sample;

✓ Define experimental design, sampling methods and acceptance criteria;

✓ Provide any validation reports for methods under transfer and demonstrate their robustness;

✓ Provide details of the equipment used, as necessary (part of validation report, if available) and any standard reference samples;

✓ Provide approved procedures used in testing;

✓ Review and approve transfer reports.

- **The RU's responsibilities are to:**

✓ Review analytical methods provided by the SU, and formally agree on acceptance criteria before execution of the transfer protocol;

✓ Ensure that the necessary equipment for QC is available and qualified at the RU site. The equipment used by the RU during the analytical transfer should meet appropriate specifications to ensure the requirements of the method or specification are met;

✓ Ensure that adequately trained and experienced personnel are in place for analytical testing;

- ✓ Provide a documentation system capable of recording receipt and testing of samples to the required specification using approved test methods, and of reporting, recording and collating data and designation of status (approved, rejected, quarantine);
- ✓ Execute the transfer protocol;
- ✓ Perform the appropriate level of validation to support the implementation of the methods;
- ✓ Generate and obtain approval of transfer reports.

Qualification and Validation

- Extent to qualification and validation to be performed should be determined.
- Based on risk management principles
- Should be documented.

Thank you