D.PHARM • SECOND YEAR

Pharmacy Law & Ethics

CHAPTER 14

BCS System, Clinical Trials, ANDA, NDA, New Drugs and Patent Law



ENGLISH CHAPTER NOTES

DIPLOMA IN PHARMACY

BIOPHARMACEUTICS CLASSIFICATION SYSTEM (BCS)

DEFINITION

The Biopharmaceutics Classification System (BCS) groups an orally administered drug substance by its aqueous solubility and intestinal permeability.
It helps predict whether dissolution or membrane permeation may limit absorption.

INTESTINAL PERMEABILITY

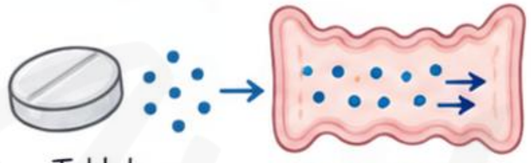
High

Low

CLASS I — HIGH SOLUBILITY + HIGH PERMEABILITY

Usually dissolves and crosses the intestinal membrane well.

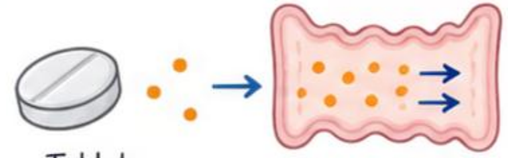
Example: metoperlol.



CLASS II — LOW SOLUBILITY + HIGH PERMEABILITY

Dissolution is often the main limitation; formulation can improve absorption.

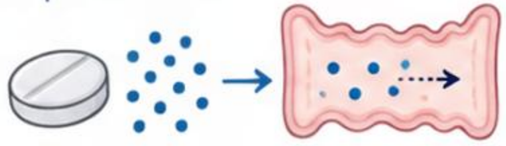
Examples: ibuprofen, ketoprofen.



CLASS III — HIGH SOLUBILITY + LOW PERMEABILITY

Dissolves readily, but membrane permeation is the main limitation.

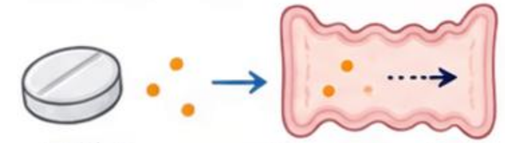
Examples: cimetidine, acyclovir.



CLASS IV — LOW SOLUBILITY + LOW PERMEABILITY

Both dissolution and permeation are difficult; oral development is challenging.

Example: hydrochlorothiazide.



High — SOLUBILITY — Low

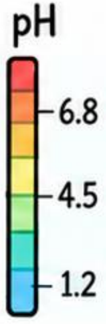
USES

Formulation design • bioavailability and bioequivalence planning • deciding whether a BCS-based biowaiver may be considered.
BCS class is assigned using defined dose, pH, temperature and evidence—not by guesswork.

BIOPHARMACEUTICS CLASSIFICATION SYSTEM (BCS)

HIGH SOLUBILITY — ICH M9

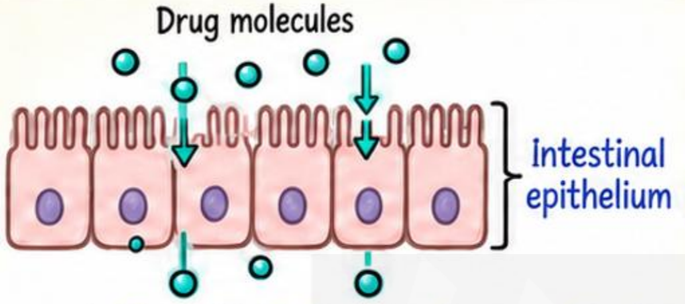




The highest single therapeutic dose is completely soluble in 250 mL or less of aqueous medium from pH 1.2 to 6.8 at 37 ± 1°C.

Check at least pH 1.2, 4.5 and 6.8, and at the pKa when it lies within the range.

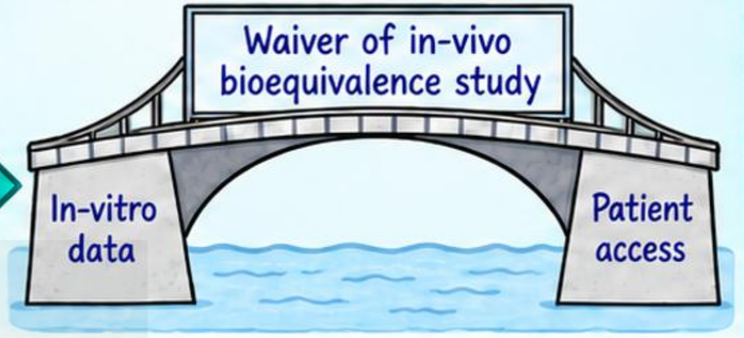
HIGH PERMEABILITY



Supported by suitable human pharmacokinetic or mass-balance data, or by an appropriately validated permeability method accepted for the purpose.

A fixed **90%** absorption statement is not a universal ICH M9 rule.

BCS-BASED BIOWAIVER



A regulator may waive an in-vivo bioequivalence study for an eligible immediate-release solid oral product when all guideline conditions are met.

It is mainly considered for Class I and Class III drug substances—not Class II or IV.

DISSOLUTION CONDITIONS

CLASS I: test and reference are very rapidly dissolving, or rapidly dissolving with similar profiles.



VERY RAPID: ≥85% in 15 min

OR



RAPID: ≥85% in 30 min with similar profiles

CLASS III: both should be very rapidly dissolving—at least 85% in 15 minutes—and excipient similarity is stricter.



VERY RAPID: ≥85% in 15 min

IMPORTANT

A biowaiver is a scientific and regulatory decision, not an automatic right. Dose, formulation, excipients, dissolution, therapeutic index and product eligibility all matter.

BASIC CONCEPTS OF CLINICAL TRIALS

CLINICAL TRIAL

A planned study in human participants that evaluates a health intervention according to a written protocol.





PHASE I – FIRST HUMAN STUDIES

Usually **20–80** participants.
Main questions: safety, tolerability, dose range, pharmacokinetics and pharmacodynamics.

Often healthy volunteers; patients may be used when healthy exposure is unsutablle, such as some anticancer drugs.



PHASE II – EARLY THERAPEUTIC EXPLORATION

Usually a few dozen to about **300** patients with the target condition.

Main questions: preliminary efficacy, dose selection and short-term adverse effects.



PHASE III – CONFIRMATORY STUDIES

Usually several hundred to about **3,000** patients, sometimes more.

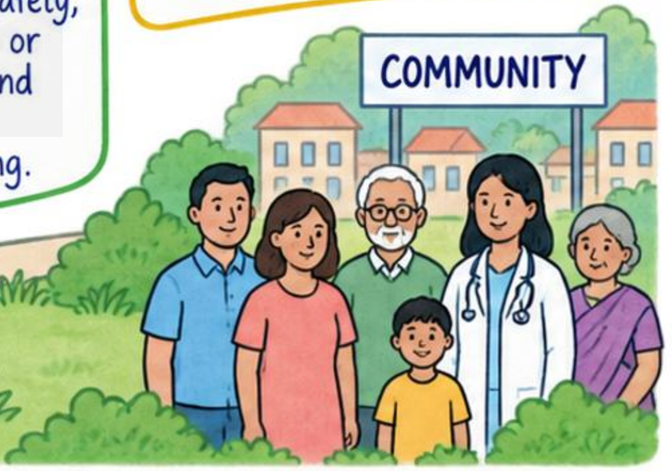
Confirms benefit and safety, compares with placebo or standard treatment, and supports marketing application and labeling.



PHASE IV – AFTER APPROVAL

Post-marketing studies and pharmacovigilance in wider use.

Detects rare or long-term risks, effectiveness in practice and additional uses when properly studied.



NOTE Participant numbers are typical ranges—not legal fixed limits. Design depends on the disease, product, outcome and regulator.

BASIC CONCEPTS OF CLINICAL TRIALS



1. SCIENTIFIC PROTOCOL
clear objective, design, eligibility, treatment, monitoring and stopping rules.

2. REGULATORY PERMISSION
obtained from the Central Licensing Authority when required.

3. REGISTERED ETHICS COMMITTEE
independently reviews risk, benefit, consent and participant protection.

4. CTRI REGISTRATION
Indian clinical trial is registered before the first participant is enrolled.

5. INFORMED CONSENT
voluntary decision after understandable information about purpose, procedures, risks, benefits, alternatives, privacy and right to withdraw.

6. GCP CONDUCT
trained team follows protocol, protects participants and produces reliable data.

7. SAFETY MONITORING
adverse events are detected, treated, documented and reported.

8. MEDICAL MANAGEMENT / COMPENSATION
trial-related injury is managed and compensation is determined under applicable rules.

9. DATA INTEGRITY
records are accurate, attributable, confidential, traceable and available for audit.

ETHICAL CORE
Respect for persons • beneficence • non-maleficence • justice • privacy.
Consent is a continuing process—not only a signature.

INDIA — SAE TIMELINE
Investigator sends an initial serious adverse event report within **24 hours** and a due-analysis report within **14 days** as required by **NDCTR 2019**.

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