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B. Pharmacy — 8th Semester

BIOSTATISTICS AND RESEARCH METHODOLOGY

UNIT 3 — Non-Parametric Tests | Research Design | Graphs | Clinical Trials

Subject Code	Semester	Unit	Platform
BP801T	8th Semester	Unit 3 of 5	Noteskarts.com

UNIT 3 SYLLABUS AT A GLANCE

S.N.	Topic	Sub-topics
1	Non-Parametric Tests	*Wilcoxon Rank Sum, Mann-Whitney U, Kruskal-Wallis, Friedman Test*
2	Introduction to Research	*Need for research, Experimental Design, Plagiarism*
3	Statistical Graphs	*Histogram, Pie Chart, Cubic Graph, Response Surface, Contour Plot*
4	Research Methodology	*Sample size, Power, Report writing, Protocol, Cohort, Clinical Trials & Phases*

Non-Parametric Tests

Non-parametric tests (also called distribution-free tests) do not assume that data follows a normal distribution. They are used when:

- Sample size is small ($n < 30$)
- Data is ordinal or ranked
- Data is not normally distributed
- Population parameters (μ, σ) are unknown
- • Outliers are present that cannot be removed

◆ Parametric vs Non-Parametric Tests

Feature	Parametric Tests	Non-Parametric Tests
Assumption	Normal distribution required	No distribution assumption
Data type	Interval / Ratio (continuous)	Ordinal / Nominal / Ranked
Sample size	Preferred $n \geq 30$	Works for small n
Parameters tested	μ, σ (population parameters)	Median, ranks
Statistical power	Higher (more sensitive)	Lower (less sensitive)
Examples	t-test, ANOVA, Z-test	Wilcoxon, Mann-Whitney, Kruskal-Wallis
Pharma use	Drug concentration data	Pain scale, ordinal efficacy scores

◆ Wilcoxon Rank Sum Test (Signed-Rank Test)

- The Wilcoxon Signed-Rank Test is the non-parametric equivalent of the PAIRED t-test.
- It tests whether the median difference between paired observations is significantly different from zero.

When to use:

- Paired data (before-after design) that is NOT normally distributed
- Small sample size with ordinal data
- Pharma example: Pain score before and after analgesic drug in same patients

Steps for Wilcoxon Signed-Rank Test:

1. **Formulate Hypotheses**:
   - H_0: There is no significant difference between the pairs.
   - H_1: There is a significant difference between the pairs.
2. **Find the Difference (D)** between paired observations (i.e., D = B − A).
3. **Calculate the Absolute Difference (|D|)** for each pair.
4. **Assign Ranks** to the absolute differences from lowest to highest. For tied ranks (duplicate absolute differences), assign them the average rank.
   Example for ties: If two absolute differences are both 3, assign them a rank of 3+42=3.523+4 =3.5.
5. **Calculate the Sum of Ranks**:
   - **T+**: Sum of ranks for positive differences.
   - **T-**: Sum of ranks for negative differences.
6. **Find the Wilcoxon Rank Statistic (Wcalc)**: $W_{calc} = \min[f_0](T+, T-)$
7. **Compare Wcalc to Wtable**:
   - Use the sample size n and the significance level α (commonly 0.05) to find the critical value W_{table} from a table of critical values for the Wilcoxon Signed Rank Test.
8. **Interpret the Result**:
   - If $W_{calc} < W_{table}$, reject H_0.
   - If $W_{calc} > W_{table}$, accept H_0.

Interpretation of Results

- **Rejecting H0**: If W_{calc} is less than the critical value W_{table}, it indicates that the two groups are not identically distributed and there is a significant difference.
- **Accepting H0**: If W_{calc} is greater than W_{table}, it means the two groups are identically distributed and there is no significant difference.

Example: Smog Concentration Comparison

Let's consider an example where we compare smog concentrations in India from May to December. The data is presented for 13 states with measurements in both months.

States	Smog in May (A)	Smog in December (B)	Difference [D]	Absolute Difference [Abs-D]	Rank
Delhi	13.3	11.1	-2.2	2.2	5
Mumbai	10.0	16.2	6.2	6.2	9
Chennai	16.5	15.3	-1.2	1.2	3
Kerala	7.9	19.9	12.0	12.0	11

States	Smog in May (A)	Smog in December (B)	Difference [D]	Absolute Difference [Abs-D]	Rank
Karnataka	9.5	10.5	1.0	1.0	2
Tamil Nadu	8.3	15.5	7.2	7.2	10
Orissa	12.6	12.7	0.1	0.1	1
UP	8.9	14.2	5.3	5.3	7
MP	13.6	15.6	2.0	2.0	4
Rajasthan	8.1	20.4	12.3	12.3	12
Gujarat	18.3	12.7	-5.6	5.6	8
West Bengal	8.1	11.2	3.1	3.1	6
Jammu	13.4	36.8	23.4	23.4	13

Step 5: Calculate T+ and T−

- ***Sum of positive ranks (T+):*** *T+ = 9 + 11 + 2 + 10 + 1 + 7 + 4 + 12 + 8 + 6 + 13 = 82*
- ***Sum of negative ranks (T-):*** *T- = 5 + 3 = 8*

Step 6: Calculate Wcalc

$W_{calc} = \min(T+, T-) = \min(82, 8) = 8$

Step 7: Find Wtable

For n = 13 and α = 0.05 for a two-tailed test, the critical value is 17.

Step 8: Interpret the Result

Since $W_{calc} = 8$ is less than $W_{table} = 17$, we reject the null hypothesis H_0. This means that there is a significant difference in the smog concentrations between May and December.

◆ Mann-Whitney U Test

The Mann-Whitney U test is the non-parametric equivalent of the UNPAIRED (independent) t-test. It tests whether two independent groups have the same distribution/median. Also called Wilcoxon Rank-Sum Test.

When to use:

- Two independent groups, non-normal data
- Ordinal data (e.g., pain scales, clinical scores)
- Pharma: Comparing adverse effect severity scores of Drug A vs Drug B

Steps for Mann-Whitney U Test:

- Step 1: Combine all observations from both groups and rank them (1 = smallest)
- Step 2: If tied values, assign average rank to each
- Step 3: Calculate rank sums: R_1 (Group 1) and R_2 (Group 2)
- Step 4: Calculate U statistics:

U_1	$U_1 = n_1n_2 + n_1(n_1+1)/2 - R_1$	R_1 = sum of ranks for group 1
U_2	$U_2 = n_1n_2 + n_2(n_2+1)/2 - R_2$	R_2 = sum of ranks for group 2
Check	$U_1 + U_2 = n_1 \times n_2$	Verification formula

- Step 5: $U = \min(U_1, U_2)$ → Compare with U_critical from table
- Step 6: If $U \leq U\_critical$ → Reject H_0 (significant difference)

◆ Kruskal-Wallis Test

The Kruskal-Wallis test is the non-parametric equivalent of ONE-WAY ANOVA. It tests whether 3 or more independent groups have the same distribution/median. Uses ranks of combined data.

When to use:

- 3 or more independent groups with non-normal data
- Ordinal measurements across multiple treatment groups

- Pharma: Comparing pain scores across 3 different dose groups (Low/Medium/High)

H statistic	$H = \frac{12}{n(n+1)} \sum \frac{R_j^2}{n_j} - 3(n+1)$	N=total obs, n_i=group size, R_i=rank sum of group i

Decision Rule:

- H follows chi-square distribution with df = k−1 (k = number of groups)
- If H_calc ≥ χ^2_critical(df=k−1, α=0.05) → Reject H_0
- If significant → Apply post-hoc (Dunn's test) to find which groups differ

◆ Friedman Test

The Friedman Test is the non-parametric equivalent of TWO-WAY ANOVA (with one observation per cell) or REPEATED MEASURES ANOVA. It tests whether k related groups have the same distribution. Data is ranked within each block (row).

When to use:

- Repeated measurements on the same subjects under different conditions
- Non-normal data with related/matched groups (like blocks in RCB design)
- Pharma: Comparing drug effect at different time points in the same patients

Friedman χ^2r	$Fr = [12/(nk(k+1))] \times \Sigma R_j^2 - 3n(k+1)$	n=subjects, k=treatments, R_j=rank sum for each treatment

Steps:

- Step 1: Arrange data in table (rows = subjects/blocks, columns = treatments)
- Step 2: Rank within each row (1=lowest to k=highest) separately
- Step 3: Sum the ranks for each column: R_1, R_2, ..., Rk
- Step 4: Calculate Fr statistic using formula
- Step 5: Compare with χ^2_critical(df=k−1, α=0.05); if Fr ≥ χ^2_critical → Reject H_0

Introduction to Research

Research is a systematic, logical, and unbiased investigation conducted to discover new facts, verify existing knowledge, and develop new applications. In pharmacy, research is the backbone of drug discovery, development, and patient safety.

◆ Need for Research in Pharmacy

Area of Need	Why Research is Essential
Drug Discovery	To identify new chemical entities (NCEs) with therapeutic potential; without research no new drugs would be developed
Drug Safety	Clinical research detects adverse effects, drug interactions, and contraindications before market approval
Evidence-Based Medicine	Research provides scientific evidence for treatment guidelines, dosing regimens, and therapeutic protocols
Pharmacoeconomics	Research evaluates cost-effectiveness of therapies to optimize healthcare resource allocation
Regulatory Compliance	CDSCO, FDA, WHO require research data (clinical trial results) before drug approval
Quality Control	Analytical research ensures drug purity, potency, stability, and bioavailability standards are met
Disease Management	Epidemiological research identifies disease burden, risk factors, and preventive strategies
Generic Drug Development	Bioequivalence research validates that generic drugs perform like the innovator brand

◆ Need for Design of Experiments (DoE)

Design of Experiments (DoE) is a systematic approach to planning experiments so that valid, relevant, and precise data is obtained with minimum resources and maximum efficiency.

Why DoE is Essential:

- Reduces the number of experiments needed — saves time, cost, and materials
- Controls confounding variables to isolate the true effect of each factor

- Allows simultaneous study of multiple factors (factorial designs)
- Helps optimize formulation parameters (e.g., drug release, hardness, dissolution)
- Mandated by ICH Q8 (Pharmaceutical Development) for Quality by Design (QbD) approach

▸ Principles of Experimental Design:

Principle	Definition & Pharmaceutical Application
Replication	Repeating the experiment multiple times to get reliable estimates of experimental error. Ex: Testing 3 separate tablet batches at each formulation setting
Randomization	Random assignment of subjects/samples to treatments to eliminate systematic bias. Ex: Randomly assigning patients to drug vs placebo groups
Blocking	Grouping experimental units with similar characteristics to reduce variability. Ex: Testing batches from 3 different manufacturing shifts as blocks
Factorial Design	Studying all combinations of multiple factor levels simultaneously. Ex: 2^2 factorial: 2 binders × 2 compression forces = 4 experiments
Confounding Control	Ensuring unknown variables do not systematically affect results. Ex: Blinding evaluators to treatment assignment

◆ Experimental Design Techniques

Design Type	Description	Pharmaceutical Application
Completely Randomized Design (CRD)	Simplest design; treatments assigned completely at random	*Comparing dissolution of 3 tablet formulations (no blocking)*
Randomized Block Design (RBD)	Subjects grouped into blocks; treatments randomly assigned within blocks	*Multi-center clinical trial with hospital as block*

Latin Square Design	Controls 2 sources of variation (row and column blocks)	*Drug stability study across 3 labs × 3 time points × 3 conditions*
Factorial Design	Studies all combinations of 2+ factors	*2^3 design: 3 variables at 2 levels each = 8 formulation experiments*
Response Surface Methodology (RSM)	Optimization design using polynomial equations to model response surface	*Optimizing drug release: Binder%, Compression force, Disintegrant%*
Crossover Design	Each subject receives all treatments in random sequence	*Bioequivalence studies comparing generic vs innovator drug*
Placebo-Controlled Design	Control group receives inert placebo; eliminates placebo effect	*Phase III clinical trials for new drug evaluation*

◆ Plagiarism in Research

⚠ PLAGIARISM: Plagiarism is the act of presenting someone else's work, ideas, data, words, or intellectual property as one's own, without proper acknowledgment or attribution. It is considered academic fraud and research misconduct.

▸ Types of Plagiarism:

Type	Description
Direct/Verbatim Plagiarism	Copying text word-for-word without quotation marks or citation
Mosaic Plagiarism	Mixing copied phrases with own words without attribution (patchwork writing)
Paraphrasing Plagiarism	Rewording another's ideas without crediting the original source
Self-Plagiarism	Reusing one's own previously published work without disclosure

Source Plagiarism	Citing a reference but distorting its meaning or fabricating the citation
Data Plagiarism	Using another researcher's experimental data without permission

How to Avoid Plagiarism:

- Always cite sources using standard referencing formats (APA, Vancouver, Harvard)
- Use quotation marks for direct quotes and cite the page number
- Paraphrase in your own words AND still cite the original source
- Use plagiarism detection software: Turnitin, iThenticate, PlagScan before submission
- Maintain a research log recording all sources consulted
- Understand institutional plagiarism policy — most universities allow <10% similarity

Consequences of Plagiarism: Retraction of published paper, suspension/expulsion from institution, damage to scientific reputation, legal action for copyright violation, disqualification from research grants.

Statistical Graphs in Pharmaceutical Research

Graphical representation of data helps visualize patterns, trends, and relationships that may not be apparent from tables alone. Choosing the right graph type is essential for accurate data interpretation and scientific communication.

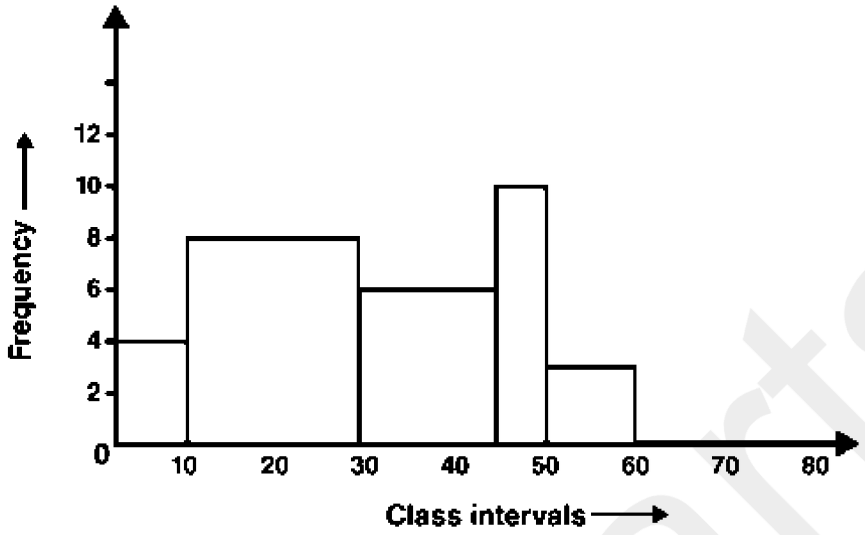
◆ Histogram

A Histogram is a bar chart that displays the frequency distribution of continuous data. Unlike bar charts, bars are ADJACENT (touching) — representing continuous class intervals.

Components of a Histogram:

- X-axis: Class intervals (continuous variable, e.g., dissolution %, tablet weight)
- Y-axis: Frequency or frequency density
- Bars are contiguous (touching) — representing continuous data

- Area of each bar = frequency of that class
- Shape reveals distribution: normal, skewed, bimodal



Pharmaceutical Uses of Histogram:

- Quality control: Tablet weight, hardness, and dissolution uniformity assessment
- Particle size distribution analysis of drug powders and excipients
- Detection of batch non-uniformity and process capability assessment
- Identifying normal vs skewed distribution of pharmacokinetic parameters

◆ Pie Chart

A Pie Chart is a circular graph divided into sectors, where each sector represents a proportion (percentage) of the whole. Sector angle = (frequency/total) × 360°.

Pharmaceutical Uses:

- Market share of drug categories in a therapeutic class
- Proportion of adverse drug reactions by type (mild/moderate/severe)
- Distribution of disease burden across demographic groups
- Composition of a formulation (% of each excipient)

◆ Cubic Graph (3D Surface Graph)

A Cubic Graph (3D graph) represents data with three variables simultaneously — X, Y, and Z axes. It shows a three-dimensional relationship and is used in advanced pharmaceutical formulation optimization.

Features:

- Three axes: X (Factor 1), Y (Factor 2), Z (Response variable)
- Creates a 3-dimensional visual surface
- Useful for visualizing interactions between two independent variables and their combined effect on a response
- Generated using polynomial regression equations from DoE

◆ Response Surface Plot

A Response Surface Plot is a 3D or 2D graph used in Response Surface Methodology (RSM) to visualize the relationship between two or more independent variables and the response (dependent variable). It helps identify optimal formulation conditions.

Types of Response Surface Designs:

- Central Composite Design (CCD): Used to build second-order response surface models
- Box-Behnken Design (BBD): 3-factor design without corner points; more efficient
- Doehlert Design: Uniform distribution of experimental points

Polynomial Equation for Response Surface:

RSM Equation	$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2$	2nd order polynomial model

◆ Contour Plot Graph

A Contour Plot is the 2D 'top view' (overhead projection) of a Response Surface Plot. Lines on the contour plot connect points with equal response values — similar to topographic maps. It helps identify optimal zones more precisely.

How to Read a Contour Plot:

- Each contour line represents a constant response value (isoresponse line)
- Closer contour lines = steeper change in response (high sensitivity)
- Oval/circular contours = interaction between factors is absent
- Elongated/tilted contours = significant interaction between factors
- The 'bullseye' center of smallest contour oval = optimal point

Graph Type	Best Used For	Pharmaceutical Application
Histogram	Frequency distribution of continuous data	*Tablet weight uniformity, particle size*
Pie Chart	Proportion/percentage breakdown	*ADR types, market share, formulation composition*
Cubic/3D Graph	3-variable relationship visualization	*DoE factor-response 3D relationships*
Response Surface	Optimization of formulation parameters	*RSM in pharmaceutical QbD*
Contour Plot	Identifying optimal zone in 2D map	*Formulation optimization, design space*

Designing the Methodology

Research methodology encompasses the entire strategy and framework for conducting a study: how data will be collected, analyzed, and reported. A well-designed methodology ensures valid, reproducible, and reliable research outcomes.

◆ Sample Size Determination

Sample size is the number of subjects/units needed in a study to detect a statistically significant result with adequate confidence. Too small = underpowered study (missed effects). Too large = waste of resources and unethical over-enrollment.

Factors Affecting Sample Size:

- Level of significance (α): Usually 0.05 → corresponds to $Z_{\alpha/2} = 1.96$ (two-tailed)
- Power of the test (1−β): Usually 80–90% → β=0.20, $Z_{\beta} = 0.842$
- Effect size (d): Minimum clinically important difference to detect
- Standard deviation (σ): Estimated from pilot study or literature
- Type of test: One-tailed or two-tailed

Sample Size (comparing 2 means)	$n = 2\sigma^2(Z_{\alpha/2} + Z_{\beta})^2 / d^2$	σ=SD, d=effect size, α=significance, β=type II error
Sample Size (proportion)	$n = Z^2_{\alpha/2} \times p(1-p) / e^2$	p=proportion, e=margin of error

◆ Power of a Study

Statistical Power (1−β) is the probability that a study will correctly detect a real effect when it truly exists. A study with 80% power has an 80% chance of finding a significant result if the true effect size is as hypothesized.

Power Level	Interpretation	Standard in Research
< 0.50 (50%)	Study very likely to miss real effects	*Insufficient — redesign required*
0.80 (80%)	80% chance of detecting true effect	*Minimum acceptable standard (ICH E9)*
0.90 (90%)	90% chance of detecting true effect	*Preferred for pivotal clinical trials*
0.95 (95%)	Very high sensitivity	*Used in critical safety studies*

Factors that INCREASE Power:

- Larger sample size (n) — most controllable factor
- Larger effect size (d) — more pronounced treatment effect
- Higher α level (e.g., 0.10 vs 0.05) — increases power but increases Type I error risk
- Smaller variability (σ) — more precise measurements
- One-tailed test — more powerful than two-tailed (when direction is known)

◆ Report Writing & Presentation of Data

▸ Structure of a Research Report / Scientific Paper (IMRaD Format):

Section	Content & Guidelines

Title	Concise, specific, informative; includes key variables. Max 15 words. Ex: 'Formulation and Evaluation of Sustained-Release Metformin Tablets'
Abstract	Brief summary (250 words): Background, Objective, Methods, Results, Conclusion. Structured or unstructured format
Introduction	Background, problem statement, rationale, literature review, objectives, and hypothesis
Materials & Methods	Detailed description of study design, materials, equipment, procedures, statistical methods — sufficient for reproducibility
Results	Objective data presentation using tables, graphs, statistical values (mean ± SD, p-values). No interpretation
Discussion	Interpretation of results, comparison with literature, limitations, clinical relevance
Conclusion	Clear, concise summary of key findings and their significance
References	All cited sources formatted as per journal style (Vancouver, APA, etc.)
Acknowledgements	Funding sources, institutional support, technical assistance

Data Presentation Guidelines:

- Tables: Use for precise numerical data; include units, mean, SD, p-values; title above table
- Figures: Use for trends and distributions; title below figure; error bars for variability
- Statistical reporting: Always report test statistic, degrees of freedom, p-value. Ex: t(10)=3.45, p=0.006
- Significant figures: Report to appropriate decimal places (3 significant figures for pharma data)

◆ Research Protocol

A Research Protocol is a written document that describes the objectives, design, methodology, statistical considerations, and organization of a clinical

trial or research study. It is the binding document that guides how the study is conducted.

Essential Components of a Clinical Research Protocol:

- Title and Protocol Number (unique identifier)
- Background and Rationale — why this study is needed
- Study Objectives — primary and secondary endpoints
- Study Design — type of study, duration, phases
- Subject Population — inclusion/exclusion criteria
- Interventions — drug dose, route, frequency, duration
- Randomization and Blinding procedure
- Sample size justification and power calculations
- Statistical Analysis Plan (SAP)
- Ethical considerations — Informed Consent Form (ICF), IRB/IEC approval
- Adverse Event monitoring and reporting procedures
- Data collection forms (Case Report Forms — CRFs)
- Regulatory approvals required (CDSCO for India, FDA for USA)

◆ Types of Studies

▸ A) Cohort Studies

A Cohort Study is a prospective/retrospective observational study that follows a group of people (cohort) over time to determine how certain exposures affect the incidence of outcomes (disease or event).

Feature	Prospective Cohort	Retrospective Cohort
Direction	Forward in time	Backward in time
Data collection	Collected as study progresses	Uses existing records
Time	Long (years)	Short (uses past data)
Cost	Expensive	Economical
Pharma example	Following statin users for 10 years to monitor cardiovascular outcomes	Using hospital records to study past drug exposure and cancer incidence

▸ B) Observational Studies

Observational studies collect data without intervening in the exposure of subjects. The researcher only observes and records events.

Type	Description & Pharmaceutical Example
Cross-Sectional Study	Data collected at a single point in time. Ex: Survey of diabetes prevalence and medication use in a population in 2024
Case-Control Study	Compares subjects WITH a disease (cases) to those WITHOUT (controls) looking backward for exposure. Ex: Studying past NSAID use in patients with GI bleeding vs controls
Cohort Study	Follows exposed and unexposed groups forward to compare disease incidence (see above)
Ecological Study	Studies populations rather than individuals. Ex: Correlation between antibiotic sales data and resistance rates by country

▸ C) Experimental Studies

Experimental studies involve active manipulation of an independent variable (e.g., drug treatment) by the researcher. They provide the strongest evidence for causality.

Type	Description & Example
Randomized Controlled Trial (RCT)	Gold standard. Subjects randomly assigned to treatment or control. Ex: Phase III drug trial with randomization and blinding
Non-Randomized Experimental	Treatment assigned by non-random method. Ex: Comparing drug effect in patients who chose vs declined treatment
Before-After Study	Measurements taken before and after intervention without control group. Ex: HbA1c before and after 3 months of Metformin
In Vitro Study	Conducted in laboratory setting (cell cultures, test tubes). Ex: Cytotoxicity assay of anticancer compound on HeLa cells
In Vivo Study	Conducted in living organisms (animals or humans). Ex: Pharmacokinetic study in Wistar rats

◆ Designing a Clinical Trial

A Clinical Trial is a carefully designed research study conducted in human subjects to evaluate the safety, efficacy, pharmacokinetics, and pharmacodynamics of a new drug or therapeutic intervention.

Design Elements of a Clinical Trial:

- Hypothesis: Clear primary and secondary objectives
- Population: Inclusion and exclusion criteria defining eligible subjects
- Randomization: Method of assigning subjects to groups (computer-generated, block randomization)
- Blinding: Single blind (patient unaware), Double blind (patient + investigator unaware), Triple blind (patient + investigator + statistician unaware)
- Control: Placebo, active comparator, or dose-comparison
- Duration: Acute (days), Sub-chronic (weeks), Chronic (months/years)
- Endpoints: Primary (efficacy/safety) and Secondary (quality of life, biomarkers)
- Statistical Analysis: Pre-specified SAP with ITT (Intent-to-Treat) and PP (Per-Protocol) analyses

◆ Phases of Clinical Trials

Phase	Subjects	Duration	Primary Focus	Pharmaceutical Objectives
Pre-clinical	**Animals (in vitro, in vivo)**	2–5 years	**Safety & Toxicology**	Determine MLD, LD50, NOAEL, pharmacokinetics in animals. IND application filed with CDSCO/FDA
Phase 0	**10–15 humans (healthy volunteers)**	Weeks	**Pharmacokinetics**	Microdosing studies (<1% therapeutic dose); no therapeutic intent; PK/PD profiling
Phase I	**20–100 (healthy volunteers)**	Months	**Safety & Dosing**	First-in-human study; MAD/SAD studies; dose escalation; determine MTD; PK parameters; identify adverse effects
Phase II	**100–300 patients**	Months–1 year	**Efficacy & Safety**	Dose-finding; proof of concept; identify therapeutic dose range; monitor short-term side effects; Phase IIa (proof

				of concept) and IIb (dose finding)
Phase III	**1000–5000+ patients**	1–4 years	**Confirm Efficacy & Safety**	Pivotal trials; randomized controlled; compare with placebo or standard treatment; NDA/MAA submission to regulators; ICH E9 statistical guidelines
Phase IV	**Post-marketing (thousands)**	Ongoing	**Post-marketing Surveillance**	Pharmacovigilance; detect rare ADRs; long-term safety; new indications; real-world effectiveness; PSUR submission

Indian Regulatory Context:

- Phase I–III trials require CDSCO (Central Drugs Standard Control Organisation) approval under Schedule Y of Drugs & Cosmetics Act, 1940
- Ethics Committee (IEC/IRB) approval mandatory before first patient enrollment
- Good Clinical Practice (GCP) guidelines per ICH E6(R2) must be followed
- • Informed Consent (IC) must be obtained from each subject before participation.
- New Drug and Clinical Trials (NDCT) Rules 2019 govern clinical research in India

◆ Expected Exam Questions — Unit 3

Q	Question	Marks
1	What are non-parametric tests? How do they differ from parametric tests?	3–5
2	Explain Wilcoxon Signed-Rank test with a pharmaceutical example (before-after design).	5–10
3	What is Mann-Whitney U test? When is it used? Solve a problem with two groups.	5–10
4	Explain Kruskal-Wallis test. Compare it with one-way ANOVA. Solve a 3-group problem.	5–10

5	Write a note on Friedman test. Give its pharmaceutical significance.	5
6	What is the need for research in pharmaceutical sciences? Explain different types of research.	5
7	What is Design of Experiments? Explain its principles with pharmaceutical examples.	5
8	Define plagiarism. What are its types and how can it be avoided in research?	3–5
9	Differentiate: Histogram vs Bar chart; Pie chart vs Histogram. Give pharma examples.	5
10	What is a Response Surface Plot? How does it differ from a Contour Plot? Pharma application.	5
11	How is sample size determined for a clinical trial? Calculate for given parameters.	5–10
12	What is Power of a study? What factors affect it? How can power be increased?	5
13	Explain the phases of clinical trials (Phase 0 to Phase IV) with objectives and sample sizes.	10
14	What is a Research Protocol? List its essential components.	5
15	Differentiate: Cohort vs Case-Control studies; Observational vs Experimental studies.	5
16	Write a short note on: (a) GCP Guidelines (b) Informed Consent in Clinical Trials.	5