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**(CONTENTCREATER/TEACHER)**

**Syllabus**

| UNIT | CONTENTS |
|---|---|
| **UNIT-2** | **Technology development and transfer;** WHO guidelines for Technology Transfer (TT): Terminology, Technology transfer protocol, Quality risk management, Transfer from R & D to production (Process, packaging and cleaning), Granularity of TT Process (API, excipients, finished products, packaging materials) Documentation, Premises and equipments |

## UNIT-II

**TECHNOLOGICA L DEVELOPMENT:**

1. Technological development, including improvement and reassessment of existing technologies, is urgently needed to:
   (a) limit or reduce anthropogenic greenhouse gas emissions;
   (b) absorb greenhouse gases—i.e., protect and increase greenhouse gas sinks;
   (c) adapt human activities to the impacts of climate change;
   (d) Monitor, detect, and predict climate change and its impacts.
2. Technological actions designed to limit or adapt to climate change must be founded on a sound scientific basis, and must be consistent with the concept of sustainable development.
3. Criteria
   (a) In selecting technologies, priority should be given to those technologies that provide. significant economic and social benefits in addition to benefits in limiting or adapting to climate change,
   (b) (b) Appropriate criteria for selecting technologies (and for technology transfer measures) also include economic efficiency, taking into account all the external costs and benefits. Account must also be taken of suitability to local needs and conditions, additional benefits, ease of administration, information needs, legal and institutional constraints, national security (including defense, economy, energy, and food), and acceptability to the public.

4.

   a) Technological development will have to be pursued in a wide range of sectors and activities such as energy (including noncommercial sources), industry, agriculture, and transport and management of natural resources.
   b) (b) Adequate and trained human resources in all the countries are a prerequisite for development and transfer of technologies.
   c) (c) The growth of industrial and agricultural activities is one of the main anthropogenic components of the greenhouse effect. Technological advances to limit or adapt to climate change are critically important to provide a sound basis of sustainable development.

**WHO guidelines for Technology Transfer:** These guiding principles on transfer of technology are intended to serve as a frame work which can be applied in a flexible manner rather than as strict rigid guidance. Focus has been placed on the quality aspects, in line with WHO's mandate.

1. Transfer of technology is defined as "a logical procedure that controls the transfer of any process together with its documentation and professional expertise between development and manufacture or between manufacture sites". It is a systematic procedure that is followed in order to pass the documented knowledge and experience gained during development and or commercialization to an appropriate, responsible and authorized party.

2. Technology transfer embodies both the transfer of documentation and the demonstrated ability of the receiving unit (RU) to effectively perform the critical elements of the transferred technology, to the satisfaction of all parties and any applicable regulatory bodies.
3. Transfer of processes to an alternative site occurs at some stage in the life-cycle of most products, from development, scale-up, manufacturing, production and launch, to the post-approval phase.
4. The ever changing business strategies of pharmaceutical companies increasingly involve intra- and intercompany transfers of technology for reasons such as the need for additional capacity, relocation of operations or consolidations and mergers.
5. Some of the principles outlined in this document may also be applicable to manufacturing investigational pharmaceutical products for clinical trials as part of research and development, but this is not the main focus of this guidance and has been excluded due to the complexity of the processes.

**Technology transfer protocol:**

Transfer protocol to include;

1. Objective and scope.
2. Key personnel and their responsibilities.
3. A parallel comparison of materials, methods and equipment.
4. Transfer stages.
5. Identification of critical control points.
6. Experimental design and acceptance criteria for analytical methods.
7. Information on trial production batches, qualification batches and process validation;
8. Change control and deviations encountered;
9. Assessment of end-product;
10. Arrangements for keeping retention samples
11. Conclusion and approval

**Quality risk management:**

Principles of quality risk management. It is not always appropriate nor always necessary to use a formal risk management process (using recognized tools and/or internal procedures, e.g. standard operating procedures (SOPs)). The use of an informal risk management process (using empirical tools or internal procedures) can also be considered acceptable. The two primary principles of QRM are that:

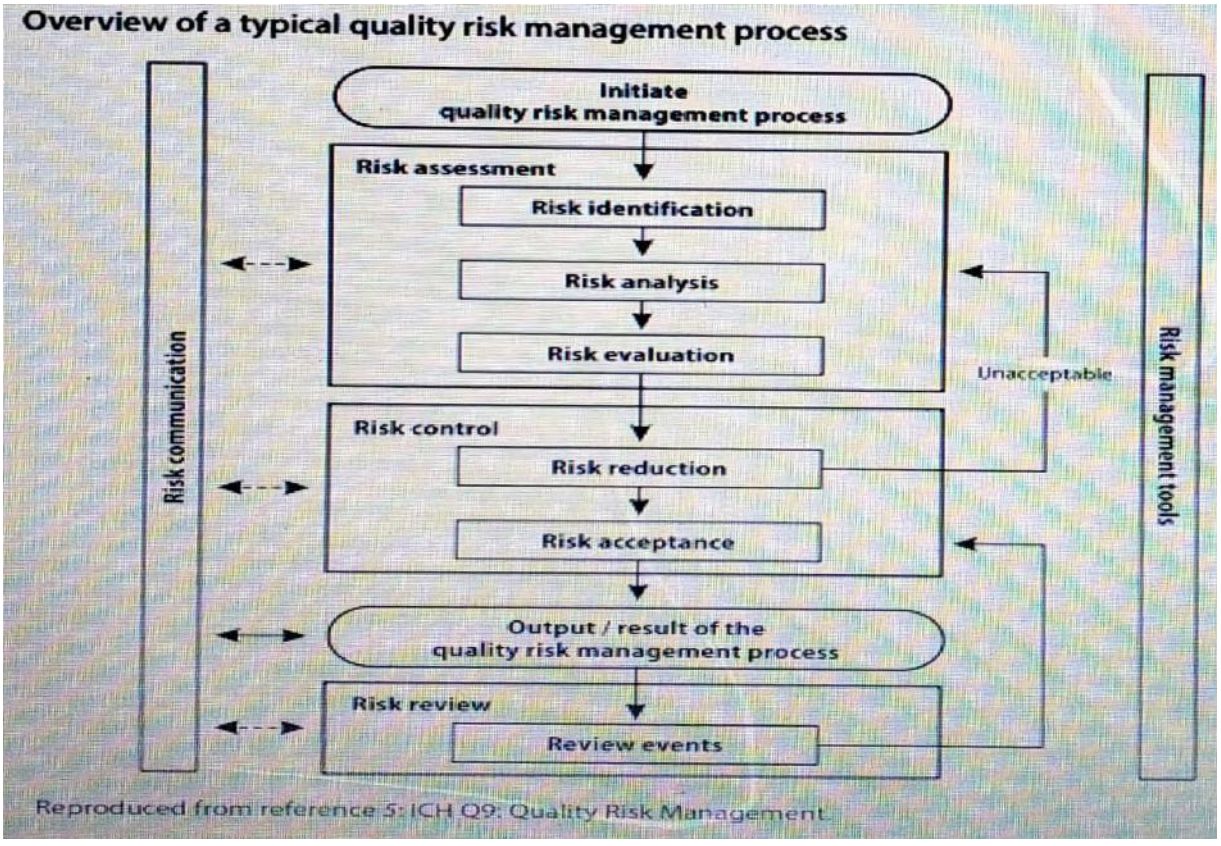
**1.** The evaluation of the risk to quality should be based on scientific knowledge and ultimately linked to the protection of the patient.

2. The level of effort, formality and documentation of the QRM process should be commensurate with the level of risk

**Quality risk management process:**

QRM activities should be performed using systematic processes designed to coordinate, facilitate and improve science-based decision-making with respect to risk. The possible steps to be taken in initiating and planning a QRM process might include the following:

1. Define the problem and/or risk question, including pertinent
2. Assumptions identifying the potential for risk;
3. Assemble background information and/or data on the potential hazard, harm or human health impact relevant to the risk assessment;
4. Identify a leader and the necessary resources;
5. Specify a timeline, the deliverables, and an appropriate level of decision-making for the risk management process




**Quality risk management Responsibilities**:

Quality risk management activities are usually, but not always, undertaken by interdisciplinary teams. When teams are formed, they should include experts from the appropriate areas (e.g., quality unit, business development, engineering, regulatory affairs, production operations, sales and marketing, legal, statistics and clinical) in addition to individuals who are knowledgeable about the quality risk management process.

**Scope of Quality risk management:**

This guideline provides principles and examples of tools for quality risk management that can be

applied to different aspects of pharmaceutical quality. These aspects include development, manufacturing, distribution, and the inspection and submission/review processes throughout the lifecycle of drug substances, drug (medicinal) products, biological and biotechnological products (including the use of raw materials, solvents, excipients, packaging and labeling materials in drug (medicinal) products, biological and biotechnological products).

**Transfer from R & D to production:**

The RU should be able to accommodate the intended production capacity. If possible, it should be established at the outset whether the intention is to perform single-batch manufacture, continuous production or campaigns. 5.2 Consideration should be given to the level and depth of detail to be transferred to support production and any further process development and optimization at the RU **(Receiving unit)** as intended under the transfer project plan. 5.3 Consideration should be given to the technical expertise, site technology and site capabilities for the RU. It should be identified upfront by the SU of any process robustness issues so that plans may be put in place at the RU. 5.4 The SU **(Sending unit)** and the RU should jointly develop a protocol for the transfer of relevant information related to the process under consideration from the SU to the RU, as well as the development of a comparable process at the RU.

**Process:** Each product needs to be transferred from R&D scale to commercial manufacturing scale. This requires precise project planning at an early stage, a competent project team. Including its qualitative and quantitative composition, physical description, method of manufacture, in-process controls, control method and specifications, packaging components and configurations, and any safety and handling consideration.

- Information on clinical development,
- Information on scale-up activities,
- Information or report on full-scale development activities,
- The change history and reasons,
- Information on investigations of problems and the outcomes of the investigations.

**Packaging:** The transfer of packaging operations should follow the same procedural patterns as those of the production transfer.

Information on packaging to be transferred from the SU to the RU includes specifications for a suitable container or closure system, as well as any relevant additional information on design, packing, processing or labeling requirements. For QC testing of packaging components, specifications should be provided for drawings, artwork and material (for example, glass, card or fibre board).

**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.

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
- Recovery studies to validate the sampling methodology.

**Active pharmaceutical ingredients (API):** The SU should provide the RU with the open (applicant's) part of the API masterful (APIMF or drug master file (DMF) or active substance master file (ASMF)), or equivalent information and any relevant additional information on the API of importance for the manufacture of the pharmaceutical product. The following are examples of the information which may typically be provided; however the information needed in each.

1. Manufacturer and associated supply chain;
2. Step of the API to be transferred;
3. Flow chart of synthesis pathway, outlining the process, including entry points for raw materials, critical steps, process controls and intermediates;
4. Where relevant, definitive physical form of the API (including photomicrographs and other relevant data) and any polymorphic and solvate forms;
5. solubility profile;
6. The input quantity of API for product manufacturing, providing example calculations; and special considerations with implications for storage and or handling

**Excipients:**

The excipients to be used have a potential impact on the final product. Their specifications and relevant functional characteristics should, therefore, be made available by the SU for transfer to the RU site. The following are examples of the information which may typically be provided; however, the information needed in each specific case should be using the principles of QRM:

- manufacturer and associated supply chain;
- description of functionality, with justification for inclusion of any antioxidant, preservative or any excipient;
- definitive form (particularly for solid and inhaled dosage forms);
- solubility profile (particularly for inhaled and transdermal dosage forms);
- partition coefficient, including the method of determination (for transdermal dosage forms);

**Finished pharmaceutical products:**

The SU should provide a detailed characterization of the product, including its qualitative and quantitative composition, physical description, method of manufacture, in-process controls, control method and specifications, packaging components and configurations, and any safety and handling considerations.

The SU should provide any information on the history of process development which may be required to enable the RU to perform any further development and or process optimization after successful transfer.

Such information may include the following:

- information on clinical development, e.g. information on the rationale for the synthesis, route and form selection, technology selection, equipment, clinical tests, and product composition;
- information on scale-up activities: process optimization, statistical optimization of critical process parameters, critical quality attributes, pilot report and or information on pilot-scale development activities indicating the number and disposition of batches manufactured;
- information or report on full-scale development activities, indicating the number and disposition of batches manufactured, and deviation and change control (sometimes referred to as change management) reports which led to the current manufacturing process;
- the change history and reasons, e.g. a change control log, indicating any changes to the process or primary packaging or analytical methods as a part of process optimization or improvement; and

**Premises and equipments:**

**Premises -** The SU should provide information on relevant health, safety and environmental issues, including:

- inherent risks of the manufacturing processes (e.g. reactive chemical hazards, exposure limits, fire and explosion risks);
- health and safety requirements to minimize operator exposure
- emergency planning considerations (e.g. in case of gas or dust release, spillage, fire)
- Identification of waste streams and provisions.

**Equipment:**

The SU should provide a list of equipment, makes and models involved in the manufacture, filling, packing and or control of the product, process or method to be transferred, together with existing qualification and validation documentation. Relevant documentation may include:

- drawings;
- manuals;
- maintenance logs;
- calibration logs; and

- Procedures (e.g. regarding equipment set-up, operation, cleaning, Maintenance, calibration and storage).

**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 the test of pharmaceutical products, starting materials, packaging components and cleaning (residue) samples.

A protocol defining the steps should be prepared for transfer of analytical methods. The analytical methods transfer protocol should include a description of the objective, scope and responsibilities. The materials and methods; the experimental design and acceptance criteria; documentation (including information to be supplied with the results, and report forms to be used, if any); procedure for the handling of deviations; references; signed approval; and details of reference samples.

1. provide method-specific training for analysts and other quality control staff, if required
2. assist in analysis of QC testing results;
3. provide details of the equipment used, as necessary
4. provide approved procedures used in testing; and
5. Review and approve transfer reports.

**References:**


1. ISPE Good practice guide. Technology transfer. Tampa, FL, International Society for Pharmaceutical Engineering, 2003.
2. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-second report. Geneva, World Health Organization, 2008 (WHO Technical Report Series, No. 948).