Unit - 1

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Definition of Quality

→ Quality can be defined as a product with zero defect or a product that meets customer satisfaction.

→ These definition are accepted as quality that refers to a degree of excellence.

IMP → 2 Marks

Definition and concept of Quality Control [QC]

→ Quality controls refers to sum of all procedure undertaken to ensure the identity and purity of a particular pharmaceutical product.

→ The testing of Pharmaceutical product involves chemical, physical and some time microbiological evaluation or test.

→ ISO 9000 define quality control as "A part of the quality management system focused on fulfilling quality requirement

→ It is that part of GMP which concerned with sampling, specification, testing and documentation and release procedure which ensure that necessary test are performed on product.

- Responsibilities of Quality Control ↓

1) It is responsible for day to day control of quality within the company.

2) It is responsible for analytical testing of incoming raw materia and inspection of packaging component.

3) Role in selection of qualified vendors from which raw material are purchased.

IMP
4) It inspect environmental area for manufacturing of dosage Forms.

5) It also test Finished product.

- Objective of Quality control ↓

1) To establish the desired quality standard which are acceptable to the customer and consumer.

2) To discover or finds Flaws and variation in the raw material and manufacturing process.

3) To improve quality and increase employee motivation.

4) It promote teamwork in group.

IMP → 2 Marks
Definition and concept of Quality Assurance (QA)

→ Quality assurance is process to become assure regarding the quality of any manufactured product.

→ In this process we compare the quality of finished product with it pre-design sample.

→ This is an important step for the satisfaction regarding quality.

→ ISO good define quality assurance as a part of quality management system focused on providing confidence that quality will be fulfilled.

- Responsibilities of Quality Assurance ↓

It
1) Ensuring proper warhousing practice.

2) It check the manufacturing process and batch record reviews.

3) It is responsible for making the master plan for the entire process.

4) It is responsible for stability testing and self life evaluation.

5) It is responsible for arrangement are made for the manufacturer, supply and use of correct starting and the packaging material.

- Objective of Quality Assurance ↓

1) To enhance the efficiency of product.

2) To assuring the quality of row material.

3) To assuring the quality of finished product.

4) To evaluate the plant environment.

IMP → 7 Marks ④

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Difference b/w Quality Control (QC) and Quality Assurance (QA)

	Quality Controls	Quality Assurance
1)	It aims to identify and fix the defects.	1) It aims to prevents the defects.
2)	It is a corrective technique.	2) It is a preventive technique.
3)	It ensure that standards are followed while working on the product	3) It define standard & procedure need to adhere in order to meet customer requirement.
4)	It helps implement the existing processes	4) It helps in building the processes
5)	The activities are performed after product is developed.	5) The activities are performed before product is developed.
6)	It is a corrective tools.	6) It is a managerial tools.
7)	It comes under the category of validation.	7) It comes under the category of verification.
8)	It is a product oriented exercise.	8) It is process oriented exercise.
9)	It is a time consuming activity.	9) It is not time consuming activity.
10)	It is done only after quality assurance.	10) It is done before quality control.

IMP → 2 Marks ⑤

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GMP - Good Manufacturing Practices.

→ GMP is the part of QA which ensure that the product are consistently produced and controlled according to quality standard for their intended use.

→ GMP is a set principle and procedure which whe Followed by manufacturer for the therapeutic goods a help to ensure that the product manufacture will have required quality.

→ GMP is designed to minimize the risks involved in any pharmaceutical production that can not be the eliminated through testing the Final product.

- Objective →

1) To reduce dependence of one another.
2) To reduce materials handling costs.
3) To obtain reasonable utilization of people & equipme
4) To maximize the customer service.
5) Longer Production runs and avoid stock out an the shortage.
6) Flexibility in production scheduling.

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• Principle → 1) It is clear defined and controlled process.

2) It has well documented procedure and risk management.

3) It controlled environment to prevent cross contamination.

4) It Follow written procedure and instruction.

5) It monitors the facilities and equipments.

6) It investigate the customer complaints.

IMP → 10 Marks, 7 Marks, 2 Marks.

TQM – Total Quality Management

→ TQM is a management approach in which quality is emphasized in every aspect of the business and the organisation.

→ Its goals are aimed at long term development of quality products and services.

Total – Made up of the whole
Quality – Degree of excellence a product or service provides
Management – Act, art or manner of planning, controlling and directing.

→ Therefore, TQM is the art of managing the whole to achieve excellence.

→ TQM is method by which management and employes can become involved in improvement of product and business.

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IMP

• Elements → The element can be divided into 4 groups according to their Function.

→ The groups are ↓

1) Foundation – It include – Ethics, Integrity and Trust

2) Building Bricks – It include – Traning, Teamwork and Leadersh

3) Binding Mortar – It include – Communication

4) Roof – It include – Recognition

(1) Foundation → TQM is built on a Foundation of ethics, integrity and trust.

→ These three elements moves together and offers the something different to TQM concept.

(a) Ethics → Ethics is the discipline concerned with good and bad in any situation.

→ Organizational ethics establish a business code of ethics that outline guideline that all employee are to adhere to in the performance of their work.

→ Individual ethic include personal rights or wrongs.

(b) Integrity → Integrity implies honesty, morals, values, fairness and adherence to the facts and sincerity.

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(c) Trust → Trust is a by product of integrity and ethical conduct.

→ Without trust, the Framework of T&M cannot be built.

→ Trust is essential to ensure customer satisfaction.

2) Building Bricks → These bricks are placed to reach the roof of recognition. It include are ↓

(a) Training → Training is very important for employees that give highly productive function within the team which help in solving problems, making decisan technical skills and improvements.

(b) Team work → Team work is important key element of T&M to become successful in business.

(c) Leadership → It is important key element of T&M to require the manager to provide an inspiring vision make strategic direction that are understood by all.

3) Binding Mortar → (a) Communication → communication means a common understanding of ideas b|w sender and receiver.

→ So communication binds everything together to form a foundation which is the roof of T&M.

4) Roof → (a) Recognition → Recognition is last and final element of T&M which provide suggestion of the

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achievement for team as well as individuals.

IMP

Philosophies of T&M → The philosophies of T&M are ↓

1) Dr. W. Edward Deming → He introduced satisfical quality control into industrial operation.

→ He define quality as being the direct result of quali design, quality of conformance and quality of sales and service function.

→ His beliefs were that quality management and improvement were the responsibility of all employe in a company.

→ He developed a set of 14 points. For management

2) Joseph M. Juran → Juran defined quality as being fitness for use and riably emphasized the cost of quality.

→ He developed his 10 points plans which is backbone of T&M implementation nowdays.

3) Armand V Feigenbaum → He believed that significant quality improvement could not be achieved by the participation of everyone in the organisation.

→ He believed that goals of quality improvement was to reduce the total cost of quality to as low percentage as possible.

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International Conference on Harmonization [ICH] Guideline

→ It is a joint association which involve industry & regulatory bodies together as equals partner in scientific and technical discussion of testing procedure which is required to ensure the quality, safety and the efficacy of medicine.

- Mission → 1) To make recommendation towards achieving greater harmonization.

2) To improve efficiency of new drug development and registeration process.

3) To promote public health and minimize the use of animal testing.

- Purpose →

1) Ensuring quality, safety and efficacy of drugs.

2) Harmonization of drug technical requirement.

3) Avoid duplication of human clinical trials.

4) Reduce use of the animal testing.

5) Safety of drugs.

- Participants →

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→ ICH is comprised from the 6 cosponsoring parties as well as three observer and IFPMA - International federation of Pharmaceutical Manufacture Association.

(1) Japan - MHW [Ministry of Health and Family welfare]

JPMA [Japan Pharmaceutical Manufacture Association]

(2) Europe - EC [European Commission]

~~EFPIA~~

EFPIA [European federation of Pharmaceutical Industries Association]

(3) USA - FDA [Food and Drug Administration]

~~EFPIA [European federation of Pharmaceutical~~

PhRMA [Pharmaceutical Research and Manufacture of America]

- Process → The harmonization activities of ICH may fall into one of 4 categories ↓

1) Formal ICH Procedure - New topic for harmonization.

2) Q and A Procedure - Clarification for an existing ICH guideline.

3) Revision Procedure - Adding new information to an existing ICH guideline.

4) Maintenance Procedure - Change to be made to maintain guideline.

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Brief overview of QSEM

→ The ICH guideline are covered under the acronym QSEM - Quality, Safety, Efficacy and Multidisciplinary.

① Quality guideline → These guideline covers the area of quality of drug product such as impurity testing and stability studies and a flexible approach to a Pharmaquality on the basis of GMP risk management.

② Safety guideline → They help to detect potential risks such as genotoxicity, carcinogenicity and reprotoxicity.

③ Efficacy Guideline → These guideline provide guidance about designing, conducting, safety aspects and reporting of clinical trials for pharmaceutical product.

④ Multidisciplinary guideline → These guideline also include details of [MedDRA], CTD and standard such as electronic standard for the transfer of Regulatory Information [ESTRI].

INP → 2 Marks

Quality [Q] - series guideline → Out of all these guideline, the one most relevant to us is the quality guideline.

→ The areas covered under this are labeled from Q1 to Q11 and deal with different aspect of quality assurance relating to pharmaceutical.

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	Guideline	Subpart	Area covered
①	Q1 Stability	Q1A	Stability testing of new drug products.
		Q1B	Photostability testing of new drug product
		Q1C	Stability test of dosage for
		Q1D	" " " "
		Q1E	Evaluation of stability data
		Q1F	Stability data package for registeration application
②	Q2		Validation of analytical procedure
③	Q3 Impurities	Q3A	Impurities in new drug substance
		Q3B	" " " " " product
		Q3C	Guideline for residual solvents
④	Q4 Pharmacopeial	Q4A	Pharmacopoeial harmonization
		Q4B	Evaluation and recommendation of pharmacopeial text for use in ICH guideline region
⑤	Q5 Quality of biotechnological product	Q5A	Viral safety evaluation of biotechnology product
		Q5B	Production of r-DNA
		Q5C	Stability test of biological product

(6)	Specification	Q6A	Test procedure of new drugs
		Q6B	" " " biological products
(7)		Q7	Good manufacturing practice
(8)		Q8	Pharmaceutical development
(9)		Q9	Quality risk management
(10)		Q10	Pharmaceutical quality system
(11)		Q11	Development & manufacture of drug substance

ICH Stability testing guideline

→ The ICH guideline for stability testing define what the information must be provided at the time of applying to register a new drug molecule.

→ Stability testing is important because drug product must be stable when administered to the patients.

→ Stability testing data must provide information about how the drug molecule changes over time under different storage conditions.

• Types of stability testing ↓

1) Real time testing → This involve testing drug product for a longer duration to find out what is the maximum product degradation when stored as recommended.

2) Accelerated stability testing → Here, product is subject to stress in the form of higher temperature, moistur agitation, light, pH and packaging condition.

3) Retained sample stability testing → This is testing of sample retained from each batch has been sent into the market.

4) Cyclic temperature stress testing → It involve the subjecting the product to temperature stress in wo to mimic likely market storage condition.

• Stability Testing Protocol ↓

1) Batch selection - how many batches to be tested.

2) Container & closure must be used for the testing.

3) Method to be used for testing and their validation.

4) Parameter to be tested to evaluate the product stability

5) Frequency of drawing sample for analysis.

6) The data obtained by performing stability studies is used for expiration dating of drug product and to determine its shelf life.

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- Overview of ICH stability Guideline contents ↓

→ Some of the area covered by ICH guideline on stability testing include ↓

(a) Stress testing → Study of degradation pathway, effect to change the temperature, relative humidity, PH change.

(b) Photostability testing → Study of effect of light on drug chemistry.

(c) Batch selection for stability testing → not less than 3 primary batches of drug substance.

(d) Testing of container closure system → 1 in 3months, 1yrs in 6 months, 2yrs in annually testing.

(e) Storage condition for the drug substance and product.

IMP → 5 MARKS

Quality by Design [QbD]

- Definition → Quality by design (QbD) is a defined as the a systemic approach to development that begins with predefined objective and emphasize product and process understanding and process control based on sound science of quality risk management.

→ QbD is a concept 1st edition or outline by Dr. Joseph M. Juran.

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→ QbD is describe in ICH guideline Q8, Q9 and Q10.

→ Juran explained that most of quality crises and issue i product is only due to lack of importance of produc during product planning.

- Objective → 1) To achieve the quality product.

2) To achieve positive performance testing.

3) To ensure combination of product and process, kno ledge gained during development.

- Benefits → 1) Better design of product with fewer proble

2) Eliminate batch failure.

3) Continuous improvement.

- Elements →

1) QTPP [Quality Target Product Profile] → QTPP is summar of quality characteristic of a drug that ideally wi be achieve to ensure the desired quality and efficacy drug product.

→ It is quality characteristics that a drug product should posses in order to give therapeutic effect.

→ It include identity, assay, dosage forms, purity stability.

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→ It forms basis for design of development of product.

2) Critical Quality Attribute [CQA] → A characteristics of a drug that when controlled within a defined limit of range it ensure the desired product quality.

→ It is a physical, chemical, biological or microbiological property of drug that should be within an appropriate limit range of distribution to ensure the desired quality.

→ It is used to describe the element of QTPP. (CMAs)

3) Critical Material Attribute → It is defined as physical, chemical, biological and microbiological property of raw material that need to be monitored to ensure the quality of product.

4) Process Parameter [PP] → This is any input operational parameter of a system or unit operation.

5) Design Space → A design space can be designed for single and multiple unit operation.

• Tools →

1) Screening → Its design are made to screen large number of factors by using less number of experiment to identify the significant one.

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→ The main purpose of these design is to identify main effect.

Ex- Fractional factorial design

2) Optimization → These design are only applied at once to a selected factor in formulation process.

→ The main purpose of these design is to identify main effect.

Ex- Full Fractional design

Imp → 4 Marks

(A) ISO 9000 → • Definition → ISO 9000 is family of standard that are related to the quality management system.

→ International Standard Organisation

ISO 9000 and ISO 14000

→ It is designed to help the organisation to ensure that they meet the need of customer and other stakeholder.

→ It helps a company to satisfy its customer, meet regulatory requirement and achieve continual improvement.

→ It provide base level of quality system, not a complete gurantee of quality.

• Benefits → 1) Quality is maintained.

2) opportunity to complete with large companies.

3) More time spent on customer focus.

4) May facilitate trade and increased market opportunities.

5) Increase customer confidence and satisfaction.

6) Confirmation that you company is committed to quality.

- Elements → 1) Management Responsibility 2) Quality System 3) Resource Management 4) Contract review 5) Design control 6) Document Control 7) Purchasing 8) Process control 9) Inspection & Testing 10) Corrective action 11) Quality records 12) Training 13) Servicing 14) Satistical Technique

- Steps for registeration →

Set the registeration objective
↓
Select the appropriate standard
↓
Develop and implement quality system
↓
Select a third party registar and apply
↓
Perform the self analysis audit
↓
Submit quality mannual for approval
↓

Pre-assessment by registar
↓
Take corrective actions
↓
Final assessment by registrar
↓
Registeration

(B) ISO 14000 → • Deffinition → ISO 14000 focus on environment thus encourage a clean, safter, heatheir world for us all.

→ They promise to improve environmental problem which in turn can facilitate trade of improve environmental performance world wide.

→ It comprises the international standard, technical reports and guide for environmental management by organization.

- Benefit → 1) Improving market access.
2) Adopting a process of continual improvement.
3) Improvement environmental performance.
4) Credibility with stakeholder
5) Improving cost control

- Elements → 1) Environmental Policy → Requirement to pursure this policy,

2) Planning → Analysis of all environment aspect of organisation.

3) Implementation and Operation → Implements all the plans.

4) Checking and corrective action → This action done by the monitoring the plan performance.

5) Management Review → It review by the organization top management to ensure its continuing the suitability, adequacy and effectiveness.

6) Continual improvement → The concept of continual improvement is a key component of environmental management.

- Steps for registeration → Same as ISO 9000;

10 Months ← IMP ← NABL accreditation → (मिलता)

- Definition → National accreditation Board for testing and calibration Laboratories [NABL] is a constituent beard of quality council of India.

→ It specifies the general requirement for the competence to carry out test and calibration including sampling.

→ It covers testing and calibration performed using standard method, non-standard method and laboratory developed method.

- Benefits → 1) national and International recognition.

2) Enhanced customer confidence and satisfaction.

3) Time and money efficient.

4) Increase quality management system.

5) Potential increase in business.

- Principle and Procedure ↓

1) Awarness Training → The separate training session for top management, middle and junior management.

2) Quality Policy and Objective → It workshop with top management on development of quality policy and and quality objective.

3) Gap Analysis → It understanding of all operation of organization and development of process map for activities of the organisation.

4) Documentation or Process design → It makes the proper formate and documentation.

5) Process Implementation → It involve the individual assistance in implementing the new process.

6) International Audit → It suggest preventive action for improvement in each audited department.

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7) Management review meeting → result of internal audit, result of customer complaints, result of feedback by customer.

8) Shadow Audit → It give an idea to employee about the conduct of final certification audit.

9) Corrective & Preventive action → On the basis of shadow audit conducted in last step, all the non conformities will be assigned corrective and preventive action.

10) Final certification Audit → After completing all stage of accrediation your organization will be awarded accreditation.

THANK // YOU //