



UNIT - II

Long Essay Questions:

Q) What are contents of NDA:

Ans:

A New Drug Application (NDA) is a comprehensive data that is submitted to the regulatory bodies such as USFDA for the approval to sell and market the new pharmaceutical product.

- The NDA contains detailed information about the drug safety, Efficacy, Manufacturing process, packaging and Labelling.

- NDA must provide all the relevant data and information that is collected during product's research and development.

The key contents of NDA includes:

1) Cover Letter:

It includes a brief information about the purpose and submission of the application to the regulatory authorities.

2) Index:

The NDA index is a overall comprehensive table of contents that helps to find the specific information in the document very quickly.

3) Summary of NDA:

- It includes an overall overview that provides the summary of entire NDA, including key elements, conclusions and recommendations.

- ❖ The Application Summary may include:
- pharmacological class, intended use, potency, clinical benefits
 - Chemistry, Manufacturing & Control Summary
 - Non-clinical pharmacology & toxicology summary
 - Human pharmacokinetics & Bioavailability Summary
 - Microbial Summary
 - clinical data Summary
 - Results of statistical analysis
 - Discussion of benefit/risk relationship

4) Chemistry, Manufacturing and Controls (CMC)

Information:

- It includes detailed information about the drug's composition, manufacturing process and quality control measures to ensure the safety, consistency and efficacy.

5) Non-clinical studies:

- It includes data from the pre-clinical studies conducted in animals
- It also includes data for evaluating the drug's safety profile, pharmacology and toxicology.
- It provides individual study reports including the drug-interactions

6) Clinical studies:

- It includes a comprehensive data from the clinical trials conducted in humans
- It gives overall profile including the adverse effects, side effects and potential risks



- It gives summary of effectiveness and Safety information.

- It also includes over-dosage information

7) Safety Data:

- It includes precautions, warnings, adverse effects and data on contra-indications demonstrating the safety and effectiveness

8) Efficacy Data:

- It includes the results from clinical trials demonstrating the drug's efficacy in treating the targeted condition (or) disease.

9) Proposed Labelling:

- Data on proposed labelling, including the prescribing information, dosage, and patient package insert and other relevant labelling components are included.

10) Pharmacovigilance plan:

- It is a plan that outlines how the applicant monitor and report any adverse events (or) safety concerns related to the drugs, once the drug is in the market

11) Environmental Impact:

- If the drug may have any potential environmental effects, including on disposal, packaging and other necessary precautions are included

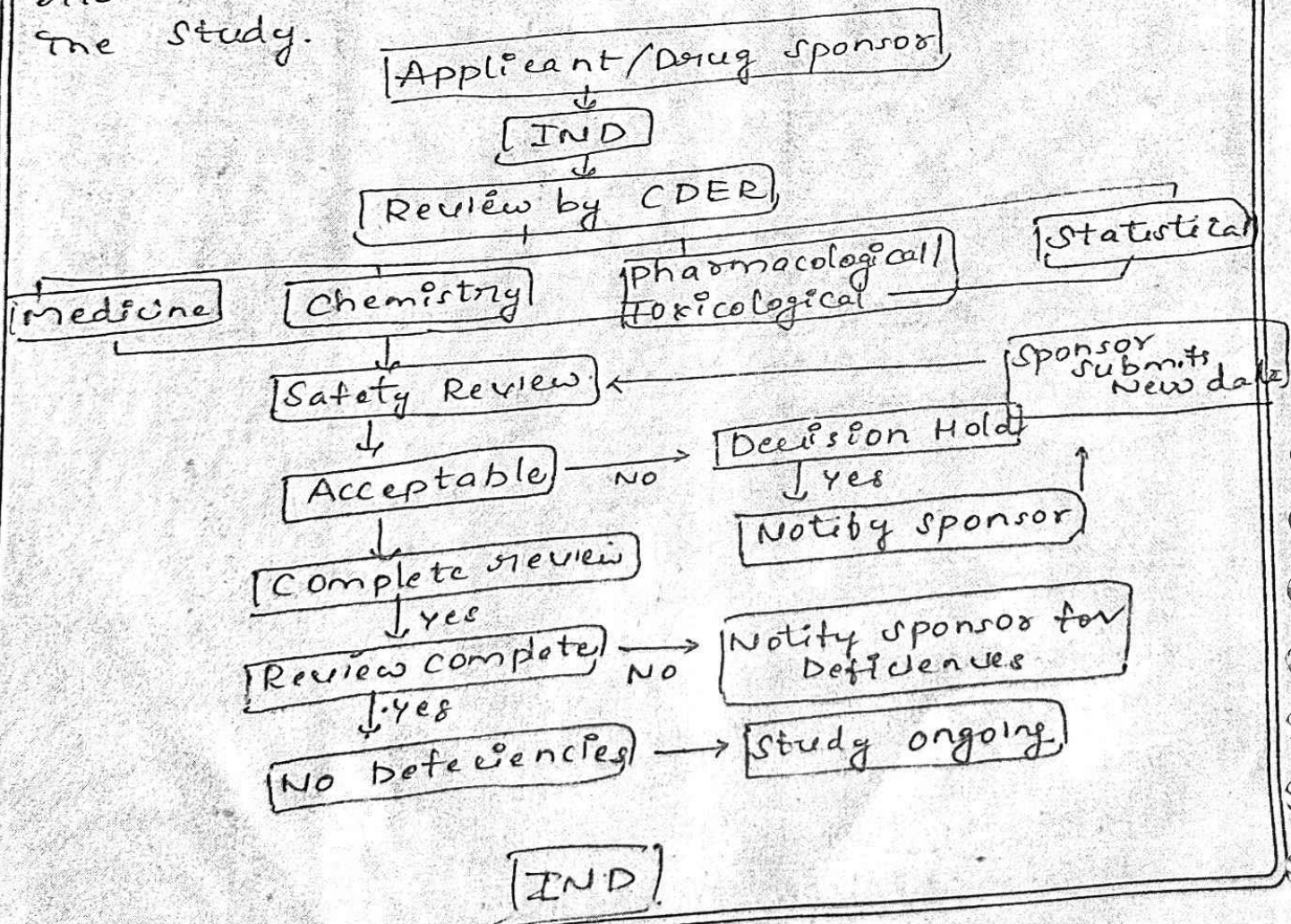
12) Payment of fees:

- Documentation of payment of required application fees.

2) Contents of IND:

IND: Investigational New Drug.

- An IND is a submission to the Food & Drug Administration (FDA) requesting permission to initiate a clinical study of new drug product.
- The IND application allows the company to initiate and conduct clinical studies for their new drug products.
- The IND application must provide FDA, the necessary data to decide whether the new drug and the proposed clinical trial pose risk to Human subjects participating in the study.





Contents

1) Introduction:

The Introduction section provides an overview of drug characteristics, including its chemical structure, properties and a brief summary of pre-clinical studies supporting the development of the drug.

2) Investigational Brochure:

- The IB contains a comprehensive information about the drug's candidate, including the pharmacology, toxicology and any available data from the prior clinical studies.

- It serves as a reference document for investigators involved in clinical trials.

3) Chemistry, Manufacturing & Controls:

- The CMC section focus on the drug's manufacturing process, quality control and stability.

- It includes details on the drug substance, drug product formulation, manufacturing facilities, analytical methods and specifications.

4) Non-clinical studies:

This section provides detailed information on non-clinical studies conducted to evaluate the drug's safety, pharmacology and toxicology.

- It includes data from in vitro studies, animal pharmacokinetics & toxicology studies.

5) Clinical Trial protocol;

- It includes the design, objectives and methodology of the proposed clinical trials.
- It includes details on study population, dosage, treatment duration, primary and secondary endpoints and statistical analysis.

6) Investigational plan:

- The Investigational plan describes the overall strategy for clinical development
- It includes proposed clinical trials, their phases, timelines etc.
- It includes details on patient selection, monitoring and safety assessment.

7) pharmacology & pharmacokinetics

- This section provides information on drug's pharmacological activity, mechanism of action and pharmacokinetic properties.
- It includes data from *in vitro* and *in vivo* studies, and drug-drug interactions.

8) Safety update:

- It includes information on adverse events observed in pre-clinical studies, previous clinical trials and any other relevant safety data.
- It also includes description of the safety monitoring for the proposed clinical trials.

9) proposed labelling;

- It includes outlines for usage, dosage and administration instructions, contraindications, warnings, precautions and potential Adverse Effects



10) Additional supporting Documents

- It may include additional supporting documents such as previous clinical trial data, published literature, patents and any other relevant information.

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3) Explain the submission of IND:

Ans. An Investigational New Drug (IND) application is a crucial step in the process of bringing a new drug (or) biological product to the market.

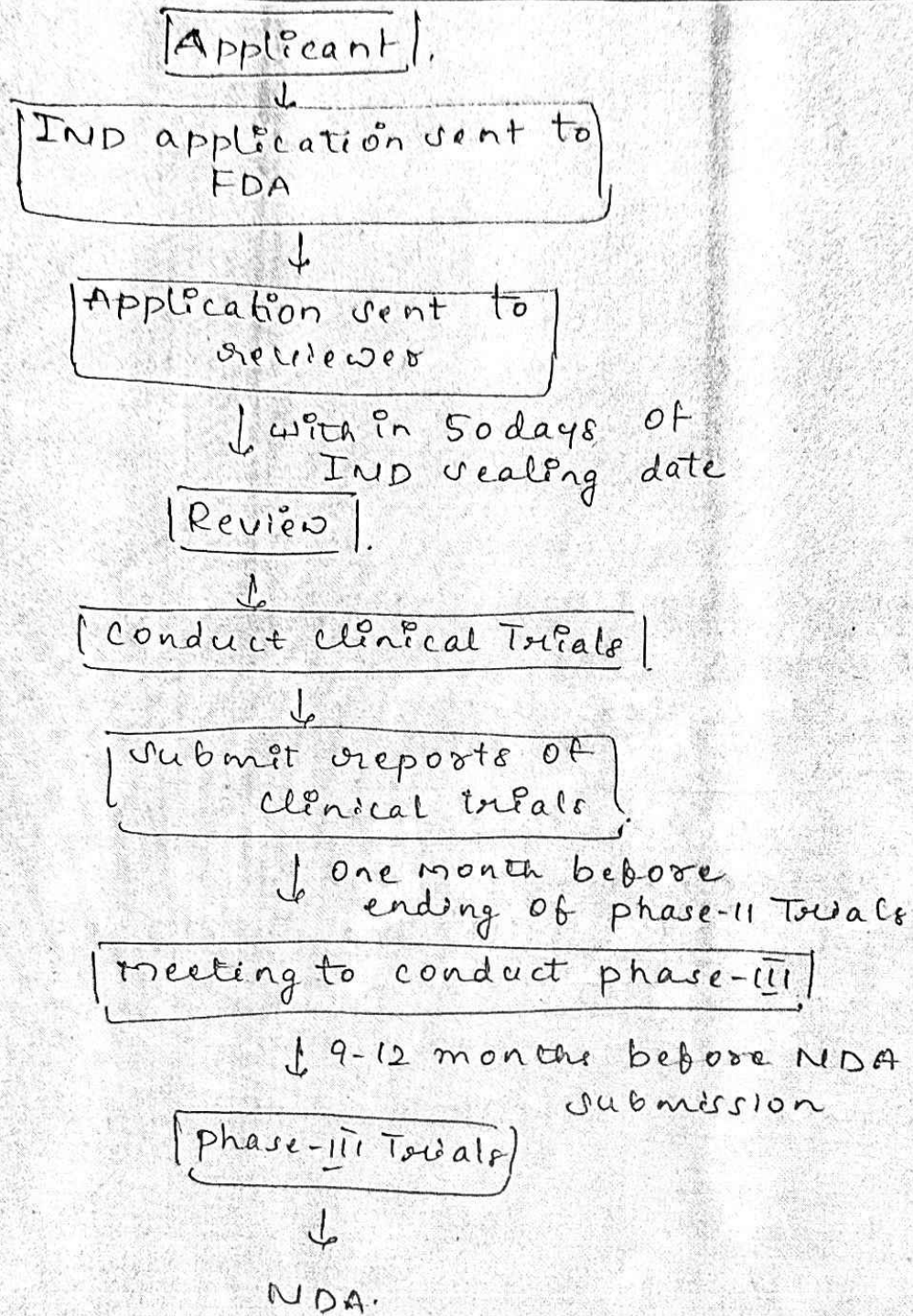
- It is a regulatory submission made to USFDA, seeking permission to conduct clinical trials with the investigational product in the human subjects.

- The submission and subsequent approval are necessary before starting the clinical trial.

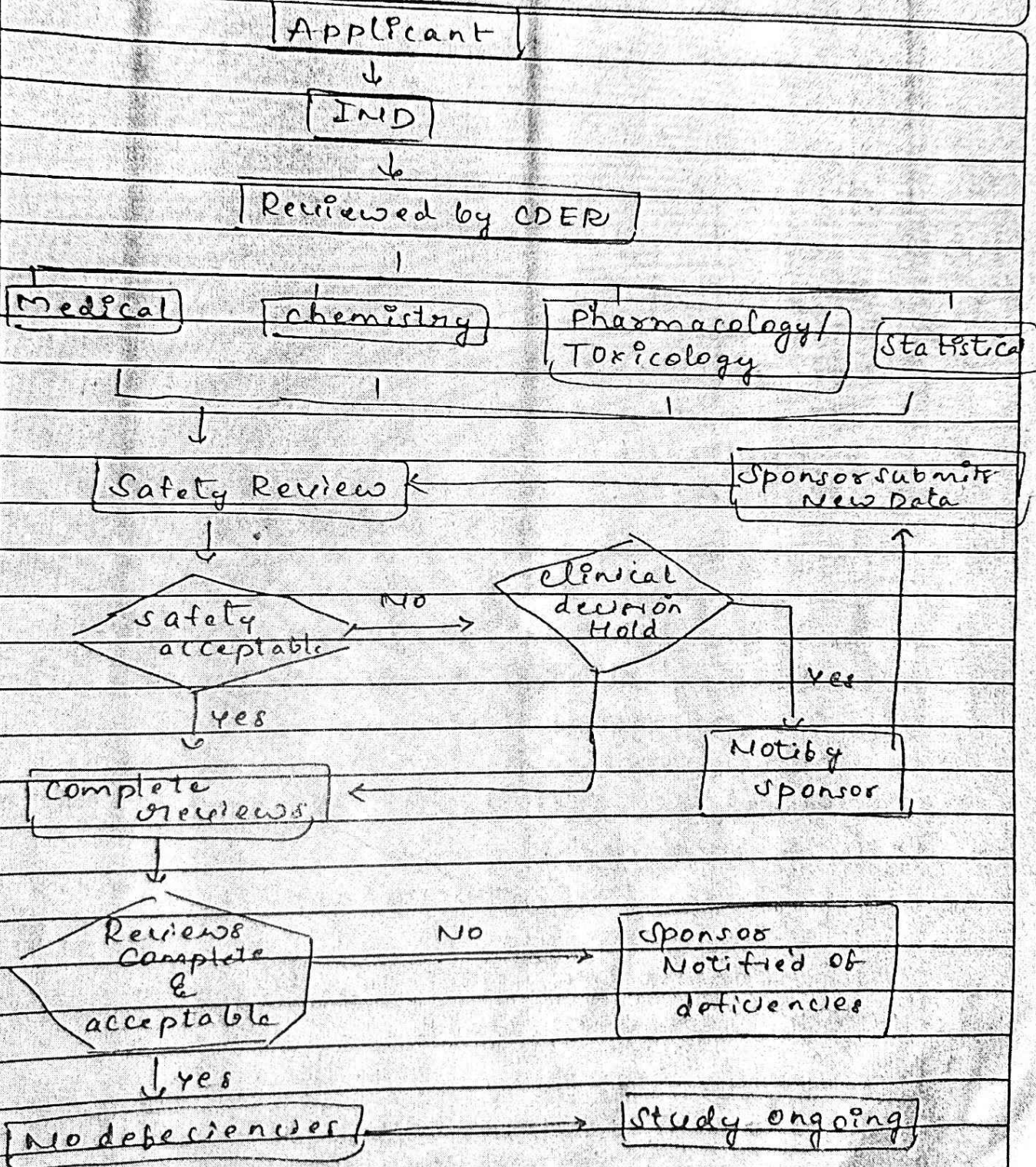
- Submission of IND is a very important step.

- It requires careful planning, documentation and acceptance with respect to the regulatory authorities.

- It includes pre-clinical data, manufacturing information and a detailed clinical development plan.



Drug Approval process



Submission process

1) Initial IND submission:

- The sponsor/Applicant submits the application to the appropriate regulatory authority such as FDA.

- The application is reviewed for completeness and acceptance with regulatory authorities

2) IND Review and Response:

- The regulatory authority reviews the submitted IND and provides feedback (or) requests for additional information within a specified time frame.

- The applicant must respond to any concerns/questions raised by the authority within 30 days

3) IND Approval:

- Once the regulatory authority is satisfied that IND meets the necessary requirements for conducting clinical trials, they have to issue an approval letter.

- The sponsor/applicant can proceed with the proposed clinical trials mentioned in IND.

4) IND Amendments:

- During IND, the sponsor/applicant need to submit amendments to address changes in the study design, protocol, safety information (or) other relevant data.

5) IND Safety Reporting:

The sponsor/applicant is responsible for monitoring and reporting any adverse events



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that arise during clinical trials.

- Timely reporting of safety information is crucial for ensuring the subject safety.

SHORT QUESTIONS

Q) Explain the contents of IB:

Ans) IB → Investigational Brochure.

- It is a document that contains summary of the Investigational product (IP) obtained during drug trial.

- It is a document that contains all the critical information through out the drug development process.

- It gives key aspects of safety measures of a clinical trial protocol such as

✓ Dose

✓ Mode of Action

✓ Method of Administration

✓ Safety monitoring procedures

Contents:

IB contains.

1) Cover page:

The title of the Investigational product and purpose of the study

2) Introduction:

- A brief Intro to the Investigational product and the medical condition it is used for.

3) Study overview:

- A description of clinical trial, including its phases, objectives and study design.

4) Study Inclusion and Exclusion criteria

- Details about the eligibility criteria for the participants enrolled in trial.

5) Benefits & risks:

- A thorough discussion of benefits and risks associated with the product.

6) Mechanism of Action:

- A clear description of how the investigational product works.

7) pre-clinical data:

- Info on the results of animal studies that support the human clinical trials.

8) clinical trial info

- Details about the ongoing clinical trials, number of subjects, estimated completion date.

9) patient responsibilities and Informed Consent

- Info about the rights and responsibilities of the subject.

Investigational Brochure

Investigational product: _____

Compound No: _____

Chemical/Genetic Name: _____

Trade Name _____

Effective Date: _____

Previous version No.	Effective Date



Specific requirements; Content & format of NDA

Requirements of NDA:

The requirements include:

1) Chemical & Pharmaceutical Information:

- Information of Active Ingredients
- Physicochemical Data
- Physical properties
- Analytical Data
- Dosage form and composition
- Stability Data

2) Pharmacology:

- Specific pharmacological actions
- Pharmacokinetics - ADME

3) Toxicology

- General aspects
- Systemic Toxicity studies
- Carcinogenicity
- Genotoxicity

4) Human/Clinical Pharmacology (Phase 1)

- Pharmacokinetics - ADME
- Pharmacodynamics - measurement of drug activity

5) Therapeutic Trials (Phase 2)

- Study reports

6) Therapeutic Confirmatory Trials (Phase 3)

- Individual study reports

7) Special Studies:

- Bioavailability, Bio-equivalence
- Geriatrics, pediatrics, pregnant women etc



Manufacturing control requirements of NDA

Ans: The Manufacturing control requirements of NDA are critical for ensuring the safety, quality and efficacy of the pharmaceutical product.

- while submitting the NDA, the pharmaceutical companies must have strict control over the manufacturing process of their drug products

Some key Manufacturing control requirements include:

1) CGMP:

- The NDA should provide a detailed information about the CGMP guidelines including documentation of SOP, batch records, equipment qualification, personnel training and records.

2) Manufacturing process description.

- A comprehensive description of manufacturing process should be included in NDA. This includes information on Raw materials, their specifications and steps involved in their production.

3) Process validation:

- process validation involves establishing documented evidence that a manufacturing process, consistently produces drug that meets pre-determined specifications

- Manufacturers must show that their manufacturing process are capable of producing drug meeting its specifications.

4) Quality Control & Quality Assurance

- Quality control & Quality assurance are vital for ensuring safety & Efficacy of drug
- Quality control involves testing of RM, IP and FP to ensure they meet the pre-determined criteria
- Quality assurance involves implementing the GMP.

5) Product Stability Testing

- It involves testing the drug's physical, chemical and microbial properties to determine the shelf life and storage conditions.
- Manufacturers must provide sufficient data to determine the drug's stability

The other aspects include

- ✓ Record keeping
- ✓ Handling of critical materials
- ✓ Risk Management
- ✓ Contamination
- ✓ Quality management system