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Unit II

Technology development and transfer

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Abstract: WHO sets standards for technology transfer (TT), which includes quality risk management, terminology, the technology transfer method, and the steps that are taken from research and development to manufacturing, such as cleaning, processing, and packaging. It also talks about paperwork, the level of detail in the TT process (which includes APIs, excipients, final products, and packaging materials), facilities and tools, certification, and verification methods. Part of the standards are also quality control and the sharing of analytical methods. These are the jobs of approved authorities and regulatory agencies. Case studies show different parts of commercialization, such as difficulties and useful things to think about. APCTT, NRDC, TIFAC, BCIL, and TBSE/SIDBI are some of the TT bodies in India that help with this process. Also, paperwork linked to TT includes agreements to keep information private,

Keywords: Quality Risk Management, Analytical Methods, Regulatory Agencies Commercialization, Confidentiality Agreements

1.1 Introduction

What is technology transfer?

"Systematic process that governs the exchange of any procedure along with its documentation and expert knowledge between developers or manufacturing locations" is what "technology transfer" means. It is also what makes it possible to find and create new medical products. It assists in the creation of dosage forms in several ways: it improves process efficiency, maintains product quality, and helps set up standard methods that make production cost-effective. In this process, the person who came up with the idea for a technology gives it to a business partner who will use it.

"Technology transfer" in the pharmaceutical industry refers to the steps that are taken from finding a new drug to developing it, testing it in humans, and finally putting it on the market. This step is very important for researchers who want to share their discoveries with a wider audience, especially when they are making new goods. Technology transfer includes more than just the parts of manufacturing that can be patented. It also includes business practices that require knowledge and skill.

Figure shows the different steps that are needed to move technology.

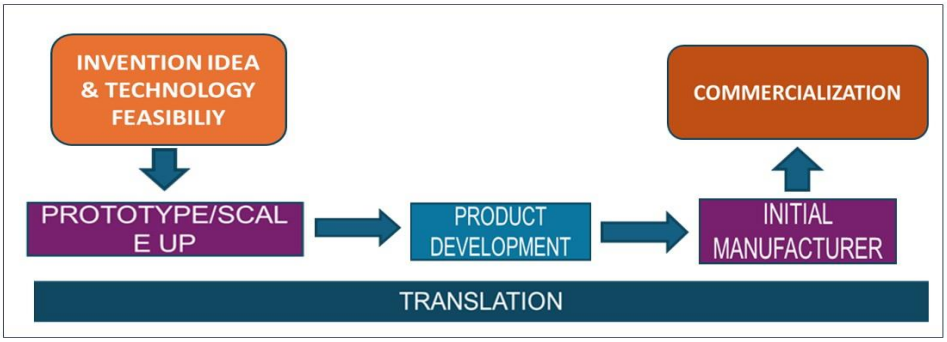

Fig. No.2.1: In different steps, technology is transferred

Facts of technology transfer

There are a few different ways that technology can be transferred:

- From private businesses to government labs.
- Between private companies in the same country.
- When it comes to private companies in different countries.
- From public and private schools to businesses.

1.2 Who Guidelines for Technology Transfer (Tt):

These principles for technology transfer are not meant to be rigid rules that can't be changed. Instead, they are meant to be a framework that can be used in different ways. As suggested by WHO, more attention has been paid to the quality aspects (INDIAN REGULATORY REQUIREMENTS, n.d.; Introduction, n.d.). Transfers to different locations happen at different points in the life cycle of most goods, from the development and scale-up stages to the manufacturing and production stages to the launch and post-

approval stages.

You can think of technology transfer as "a structured process that governs the transfer of any procedure along with its accompanying documentation and expertise from development to manufacturing or between manufacturing locations." It is a planned way to give the written knowledge and experience gained during development or commercialization to the right, responsible, and authorized group. A review of the literature showed that neither national nor regional regulatory bodies had much to say about this subject. The International Society for Pharmaceutical Engineering (ISPE) has put together guidelines for moves within the same company.

Pharmaceutical companies are always changing their business plans. One way they do this is by sharing technology within and between companies. This can happen because of things like needing more space, moving operations, or consolidations and mergers. In its 42nd report, the WHO Expert Committee on Specifications for Pharmaceutical Preparations said that the WHO should make rules about this problem. To transfer technology, you need a structured, well-documented process with trained, informed staff working within a quality framework All of the data used for advancement, manufacturing, and quality assurance must also be documented. The most prevalent categories are a sending unit (SU), a receiving unit (RU), and a unit that is in control of the process but may or may not be distinct from the others. The following fundamental guidelines and conditions must be fulfilled for a transfer to proceed smoothly: The project plan should include the quality parts of the project and be based on the principles of quality risk management (QRM).

- It's not necessary for the Sending Unit (SU) and the Receiving Unit (RU) to have exact the same powers, but they should be similar. The facilities and equipment should also work in a similar way.
- A thorough operational evaluation of gaps between the SU and RU shall be conducted if necessary. This should include a look at technical risks and possible legal inconsistencies.
- The people who work at the RU should be properly trained or should get training, taking into account the rules in both the SU and the RU, as well as the rules of any other countries where the product is going to be sold. This should be interpreted the same way throughout the whole project, making sure that information transfer about products and processes works well.

A technology transfer is considered successful when there is written proof that the receiving unit (RU) can regularly make the transferred product, process, or method according to a set of rules agreed upon by both the sending unit (SU) and the receiving

unit (RU). It is very important for ongoing knowledge management that if the RU runs into specific problems with the process during the move, they tell the SU about them. There are legal and financial things to think about when working on projects that involve sharing technology, especially when those projects involve two different companies.

Before and during the planning and implementation stages of the transfer, problems like intellectual property rights, royalties, pricing, conflicts of interest, and privacy should be dealt with if they are likely to get in the way of open talks about technical issues. A lack of openness could make the spread of technology fail.

It's possible that some of the tasks listed in this paper for the SU are also the management unit's job. The rules cover the following areas:

- The movement of production and growth (packaging, cleaning, and processing).
- The sharing of scientific methods that are meant to improve and guarantee quality.
- Taking a look at skills and giving training.
- How the move process is set up and supervised.
- An evaluation of the building and its tools.
- Documentation, as well as verification and qualification.

Terminologies used in technology Transfer

1. ***Acceptance criteria*:** The criteria that can be used to measure when test results are considered good should be kept in a verified state.
2. ***Bracketing*** is a type of experiment design that looks at only the most extreme values, like dose strength. The idea behind this design is that the extremes will show the traits of all samples that fall in between them.
3. ***Change control*** is a planned process where qualified professionals from related fields look over suggested or existing modifications that might impact a confirmed status. Determining what must be done to ensure that the system remains in an authorized state is the aim.
4. ***Commissioning*** During commissioning, equipment or a system is set up, calibrated, and checked to make verify that it satisfies every criterion listed in the user requirement specification and operates within the parameters established by the developer or originator. Commissioning occurs prior to qualification and proof.
5. ***Corrective action (C/A)*** is any necessary action when monitoring findings at a critical control point indicate that control has been lost.

6. ***Critical*** Being able to have a big effect on the quality or performance of a product.
7. ***Critical control point (CCP)*** is an important spot where control can be put in place to stop or get rid of a danger to the quality of drugs or reduce it to a level that is safe.
8. ***Design qualification (DQ)*** Records demonstrate that the structures, services, tools, systems, and procedures were developed using good manufacturing practices (GMP). This is called design qualification (DQ).
9. ***Design space*** is the complicated mix and interaction of input factors (like the properties of the material) and process settings that have been shown to ensure quality.
10. ***Drug master file (DMF)*** The pharmaceutical regulatory agency receives a lot of information on a facility, process, or product so that it may be added to the application for marketing approval.
11. ***Gap analysis***: identifying the key components of a procedure that are absent at the RU but present at the SU.
12. ***Good Manufacturing Practices (GMP)*** are a component of quality assurance that guarantees products are consistently manufactured and operated to satisfy the requirements of quality necessary for their intended use as well as those mandated by the marketing authorisation.
13. ***Inter-company transfer*** Technology moving from one firm to another is known as an inter-company transfer.
14. ***In-process control (IPC)*** Examinations In-process control (IPC) inspections are carried out during production to monitor the procedure and, if required, alter it to ensure that the end product satisfies the specifications. Taking care of the surroundings or the machines can also be seen as a part of in-process control.
15. ***Installation qualification (IQ)*** Installation qualification (IQ) is the process of ensuring that the equipment, measuring devices, services, and production spaces utilised in a manufacturing process are appropriately selected, installed, and operating in accordance with established standards.
16. ***Operational qualification (OQ)*** Verified evidence that the system or subsystem operates as planned within all anticipated operating ranges. We refer to this as operational qualification, or OQ.
17. ***Performance qualification (PQ)*** Documentation that proves the equipment or system works effectively and consistently within certain parameters and requirements for long periods of time. This is called performance qualification (PQ).
18. ***Process validation*** is the recording of information that gives a lot of trust that a certain process will consistently make a product that meets its quality standards and specifications.

19. ***Quality assurance (QA):*** Quality assurance is a broad term for a lot of different ideas that can change the quality of a product, either on their own or together. It includes all the steps that are taken to make sure that pharmaceutical goods meet the quality standards they need to do their job.
20. ***Quality control (QC):*** QC includes all the steps that are taken to make sure that starting materials, intermediates, packaging materials, and finished pharmaceutical products meet the set standards for identity, strength, purity, and other factors. These steps include defining specifications, sampling, testing, and performing analytical checks.
21. ***Qualification*** is the process of showing and writing down that all facilities, systems, and equipment are set up properly and work as they should, producing the desired results. As a preliminary step, qualification is often used as part of validation. However, the steps of qualification do not meet the standards of process validation on their own.
22. ***Quality Risk Management (QRM)*** there is a structured way to evaluate, control, communicate, and review risks that could affect the quality of pharmaceutical goods throughout their life cycle. This is called quality risk management (QRM).
23. ***Receiving unit (RU):*** The different parts of a company that are likely to share a certain product, process, or method.
24. ***Sending unit (SU):*** The different areas of a company from which a certain technique, procedure, or material will be supplied.
25. ***Spiking*** is when a known amount of a chemical is added to a standard, sample, or fake substance. This is usually done to make sure that an analytical method works.
26. ***Standard operating procedure (SOP)*** is an officially approved document that tells people how to do things that aren't specific to a certain product or material. For example, it tells people how to clean, maintain, and run machines; how to clean and keep facilities clean and in line with environmental standards; and how to do things like sampling and inspection.
27. ***Transfer of technology (TOT)*** is an organised procedure that transfers a certain process, its supporting functions, and its documentation to a location that can replicate the process to a specified degree of performance.
28. ***Validation*** is the process of demonstrating and documenting how a procedure, approach, or methodology consistently produces the desired outcomes.
29. ***Validation master plan (VMP)*** is a detailed document that explains the overall mindset and method of the manufacturer as well as a general validation strategy for the whole project. Its purpose is to help with the evaluation of performance sufficiency. This document gives information about the manufacturer's validation work program and lists the specifics and due dates for the validation activities that

need to be carried out. It also lists the duties of the people who are carrying out the plan.

30. ***Validation protocol (or plan) (VP)*** outlines the steps that must be taken during validation and the requirements that must be fulfilled for a manufacturing process (or a portion of it) to be utilized regularly.
31. ***Validation report (VR),*** A single document contains all of the documentation, findings, and assessments from a finished validation program. It could also provide suggestions for improving machinery and/or procedures.

1.3 Technology Transfer Protocol

A conversion protocol must provide the recommended sequence of the transfer stages. It must contain:

- Reason
- The Policy
- Important People and What They Do;
- A Look at How Different Materials, Methods, And Tools Compare
- The Stages of Transfer, along with Written Proof That Each Important Step Has Been Properly Finished Before Moving On to The Next
- Being Aware of Important Control Points
- The Plan for The Study and The Requirements for Accepting Analytical Methods
- Information On Test Runs, Qualification Groups, And Making Sure Processes Work
- Steps For Dealing with Any Process Changes That Happen
- A Review of the Finished Item
- Plans for storing samples of finished goods, intermediates, and chemical components for A Certain Amount of Time, along with Information On Reference Materials When Needed;
- A Summary That Includes a Name from The Project Manager Indicating That Everything Is Okay.

1.4 Technology Transfer Protocol

There are two basic rules for good risk management, which are:

- Figuring Scientists' knowledge and, above all, patient safety should be the basis for determining the danger to quality; and
- The level of possible risk should determine how much work, ceremony, and paperwork is needed for the quality risk management process.

- Quality risk management is a planned way to find, handle, talk about, and look over risks to the quality of drug products all the way through their lifecycle. Figure 2 shows an example of how to handle quality risks.

Duties - Quality risk management tasks are typically, yet not constantly completed by teams of individuals from several disciplines. Experts from a range of disciplines, including manufacturing, sales and marketing, engineering, quality assurance, expanding a company, legal, statistics, clinical research, and more, should be included in these teams. These professionals have to be proficient in the quality risk management approach as well.

Initiating a Quality Risk Management Process

Organizational steps must be used in good risk management to coordinate, simplify, and improve decisions about risk that are based on science. Some steps that can be taken to begin and plan a good risk management process are listed below:

- Write out the issue and/or risk inquiry, making sure to include important assumptions that take risk into account;
- Assemble historical information and/or current data concerning potential harm, danger, or health effects on individuals that is pertinent to the risk evaluation;
- Select a supervisor and provide them with the necessary resources;
- Set a deadline, list the results you want, and decide on the right amount of decision-making for the process of managing risk.

Risk Assessment

Risk assessment is the process of looking for possible dangers and weighing the risks that come with being near them. A clearly defined problem or risk inquiry is the first step in doing a good risk assessment. There are three main questions that are often helpful:

- What are some things that might go wrong?
- How likely is it that it will happen?
- What would happen (how serious)?

Risk Identification

With this method, you can use information to find risks that are linked to the risk inquiry or issue description. This data could include things like historical facts, theoretical assessments, expert opinions, and worries from stakeholders. The question "What could possibly go wrong?" is at the heart of risk detection.", which includes being aware of the

possible results.

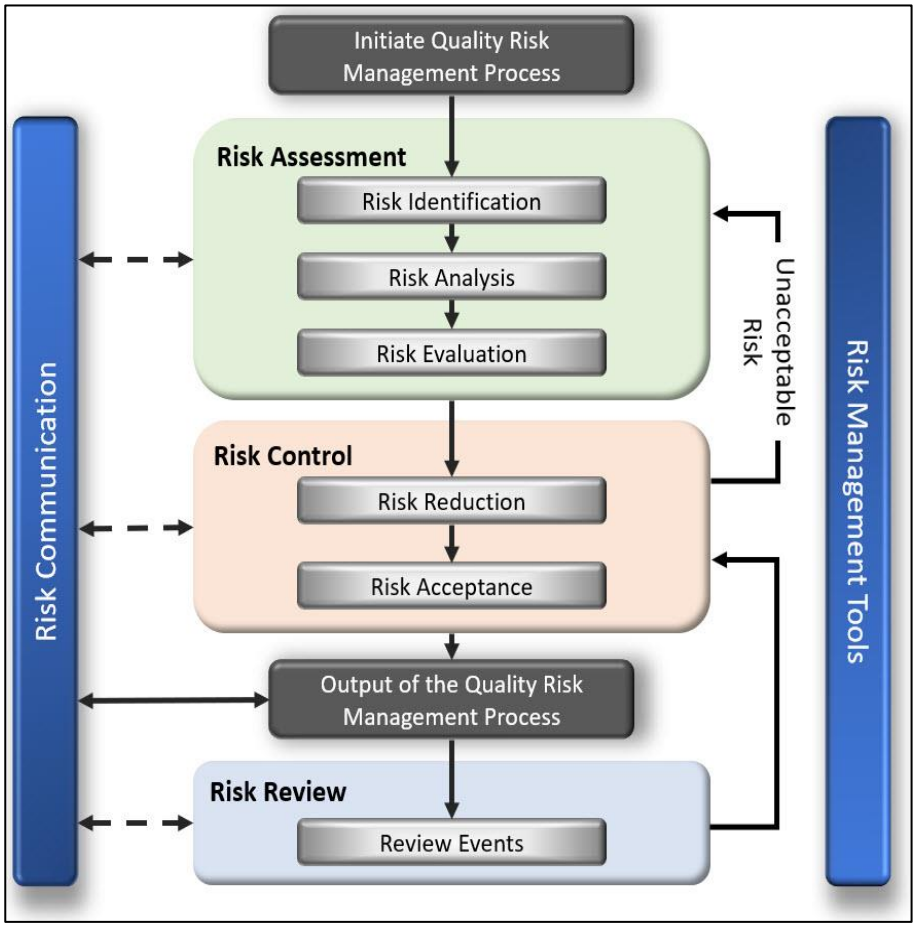

Fig. No.2.2: A look at a common process for managing quality risks

Analysis of risk

Risk analysis is the process of figuring out how dangerous something is and how dangerous it is. It is the process, which can be qualitative or numeric, of relating the likelihood of something happening to how bad it could be if it does.

Risk analysis

The known and looked at risks are judged by how well they meet set risk criteria. There are There are two possible results from a risk assessment: a qualitative overview of the

various risk categories or a numerical estimation of hazard. A certain chance number is used when the question is asked in a quantitative way. On the other hand, danger can also be described by words like "high," "medium," or "low," which should be clearly explained.

Risk Control

Managing risks means making decisions about how to reduce and/or recognize risks. The goal of managing risk is to bring it down to a level that can be handled. These main questions may be at the centre of risk management:

- Does the risk go beyond what can be tolerated?
- What steps can be taken to lower or get rid of risks?
- What is the best number of resources, risks, and advantages?
- Does managing the risks that have already been discovered lead to new risks?

Risk Reduction

Risk reduction is all about coming up with ways to lower or get rid of quality risk when it gets too high. As part of this process, steps may be taken to lower both the chance of harm happening and its effects. In addition, steps that make it easier to find dangers and quality risks can be included into a risk management plan.

Risk communication

Risk communication is when decision-makers and other stakeholders share knowledge about risk and how to handle it. At any point in the risk management process, people can talk to each other. Effective risk management means making sure that the results of the process are shared clearly and properly recorded.

Risk review

There needs to be a way to look back on or keep an eye on events. The results of the risk management method should be looked at again with new information and knowledge in mind. How often these reviews happen should depend on how dangerous the situation is. As part of assessing risk, choices about accepting risk may need to be reevaluated.

Risk management methodology

A scientific and practical way to make choices is made easier by good risk management. It gives written, easy-to-understand, and repeatable steps for each step of the quality risk management process. These steps show the most up-to-date knowledge on how to figure

out how likely, harmful, and sometimes even detectable risks are. Risks can be found and managed by the pharmaceutical industry and regulatory bodies using well-known internal procedures, such as standard operating procedures, and/or risk management tools. A brief summary of some of these tools is provided below: Simple risk management instruments such as check spreadsheets, diagrams, and so on;

FMEA stands for Failure Mode Effects Analysis.

FMECA stands for Failure Mode, Effects, and Criticality Analysis.

- Analysis of fault trees (FTA);
- Failure Modes and Critical Control Points (HACCP);
- Risk Analysis and Operational Capability (HAZOP);
- A preliminary risk assessment (PHA);
- List and sorting of risks;
- Helping with research tools.

1.5 Transfer From Research and Development to Production (Processing, Packing, And Cleaning)

- First, it's important to figure out if the goal is single-batch production, ongoing manufacturing, or production campaigns. It's also important to see if the RU can handle the production capacity that is wanted.
- It is important to pay attention to the amount and specifics of information that needs to be sent to make production easier and to help with any future growth. Alternatively, as outlined in the relocation project plan, procedure enhancement at the RU.
- The SU and the RU should work together to come up with a way for important information about the manufacturing process to be sent from the SU to the RU and for the RU to set up a similar process.

Process

The SU has to give a full description of the product, including its quality and quantity, physical features, how it was made, any in-process controls and criteria, the parts and arrangements of its packaging, and any additional handling and safety guidelines. The SU has to give the RU any useful information about the history of process development that could help them do more development or process optimization after the transfer goes well.

- ***Information on clinical development***, e.g. Details about clinical development, such as the reasons behind the synthesis, the choice of route and form, the technology used,

the equipment that was used, clinical evaluations, and the product's makeup;

- ***Information on scale-up activities***: Details on activities that will be done on a larger scale, such as improving processes and looking at statistical optimization of key process variables; there should also be a details on pilot-scale development and/or a pilot report that show how many batches were made and their state.
- **I*nformation or report on full-scale development activities:*** Details or a report on all the work that went into full-scale development, including how many batches were made and their current state, as well as details on any deviations or changes that resulted in the production procedure used today.
- Any safety, health, or sustainability issues that may arise from the new methods of production should be discussed by the SU with the RU., along with any effects that will happen as a result, like the need for protected clothing or gowns.
- The SU is supposed to give the RU information about what is being processed and made right now. This information should include, but isn't limited to:
- A full list of all the tools and supplies needed for the building
- Selecting an appropriate process technology Information on starting materials, related MSDs, and how to store both raw materials and finished goods
- A description of the steps used in the manufacturing process, including the qualifications for in-process descriptions of bulk transfers between processing processes, hold periods and conditions, and the sequence and technique of adding raw materials. Included should be the analytical techniques that were employed.
- There are in-process control measures, such as identifying process control points, assessing product quality qualities, confirming important processing parameter ranges, and identifying critical performance aspects for certain dose forms. Additionally, there are charts for statistical process control (SPC).
- Details about validation, like validation plans and results, as well as yearly product evaluations
- Information about stability, along with a set of approved Standard Operating Procedures (SOPs) and guidelines for how to make things.

Packaging

The steps should be the same as those used for the production move.

- ***Information on packaging*** The information on packaging items that need to be moved from the SU to the RU should include information on the right container/closure system and any other information that is needed for the qualification of packaging parts at the RU in terms of design, packing, processing, or labelling.

Specifications must be given for drawings, artwork, and materials (like glass, cardboard, fibreboard, etc.) used in quality control tests for packaging parts. Using the information given, the RU should do a review of the packaging components' suitability for the first qualification.

- ***For quality control testing*** If the packaging protects the drug well (keeping it from breaking down in the environment), keeps the product safe (not letting any unwanted substances into it), works well with other products (not interfering with the drug's quality), and works well at delivering the drug, then it's a good package.

Cleaning

If different goods are processed right after each Pharmaceutical goods and active pharmaceutical ingredients (APIs) may get contaminated during the production process. Having good cleaning methods in place is important to lower the risk of contamination and cross-contamination, as well as the risk of user exposure and damage to the environment. The SU should describe the cleaning procedures used to prevent cross-contamination from leftovers from earlier manufacturing processes, as well as the effects on workers and the environment. The SU should also include details on how well active ingredients, excipients, and vehicles dissolve in water.

1.6 Granularity Of TT Process (Api, Excipients, Finished Products, Packaging Materials) Starting Materials

At the RU, the specs for the starting materials (APIs and excipients) must match those of the reference batches, which could be development batches, bio batches, or batches made at the SU. It is important to find and fully describe any features that could impact the process or result.

Active Pharmaceutical Ingredients (API)

The SU must give the RU the drug master file (DMF) and any other relevant information about the API so that it can be checked against the API standards. The following information needs to be included:

- Maker of
- A flow chart showing the synthetic route, including where the raw materials come in, the important steps, the controls for the process, and the intermediates.
- The stable form of the solvate forms and any polymorphisms of the active pharmaceutical ingredient (API); photomicrographs and other pertinent

information should be included. Characteristics of solubility

- Partition coefficient (along with the way it was found)
- The intrinsic breakdown rate and the way it was found are both important.
- The size and location of the particles (including how they were measured)
- Physical properties of the bulk, such as density, surface area, porosity, and tap density, if relevant
- The amount of water present and an evaluation of its hygroscopicity, along with information on water activity and special handling instructions
- Microbiological factors, such as bacterial endotoxins, sterility, and bioburden levels where the API can support microbe growth, in line with regional Pharmacopoeia standards
- Details about release and end-of-life limits, along with reasons for them
- A summary of stability studies that were done according to existing rules, with results and suggestions for when to do the next test
- A list of possible and real synthetic impurities, along with data that backs up suggested standards and levels that are usually seen
- Information on degradants, such as a list of possible and observed degradation products; and Data to back up proposed specifications and normally observed levels of potency factor, showing observed purity and giving reasons for any suggested changes to the amount of API used to make the product, with examples of calculations; and
- Special things to think about when storing and/or handling, like environmental and safety concerns, as well as how sensitive the item is to heat, light, or moisture.

Finished Products

The finished product may be different depending on the excipients used. So, the SU needs to send their specs along with the DMF so that they can be sent to the RU site. For each type of excipient, the following information should be given:

- A full explanation of how it works, including why any antioxidants, preservatives, or other ingredients that are added in amounts that are higher than what is suggested is used.
- The name of the company that made it.
- For compendial excipients, the specifications should include monographs and any other details that could affect the processing or quality of the product. For non-compendial excipients, the specifications should include analytical methods and reasons for release limits. The same amount of detail must be given for excipients that are being used in a human drug product for the first time or

through a new route of administration.

- Other things to think about that might affect how it is stored and/or handled, like how it reacts to heat, light, or water solubility; these could include safety and outdoor factors, like those listed in material safety data sheets.
- Regulatory issues, such as the status of the compendial and any necessary regulatory data for non-compendial excipients; details about any remaining solvents or organic volatile impurities; and proof that the product meets the requirements for transmissible animal spongiform encephalopathy certification, if that's the case.
- Completed Items
- Depending on the dosage type used, the SU must give the RU relevant information about the physical properties of the excipients, such as:
- Final preparation (for dosage forms that are solid or inhaled)
- How well it dissolves (for solid, oral, and transdermal dosage forms)
- The partition coefficient and the evaluation technique are crucial for transdermal dose forms. For transdermal dose forms, this also applies to the intrinsic dissolving rate and the evaluation technique. Details on particle size and distribution, as well as the evaluation technique, are equally crucial.
- The physical properties of the bulk, such as its density, surface area, and porosity (for solid and inhaled dose forms), as needed.
- Compaction characteristics (for solid dosage forms)
- Melting point range for topical and semi-solid dosage forms
- range of pH (for oral, topical, semisolid, or liquid dosages)
- Strength of the ions (for parenteral dose forms)
- A precise weight or porosity (for transdermal, liquid, injectable, and semi-solid/topical dose kinds)
- For parenteral, semi-solid/topical, liquid, and transdermal dosage types, viscosity and/or viscoelastic qualities are important.
- osmolarity (for dose forms that are injectable)
- Checking the amount of water and hygroscopicity, along with Information on water activity and specific handling guidelines (for solid and inhaled dosage forms)
- The range of moisture content for liquid, transdermal, semi-solid/topical, and parenteral medication forms
- Microbiological variables for parenteral, liquid, inhalation, transdermal, and semi-solid/topical dose forms must comply with local pharmacopoeia criteria.
- For transdermal dosage forms, information on adhesives that meet design

standards for peeling, shearing, and sticking.

Packaging

The information about packaging that needs to be sent from the SU to the RU includes the right container/closure system specifications as well as any other design, packing, processing, or labelling rules that are needed for the RU to approve the packaging components. For the quality control check of package parts, it is important to give details about the drawings, artwork, and materials that will be used.

Documentation: Table 1 shows the things that are needed to share technology.

Table No.2.1: Documentation for transfer of technology (TOT)

Key task	**Documentation provided by SU**	**Transfer documentation**
Project definition	Project plan and quality plan (where separate documents), protocol, risk assessments, gap analysis	Project implementation plan
Quality agreementFacility assessment	Plans and layout of facility, buildings (construction, finish) Qualification status (DQ, IQ, OQ) and reports	**TOT protocol** Side-by-side comparison with RU facility and buildings; gap Analysis **Qualification protocol and report**
Health & Safety assessment	Product-specific waste management plans Contingency plans	
Skill set analysis andtraining	SOPs and training documentation (product-specific operations, analysis, testing)	Training protocols, assessmentresults
Analyticalmethod	Analytical method specifications and validation, including in-	Analytical methods transferprotocol and

transfer	process quality control	report
Starting material Evaluation Equipment selection and transfer	Specifications and additional information on APIs, excipients Inventory list of all equipment and systems, including makes, models, qualification status (IQ, OQ, PQ). Drawings, manuals, logs, SOPs(e.g. set-up, operation, cleaning, maintenance, calibration, storage)	Side-by-side comparison with RU equipment (makes, models, qualification status) Gap analysis. **Qualification and validation protocol and report**
Process transfer: manufacturingand packaging	Reference batches (clinical, dossier, bio-batches) Development report (manufacturing process rationale), History of critical analytical data Rationale for specifications, Change control documentation, Critical manufacturing process Parameters Process validation reports Drug master file. API validation status and report(s) Product stability data Current master batch manufacturing and packaging records List of all batches produced Deviation reports, Investigations, complaints, recallsAnnual product review	History of process development at RU, Experiences at RU should be recorded for future reference Provisional batch mfg. document (RU to develop) Provisional batch packaging document (RU to develop) Description of process at RU (narrative, process map, flow chart) **Process validation protocol** **and report**
Cleaning	Cleaning validation, Solubility information; therapeutic doses; category (toxicology); existing	Product- and site-specific cleaning SOPs at RU

	cleaning SOPs; validation reports chemical and micro; agents used; recovery study	**Cleaning validation protocol and report**

Premises and Equipment Premises

All structures and utilities (such as heating and ventilation, temperature, relative humidity, water, electricity, and compressed air) that are related to the technique, procedure, or substance being transferred must be designed, constructed, and completed, and the SU must provide the RU with this information.

The SU must also give details about important environmental, health, and safety issues, such as:

- The risks that come with the industrial processes themselves, such as reactivity of chemicals, exposure thresholds as well as the dangers of fire and explosion.
- Safety and health rules that must be followed to protect workers from harm, like keeping medicine dust out of the air.
- The SU and RU will have different building designs, layouts, and services, so the following should be taken into account when comparing them:
- GMP says that the structures and RU services must be able to support the technique, process, or product. that is being transferred so that it can meet the quality standards and output volumes that were agreed upon.

DQ stands for "design qualification," IQ for "installation qualification," OQ for "operational qualification," API for "active pharmaceutical ingredient," SOPs for "standard operating procedures," and RU for "receiving unit."

- To do their jobs well, quality control labs need to have the right tools and be able to test all APIs, cleaning validation samples, excipients, intermediates, final products, and packaging components.
- The buildings that are used to make highly sensitizing materials (like penicillin's and harmful substances) should be kept separate from other factories so they can only be used for this purpose.
- Health, safety, and the environment issues should be handled at the production unit in line with any rules, regulations, and limits set by the company or by the government. This includes managing waste, being ready for emergencies,

limiting operator exposure, and minimizing environmental impact.

Equipment

Along with the current qualification and validation papers, the SU must give a full list of all the equipment, along with its makes and models, that was used to make, fill, package, or check the quality of the product, process, or method that is being transferred. Documentation that is relevant may include:

- Detailed plans
- Rules and instructions
- Records of service
- Setting up
- Standard Operating Procedures (for example, how to set up, use, clean, fix, calibrate, and store equipment).

The RU should look at the SU's information along with its own inventory list, which includes the qualification status (IQ, OQ, PQ) of all systems and equipment. It should then compare the equipment at both locations in terms of their functionality, makes, models, and qualification status.

After comparing, the RU should do a gap analysis to see what changes need to be made to current equipment or what new equipment needs to be bought so that the RU can copy the process that is being moved. In addition to adhering to GMP regulations, intended production quantities and batch sizes (such as the same, scaled-up, or campaign) must be considered. The following factors need to be considered: when comparing:

- The lowest and largest capacities
- Materials for building
- Conditions necessary for operation
- Important pieces of equipment, like filters, screens, and temperature and pressure gauges
- The types of uses that are planned.

When making process maps or flow plans for the manufacturing process that is going to be moved, all of the RU's equipment should be carefully thought out in terms of where it is located in the facility and building (Asit et al., n.d.). This includes the movement of people and things.

It is important to think about what might happen to current products when new ones are

made with the same tools.

If the current production equipment needs to be changed so that the transferred process can be repeated, a full development project needs to be built into the transfer procedure.

You should make sure that any new equipment you buy is built to support the process and make cleaning and upkeep easier. Any brand-new equipment has to go through a licensing process that ends with the OQ level. Setting up, using, cleaning, storing, and maintaining the equipment should all have clear operational processes set up by the end of the OQ. Supporting records should be kept, like drawings of the equipment, diagrams for installing pipes, manuals calibration records, repair logs, and so forth.

Qualification and Validation General

- ✓ It is important to qualify and Verify systems, methods, infrastructure, and equipment to demonstrate that all crucial components of the transfer project have been effectively finished. This will enable the RU to reliably produce the product, procedure, or technique in accordance with the guidelines that were established in consultation with the SU. A validation master plan (VMP) should keep track of the validation that was done as part of the move project. In this plan, it should be clear which steps need to be validated and what the acceptance factors are.
- ✓ When people move within the same business, The SU and the RU must adhere to the same VMP. A VMP needs to be established at the RU prior to a transfer between firms.
- ✓ In order to complete each step, the RU has to make a validation process (VP). A validation report (VR) must be used to show that each VP was completed successfully.
- ✓ Until all of the tools have been configured and tested, the RU cannot do qualification and validation. This guideline lists all the steps that need to be taken for this process, including buildings, services and tools, manufacturing, packaging, cleaning, and analytical testing. To sum up, the following important steps apply to all of these areas:
- ✓ The SU is in charge of giving information about the parts, systems, and steps that were used to create the process, product, or technique that will be passed on.
- ✓ The RU needs to look over the information the SU gave them and do an audit of their current systems, tools, and processes, as well as any practices and services that aren't related to the process but still affect it.
- ✓ In order to create site-specific SOPs, training programs, and procedures that will be utilised for certification and validation, the RU should either approve the material they received or continue working on it after this review.

- ✓ All the important people, like operators and researchers, need to be trained on any new processes that need to be used.
- ✓ Once the RU has put in place the necessary systems and procedures and training has been recorded as successful, the facility and its equipment should be qualified and validated. This should be followed by the validation of analytical testing methods, process validation for manufacturing and packaging, and cleaning validation.
- ✓ Upon reviewing the gap analysis, the RU should create validation plans (VPs) for the building, services, and tools, if necessary.
- ✓ VPs must be followed for both new as well as used equipment when it comes to purchasing and designing requirements, installation qualification (IQ), operational qualification (OQ), and factory acceptance testing (FAT), if feasible.
- ✓ At the start of trial batches, performance qualification should be set up. This includes checking the working parameters in relation to the product characteristics.
- ✓ A report must show that the qualification and validation steps were completed successfully.

1.7 Quality Control:

All the tests that need to be done to make sure the product meets the registered standards must be part of the transfer of analytical methods. Before doing process validation studies for manufacturing operations, it's necessary to set up the Transmission of analytical techniques for assessing cleaning residue samples, medicinal products, and their components. The SU must create a protocol outlining the procedures for exchanging analytical techniques. The purpose, scope of applications, responsibilities of the SU and RU, materials, techniques, and equipment to be used, experiment design and acceptance criteria, documentation (including information to be included with the results and any report forms to be used), deviations, references, approval signatures, and details about reference samples (APIs, intermediates, and finished products) should all be included in the analytical methods transfer protocol.

- SU is in charge of the changeover of scientific methods, which includes:
- Give analysts and other quality assurance staff method-specific training;
- Make a list of the requirements and steps for validating any RU training events;
- Help with judging the results of quality control tests;
- List and explain all the ways that will be used to test a certain product,

ingredient, or cleaning sample;

- Explain the experiment's design, sample procedures, and acceptability standards;
- To ensure the validity of the techniques being sent, present any validation documents;
- Provide details on the instruments utilised and any common reference materials; &
- Provide the approved SOPs that are utilised during the testing procedure.
- The RU is responsible for the following:
- Looking over the SU's analytical methods and officially agreeing on acceptance criteria before putting the transfer process into action;
- Making sure that the RU site has all of the necessary quality control tools that is in good working order. It is better to have duplicated equipment, However, it is known that several kinds, such as chromatographs and spectrometers, may be currently in use.
- Making sure as people who are properly trained and experienced are ready to do analytical tests;
- Setting up a method for keeping records of when samples are received and tested.

Analysts from both SU and RU do tests on two samples that were kept from SU:
Next, experts from SU and RU do tests on two sub-potent samples, which can come from SU or be spiked.
Analysts from SU and RU look at samples from RU production
The analyst at RU does enough duplicate analyses to allow a significance test (e.g., student's t) to be done compared to the method that is already in place at SU.
A similar process should be used to look at APIs that are present in small amounts.
All actions and results of training must be written down.

1.8 Analytical Methods Transfer

These parts should be in the process for sending analytical methods:

- Aim
- Range
- SU & RU jobs
- Tricks, tools, equipment
- The paperwork for the experiment's design and acceptance criteria, which includes information that will go with the results and any report forms that may be used.
- Slight changes

- List of sources
- Written permission; and
- Information about reference samples, which can be APIs, intermediates, or finished goods. A record should show that the analytical methods were successfully transferred and checked.

1.9 Approved Regulatory Bodies and Agencies

The major government agencies in India that are in charge of making sure that only high-quality medicines are approved, made, and sold at fair prices are

- ✓ ***The Central Drug Standards and Control Organization (CDSCO),*** which is directly overseen by Ministry of Health and Family Welfare. CDSCO makes rules and standards to make sure that all medicines, cosmetics, diagnostics, and devices in country are safe, effective, and of good quality. controls need for clinical trials and the approval of newly marketed medications; it also keeps an eye on drug imports and issues licenses for making those things.
- ✓ ***The Drugs Controller General of India (DCGI),*** The Central Drug Controller The Ministry of Science and Technology, Department of Biotechnology (DST), the Ministry of Environment, the Ministry of Environment and Forests, and the Ministry of Health and Family Welfare are in charge for market authorization. They are also being responsible of quality assurance and licensing. Controllers of drugs in each state can make sure that medicines are made safely and properly and give licenses to companies that want to make approved medicines.
- ✓ ***Central Drug Standards Control Organization (CDSCO).***
- ✓ ***The Food and Drug Administration (FDA or USFDA)*** It is a federal body of the Department of Health and Human Services and one of the executive departments of the United States. The Food and Drug Administration (FDA) is in charge of making sure that tobacco products, dietary supplements, pharmaceutical drugs (both over-the-counter and prescription), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), cosmetics, animal foods and feed [4], and veterinary products are safe and effective. This is all part of the FDA's mission to protect and improve public health.
- ✓ ***The Therapeutic Goods Administration (TGA)*** Australia's Department of Health is in charge of the Therapeutic Goods Administration (TGA). The TGA is in charge of regulating therapeutic items like prescription drugs, vaccines, sunscreens, vitamins, minerals, medical tools, blood and blood products. A lot of medicines that claim to be therapeutic must be Prior to being marketed in

Australia, they must be listed on the Australian Register of Therapeutic Goods (ARTG).

- ✓ ***Medicines and Healthcare Products Regulatory Agency (MHRA)*** In the UK, the Medicines and Healthcare Products Regulatory Agency (MHRA) oversees blood components used in transfusions, medicines, and medical tools.
- ✓ ***Commercialization: problems and issues in the real world (case studies)***

Some real-world studies are used to talk about technology transfer.

Case Study 1: Table 2 shows how the drug and excipients were mixed. [3] ***Factors considered in the proposed technology transfer (scale up)*** Maintaining Forces (Froude number) is an example of dynamic similarity; the proportion for all lengths stays the same (constant ratio of fill).

Kinematic similarity means keeping the same number of turns.

Table No.2.2: Scale-up in QbD Approach: Blending

Scale	Amount (kg)	Blender Capacity	Blending Speed (rpm)	Blending Time (min)	Nrev	Volume Fill Ratio (%)
Laboratory	2	8 qt	25	12	300	~50
Pilot	40	7.5 cu.ft	15	20	300	~50
Commercial	180	30 cu. ft	10	30	300	~50

Conclusion of case study 1: By adjusting the blending speed and duration, among other things, the required content homogeneity was achieved.

Case Study 2: Drug stacking on MCC spheres [3]

If you use manufacturing equipment that is most like the commercial-scale process you want, you can keep the same process factors as you scale up, except for air flow, which goes up in a straight line.

(Figure 3, Table 3).

Conclusion of case study 2

To achieve a consistent drug coating on the MCC spheres, the air flow rate and total spray rate were adjusted. In both the commercial and pilot runs, the formulation's assay had a 99.9% success rate.

Fig. No.2.3A: Pilot Scale Studies (40 kg each) using 18'' Wurster HS insert

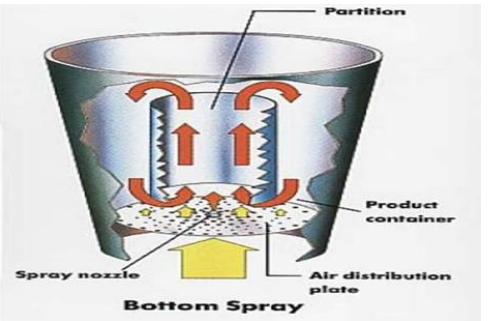

Fig. No.2.3B: Commercial Scale (140 kg) using 32'' Wurster HS insert

Table No.2.3: Parameters for pilot and verification batches at commercial scale

Particular	**Pilot batches**	**Commercial scale**
Starting Batch Size	40 kg	140 kg
Ending Batch Size	56 kg	198 kg
Estimated use of capacity	50%-70%	56%-79%
Number of Partition(s)	1	3
Partition height	30-50 mm	30-50 mm
Nozzle	1.2 mm	1.2 mm
Product Temperature	44-48 C	44-48 C
Air Flow Rate	**810±90 cfm**	**2430±270 cfm**
Spray Rate per nozzle	135±25 g/min	135±25 g/min
Total Spray Rate	**135±25 g/min**	**405±75 g/min**
Atomization Pressure per nozzle	2.5-2.9 bar	2.5-2.9 bar

1.10 TT agencies in India - APCTT, NRDC, TIFAC, BCIL, TBSE /SIDBI [4]

Asian and Pacific Centre for Transfer of Technology (APCTT

It is a regional organization of the United Nations that was set up in 1977 in Bangalore, India. It is part of the Economic and Social Commission for Asia and the Pacific (ESCAP). In 1993, the Centre moved to New Delhi, India. APCTT promotes the exchange of technology between and among small and medium-sized businesses (SMEs) in Asia and the Pacific. APCTT runs development projects that are paid for by foreign donors to make it easier for small and medium-sized businesses to share technology. The APCTT's goals are to improve the region's ability to share technologies and make it easier for member countries to bring and send environmentally friendly technologies to and from each other.

The National Research and Development Corporation (NRDC)

The National Research Development Corporation (NRDC) was created by the Indian government in 1953. Its main goal is to promote, develop, and commercialize technologies, know-how, inventions, patents, and processes that come from different national R&D institutions and universities. It is currently run by the Department of Scientific & Industrial Research, Ministry of Science & Technology. In its six-decade history, NRDC has built strong relationships with the scientific and business communities in India and around the world in order to further its business goals. It is known to have a huge collection of technologies from almost every industry, such as building materials, mechanical, electrical, and electronic systems, biotechnology, metallurgy, chemicals (including pesticides, pharmaceuticals, and chemicals), agriculture, and agro-processing. Over 4800 business owners have been given rights to use the indigenous technology, which has helped many small and medium-sized businesses get started. NRDC also does a lot of other things, such as providing rewards for good ideas, helping businesses use technology, providing financial and technical support for protecting intellectual property rights, providing value-added services, and supporting the progress of technologies, to name a few.

Technology information, Forecasting and assessment Council (TIFAC)

TIFAC is a separate organization that was created in 1988 by the Department of Science and Technology. It looks ahead in the field of technology, reviews its paths, and encourages innovation through coordinated efforts in a few key areas of national importance. TIFAC was given the important job of creating a national technological strategy in a number of very new technology areas. Vision 2020's technical work, which

was led by Dr. APJ Abdul Kalam, resulted in 17 publications, one on services and sixteen on scientific areas. In its more than 25 years of service to the country, it has done a number of studies on evaluating and planning for new technologies. Prime Minister Narendra Modi showed off the Technology Vision 2035, a plan made by TIFAC, at the 103rd Indian Science Congress in Mysuru. This detailed plan covers 12 important areas for the whole country, such as healthcare, education, agriculture, energy, transportation, and more. This inspiring document is meant to shape India's technological future and meet the country's urgent needs. It focuses on progress and new ideas. The Prime Minister's announcement of this big plan shows a renewed dedication to advancing science and making everyone's life better in India.

Biotech Consortium India Limited (BCIL)

Biotech Consortium India Limited (BCIL) is a public business that was set up in 1990 to help biotechnology become more widely used in India. BCIL's goal is to create and share cutting-edge biotech technologies, offer expert project consulting, raise biosafety knowledge, and develop industry talent. It is backed by the government's Department of Biotechnology and financial institutions. Over the years, BCIL has run several important programs for the Department of Biotechnology well. These include the Biotechnology Industry Partnership, Biotechnology Industrial Training, and Small Business Innovation Research programs. BCIL is slowly changing India's biotech scene and making the country a global centre for innovation and business through these active efforts.

Technology Bureau for Small Enterprises (TBSE)/ Small Industries Development Bank of India (SIDBI).

The Technology Bureau for Small Enterprises (TBSE) is a website that helps small businesses find global chances to buy new technology or work together on projects. The UN's technology transfer centre and India's Small Industries Development Bank joined forces to make TBSE in 1995. TBSE is a professional system that helps small businesses explore technology and collaboration options, build trust with potential partners, and network their way into the global technology market. The group also helps with business planning and evaluating projects. China, the Philippines, South Korea, Australia, Germany, and the United States are some of the places where TBSE gets new technologies.

Overall, TBSE is a fun platform that gives small businesses the tools they need to grow by using global resources.

TT related documentation - confidentiality agreement, licensing, MoUs, legal issues.
Confidentiality Agreements

The goal of a secrecy agreement is to keep all of the parties' information safe before they start talking. Before any official talks about the transfer of technology can start, everyone involved must be able to evaluate it. So, the offer's economic and technological possibilities will be taken into account. Before letting anyone use your technology, you should make a secrecy agreement. It should list the main points that will be talked about in the agreement, as well as all the usual terms, like the parties, the length of the agreement, how it can be ended, and any laws that apply.

The first thing that should be in any secrecy agreement is a short but clear description of the technology that will be sent. What are the main features of this technology, and what is the right way to use it? In the same part of the deal, the party offering may talk about their property rights.

1.11 Licensing

A licensing deal is what the law says about sharing technology. By signing this deal, the owner of a technology (called the "licenser") lets another business (called the "licensee") use the technology. A license does not change the owner's property rights; he is still the only one who owns the technology. It's also possible for him to sell his technology. If someone bought it, they would own it and be the seller. But if the owner of the technology wants to make a deal with a partner, he has to give the licensee some rights. The licensee is allowed to use the technology, but they can't throw it away.

This use will be limited in some ways. It's possible for a license to have limits on time, place, product, or use. The license will be the link between the licenser and user for as long as they work together, and there are some things that need to be cleared up before they can start working together.

1.12 Memoranda Of Understanding (MOUs)

Memorandums of Understanding (MOUs) are often used to plan joint study projects with outside organizations before other agreements are signed. An MOU generally spells out the roles and responsibilities of each party, as well as how intellectual property will be shared. If you want to work with someone from outside your company, you should talk

about possibility of an MOU. MOUs are draughted by the Office of Technology Commercialisation for researchers who wish to collaborate. MOUs usually say how the money from licenses will be split and name an institution that will be in charge of managing intellectual property.

1.13 Legal Issues

When technology is transferred, the following types of legal issues come up all the time.

Contracts that are legal

- Effects on taxes
- Legal issues in deals about intellectual property
- Things that have to do with IPR lawsuits

- Laws in India that guide IPRs

Review Questions

Short Answer 02 marks

1. Describe the goals and reach of TT.
2. Describe the aspects of technology transfer; write a comment on CDSCO and DCGI; and write the CDSCO vision and mission.
3. What does FMECA signify to you?
4. Describe the purpose and function among the following:
   i. NRDC
   ii. APCTT
   iii. TIFAC
   iv. BCIL
   v. TBSE
   vi. SIDBI

Short Essay 05 marks

1. Describe the WHO's TT recommendations.
2. Explain what is QRM.
3. Outline the functions of the various regulatory bodies and agencies in TT.

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