Unit-5

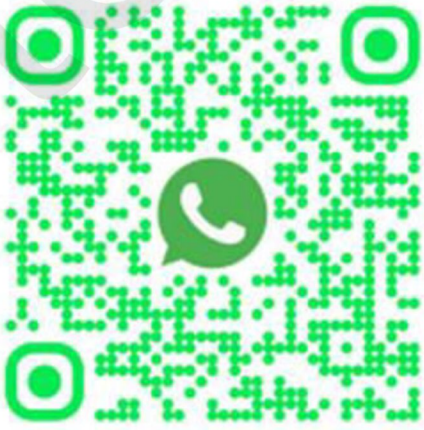
Industrial Pharmacy 2

B.Pharma 7 Sem Notes

Unit: 5

Indian Regulatory Requirements:

- **Central Drug Standard Control Organization (CDSCO) and State Licensing Authority: Organization, Responsibilities, Certificate of Pharmaceutical Product (COPP), Regulatory requirements and approval procedures for New Drugs.**



Introduction to Drug Regulation in India

Drug regulation in India is the process of ensuring that all medicines, cosmetics, and medical devices available in the country are safe, effective, and of good quality. The Indian government has put in place a strong system of laws and organizations to protect public health.

Legislation:

The main law governing drugs in India is the **Drugs and Cosmetics Act, 1940** and the **Drugs and Cosmetics Rules, 1945**. These laws cover the import, manufacture, distribution, and sale of drugs and cosmetics throughout India.

Two-Tier Regulatory System

India follows a unique two-tier system for drug regulation, meaning the work is divided between the Central Government and the State Governments:

Central Level	State Level
CDSCO (Central Drug Standard Control Organization)	State Drug Control Departments
Headed by DCGI (Drugs Controller General of India)	Headed by State Drug Controller / Commissioner
Controls new drugs, imports, clinical trials, and standards	Controls manufacturing licenses, sales licenses, and local enforcement

Remember This!
Central Government = Policy, Standards & New Drug Approvals
State Government = Licensing, Manufacturing & Local Enforcement
Both work together to ensure safe drugs reach patients.

Central Drug Standard Control Organization (CDSCO)

The CDSCO is the national regulatory body for pharmaceuticals and medical devices in India. It works under the Ministry of Health and Family Welfare, Government of India. Think of CDSCO as the central command center for drug regulation in the country.

Basic Information

Detail	Information
Full Name	Central Drug Standard Control Organization
Under	Directorate General of Health Services (DGHS), Ministry of Health & Family Welfare
Headquarters	FDA Bhawan, New Delhi
Headed By	Drugs Controller General of India (DCGI)
Established Under	Drugs and Cosmetics Act, 1940
Website	cdsco.gov.in

Vision of CDSCO

To protect and promote public health in India by ensuring the safety, efficacy, and quality of drugs, cosmetics, and medical devices.

Areas of Control

- Approval of new drugs and clinical trials.
- Import of drugs into India.
- Setting quality standards for drugs.
- Regulation of medical devices.
- Monitoring adverse drug reactions (Pharmacovigilance).
- Coordination with state drug authorities.
- Blood banks and blood products regulation.

Drugs Controller General of India (DCGI)

The DCGI is the head of the CDSCO and is the most important regulatory official for drugs in India. The DCGI is appointed by the Central Government and has wide-ranging powers under the Drugs and Cosmetics Act.

Powers and Duties of DCGI

- Approves new drugs for manufacture and marketing in India.
- Grants permission for conducting clinical trials.
- Approves import licenses for drugs.
- Bans drugs that are found to be harmful or ineffective.
- Sets standards for drug testing and quality.
- Issues guidelines and notifications regarding drug regulation.
- Coordinates with international regulatory agencies (WHO, USFDA, EMA, etc.).
- Acts as the licensing authority for certain categories of drugs (biologicals, vaccines, new drugs).

Fact
The DCGI directly approves: New Drugs, Clinical Trials, Vaccines, Blood Products,
Biologicals, Medical Devices (notified), IV Fluids, and Sera.
For other drugs, licensing is done by State Authorities.

Organizational Structure of CDSCO

CDSCO has a well-defined structure with its headquarters in New Delhi and zonal offices spread across India. This ensures effective regulation at both national and regional levels.

Headquarters (New Delhi)

The headquarters is responsible for policy-making, new drug approvals, and coordination with international bodies. It houses the office of the DCGI along with various technical divisions.

Zonal Offices

CDSCO has zonal and sub-zonal offices across major cities in India to oversee drug regulation at the regional level:

Office Type	Locations
Zonal Offices (6)	Mumbai, Kolkata, Chennai, Ghaziabad, Hyderabad, Ahmedabad
Sub-Zonal Offices (7)	Chandigarh, Bengaluru, Jammu, Guwahati, and others
Port Offices	Major sea and air ports for import/export control
Testing Labs	Central Drug Testing Laboratories (CDL, Kolkata; CDTL, Mumbai; etc.)

Divisions at Headquarters

- New Drug Division — Handles applications for new drug approvals and clinical trials.
- Import & Registration Division — Manages drug import licenses.
- Medical Devices Division — Regulates medical device approvals.
- Cosmetics Division — Regulates cosmetic products.
- Pharmacovigilance Division — Monitors adverse drug reactions (ADRs).
- Biologicals Division — Handles vaccines, sera, and biological products.
- IT & Data Management — Manages SUGAM portal (online application system).

Advisory Bodies

CDSCO is supported by various expert advisory committees, including the **Drug Technical Advisory Board (DTAB)** and the **Drug Consultative Committee (DCC)**. These bodies advise the government on technical and policy matters related to drugs.

Advisory Body	Role
DTAB	Advises the Central Government on technical matters; recommends amendments to the Drugs Act and Rules.
DCC	Ensures uniformity in drug administration across states; coordinates central and state drug authorities.
Subject Expert Committees (SECs)	Review new drug and clinical trial applications; provide scientific evaluation.
Pharmacovigilance Programme Committee	Oversees national pharmacovigilance and ADR monitoring.

Responsibilities and Functions of CDSCO

CDSCO has a wide range of responsibilities that ensure the safety and quality of drugs available in India. Here are the major functions:

1. Regulatory Functions

- Approval of new drugs, clinical trials, and fixed-dose combinations (FDCs).
- Licensing of drugs manufactured by government-owned units.
- Grant of import licenses (NOCs) for drugs and medical devices.
- Registration of foreign manufacturers exporting drugs to India.
- Approval of medical devices and in-vitro diagnostic devices.

2. Standard-Setting Functions

- Laying down standards for drugs, cosmetics, diagnostics, and devices.
- Publishing the Indian Pharmacopoeia (IP) through the Indian Pharmacopoeia Commission (IPC).
- Setting guidelines for bioavailability and bioequivalence studies.
- Updating schedules (Schedule H, H1, X, etc.) for drug classification.

3. Quality Control Functions

- Testing drug samples through Central Drug Laboratories.
- Monitoring quality of drugs in the market through surveys.
- Taking action against spurious, adulterated, and not-of-standard-quality (NSQ) drugs.
- Recall of unsafe or substandard drugs.

4. Enforcement Functions

- Inspection of manufacturing units and blood banks.
- Prosecution of offenders under the Drugs and Cosmetics Act.
- Monitoring import/export of controlled substances.
- Coordinating with state authorities for joint inspections.

5. International Functions

- Issuing Certificate of Pharmaceutical Products (COPP) for exports.
- Liaising with WHO, USFDA, EMA, TGA, and other global regulatory bodies.
- Participating in international harmonization efforts (ICH, etc.).
- Representing India at international drug regulation forums.

State Licensing Authority (SLA)

The State Licensing Authority is the regulatory body at the state level responsible for the day-to-day regulation of drug manufacturing, sale, and distribution within each state. Every state and union territory in India has its own drug control administration.

What is the State Licensing Authority?

Under the Drugs and Cosmetics Act, the **State Government appoints a State Drug Controller** (also called State Drugs Controller or Commissioner of Food and Drug Administration) who acts as the licensing authority for that state. This officer and the department under them form the State Licensing Authority.

Points

- Each state has its own FDA or Drug Control Department.
- The State Drug Controller is the head of this department.
- They issue manufacturing and sales licenses for drugs.
- They conduct inspections of pharmacies, drug stores, and manufacturing plants.
- They take legal action against violations within the state.

Easy Way to Remember
CDSCO = Central Level = New Drugs, Imports, Standards, Clinical Trials
SLA = State Level = Manufacturing Licenses, Sales Licenses, Local Inspections
Both work under the same law: Drugs and Cosmetics Act, 1940

Organization of State Drug Control

Each state's drug control department has a hierarchical structure designed to manage drug regulation from state headquarters down to the district level.

Typical Organizational Hierarchy

Position / Level	Responsibility
State Drug Controller / Commissioner FDA	Overall head of drug regulation in the state; policy decisions and major approvals.
Joint / Additional Drug Controller	Assists the State Drug Controller; handles specific zones or divisions.
Deputy Drug Controller	Manages regional offices; reviews license applications.
Assistant Drug Controller	Conducts inspections of manufacturing units.
Drug Inspector	The field-level officer who inspects drug stores, pharmacies, hospitals, and takes samples for testing.
Government Analyst	Head of the State Drug Testing Laboratory; tests drug samples and issues reports.

State Drug Testing Laboratories

Every state has at least one State Drug Testing Laboratory where samples collected by Drug Inspectors are tested. If a drug fails the test, legal action is taken against the manufacturer or seller. If there is any dispute, the sample can be sent to the Central Drug Laboratory (CDL) in Kolkata for a final verdict.

Responsibilities of State Licensing Authority

A. Licensing Functions

- Issue, renew, suspend, or cancel manufacturing licenses for drug products.
- Issue, renew, suspend, or cancel retail and wholesale sales licenses.
- License pharmacies and drug stores.
- Issue licenses for manufacturing of cosmetics.
- Grant licenses for restricted drugs (Schedule X drugs like narcotics and psychotropic substances).

B. Inspection & Enforcement

- Regular and surprise inspections of drug manufacturing units.
- Inspection of drug retail and wholesale shops.
- Collection of drug samples for quality testing.
- Investigation of complaints regarding drug quality.
- Prosecution of offenders selling spurious, misbranded, or adulterated drugs.
- Seizure of stocks found to be not of standard quality (NSQ).

C. Quality Monitoring

- Running State Drug Testing Laboratories.
- Participating in the Drug Survey Programme to check market quality.
- Reporting findings to CDSCO and taking coordinated action.

D. Administrative Functions

- Maintaining registers of licensed manufacturers and sellers.
- Submitting reports to CDSCO and state government.
- Implementing orders and notifications from Central Government.
- Creating awareness about drug safety among the public.

CDSCO vs. State Licensing Authority — Comparison

Aspect	CDSCO (Central)	State Licensing Authority
Level	Central (National)	State (Regional)
Head	DCGI	State Drug Controller
New Drug Approval	Yes — Sole authority	No
Clinical Trials	Yes — Approves clinical trials	No
Import License	Yes — Issues import NOCs	No
Manufacturing License	Only for biologicals, vaccines, etc.	Yes — For most drugs
Sales License	No	Yes — Retail & wholesale
Inspections	Importers, blood banks, central units	Factories, pharmacies, drug stores
Drug Testing	Central Drug Labs	State Drug Testing Labs
Standards	Sets national drug standards (IP)	Follows central standards
COPP	Issues COPP for export	No

Certificate of Pharmaceutical Product (COPP)

The Certificate of Pharmaceutical Product (COPP) is an official document issued by the CDSCO (on behalf of the Government of India) that certifies that a specific pharmaceutical product is approved and can be legally manufactured and sold in India.

What is COPP?

COPP is based on the **WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce**. It is needed when an Indian company wants to export its pharmaceutical products to other countries. The importing country often asks for this certificate to verify that the drug is properly regulated in its home country.

Purpose of COPP

- Facilitates international trade of pharmaceutical products.
- Confirms that the product is authorized for sale in India.
- Assures importing countries about the quality and regulatory status of the drug.
- Certifies that the manufacturing facility is inspected and follows GMP standards.
- Builds trust between exporting and importing nations.

Information Contained in COPP

Field	Details Provided
Product Name	Name of the drug product being exported.
Dosage Form & Strength	Tablet, capsule, injection, etc. with its strength.
Active Ingredients	Name and quantity of each active pharmaceutical ingredient (API).
Manufacturer Details	Name, address, and license number of the manufacturing unit.
Marketing Authorization	Confirmation that the product is approved for sale in India.
GMP Status	Whether the plant is inspected and follows Good Manufacturing Practices.
Market Status	Whether the product is actually marketed (sold) in India or not.

Procedure to Obtain COPP

1. The manufacturer applies online through the SUGAM portal (sugam.cdsco.gov.in).
2. Application is submitted with required documents (drug license, GMP certificate, product details, etc.).
3. The concerned zonal office of CDSCO verifies the documents.
4. If everything is in order, the zonal office recommends approval.
5. CDSCO headquarters issues the COPP.
6. The COPP is valid for 2 years from the date of issue.

Types of COPP

Type	Description
COPP (Product Marketed)	Product is approved AND actively sold in India.

COPP (Product Not Marketed)	Product is approved but NOT currently sold in India (manufactured only for export).

Important Points about COPP
COPP is issued ONLY by CDSCO, not by State Authorities.
It follows the WHO Certification Scheme format.
Validity: 2 years (renewable).
Applied online through SUGAM portal.
Essential for pharmaceutical export business.

Regulatory Requirements for New Drugs

What is a New Drug?

As per the **Drugs and Cosmetics Rules, 1945 (Rule 122-E)**, a New Drug includes:

- A drug that has not been used in the country before (not approved in India).
- A drug already approved but proposed in a new dosage form, new route of administration, or a new indication.
- A fixed-dose combination (FDC) not already approved.
- A modified or sustained-release form of an already approved drug.
- A vaccine, r-DNA product, or biological product used for the first time in India.

Important Note
A drug continues to be classified as a 'New Drug' for 4 years from the date of its first
approval in India. After 4 years, it becomes an 'existing drug' and can be licensed
by State Licensing Authorities directly.

Regulatory Framework

New Drug applications in India are governed by:

- Drugs and Cosmetics Act, 1940
- Drugs and Cosmetics Rules, 1945 (Schedule Y)
- New Drugs and Clinical Trials Rules, 2019 (NDCT Rules) — the latest and most comprehensive rules.
- Various guidelines and notifications issued by CDSCO.

Schedule Y / NDCT Rules 2019

The **New Drugs and Clinical Trials Rules, 2019** replaced the older Schedule Y and brought in a modernized, transparent, and time-bound framework for new drug approvals and clinical trials in India.

Features of NDCT Rules, 2019

- Defined timelines for approval of applications (30 to 90 working days).
- Provisions for accelerated approval for breakthrough therapies.
- Ethics Committee registration is mandatory.
- Compensation framework for clinical trial-related injuries.
- Academic clinical trials are recognized and regulated.
- Post-trial access provisions for patients who benefit from the trial drug.
- Risk-based approach to regulation.

New Drug Approval Procedure in India

Getting a new drug approved in India involves a systematic, step-by-step process. The entire process is designed to ensure that only safe, effective, and quality drugs reach patients.

Step-by-Step Approval Process

STEP 1: Pre-Clinical / Non-Clinical Studies

Before testing on humans, the drug is tested on animals in a laboratory setting. These studies include:

- Pharmacological studies (how the drug works in the body)
- Toxicological studies (how toxic / harmful the drug could be)
- Acute, sub-acute, chronic toxicity, reproductive toxicity, carcinogenicity
- These studies must follow GLP (Good Laboratory Practice) guidelines.

STEP 2: Application to CDSCO (IND Application)

The sponsor/applicant submits an application (Form CT-04) to the DCGI through the SUGAM portal with:

- Complete pre-clinical data and results
- Proposed clinical trial protocol
- Investigator's Brochure
- Chemistry, Manufacturing, and Controls (CMC) data
- Ethics Committee approval from the proposed clinical trial sites

STEP 3: Review by Subject Expert Committee (SEC)

The application is reviewed by the Subject Expert Committee (SEC), which is a panel of medical and scientific experts. They evaluate:

- Safety data from pre-clinical studies
- Scientific merit and design of the proposed clinical trial
- Risk-benefit ratio for Indian patients

STEP 4: Clinical Trials (Phase I to Phase IV)

Once approved, clinical trials are conducted in phases (explained in detail in Section 13).

STEP 5: New Drug Application (NDA) / Marketing Authorization

After successful completion of clinical trials, the applicant submits an NDA with:

- Complete clinical trial data and results
- Safety, efficacy, and tolerability data
- Proposed prescribing information / package insert
- CMC data, stability data, and proposed labelling

STEP 6: Marketing Approval by DCGI

If the SEC and CDSCO are satisfied with all the data, the DCGI grants marketing authorization (permission to manufacture and sell the new drug in India). The manufacturer then obtains a manufacturing license from the State Licensing Authority.

Clinical Trials in India

Clinical trials are scientific studies conducted on human volunteers to test the safety and effectiveness of new drugs. In India, clinical trials are regulated by CDSCO under the NDCT Rules, 2019.

Phases of Clinical Trials

Phase	Subjects	Number	Purpose
Phase I	Healthy volunteers	20–100	Test safety, dosage, side effects, and how the drug moves in the body (pharmacokinetics).
Phase II	Patients with the disease	100–300	Test effectiveness (efficacy), determine optimal dose, and monitor side effects.

Phase III	Large patient groups	300–3,000+	Confirm efficacy, monitor adverse reactions in a larger population, and compare with existing treatments.
Phase IV	General population (post-marketing)	Thousands	Long-term safety monitoring after the drug is approved and marketed. Also called Post-Marketing Surveillance.

Ethics Committee (EC)

Every clinical trial must be approved by an Ethics Committee (also called Institutional Review Board) before it can begin. The EC ensures that the rights, safety, and well-being of trial participants are protected.

- Must be registered with CDSCO.
- Reviews the trial protocol, informed consent form, and investigator qualifications.
- Monitors the trial throughout its duration.
- Has the power to stop a trial if safety concerns arise.

Informed Consent

Every participant in a clinical trial must give written informed consent in a language they understand. The consent form explains the purpose of the trial, risks, benefits, and the participant's right to withdraw at any time.

Requirements for Clinical Trials in India

- Permission from DCGI is mandatory before starting any trial.
- Ethics Committee approval is required for each trial site.
- Audio-visual recording of informed consent is mandatory for vulnerable populations.
- Compensation must be provided for any trial-related injury or death.
- All trials must be registered on the Clinical Trials Registry of India (CTRI).
- Data must be maintained for at least 5 years after trial completion.

Post-Approval Requirements

Once a new drug is approved, the manufacturer has certain ongoing responsibilities to ensure continued safety and quality:

A. Phase IV / Post-Marketing Surveillance (PMS)

- The manufacturer must monitor the drug's performance in the general population.
- Any new or rare adverse effects that appear after large-scale use must be reported.
- Periodic Safety Update Reports (PSURs) must be submitted to CDSCO.

B. Adverse Drug Reaction (ADR) Reporting

- Serious and unexpected adverse drug reactions must be reported within 15 days.
- India has the Pharmacovigilance Programme of India (PvPI) coordinated by the Indian Pharmacopoeia Commission (IPC), Ghaziabad.
- Healthcare professionals, patients, and manufacturers can report ADRs.

C. Labelling and Packaging

- The approved drug must follow the labelling requirements under the D&C Rules.
- Package insert with detailed prescribing information is mandatory.
- The label must include: batch number, manufacturing date, expiry date, MRP, storage conditions, and warnings.

D. Renewal of Approval

- New drug approval is initially valid for a specific period.
- The manufacturer must apply for renewal before expiry.
- Any changes in formulation, manufacturing process, or labelling require prior CDSCO approval (through change control / variation application).

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