19/4/24

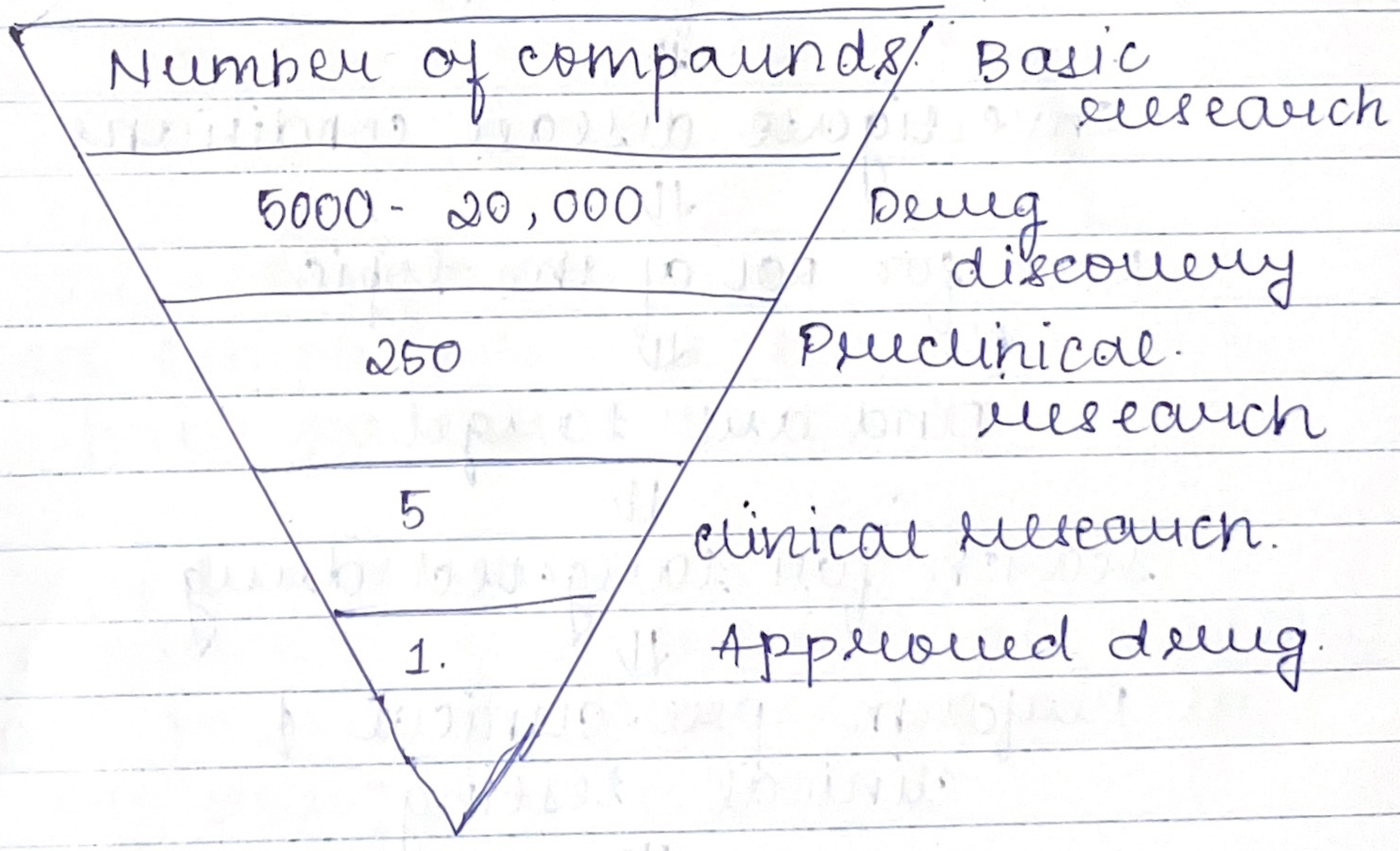
Clinical research.

Q1.(a) Draw flow chart of drug development process. Discuss advantage and disadvantages of micro. dosing trial.

⇒ It is defined as a series of well defined steps for a drug of new, safe. and effective t/t to increase health & quality of life.

Drugs are perhaps, the most important concern to research based pharmaceutical industry.

The pyramid shows the steps of DD:



The steps involved in drug discovery are:

(A) Basic research
(B) New drug discovery
(C) Screening
(D) Preclinical study
(E) Formulation development
(F) IND Application
(G) Clinical studies
(H) Office license / Marketing.

(A) Basic research - The target to study is decided.

Studying normal & abnormal functions.

⇓

Investigate disease conditions.

⇓

Look for ROL of the topic

⇓

Find out target

⇓

Search for targeted drug.

⇓

Perform pre-clinical & clinical testing.

⇓

Drug developed must be approved before entering to market

(B) New drug discovery : It has 3 steps.

(i) Target identification & Validation.-

Target identification

⇓

Find the drug that act on either cellular or genetic part.

⇓

Drug is tested upto 5000-10,000 molecules for which each patent drug candidates are subject to screening.

⇓

Confirm interaction b/w drug target

(ii) Lead identification

- Lead compounds are the ones that have potential to treat diseases.

- They are developed as collections or libraries of individual molecule that possess properties needed in the drug.

(iii) Lead optimization:

- By selecting compound b/w great potential to be developed in safe & effective medicine.

- Testing is done in (IN-VIVO) & in cell in test tubes.

(C) Pre-clinical studies -

- carried out in animals using in-vivo or in-vitro technique.

- It carries out activity, MOA, PK, & at effective dose.

- It also help in toxicological study to evaluate & minimize harm of drug.

(D) Clinical study -

- Here, only 16 out of 100 drugs enter in phase-I and will be approved by FDA.

- There steps are:

Phase I - Safety checking. (20-100 volunteers)
↓
Phase II - checking efficacy (100-800 vount.)
↓
Phase III - confirm result (1000-5000)
↓
Phase IV - FDA approval → safety surveillance.

(E) Approval -

- New drug application (NDA) is a vehicle through sponsor formally propose the FDA for licensing the drug.

⇒ Micro-dosing :

- In phase 0 of clinical trials, the dose of the new drug are given in micro-unites and hence, it is called as micro-dosing stage in clinical trial.

Advantages -
- Helps in selection of parent compounds.
- Less chance of ADR.
- Avoid unnecessary exposure.
- cost effective stage.
- Lower no. of subject can be used.
- Help to adjust the dosing of drug.
- Initial dose information obtained.
- Time effective.

Limitations:
- May get false negative result or false positive.
- Caution is necessary as drug may show non-linear kinetics.
- Difficult to find susp. at various doses

Q1(b) Roles and responsibilities of sponsor

⇒ sponsor is an individual, company or an organization, which takes responsibilities for the initiation, management & financing of CT.

FDA regulation and Indian ICH & GCP guidelines defines the roles & responsibilities of sponsor as follows:

(1) selection of investigator & institution:
- The sponsor should select a well qualified, trained & experienced investigator.

(2) contract and agreement:
- The agreement should clearly define about -
(a) Trial should obey the protocol
(b) sponsor make sure trial follows SOP

(c) sponsor has the right to monitor, inspect and audit the site at any time.
(d) Financial aspect, if any.

(3) Allocation of duties & functions.

(4) CT. management, data collection, handling and record keeping:
- sponsor should assess the progress of the CT to check whether to continue, modify or to stop.

- Sponsor has to frame & maintain SOP
- Maintain adult trial security system and backup of data.

(5) compensation of subject & investigator:
- sponsor should provide insurance and financing coverage to investigator against any claim arising from trial.

(6) confirmation of review by IRB/IEC
- sponsor should obtain name & address of investigator to IRB/IEC
- sponsor should assure that IRB/IEC has reviewed the trial protocol.

- sponsor should ensure that IRB/IEC has approved the protocol to conduct a trial

(7) Manufacturing, packing and labelling of investigational product.

- Ensure that IP is manufactured according to acceptable GMP.

- Ensure that IP is labelled & coded accordingly.

(8) Information on IPs.

- sponsor should ensure that sufficient safety data, efficacy data from non-clinical studies are available for investigational drug.

(9) Supplying & handling IPs.

- sponsor should supply the IPs to all investigators involved in trial.

- sponsor should maintain sufficient sample from each batch & keep records & analyse them.

(10) Safety information:

- sponsor is responsible for the ongoing safety evaluation of investigational products.

- He should take appropriate measures to safeguard subject safety.

(11) ADR reporting.

- The sponsor shall report all the ADRs to the IEC.

(12) Contract research organization management

- Sponsor should transfer any or all of trial related duties and function to a CRO with an agreement.

- CRO should implement QA & QC.

(13) Record access -

- Sponsor should provide direct access to data sources & documents for trial related monitoring & audit.

(14) Audit -

- The sponsor should appoint a qualified and experienced auditors to perform audit at all sites of trial.

- They should also verify that the auditors have documented all observations.

(15) Premature termination.

(16) Clinical trial report

(17) Multicenter trials.

Q1. (c) Define IND application. and write about contents of INDA.

→ Investigational New drug application (INDA) is defined as a petition, through which a drug sponsar requests the FDA to allow human testing of drug products.

- It is submitted by the sponsar ~~to conduct studies~~ and employ CRO to conduct actual studies.
- It is submitted to drug regulatory authorities before conducting the trial.
- INDA provide the FDA with data & suggest if the trial is beneficial by ensuring & justifying risk.

There are 4 types of INDA:

(1) Investigational INDA:
These are submitted by physician, who both initiate & conduct an investigation & under whose immidiate direction, the investigation drug is dispensed.

(2) Commercial INDA -
These are submitted by companies to attain marking approval of the drug product

(3) Emergency use INDA -
This INDA allows the FDA to authorize use of experimental drug in emergency situation.

(4) Treatment INDA -
It is submited for experimental drug, showing promise in clinical testing of serious or immidiate life threatening conditions.

Contents of INDA:

(1) Cover sheet.
(a) Name, address & no. of sponsar.
(b) Identification of phases.
(c) IND approval letter.
(d) Commitment by IRB form 56.
(e) Detail of conducting trial.
(f) Name, title of monitor.
(g) Name, title of person.
(h) Name, address of CRO.
(i) Signature of sponsor.

(2) Table of contents -
It includes various titles, protocals and other parts including their respective page number.

(3) Investigational brochure.

(4) study protocol -
It must be precise & include detail of study. The part of protocol are:
(a) Title.
(b) Introduction.
(c) Rationale.
(d) Aim.
(e) Objectives
(f) Need of study.
(g) Materials & methods.

(5) Investigator facilities & IRB data:

(6) chemistry & manufacturing:
- The drug or product chemistry & other various information involved, whichever are necessary.
- The manufacturer must follow GMP guidline of drug or products.

(7) control data:
Accurate information must be mentioned in controlled manner.

(8) Previous human experience:
- It should involve data from previous research from articles, books & Journals in previous ma.

Data to be summited along with INDA:

(1) Animal p'cology and toxicology studies
(2) Manufacturing info.
(3) Clinical protocols & investigators info

(1) Preclinical data to permit an assessment as to whether the product is reasonably safe for initial testing in humans.

(2) Includes:
- composition
- Manufacturer
- Stability
- Controls used for making drug substance & drug products.

(3) - Detailed protocols & clinical studies to assess whether the initial phase trials will be exposed subjects to unecessary ~~trials~~ risks.

- Invg. info contains administrar of experimental compound to assess whether they qualified CTs.

Q2(a) Define Bias, various types of bias & methods to avoid bias.

⇒ It is defined as deviation of results or inferences from truth or process leading to such deviation.

- It is a fundamental concept in epidemiology and is a result of error & invalidation.

- A Bias can occur in many areas in a trial, such as:
  (a) study design
  (b) Data collection
  (c) Data analysis
  (d) conclusion
  (e) Publication etc.

- There are 3 types of bias:

(1) selection bias:

It occurs from the manner a study population is selected and is mainly assessed in health care.

(2) Ascertainment or information bias:

It occurs due to measurement error or miscalculation of subject according to one or more variables.

(3) Confounding:

It occurs when risk factors being studied is mixed up & other possible risk factors that its singee effect is very difficult to distinguish.

- There are multiple sources of bias, which are:

(1) Bias occured by: IPS LIO
  (a) Investigator
  (b) Participant's intention
  (c) Statistician
  (d) Literature misleading
  (e) Instrumental
  (f) Other various variables.

(2) Bias in trial phases:
  (a) Pre-clinical bias - Occurs by study design, selection of subjects.

  (b) Bias during trials - Intervieuer bias, Recall bias, transfer bias, performance bias IRTP

  (c) Bias after trial - conclusion, discussion or citation.

- There are various methods to reduce bias, which are:

(1) Randomized controlled trials (RCTs):
It helps distribute both known & unknown confounding factors to evenly balance.

(2) Blinding:
Implementing blinding such as single or double blind help to minimize bias by preventing expectations from influencing outcomes.

(3) Placebo control:
using placebo in control group ~~to~~ helps to nullify bias in effectiveness of drugs.

(4) Allocation concealment:
Concealing treatment allocation until participants are enrolled reduces selection bias.

(5) Standardized protocol:
Implementing it for recruitment, assessment & data collection reduces variability & potential bias in study procedure.

(6) Minimizing attrition bias:
Implement strategies to reduce loss to followup & ensure participants retention throughout study.

(7) Pre-registration & transpart reporting.

(8) Independant data monitoring

(9) Handling confounding variables.

Q2(b) What is randomization? Brief about static & adaptive design.

⇒ "A process of assigning of participants to treatment group."

- It gives each participant a known chance of being assigned to any of the groups.

- In a successful randomization, group assignment cannot be predicted in advance.

- It helps to ensure that any observed differences in outcomes b/w the groups are attributable to intervention being studied rather than systemic difference in baseline factors.

Static design -

- In static design, the allocation of participant to the group is determined before the study begins.

- Randomization occurs once, typically at the outset of study & participants are then assigned to their respective treatment groups. according to the pre-determined randomization scheme.

- This fixed allocation ensures that the comparision of the group remains constant over time, allowing for straightforward comparison of outcome b/w groups.

- commonly employed in:
  (i) Traditional RCTs
  (ii) studying intervention & stable characteristics.

Adaptive design -

- Allows modification to the trial design based on accumulating data and insight gained during the study.

- These modifications, which are preplanned and specified in the study protocol, may include adjustment to sample size, treatment arms, dosing regimen, patient population or other aspect of study design.

- Enables research to respond to emerging information in real-time, potentially enhance the efficiency, flexibility and ethical conduct of trial.

- It requires careful planning, robust statistical methodology & adherence to regulatory guidelines to ensure the validity, integrity & interpretability of study findings.

(Q2(a)) Give an account an Abbreviated New drug application (ANDA).

⇒ An ANDA contain data which when submitted to the FDA for drug evaluation and research, the office of generic drugs, provides for review & ultimate approval of a generic drug product.

- Once approved, the applicant may manufacture and market the generic drug product to provide safe, effective, low-cost alternative to brand-name drug it refers.

- A Generic drug product is one that is comparable to an innovator drug product in dosage form, strength, ROA, quality, performance and, intended use.

- Generic drug applications are termed "Abbreviated" because they generally are not required to include pre-clinical (animal) and clinical (human) data to establish safety and effectiveness.

- They must scientifically demanstrate that their product is has performed in the same manner as the innovator drug.

- This demonstration of "bioequivalence" gives the rate of absorption or bioavailability of the generic drug, which can then be compared to that of the innovator drug.

- To be approved by FDA, the generic drug must deliver the same amounts of active ingredients into the patient's bloodstream as the same amount of innovator drug.

ANDA requirements:

(1) Signed FDA form 356h:

- Name & address of the applicant.
- Name of the drug product
- strength.
- ROA
- Indications.
- Whether the product is prescription/OTC.

(2) Volume Index:
- Volume
- Page number for each item involved.

(3) Information on the basis for which ANDA is being submitted:

- Name of the reference drug
- Dosage form.
- Strength
- Any special information with respect to drug.

(4) Condition for use:
- Indication for use
- Labelling details for the given drug product.

(5) A statement that the AI is the same as that of the reference drug.

(6) ROA, Dosage form and strength should be the same as that of reference drug.

(7) Bioequivalence:
- Mention with evidence that the proposed drug is bioequivalent to the listed drug product.

(8) Labelling:

- Copy of currently approved & proposed labelling of listed & reference drugs.
- Comparison of both sets of labelling.

(9) Chemistry, Manufacturing & controls.

- Composition
- Manufacture
- Specifications.
- Analytical procedures.

(10) Human P'cokinetics & Bioavailability:

- Designs.
- Dosing procedures.
- Number & frequency of blood & urine collection.
- Methodology of assay.

(11) Analytical methods for drug substance and drug product:

- Specifications.
- Analytical methods.
- Validation methods.
- Stability tests
- Manufacturing details

obtaining any means of information about a product after it has been approved for public use

Q3(a). Various methods of PMS.

⇒ To market a drug, the manufacturer must provide evidence of its efficacy and safety to FDA and specified regulatory authorities.

- In pre-marketing tests, the no. & types of patients used to demonstrate drug's efficacy and safety are limited, compared to that of patients who will eventually be prescribed by the drug after it is marketed.

- PMS cannot provide knowledge about safety & efficacy of drugs at the time of introduction in the market.
But, it provides additional information about the benefits & risks of the drug.

Various types of PMS are:

(1) Spontaneous / Voluntary reporting of cases.

- Voluntary reporting of cases by physicians & other HC providers, hospitals and customers may act as

an alert to FDA & other p'ceutical firms to possiure adverse effects of drugs.

- It is done by:
  (i) WHO international system
  (ii) National P'covigilance system INDIA
  (iii) Local or regional.
  (iv) Scientific literature publications.

- In other countries:
  (i) US-FDA Medwatch.
  (ii) UK-Yellow card system.
  (iii) Australia - Blue card system.

(2) Observational studies:

(a) Case reports -

- These are descriptions of patients who are exposed to a drug and who develop suspected adverse drug reactions.

- Can be effective in alerting the medical community to very rare adverse drug reactions!

- Do not provide an estimate of the incidence of the rxn, since the no. of exposed patients is unknown.

(b) Case series:

- These are reports of a series of patients with a particular drug exposure & their subsequent clinical course.

- Useful in quantitating the frequency of medical events after exposure to a drug.

- These studies cannot determine that the drug is the cause of any of the medical events, unless the medical events is known to be extremely uncommon in the absence of the drug exposure and much more common with other drug exposure.

(c) Case control studies:

- It identifies a group of patients with disease of interest and compares them with a control group of patients without the disease.

- Both groups are examined for antecedant drug exposure & rates of exposure are compared.

Ex: Occurrence and non-occurrence of MI in pts c HTN

- This method has been used extensively in PMS and has demonstrated many important associations.

- Can be performed more quicky & less expensively than conort studies.

(d) Cohort studies:

- Compares patients exposed to a drug with a control group of unexposed patients (or) patients exposed to another drug and look forward in time at subsequent clinical events.

- Particularly useful for newly marketed drugs, looking for drug effects.

- They can measure incidence rates and thus require very large samples of patients in order to detect relatively uncommon drug effects

(e) Randomized control trials:

- Here, the investigator controls the exposure of drug.

- Performed prior to marketing, to test the efficacy of drugs.

- They are performed on highly selected groups of patients who are free from drugs & diseases.

- Thus, results are often not applicable to the typical patients who will be taking the drugs.

- They are often costly (or) impractical in specific situations.

Q3(b) various p'cological approach to drug discovery.

⇒ The following is the flowchart for drug discovery:

Target selection ⇒ Lead identification ⇒ Lead optimization

⇓

- Product development.

various approaches to drug discovery are

- Pre-clinical testing
  - P'cological testing
  - Toxicological testing
- clinical testing
  - INDA
  - Drug characterization.
  - Dosage form

- Pharmacological testing:

- These tests are to determine whether the substance has effectiveness and a reasonable safety profile.

- Components of pharmacological testing are:
  (a) selectivity testing
  (b) Pharmacological profiling
  (c) Testing in animal models of disease
  (d) safety pharmacology.

(a) selectivity testing:
  (i) screening of activity
  The selectivity of compound for a chosen molecular target needs to be assessed. Incoz it determines the potency of the drugs.

  (ii) Binding assays
  These are needed to determined the dissociation constant of the test component as a measure of affinity to the receptor.

(b) Pharmacological profiling.
  It refers to determining the p'codyn. effects of a new compound.

It is of two types:

(i) In vitro models -
- Involves studies on isolated tissues
- Applicable to study on smooth muscles, cardiac muscle & brain slices.
- Tissue is obtained from a freshly killed (or) anaesthetized animal & suspended in warmed oxygenated physiological fluids solutions.

(ii) In vivo models -
- Involves testing on normal animal bodies.
- Time consuming and very expensive.

(c) Testing in animal models of disease:
These can be divided into 3 categories -

(i) Acute physiological & p'cological models:
- They are intended to mimic certain aspects of clinical disorders.
Ex: Hot plate for analgesic drugs as a model of pain

Electrical stimulation of brain to induce seizures as a model of epilepsy.

(ii) Chronic physio & p'cological models:
- Involve the use of drugs (or) physical interventions to induce an ongoing abnormality similar to clinical condition.
Ex: Self-administration of opiates, nicotinic drugs as a model of drug dependance

(iii) Genetic models:
- These are transgenic animals provided by (or) over expression of specific genes deletion, to show abnormalities resembling the human disease.

- It has allowed inbred strains to be produced with gene abnormality to be present throughout the animal life.

(d) Safety pharmacology:
- It is the evaluation ~~and~~ of safety of potentially life threatening p'cological effects of a potential drug which is unrelated to the desired therapeutic effect & may present a hazard.

- Seeks to identify unanticipated effects of new drugs on major organ functions.

- To detect possible, undesirable (or) dangerous effects of exposure of their drug in therapeutic doses.

It involves 3 levels of study:

(i) Molecular level -
- Drug is studied for its selectivity for various receptors & its activity against selective enzyme systems.

- Cell membr. fractions from organs / glands are used.

(ii) Cellular level:
- By using cells or tissues culture & computer programs, the p'cological action is assessed to stimulate human and animal systems

- Isolated tissues like blood vessels, heart, lungs, ileum are used.

(iii) Whole animal study:
- This is to determine the effect of drugs on organ systems and disease models.

- Ex: study of anti-hypertensive effects in hypertensive rats.

Q3(c) Compare phase I & phase II clinical trials.

	Phase I	Phase II
Objectives.	Determine metabolic & p'cological action and max tolerated dose.	Evaluate effectiveness & determine the short term side effect & identify common risks for specific populations & disease.
Factors to be identified	Bioavailability Bioequivalence Dose proportionality Metabolism PK & PD.	Bioavailability Drug disease interⁿ Drug drug interⁿ Efficacy at diff. dose PK; PD & patient safety
Data focus.	Vital signs Plasma & serum lvl. ADR	Dose response & tolerance, ADR, Efficacy.
Design features	Single, ascending dose tiers, Unblinded Uncontrolled.	Placebo controlled Active controlled. well-defined entry criteria.
Duration	Upto 1 month	several months
Sample size	20 to 80	200 to 300

Population	Healthy volunteers or individuals ē target diseases.	Individuals ē target diseases.
Example.	Study of single dose of drug x in normal subjects	Double blind study evaluating safety & efficacy of drug vs. placebo in PHS. ē HTN

Q4(b) Regulatory setup in Europe.

⇒ "European Medicines Agency" (EMEA), is the regulatory authority in Europe.

- It relies on result of CT carried out by pharmaceutical company to reach its opinion on authorization of medicine.

- It ensures that GCP must be followed. and is the first regulatory authority that issues guidelines for biosimilars in 2005.

- The guideline clearly differentiates new generic & biosimilars.

- It includes quality, safety & efficacy of biosimilar guidelines.

- There are 2 procedures by which medicines are authorized:
  (a) Centralized authorization procedure
  (b) National authorization procedure

- These processes lead to single marketing authorization, which is valid across European Union.

- Centralized procedure is compulsory in human medicines which are:

(a) derived from biotechnology like genetic engineering

(b) Intended for t/t of HIV/AIDS, cancer, DM, or any immune dysfunction.

(c) Same medicines which officially designated as orphan medicines.

- EMEA only accept application through centralized procedure.

- 210 days are taken by the agency to decide that medicines should be marketed or not.

- Once community marketing grants the permission, then the medicine is made available for patients & healthcare professionals.

- In national authorization procedure, every state has its own authorization procedure & it has 2 methods of authorization.

(a) Decentralized:
- companies can apply for simultaneous authorization in more than one European country of medical product that not yet been authorized in centralized procedure.

(b) Mutual recognition procedure -
Medicine is first authorized in one European member state in accordance c the national procedure of the country.

Following this, further marketing authorization can be sought from other European countries in procedure whereby countries agree to recognize the validity of original, national authorization.

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Q5(a) Components of CR protocol & process of protocol preparation & amendment

- There are various components of protocol. They are:

(1) Title page -
It should be precise, clear & certainly explain the subject of research.

(2) Signature page -
It should consist of name, profession & signature of all participant, guide & professors.

(3) Content page -
The page of index that guides one to specific content.

(4) List of abbreviation -
All abbreviation should be listed and defined on this page; follow international abbreviation guidelines.

(5) Introduction / Abstract -
It should be of 2-3 pages and provide sufficient information to the reader & examiner.

(6) Rationale -
It is a section detailing the scientific rationale for a protocol that justify in medical & scientific literature.

(7) Inclusion & exclusion criteria -
It defines characteristic of participants eligibility to participate & excluded in CT. (Age, gender, type/stage of disease, medical history)

(8) Endpoint -
Specifies the primary & secondary endpoint outlines how these will be measured & assessed.

(9) Statistical consideration -
Describes various methods of use to analyze the clinical research.

(10) Human subject protection -
Describe the risk & benefit of CT with detail note on compensation on risk.

Preparation of Protocol & amendments:

(1) Literature review -
It is the 1st step of any clinical research to review of existing study or literature that help to develop an accurate protocol & minimize the risk of error.

(2) Study design and methodology -
It involves careful consideration of study design, methods & statistical approach that outlines the framework of data collection and analysing.

(3) Ethical consideration

(4) Inclusion & Exclusion criteria formation.

(5) Regulatory approval

(6) Identify needed amendment

(7) Overall expense of clinical research.

Q5(b) Safety issues an investigational new drug.

⇒ Safety issues in IND trials are of paramount importance, as they involve testing new p'ceutical components or biologicals in human subject for first time.

- Ensuring the safety of participants is fundamental, ethical & regulatory requirement throughout the drug development process.

- There are several safety key considerations in IND trial.
They are:

(1) Toxicity & ADR:
The 1st concern in IND trials is assessing the toxicity profile of investigational drug.

- This involves AE, which can range from mild side effect to severe reaction.

- common AEs include nausea, headache, fatigue and allergic reactions.

(2) Dose escalation & tolerance:

- IND trials often employ dose escalation protocol to gradually increase the dosage of investigational drug & assess its safety & tolerability.

- Monitoring for dose-limiting toxicities is critical during dose escalation, as DLTs can determine the maximum tolerability dose (MTD) of drug.

(3) Risk-Benefit assessment:

- safety issues must be balanced c the potential benefit of investigational drug.

- It considers factors such as severity to target diseases, the availability of alternate t/t and patient's quality of life.

- Ethical considerations dictate that the potential benefit of drug outweigh its risks & participants must provide informed consent based on thorough understanding of risk & benefit.

(4) Preclinical safety data:

Prior to initiating IND trial, sponsors are required to conduct comprehensive preclinical studies to evaluate the safety profile of investigational drug in animal model.

- Preclinical data provide valuable insight to potential toxicity concerns, p'kinetics & MOA.

- However, its important to recognize that animal studies may not always accurately predict human response, highlighting the need for careful monitoring.

(5) Monitoring & reporting:

- IND trial requires robust safety monitoring & reporting mechanism to promptly identify & address safety concerns.

(6) Risk management:

- Sponsors of IND trials develop risk management plan to pro-actively identify, evaluate & mitigate potential

safety risk associated c the investigational drug.

Q6(a) Descri
management

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Q6(a) Describe the clinical trial data management process & its benefits.

⇒ Best practices are adapted to meet with the demand & to have complete reliable data which are processed correctly.

- The collected data is sent to sponsor, who then analyzes the protocol data using statistical analysis.
- CRF is a paper or electronic questionnaire used as a tool in CTs to collect data.
- Process of data collection:

Data design ⇒ Data collection ⇒ Data entry

⇓

Data validation ⇐ Data cleanup ⇐ Data analysis ⇐ Data reporting

⇓

Data management.

(1) Data design:
- Database allows for adequate storage of study data and for accurate reporting, interpretation & verification of data.

- Two systems available: (Personal info & recruitment)
  (1) study management database.
  (2) Clinical database. → (Clinical info)

(2) Data collection:
- Validity of data collected must be ensured

(3) Data Entry:
- Different types of data entry have existed and it can also influence the method of data entry.

- It is important to have a SOP defining who is performing data entry.

(4) Data validation:
- Range, skips, inconsistencies and missing data are checked.

- check output file for data export as:
  (a) Variable names match up
  (b) Coding of category
  (c) No. Format as required (d) Format

(5) Data cleanup:
- Error / Missing data are spotted at diff. times depending on study & method used.

- Error should be corrected when possible but no change should be made w/o justification.

(6) Data Analysis:
- Majority of trial sponsors hire a trained statistician to perform data analysis.

- Different methods for analysis are:
  (1) Bayesian analysis
  (2) Decision analysis
  (3) sequential analysis.
  (4) Meta analysis

(7) Data reporting:
- Throughout the course of the study, it is the duty of data manager to report the progress of the study. It includes:

  (a) Recruitment progress.
  (b) Follow-up
  (c) Data completeness
  (d) Withdrawals.
  (e) Presentation.

Benefits :

(1) Data quality assurance.

(2) compliance with regulatory requirement. GCP and other ethical considerations

(3) Data security

(4) confidentiality

(5) Timely data analysis.

(6) Professional reporting

(7) Improved study oversight

(8) cost and time saving.