B.PHARMA
7th SEMESTER

BP-702T

INDUSTRIAL PHARMACY-II

INDUSTRIAL PHARMACY-II MODEL PAPER

VERY SHORT ANSWERS TYPE QUESTIONS (10 × 2 = 20)

1. Define pilot plant.

Answer

- A pilot plant can also be defined as the pre-commercial production system which includes new production technology and produces small volumes of new technology-based products.

2. Describe platform technology.

Answer

- Platform technologies are systems that distribute the system out into different levels of abstraction. This is done in order to differentiate between core – platform – functions, and the application layer that sits on top of, and draws upon, these underlying common services.

3. Define confidentiality agreement.

Answer

- The aim of a confidentiality agreement is to protect all information of party entering negotiations. Before any concrete negotiations on the transfer of a technology can really start all parties involved must be able to evaluate the technology offered.

4. Discuss the practical aspects of Commercialization.

Answer

Technology transfer are discussed with certain practical studies.

Case Study 1

Factors considered in the proposed technology transfer (scale-up)

- Geometric Similarity: Ratio of all lengths constant (constant fill ratio)
- Dynamic Similarity: Maintenance of Forces (Froude number)
- Kinematic Similarity: Maintaining a consistent number or revolutions

Scale-up in QbD Approach: Blending

Scale	Amount (kg)	Blender Capacity	Blending Speed (rpm)	Blending Time (min)	Nrev	Volume FillRatio (%)
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: The desired content uniformity was attained by modifying the above parameters such as blending speed and blending time.

5. Explain Drug metabolism and Toxicology.

Answer

Drug Metabolism

- The drug metabolism studies needed to characterize the fate (whether the

compound is changed and to what) of a lead or drug candidate in the body. Metabolism studies carried out by both in-vitro and in-vivo methods.

Toxicology

- Toxicology defines the preclinical part of the safety assessment during drug development. By conducting toxicity studies, possible hazards and risks are identified.
  - Acute toxicity (Single dose) and Chronic toxicity (Repeated-dose) study
  - Reproductive toxicity study
  - Genotoxicity / Mutagenicity Study

6. Quote the responsibilities of Regulatory affairs professionals.

Answer

- Ensuring that their companies comply with all of the regulations and laws pertaining to their business.
- Working with federal, state and local regulatory agencies and personnel on specific issues related to their business.
- Advising companies on the regulatory aspects and climate that would affect their proposed activities.
- Keep in touch with international legislation, guidelines and customer practices. Keep up to the date with a company's product range.

7. Define ISO 14000.

Answer

- ISO 14001 is known as a generic management system standard, meaning that it is relevant to any organization seeking to improve and manage resources more effectively.

8. Write a short note on GLP.

Answer

Good Laboratory Practice

- GLP embodies a set of principles that provides a framework within which laboratory studies are planned performed, monitored, and archived and reported.

Purpose of GLPs:

- GLP is to certify that every step of the analysis is valid or Not.
- Assure the quality & integrity of data submitted to FDA in support of the safety of regulated products.
- GLPs have heavy emphasis on data recording, record & specimen retention.

9. Define CDSCO.

Answer

- Central Drugs Standard Control Organization (CDSCO) exercises regulatory control over the quality of drugs, cosmetics and notified medical devices in the country. The CDSCO of India is main regulatory body for regulation of pharmaceutical, medical devices and Clinical Trials.

10. Define certificate of Pharmaceutical Product.

Answer

- The WHO Certification Scheme for a Certificate of Pharmaceutical Product (COPP) is an international voluntary agreement to provide assurance to countries participating in the Scheme, about the quality of pharmaceutical products moving in international commerce.

SECTION B

LONG ANSWERS TYPE QUESTIONS (2 × 10 = 20)

1. What are SUPAC guidelines. Explain the SUPAC guidelines for immediate release dosage form.

Answer

SUPAC Guidelines

- SUPAC represents the changes recommended by the US FDA at the time of scale up or approval of NDA / ANDA.
- In the process of developing a new drug product, the batch sizes used in the earliest human studies are small and the size of the batches is gradually increased (Scale-up).
- The scale-up process and the changes made after approval in the composition, manufacturing process, manufacturing equipment, and change of site have become known as Scale-Up and Post approval Changes, or SUPAC.

The SUPAC Guidelines define

- The level of changes – Minor, Moderate and Major Changes.
- Test – Application test, *in vitro* dissolution and *in vivo*
- Filing – Annual report, changes being affected supplement and Prior Approval Supplement.
- The level of changes may impact on formulation and quality performance in following levels;
  - Level 1: unlikely to have detectable Impact.
  - Level 2: could have significant impact.
  - Level 3: likely to have significant impact.

SUPAC guidelines for immediate release dosage form

- These guidelines provide recommendations for post approval changes in;
  - The components or composition change,
  - The site of manufacture change,
  - The scale-up of manufacture change
  - The manufacturing (process and equipment) change.

A) The components or composition changes:

- This section focuses on changes in excipients in the drug product.
- SUPAC-MR - Excipient critical or non-critical to the Modified drug release.

- Changes in non-release and release controlling excipients.
- SUPAC-SS - Changes in preservative in semisolid formulations.
- SUPAC-IR Changes for immediate-release solid oral dosage forms.

B) The site changes of manufacture:

- Changes in the location of the site of manufacture, packaging operations and/or analytical testinglaboratory.
- Do not include any scale-up changes, changes in manufacturing (including process and/or equipment), or changes in components or composition.
- Current Good Manufacturing Practice (CGMP) inspection.

	Level I Changes	Level II Changes	Level III Changes
Classification	Single facility where the same equipment, standard operating procedures (SOP's), environmental conditions (e.g., Temperature and humidity) and controls, and personnel common.	Same continuous campus, Common personnel, No other changes.	Different campus, Different personnel.
Test documentation	Application/ compendia requirements in chemistry, dissolution and *in vivo* Bioequivalence - None.	○ Application / compendial requirements ○ Notification of Location of newsite ○ Updated batch records ○ SUPAC – MR - Multi-point dissolution profiles	○ Application/compendial requirements. ○ Notification of Location of new site. ○ Updated batch record. ○ SUPAC - IR: Multi-point dissolution profile in the application/compendial medium. ○ SUPAC - MR: Multi-point dissolution profiles (15, 30,

		(15,30,45, 60 and 120 min) USP buffer media at pH 4.5-7.5 forextended release). ○ Three different Media (e.g., Water, 0.1N HCl, and USP buffer media at pH 4.5 and 6.8 for delayed release) until 80% of Drug Released.	45, 60 and 120 min) USP buffer media at pH 4.5-7.5 for extended release). Three different Media (e.g., Water, 0.1N HCl, and USP buffer media at pH 4.5 and 6.8 for delayed release) until 80 % of Drug Released.
Filing documentation	Annual report.	Annual report.	Annual report prior approval of supplement.

C) Changes in Batch Size (Scale-Up/Scale-Down):

- Post-approval changes in the size of a batch from the pivotal/pilot scale bio batch material to larger or smaller production batches call for submission of additional information in the application.
- Scale-down below 100,000 dosage units is not covered by this guidance.

	Level I Changes	Level II Changes
Classification	Change in batch size, up to and including a factor of 10 times the size of thepilot/bio batch.	Changes in batch size beyond a factor of ten times the size of the pilot or bio batch,No other changes.
Test documentation	Updated batch records application/compendial requirements stability.	○ Chemistry Documentation

		Application/ compendial release requirements. Notification of change and submission of updated batch records. Stability testing: One batch with three months accelerated stability data and one batch on long-term stability. ○ Dissolution Documentation-Case B testing. ○ *In Vivo* Bioequivalence - None.
Filing documentation	Annual report (long term stability data).	Changes being effected supplement; annual report (long-term stabilitydata).

D) Manufacturing Changes:

- Manufacturing changes may affect both equipment used in the manufacturing process and theprocess itself.
- **Equipment**

	Level I Changes	Level II Changes
Classification	Alternate equipment of the same design and principles as automated equipment.	Change to equipment of different design and principle.
Test documentation	Updated batch records, Application/compendial requirements and stability.	Updated batch records, Application/compendial requirements and stability. SUPAC – IR - Multi-point dissolution profiles in multiple media. SUPAC – MR - Multi-point dissolution profiles in multiple media.
Filing documentation	Prior approval supplement with justification for change; annual report(long-term stability data).	Annual report and changes being Affected Supplement.

- **Process**

	Level I Changes	Level II Changes	Level III Changes
Classification	Alternate equipment of the same design and principles as automated equipment.	This category includes process changes including changes such as mixing timesand operating speeds outside of application/ validation ranges.	Changes in the type of process used (e.g. wet granulation to direct compression).
Test documentation	Updated batch records, Application/compendial requirements and stability.	Updated batch records, Application/compendial requirements and stability. ○ SUPAC - IR - Multi-point dissolution profile. ○ SUPAC- MR - Multi-point dissolution profiles in multiple media. ○ SUPAC – SS - *In vitro* release test Documentation .	Updated batch records, Application/compendial requirements, stability,bio-study and IVIVC. ○ SUPAC - IR - Multi-point dissolution profile. ○ SUPAC- MR - Multi-point dissolution profiles in multiple media.
Filing documentation	Annual report.	Changes being effected supplement; annual report (long term stabilitydata).	Prior approval supplement with justification; annual report (long-term stability data).

2. Outline Quality risk management. Discuss the various risk management tools and methodologies.

Answer

Quality Risk Management

Two primary principles of quality risk management are:

- The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and
- The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.
- Quality risk management is a systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle. A model for 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.

Various risk Management tools and Methodologies

Initiating a Quality Risk Management Process

Quality risk management should include systematic processes designed to coordinate, facilitate and improve science-based decision making with respect to risk. Possible steps used to initiateand plan a quality risk management process might include the following:

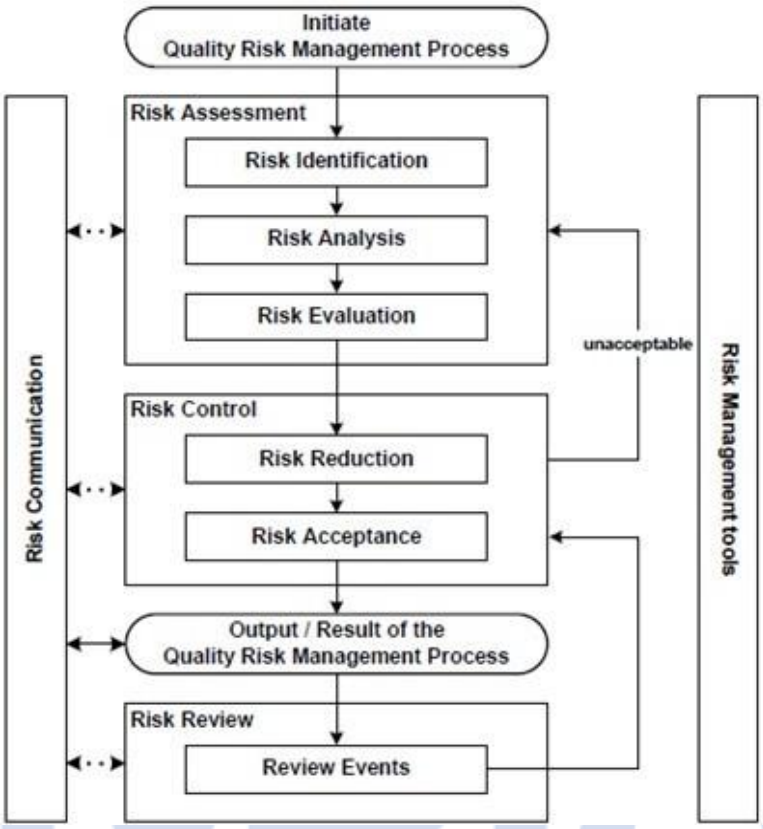
- Define the problem and/or risk question, including pertinent assumptions identifying thepotential for risk;
- Assemble background information and/ or data on the potential hazard, harm or humanhealth impact relevant to the risk assessment;
- Identify a leader and necessary resources;
- Specify a timeline, deliverables and appropriate level of decision making for the riskmanagement process.

Risk Assessment

- Risk assessment consists of the identification of hazards and the analysis and evaluation of risks associated with exposure to those hazards. Quality risk assessments begin with a well-defined problem description or risk question.
- Three fundamental questions are often helpful:
    - What might go wrong?
    - What is the likelihood (probability) it will go wrong?
    - What are the consequences (severity)?

Risk Identification

- It is a systematic use of information to identify hazards referring to the risk question or problem description. Information can include historical data, theoretical analysis, informed opinions, and the concerns of stakeholders.
- Risk identification addresses the "What might go wrong?" question, including identifying the possible consequences.



Risk analysis

- *Risk analysis* is the estimation of the risk associated with the identified hazards. It is thequalitative or quantitative process of linking the likelihood of occurrence and severity of harms.

Risk Evaluation

- It compares the identified and analyzed risk against given risk criteria. The output of a risk assessment is either a quantitative estimate of risk or a qualitative description of a range of risk.
- When risk is expressed quantitatively, a numerical probability is used.
- Alternatively, risk can be expressed using qualitative descriptors, such as "high", "medium", or "low", which should be defined in as

much detail as possible.

Risk Control

- Risk control includes decision making to reduce and/or accept risks. The purpose of risk control is to reduce the risk to an acceptable level. Risk control might focus on the following questions:
  - Is the risk above an acceptable level?
  - What can be done to reduce or eliminate risks?
  - What is the appropriate balance among benefits, risks and resources?
  - Are new risks introduced as a result of the identified risks being controlled?

Risk Reduction

- *Risk reduction* focuses on processes for mitigation or avoidance of quality risk when it exceeds a specified (acceptable) level.
- Risk reduction might include actions taken to mitigate the severity and probability of harm. Processes that improve the detectability of hazards and quality risks might also be used as part of a risk control strategy.

Risk communication

- *Risk communication* is the sharing of information about risk and risk management between the decision makers and others. Parties can communicate at any stage of the risk management process.
- The output/result of the quality risk management process should be appropriately communicated and documented.

Risk review

- A mechanism to review or monitor events should be implemented. The output/results of the risk management process should be reviewed to take into account new knowledge and experience.
- The frequency of any review should be based upon the level of risk. Risk review might include reconsideration of risk acceptance decisions.

Risk management methodology

- Quality risk management supports a scientific and practical approach to decision-making. It provides documented, transparent and reproducible methods to accomplish steps of the quality risk management process based on current

knowledge about assessing the probability, severity and sometimes detectability of the risk.

- The pharmaceutical industry and regulators can access and manage risk using recognized risk management tools and/or internal procedures (e.g., standard operating procedures). Below is a non-exhaustive list of some of these tools.
  - Basic risk management facilitation methods (flowcharts, check sheets etc.);
  - Failure Mode Effects Analysis (FMEA);
  - Failure Mode, Effects and Criticality Analysis (FMECA);
  - Fault Tree Analysis (FTA);
  - Hazard Analysis and Critical Control Points (HACCP);
  - Hazard Operability Analysis (HAZOP);
  - Preliminary Hazard Analysis (PHA);
  - Risk ranking and filtering;
  - Supporting statistical tools.

3. Explain

a. Total Quality management

Answer

- ***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.

Characteristics of TQM

- Committed management.
- Adopting and communicating about total quality management.
- Closer customer relations.
- Closer provider relations.
- Benchmarking.
- Increased training.
- Open organization
- Employee empowerment.
- Flexible production.
- Process improvements.
- Process measuring

Principles of TQM

1. Produce quality work the first time and every time.
2. Focus on the customer.
3. Have a strategic approach to improvement.
4. Improve continuously.
5. Encourage mutual respect and teamwork

The Key elements of the TQM

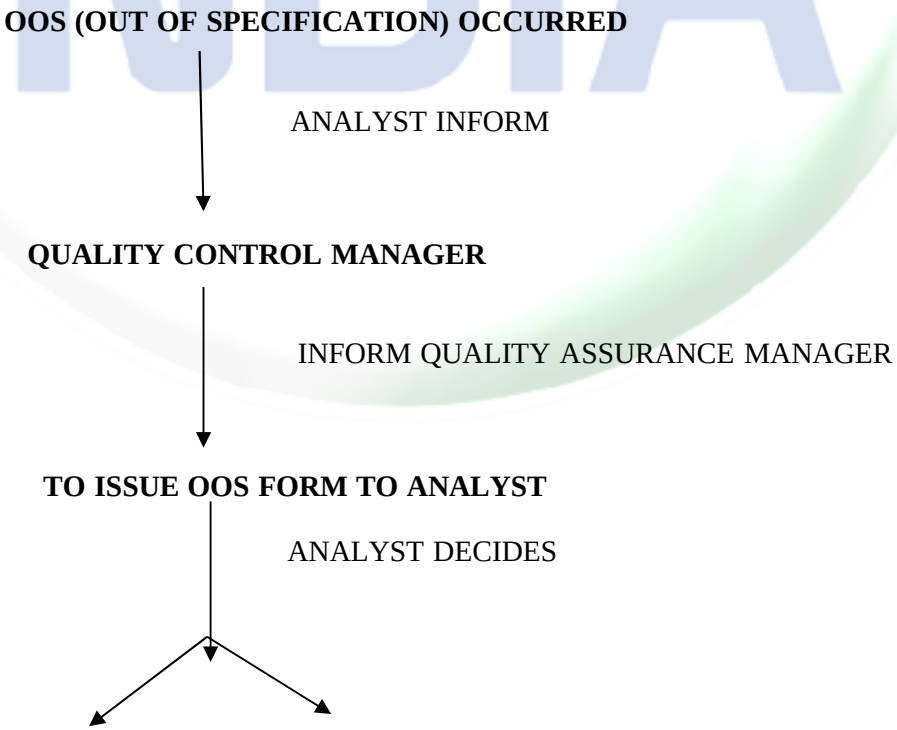
- Focus on the customer.
- Employee involvement
- Continuous improvement

b. Out of specification

Answer

- The term OOS (out of specification), is defined as those results of in process or finished product testing, which falling out of specified limits, that are mentioned in compendia,drug master file, or drug application.
- The OOS, may arise due to deviations in product manufacturing process, errors in testingprocedure, or due to malfunctioning of analytical equipment.
- The reasons for OOS can be classified as
  1. Assignable
  2. Non-Assignable.

Schematic Representation:



NON- ASSIGNABLE CAUSE ASSIGNABLE

CAUSE

c. Change control

Answer

- Change control is a systematic approach to managing all changes made to a product or system.
- The purpose is to ensure that no unnecessary changes are made, that all changes are documented, that services are not unnecessarily disrupted and that resources are used efficiently.

Procedure

- The initiating department shall initiate the change as per the change control format
- The initiating department shall furnish the details very clearly in the form for present process/use, proposed change, Justification & impact analysis and acceptance criteria.
- The initiating department shall also define changes as major or minor based on productquality or its impact of safety, health, and environmental aspects. Some of the major and minor changes are listed below:
- **Major Changes:**
  - For a substance of chemical and microbiological quality evaluation.
  - Addition or deletion of a step or addition of an alternative/new step in the formulationmanufacturing process.
- **Minor Changes:**
  - Change in the administrative references (name/company name, address) of thecertificate holder.
  - Change in the references (name/company name, address) of the manufacturing site.
  - Change or updating of the methods of analysis used to test the substance.

d. ISO 9000 series

Answer

- **ISO 9000:** Explains fundamental quality concepts and provides guidelines forthe selection and application of each standard.
- **ISO 9001:** Model for quality assurance in design, development, production,installation, and servicing.
- **ISO 9002:** Model for quality assurance in the production and installation ofmanufacturing systems.

- **ISO 9003:** Quality assurance in final inspection and testing.
- **ISO 9004:** Guidelines for the applications of standards in quality management andquality system.

SECTION C

SHORT ANSWERS TYPE QUESTIONS (5 × 7 = 35)

1. Describe the pilot plant scale-up considerations for solid dosage forms.

Answer

Pilot Plant Scale-up Consideration for Solid Dosage Forms

- The following points to be carefully consider during scaling up the solid dosage forms;
  - Batch size from intermediate to large scale production.
  - Each stage of operation.
  - Different types of equipment.
  - Use of sophisticated instruments with larger volume load.
  - Various sizes of equipment.

Material Handling:

- The handling of materials is quite different and necessary to handle carefully in medium andlarge-scale production from the laboratory scale (Mostly poured by hand or scooped).
- The characteristics of materials like density, size, shape and static charge must be taken intoconsideration while adopting the processing steps like;
  - Lifting and tilting of drums,
  - Vacuum loading system,
  - Screw feeding systems,
  - Metering pump systems.

Chemical Weighing:

- The incorrect ingredients and quantities may lead to cross contamination and misbrandedbrand during chemical weighing.
- A central weighing department should have for all the processing areas due to followingadvantages;
  - Centralization of responsibility,
  - Avoidance of duplicating weighing facility,
  - Lower labour cost.

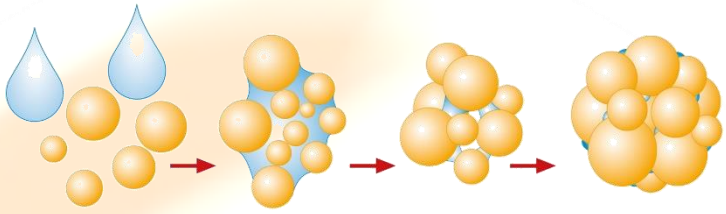
Tablet blending and Granulation:

Blending and Granulation:

- Powders to be used for encapsulation or to be granulated must be well blended to ensure gooddrug distribution.
- Inadequate blending at this stage could result in discrete portions of the

batch being eitherhigh or low in potency to avoid drug content variation.

- Steps should also be taken to ensure that all the ingredients are free of.
- The lumps and agglomerates can be removed by doing screening or milling of the ingredients should be done to avoid flow problems, non-reproducible compression and encapsulation process, to facilitate content uniformity of the product.
- In blending, segregation and mixing operation takes place which depends on particle size, shape, hardness and density.



Dry Blending and Direct Compression:

- Different blenders used in blending are V- blender, double cone blender, Ribbon blender, Slant cone blender, Bin blender, Orbiting screw blenders, vertical and horizontal high intensitymixers.
- The factors affect the optimization of blending operation of directly compressible materialsare;
  - The order of addition of components to the blender.
  - The mixing speed – Planetary type mixer, Tumbling Mixer, Cone Type Mixer.
  - The mixing time –It affects compressibility of Finished Material.
  - The use of auxiliary dispersion equipment with the mixer – Use chopper cell in Twin ShellMixer.
  - The mixing action – Determined by the Mechanics of the Mixer.
  - The blender loads Optimum working volume and normal working range.

Slugging (Dry Granulation):

- The dry powder cannot be compressed directly due to poor flow and compression properties.
- The slugging is done by using the Tablet Press of 15 tonnes.
- After compression, slugs are broken down by Hammer Mill with suitable particle sizedistribution.
- The granulation by dry compaction can also be achieved by passing powders between tworoller which put pressure of 10 Tonnes per linear inch.

Wet Granulation:

- The most common reasons given to justify granulating are;

- To impart good flow properties to the material,
- To increase the apparent density of the powders,
- To change the particle size distribution,
- Uniform dispersion of active ingredients.

➢ Traditionally, wet granulation has been carried out using Sigma blade mixer and Heavy-duty planetary mixer.

Drying:

➢ The most common conventional method of drying a granulation continues to be thecirculating hot air oven, which is heated by either steam or electricity.

➢ The important factors to consider as part of scale-up of an oven drying operation are airflow,air temperature, and the depth of the granulation on the trays.

➢ If the granulation bed is too deep or too dense, the drying process will be inefficient, and if Drying times at specified temperatures and airflow rates must be established for each product,and for each particular oven load.

➢ Fluidized bed dryers are an attractive alternative to the circulating hot air ovens.

Reduction of Particle size:

➢ Compression factors that may be affected by the particle size distribution are flowability, compressibility, uniformity of tablet weight, content uniformity, tablet hardness, and tablet color uniformity.

➢ First step in this process is to determine the particle size distribution of granulation using a series of “stacked” sieves of decreasing mesh openings.

➢ Particle size reduction of the dried granulation of production size batches can be carried out by passing all the material through an oscillating granulator, a hammer mill, a mechanical sieving device, or in some cases, a screening device.

Facilities:

➢ To avoid cross contamination in scale up and to facilitate the cleaning of equipmenteffectively, following facilities must be available that are;

- Presence of separate room with availability of more space,

- Must have granulation as unit operation,
- Must have washing and drainage facilities,

Granulation Handling and Feed System:

- The handling of the finished granulation in the compression area is either by Hand scooping for small scale or by sophisticated automated handling system with vacuum or mechanical system for large scale.
- The properties of material like size, size distribution and flow property affects the tablet properties like drug content uniformity, tablet weight, thickness and hardness.

Tablet Compression:

- The tablet press performs following functions during the compression are;

  - Filling of an empty die cavity with granulation.
  - Pre-compression of granulation.
  - Compression of granules.
  - Ejection of the tablet from the die cavity and take-off of the compressed tablet.
- The prolonged trial runs at press speeds is generally adopted to find out the potential compression problems like sticking to the punch surface, tablet hardness, capping, and weightvariation detected.
- High-speed tablet compression depends on the ability of the press to interact with granulation.

Tablet Coating:

- Many changes in Sugar coating (Carried in conventional coating pans), due to new developments in coating technology (Conventional sugar-coating pan changed to perforated pans or fluidized-bed coating columns), changes in safety and environmental regulations.

- The development of new polymeric materials has resulted in a change from aqueous sugar coating to aqueous film coating.
- The tablets must be sufficiently hard to withstand the tumbling to which they are subjected in either the coating pan or the coating column.

2. Discuss the significance of space requirements and raw materials in pilot plant set up.

Answer

Significance of Space requirements and raw materials in pilot plant set up

Space Requirements

The space required in pilot plant is divided into 4 areas that are as follows;

- **Administration and information area:**
  - Adequate office and desk space should be provided for both scientists and technicians.
  - The space should be adjacent to the working area.
- **Physical testing area:**
  - This area should provide permanent bench top space for routinely used physical- testingequipment.
- **Standard equipment and floor space:**
  - The sufficient specified space must be there for free installation, operation and easymaintenance of the equipment.
- **Storage area:**
  - Storage area for in process materials, finished bulk products, retained samples, experimental production batches, packaging materials (segregated into approved and unapproved areas).
  - Controlled environment space allocated for storage of stability samples.
  - Separate provisions for API and excipients further segregated into approved andunapproved areas according to GMP.

Raw Materials

- One major responsibility of a Pilot plant is the approval and validation of active and excipientraw materials used in the pharmaceutical products.
- This is because the raw materials used during the small-scale formulation trials may not be representative of the large volume shipment of material due to change in raw materials properties like particle size, shape,

morphology, bulk density, static charges, rate of solubility,flow property and colour.

- An alternative supplier must be arranged as stand by basis which must validate the batches formanufactured products.

3. Explain various technology transfer agencies in India.

Answer

Technology Transfer Agencies in India

Asian and Pacific Centre for Transfer of Technology (APCTT)

- It is a United Nations Regional Institution under the Economic and Social Commission for Asia and the Pacific (ESCAP) established in 1977 in Bangalore, India.

- In 1993, the Centre moved to New Delhi, India. APCTT promotes transfer of technology to and from small- and medium-scale enterprises (SMEs) in Asia and the Pacific.
- APCTT implements development projects funded by international donors aimed at strengthening the environment for technology transfer among SMEs.
- The objective of APCTT is to strengthen the technology transfer capabilities in the region and to facilitate import/export of environmentally sound technologies to/from the member countries.

National Research Development Corporation (NRDC)

- National Research Development Corporation (NRDC) was established in 1953 by the Government of India, with the primary objective to promote, develop and commercialise the technologies / know-how / inventions / patents / processes emanating from various national R&D institutions / Universities and is presently working under the administrative control of the Dept.of Scientific & Industrial Research, Ministry of Science & Technology.
- During the past six decade of its existence and in pursuance of its corporate goals, NRDC has forged strong links with the scientific and industrial community in India and abroad. It is recognized as a large repository of wide range of technologies spread over almost all areas of industries, viz.

NATIONAL RESEARCH DEVELOPMENT CORPORATION
नेशनल रिसर्च डिवेलपमेंट कारपोरेशन
(An Enterprise of DSIR)
Ministry of Science and Technology, Govt. Of India
Facilitating Technology Transfer Since 1953

Technology information, Forecasting and assessment Council (TIFAC)

- TIFAC is an autonomous organization set up in 1988 under the Department of Science & Technology to look ahead in technology domain, assess the technology trajectories, and support innovation by networked actions in selected areas of national importance TIFAC embarked upon the major task of formulating a Technology Vision for the country in various emerging technology areas.

TIFAC
Technology Information, Forecasting and Assessment Council

- Under the leadership of Dr. APJ Abdul Kalam, Technology Vision 2020 exercise led to set of 17 documents, including sixteen technology areas and one on services. In more than 25 years of its service to the nation, it has delivered number of technology assessment and foresight reports. While inaugurating the 103rd Indian Science Congress in Mysuru, Hon'ble Prime Minister of India Shri Narendra Modi released the Technology Vision 2035 prepared by TIFAC.This is being followed by release of Technology Roadmaps in 12 thematic areas of national priorities and importance.

Biotech Consortium India Limited (BCIL)

- Biotech Consortium India Limited (BCIL), New Delhi was incorporated as public limited company in 1990 under The Companies Act, 1956.

BCIL

- The consortium is promoted by the Department of Biotechnology, Government of India and financed by the All India Financial Institutions and some corporate sectors BCIL 's major functions include the development and transfer of technology for the commercialisation of biotechnology products, project consultancy, biosafety awareness and human resource development BCIL has been successfully managing several Flagship schemes and Programmes of the

Department of Biotechnology, Government of India.

- Most notable include Biotechnology Industry Partnership Programme, Biotechnology Industrial Training Programme and Small Business Innovation Research Initiative.

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

- The Technology Bureau for Small Enterprises (TBSE) is a platform for MSMEs to tap opportunities at the global level for the acquisition of technology or establishing business collaboration. TBSE is a result of the cooperative initiative of the United Nations' Asian and Pacific Centre for Transfer of Technology (APCTT) and Small Industries Development Bank of India (SIDBI) in 1995.
- TBSE also receives partial funding from the Office of DC (SSI), Government of India. Features of TBSE Offering a professionally managed system for the reasons of technology and collaboration exploration helping in the building up of confidence between potential partner. It providing an opportunity to global technology market through the process of networking.
- Taking up project appraisal and the preparation of a business plan. The new technologies for the reason of transfer are sourced from countries namely China, Philippines, South Korea, Australia, Germany, as well as the U.S.

4. Outline validation and qualification. Write a short note on Analytical Method Transfer.

Answer

Validation and Qualification

- Qualification and validation of facilities, equipment, systems and procedures are essential to demonstrate that all critical stages of the transfer project have been completed successfully, enabling the RU to reproduce the product, process or method routinely to the specifications agreed with the SU.
- Validation performed as part of the transfer project should be documented in a validation master plan (VMP). The VMP should identify the stages which need to be validated and define acceptance criteria.
- For intra-company transfers, the RU should operate under the same VMP as the SU. For inter- company transfers, a VMP should be in place at the RU before the transfer.
- The RU should prepare a validation protocol (VP) for each sequential step. Successful execution of each VP should be documented in a validation report (VR).

- Setting up and commissioning of systems at the RU need to be completed before qualificationand validation can be performed at the RU. The steps required for this purpose have been described in this guideline for buildings, services and equipment, manufacturing, packaging and cleaning and analytical testing. In brief, the following basic steps apply equally to each of these areas:
    - the SU should provide information on materials, systems and procedures involved in the manufacturing of the product, process or method to be transferred;
    - The RU should review the information provided by the SU, and audit its current systems, equipment and processes, including non-process related practices and support services that impact the process;
- Once the required systems and procedures have been commissioned at the RU, and successful training has been documented, qualification and validation of facility and equipment should be executed, followed by validation of analytical test methods, process validation for manufacturing and packaging, and cleaning validation.
- The RU should review the gap analysis and prepare, where appropriate, VPs for the facility, services and equipment.

Analytical Method Transfer

The analytical methods transfer protocol should cover the following sections:

- objective;
- scope;
- responsibilities of the SU and the RU;
- materials, methods and equipment;
- the experimental design and acceptance criteria;
- documentation (including information to be supplied with the results, and report forms tobe used if any);
- deviations;
- references;
- signed approval; and
- details of reference samples (APIs, intermediates and finished products). Successful transfer and validation of analytical methods should be documented in a report.

5. Summarize Investigational Brochure. What do you understand by IND.

Answer

Investigational Brochure

- The Investigator's Brochure (IB) is an important document, not only required as a part of the IND but also prepared for presentation to potential clinical investigators and ultimately for presentation to the investigator's IRB (Institutional Review Board or Independent Review Board).

- The IB is a compilation of the clinical and nonclinical data on the investigational product that is relevant to the study of the product in human subjects.
- Its purpose is to provide the investigators and others involved in the trial with information to facilitate their understanding of the rationale for, and their compliance with, many key features of the protocol, such as the dose, dose frequency/interval, methods of administration, and safety monitoring procedures.
- The IB should be reviewed at least annually and revised as necessary in compliance with a sponsor's writtenprocedures.
- Generally, the sponsor is responsible for ensuring that an up-to-date IB is made available to the investigator(s), and the investigators are responsible for providing the upto- date IB to the responsible IRBs.
- The following provides the information that should be included in the IB –

1. **Title Page -** This should provide the sponsor's name, the identity of each investigational product (i.e., research number, chemical or approved generic name, and trade name(s) where legally permissible and desired by the sponsor), and the release date. It is also suggested that an edition number and a reference to thenumber and date of the edition it supersedes be provided.

   TITLE PAGE OF INVESTIGATOR'S BROCHURE (Example)

   - Sponsor's Name: Product: Research Number: Name(s): Chemical, Generic (if approved)
   - Trade Name(s) (if legally permissible and desired by the sponsor) Edition Number:
   - Release Date:
   - Replaces Previous Edition Number:
   - Date:

2. **Confidentiality Statement -** The sponsor may wish to include a statement instructing the investigator/ recipients to treat the IB as a confidential document for the sole information and use of the investigator's teamand the IRB/IEC.
3. **Contents of the Investigator's Brochure -** The IB should contain the following sections, each with literature references where appropriate:
   1. Table of Contents
   2. Summary
   3. Introduction
   4. Physical, Chemical, and Pharmaceutical Properties and Formulation
   5. **Nonclinical Studies**
      a. Nonclinical Pharmacology
      b. Pharmacokinetics and Product Metabolism in Animals
      c. Toxicology
   6. **Effects in Humans**

a. Pharmacokinetics and Product Metabolism in Humans
b. Safety and Efficacy
c. Marketing Experience

7. Summary of Data and Guidance for the Investigator
8. Publications
9. Reports (these references should be found at the end of each chapter.) and Appendices (if any)

Investigational New Drug (IND)

- After the successful completion of preclinical research, Drug developer or sponsor, must submit an Investigational New Drug (IND) application to respective regulatory authority such as FDA in US,CDSCO in India etc in order to start clinical research.
- The IND filing is the formal process by which a sponsor requests approval for testing of a drug inhuman subjects.
- In the IND application, following things are must include:
  - Animal study data and toxicity data
  - Manufacturing information
  - Clinical protocols (study plans) for studies to be conducted
  - Data from any prior human research
  - Information about the investigator
  - Any additional data
- After submitting IND, respective regulatory authority reviewed all the data and if satisfied, they grant the sponsor to begin clinical trial. It will take 30 -60 days after IND submission to get approval for clinical trialfrom the FDA.

6. Describe Six sigma concepts.

Answer

- Six Sigma seeks to improve the quality of process outputs by identifying and removing the causes of defects. Six Sigma approach is a collection of managerial and statistical deficiencies in product. The concept of Variation states "NO two items will be perfectly identical.
- In a process that has achieved six sigma capability, the variation is small compared to the range of specification limit.
- A six-sigma process is one in which 99.9999966% of the products manufactured are statistically expected to be free of defects (3.4 defects per million).
- Six Sigma is a very clever way of branding and packaging many aspects of Total Quality Management (TQM). (TQM is a management approach to long–term success through customer satisfaction.)

INDUSTRIAL PHARMACY-II MODEL PAPER

The Characteristics of Six Sigma:

- **Statistical Quality Control**: Six sigma is clearly derived from Greek letter sigma which is used to denote standard deviation in statistics which is used to measure nonconformance as far quality output is concerned.
- **Methodical Approach:** The six sigma is not merely quality improvement strategy in the theory as it features a well-defined methodical approach of application in DMAIC and DMADV which can be used for quality production.
- **Fact and Data Based Approach:** The statistical and methodical aspects of Six Sigma show the scientific basis of the technique. This accentuates an important aspect of Six Sigma that it is fact and data based.
- **Project and Objective Based Focus:** The Six Sigma process is implemented for an organization's project tailored to its specifications and requirement. The process is flexedto suit the requirements and conditions in which a project is operating to get the best results. Apart from that, the Six Sigma is also objective based. The management needs some incentive to invest in the Six Sigma process. It is aimed to enhance profitability and to generate financial.
- **The Customer Focus:** The customer focus is fundamental to the Six Sigma approach.The quality improvement and control standards are based on the explicit customer requirements.
- **Teamwork Approach to Quality Management:** The Six Sigma process requiresorganizations to get organized when it comes to controlling and improving quality. Six Sigma involves a lot of training depending on the role of an individual in the Quality Management team.

Six Sigma Objectives:

- **Overall Business Improvement:** Six Sigma methodology focuses on business improvement. Beyond reducing the number of defects present in any given number of products.
- **Remedy Defects/Variability:** Any business seeking improved numbers

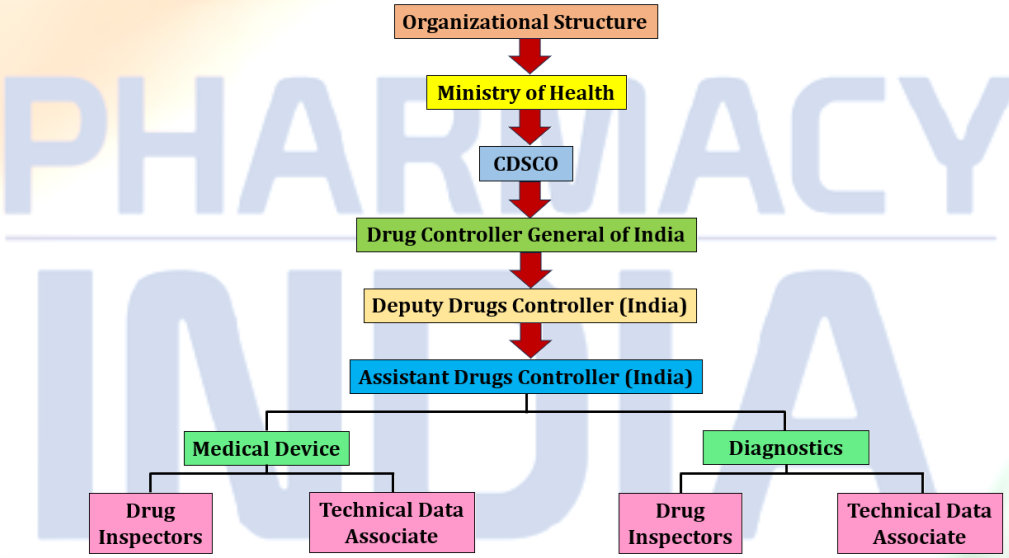
must reduce the number of defective products or services it produces. Defective products can harm customer satisfaction levels.

- **Reduce Costs:** Reduced costs equal increased profits. A company implementing Six Sigma principles must look to reduce costs wherever it possibly can--without reducing quality.
- **Improve Cycle Time:** Any reduction in the amount of time it takes to produce a product or perform a service means money saved, both in maintenance costs and personnel wages.
- **Increase Customer Satisfaction:** Customer satisfaction depends upon successful resolution of all Six Sigma's other objectives. But customer satisfaction is an objective all its own.

7. Explain the organization structure and responsibilities of CDSCO.

Answer

Organization Structure of CDSCO



Responsibilities of CDSCO

- CDSCO: For implementing and to revise the same as notified, from time to time by theauthority.
- Initiate in framing of rules, regulations and guidance documents to match the contemporaryissues in compliance with the requirements of Drugs & Cosmetics Act 1940 and Rules 1945.
- Facilitate in Uniform implementation of the provisions of the Drugs & Cosmetics Act 1940and Rules 1945.
- Function as Central license Approving Authority under the provisions of Drugs andCosmetics Act 1940 and Rules 1945.
- Collaboration with other similar International agencies. • Providing training to the Indianregulatory personnel.
- Approval of New Drugs

- Clinical Trials in the country
- Laying down the standards for Drugs
- Control over the quality of imported Drugs
- Coordination of the activities of State Drug CO
- Providing expert advice with a view of bringing about the uniformity in the enforcement ofthe Drugs and Cosmetics Act