INTRODUCTION TO REGULATORY AGENCIES

Mrs. Bhujadi P. N.

MES's College of Pharmacy, Sonai

U.S. Food and Drug Administration

FDA

Department of Health and Human Services

World Health Organization

ICH

harmonisation for better health

MHRA

Regulating Medicines and Medical Devices

Australian Government

Department of Health

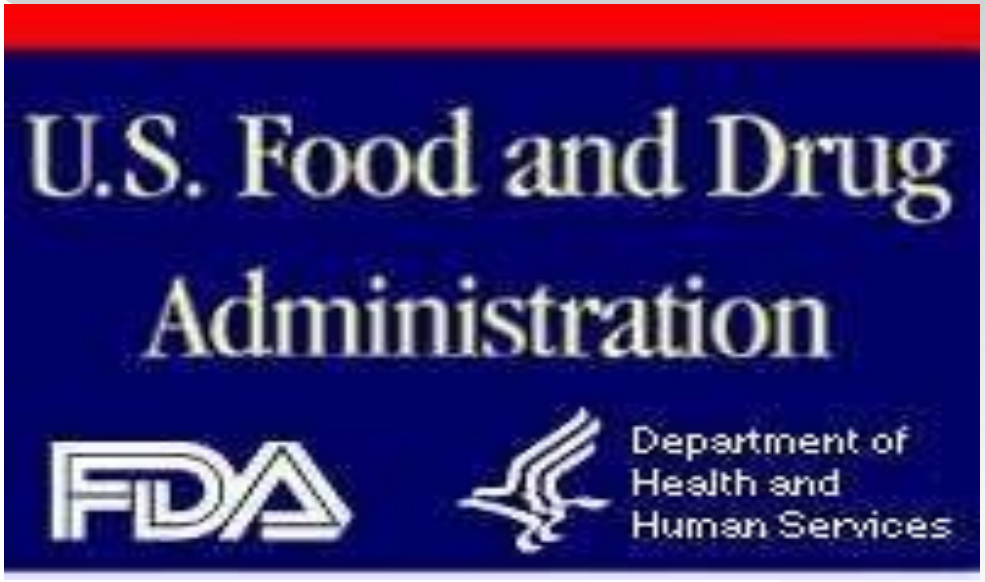
Therapeutic Goods Administration

CDSCO

Central Drugs Standard Control Organization

Regulatory Authorities Worldwide

Country/Continent	Regulatory Authorities
International	•ICH
	•WHO
	•WTO
Europe	•EMEA (European Medicine Evaluation Agency)
India	•CDSCO (Central Drug Standard Control Organization) •AYUSH (Ministry of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy)
US	•USFDA
	•DHHS (Department Of Health & Human Services)
	•NCCAM (National Center For Complementary & Alternative Medicine)
UK	•MHRA (Medicines & Healthcare Products Regulatory Authority)
Australia	•TGA (Therapeutic Goods Administration)
China	•SFDA (State Food & Drug Administration)
Brazil	•National Health Servillance Agency (NHSA)


U.S. Food and Drug
Administration
FDA
Department of
Health and
Human Services

US

FDA

INTRODUCTION

- US FDA - An agency within the U.S. Public Health Service, which is a part of the Department of Health and Human Services.

- Agency monitors the manufacture, import, transport, storage and sale of Medicines, medical devices, biological products & radiation-emitting devices.

ORGANISATION (BRANCHES)

- Centre for Biologics Evaluation and Research (CBER)
- Centre for Devices and Radiological Health (CDRH)
- Centre for Drug Evaluation and Research (CDER)
- Centre for Food Safety and Applied Nutrition (CFSAN)
- Centre for veterinary Medicine (CVM)
- Office of Regulatory Affairs (ORA)
- National Centre for Toxicological Research (NCTR)
- Office of Chief Council (OCC)
- Office of Commissioner (OC)

MISSION

- To promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner.

- With respect to such products, protect the public health by ensuring that the food are safe, Wholesome, sanitary, and properly labelled; human and veterinary drugs are safe and effective; there is reasonable assurance of the safety and effectiveness of devices intended for human use; cosmetics are safe and properly labelled, and public health and safety are protected from the electronic product radiation.

- Participates through appropriate process with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements.

WHAT USFDA REGULATES?

- Biological products
- Product manufacturing establishment Licensing
- Nations blood supply
- Research to establish product standards and to develop improved testing methods
- Cosmetics
- Labelling
- Drugs
- Product approvals

Continue….

- OTC and prescription drug labelling
- Drug manufacturing standards
- Foods
- Safety of all food products (except meat and poultry)
- Radiation-Emitting Electronic Products
- Radiation safety performance standard for microwave, ovens,diagnostic x-rays equipment, cabinet x-ray system (such as baggage x-rays at airports),Laser products,mercury vapour lamps
- Veterinary products.

WHAT USFDA DOES NOT REGULATES?

- Advertisements
- Alcohol
- Consumer products
- Drugs of abuse
- Health insurance
- Meat & poultry
- Pesticides
- Restaurants

US-FDA GUIDELINES

Part of title 21CFR	Guidelines
Part of 58	Good laboratory practice for nonclinical laboratory studies
Part of 101	Food labeling
Part of 110	Current good manufacturing practice in manufacturing, packing, or holding human food
Part of 201	Labeling
Part of 312	Investigational new drug application
Part of 314	Applications for FDA approval to market a new drug
Part of 328	Over-the-counter drug products intended for oral ingestion that contain alcohol

Continue…

Part of title 21CFR	Guidelines
Part of 331	Antacid products for over-the-counter (otc) human use
Part of 341	Cold, cough, allergy, bronchodilator, and antiasthmatic drug products for over-the-counter human use
Part of 600	Biological products: general
Part of 820	Quality system regulation
Part of 892	Radiology devices
Part of 1392	Registration of manufacturers, distributors, importers and exporters of list

WHO
(World Health Organization)

World Health Organization

Working For Health

World Health Organization

INTRODUCTION

- WHO is the United Nations specialized agency for health.
- WHO is the directing and coordinating authority for health within the world.
- It is responsible for providing leadership on global health matters shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring and assessing health trends.

World Health Organization

HISTORY

- When diplomats met to form the United Nations in 1945, one of the thing they discussed was setting up a global health organization.

- WHO's Constitution came into exist on 7 April 1948 – a date we now celebrate every year as World Health Day.

Objective of WHO

- Attainment of the highest possible level of Health by all peoples.

OFFICES

- *The headquarter is at Geneva,Switzerland.*
- *six regional offices are :*

1. Regional Office for South-East Asia:
   - at New Delhi
2. Regional Office for Africa:
   - at Congo
3. Regional Office for the America:
   - at Washington, USA
4. Regional Office for Europe:
   - at Copenhagen,Denmark
5. Regional Office for the Eastern Mediterranean:
   - at Cairo, Egypt
6. Regional Office for the Western Pacific:
   - at Manila,Philippines

World Health Organization

Governance of WHO

- The World health Assembly is the supreme decision-making body for WHO. It **meets each year in May at Geneva** & is attended by delegations from all 193 Member countries.

- The world health assembly is headed by the Director- General who is nominated by the executive board. The executive board is composed of 32 members technically qualified in the field of health.

- Members are elected for three-year terms. The main Board meeting is held in January, with a second shorter meeting in May of each year, immediately after the Health Assembly, for more administrative matters.

- Function: To approve the WHO programme & the budget for same & to decide major policy questions.

World Health Organization

Functions of WHO

1. To act as the directing & co-ordinating authority on international health work.

2. To assist governments,upon request,in strengthening health services.

3. To furnish appropriate technical assistance & in emergencies, necessary aid upon the request of governance.

4. To stimulate & advance work to eradicate epidemic, endemic & other diseases.

5. To promote & conduct research in the field of Health.

World Health Organization

Continue

6. To establish & revise as necessary international nomenclature of diseases, of causes of death & public health practices.

7. To develop, establish & promote internation standards of food,biological,pharmaceutical products.

8. To provide information ,counsel & assistance in the field of Health.

9. To promote improved standards of teaching & training in the Health,medical & related professions.

10. To establish & maintain effective co-operation with the United Nations,specializedagencies,governmental health administration & professional groups.

ICH
(International Conference on Harmonization)

Introduction of ICH

ICH - International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use.

- It is a unique project that brings together the regulatory authorities & experts from the pharmaceutical industries in the Europe,Japan & United states to discuss scientific and technical aspects of the product registration.

ICH
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PURPOSE

- To reduce the need to duplicate the testing carried out during the research & development of new medicines & thereby eliminate the unneccessary delay in the availability of new medicines.

LOCATION

- ICH secretariat is based at Geneva.

Members of ICH

ICH is comprised of six parties that represent the regulatory bodies and research based industries in the European Union,Japan and the USA.

JAPAN

- Ministry of Health,Labour and Welfare (MHLW)
- Japan Pharmaceutical Manufacturers Associations (JPMA)

Europe

- European Union (EU)
- European federation of Pharmaceutical Industries and Associations (EFPIA)

USA

- Food and Drug Administration (FDA)
- Pharmaceutical Research and Manufacturers of America (PhRMA)

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Additional members includes

Observers from the:

- World Health Organization (WHO) ,
- European Free Trade Association (EFTA) &
- Canada.

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Structure

- ICH Steering Committee,
- ICH Coordinators,
- ICH Secretariat &
- ICH Working Groups.
  - Expert Working Group (EWG),
  - Implementation Working Group (IWG).

ICH GUIDELINES (Q-Quality)

Q1A	Stability Testing of New Drug Substances & Products
Q1B	Stability Testing : Photostability Testing of New Drug Substances & Products
Q1C	Stability Testing for New Dosage Forms
Q1D	Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products
Q1E	Evaluation for stability data
Q1F	Stability Data Package for Registration Applications in Climatic Zones III and IV
Q2	Validation of AnalyticalProcedures: Text and Methodology

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Continue…

Q3A	Impurities in new drug substances
Q3B	Impurities in new drug products
Q3C	Impurities: guideline for residual solvents
Q4B	Evaluation and recommendation of pharmacopoeial texts for use in the ICH regions
Q5A	Viral safety evaluation of biotechnology products derived from cell lines of human or animal origin
Q5B	Quality of biotechnological products: analysis of the expression construct in cells used for production of r-dna derived protein products
Q5C	Quality of biotechnological products: Stability testing of biotechnological/biological products
Q5D	Derivation and characterisation of cell substrates Used for production of Biotechnological/biological products

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Q5E	Comparability of biotechnological/biological products subject to changes in their manufacturing process
Q6A	Specifications: test procedures and acceptance criteria for new drug substances and new drug poducts: chemical substances
Q6B	Specifications: test procedures and acceptance criteria for biotechnological/biological products
Q7	Good manufacturing practice guide for active pharmaceutical ingredients
Q8	Pharmaceutical development
Q9	Quality risk management
Q10	Pharmaceutical Quality System

ICH GUIDELINES (S-Safety)

S1A	Guideline on the Need for Carcinogenicity Studies of Pharmaceuticals
S1B	Testing for Carcinogenicity of Pharmaceuticals
S1C (R2)	Dose Selection for Carcinogenicity Studies of Pharmaceuticals
S2(R1)	Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use
S3A	Note for Guidace on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies
S3B	Pharmacokinetics:guidance for Repeated Dose Tissue Distribution Studies

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Continue…

S4	Duration of Chronic Toxicity Testing in Animals (Rodent and Non Rodent Toxicity Testing)
S5(R2)	Detection of Toxicity to Reproduction for Medicinal Products & Toxicity to Male Fertility
S6	Preclinical Safety Evaluation of Biotechnology derived Pharmaceuticals
S7A	Safety Pharmacology Studies for Human Pharmaceuticals
S7B	The Non-clinical Evaluation of The Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals
S8	Immunotoxicity Studies for Human Pharmaceuticals
S9	Nonclinical Evaluation for Anticancer Pharmaceuticals

ICH GUIDELINES (E- Efficasy)

E1	The Extent of Population Exposure to Assess Clinical Safety
E2A	Clinical Safety Data Management
E2B(R2)	Maintenance of The ICH Guideline on Clinical Safety Data Management
E2B(R3)	Revision of The ICH Guideline on Clinical Safety Data Management
E2C(R1)	Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs
E2D	Post-approval Safety Data Management: Definitions and Standards for Expedited Reporting

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Continue…

E2E	Pharmacovigilance Planning
E2F	Development Safety Update Report
E3	Structure and Content Of Clinical Study Reports
E4	Dose-response Information to Support Drug Registration
E5(R1)	Ethnic Factors in The Acceptability of Foreign Clinical Data
E6(R1)	Guideline for Good Clinical Practice
E7	Studies in Support of Special Population: geriatrics

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Continue…

E8	General Considerations for Clinical Trials
E8	Statistical Principles for Clinical Trials
E10	Choice of Control Group and Related Issues in Clinical Trials
E11	Clinical Investigation of Medicinal Products in The Pediatric Population
E12	Principles for Clinical Evaluation of New Antihypertensive Drugs
E14	The Clinical Evaluation of QT/QTC Interval Prolongation and Proarrhythmic Potential for Non-antiarrhythmic Drugs
E15	Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories
E16	Genomic Biomarkers Related to Drug Response

ICH GUIDELINES
(M- MULTIDISCIPLINARY)

M1- MedDRA	Medical Terminology
M2- ESTRI	Electronic Standards for the Transfer of Regulatory Information
M3- (R2):	Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals
M4- CTD	The Common Technical Document
M5	Data Elements and Standards for Drug Dictionaries

TGA
(Therapeutic Goods Administration)

Australian Government

Department of Health

Therapeutic Goods Administration

Australian Government
Department of Health
Therapeutic Goods Administration

What is TGA?

- The TGA is responsible for conducting assessment and monitoring activities to ensure that therapeutic goods available in Australia are of acceptable standards.

- Established on 15 February 1991.

Australian Government
Department of Health
Therapeutic Goods Administration

Objective of TGA…

- To provide a national framework for the regulation of therapeutic goods in Australia to **ensure the quality, safety and efficacy of medicines** and ensure the quality, safety and performance of **medical devices**.

- Essentially therapeutic goods must be entered on the **Australian Register of Therapeutic Goods (ARTG)** before they can be supplied in Australia.

Australian Government
Department of Health
Therapeutic Goods Administration

Role of the TGA

The TGA carries out an overall control through five main processes:

- **Pre-market evaluation** and approval of registered products intended for supply inAustralia;
- **Development, maintenance and monitoring** of the systems for listing of medicines;
- **Licensing** of manufacturers in accordance with international standards of GMPs

- **Post-market monitoring,** through sampling, adverseevent reporting, surveillance activities, and response to public inquiries;

- The **assessment** of medicines for export.

Australian Government
Department of Health
Therapeutic Goods Administration

TGA structure

- The TGA's offices are grouped into following core groups

1. TGA Executives
2. Market Authorization Group (MAG)
3. Monitoring and Compliance Group (MCG)
4. Regulatory Support Group
5. Office of Regulatory Integrity (ORI)

Australian Government
Department of Health
Therapeutic Goods Administration

1. TGA Executives

The TGA Executives has overall responsibility for the management of the TGA's regulatory functions and activities.

The TGA Executives comprises:

- TGA National Manager
- Principal Medical Adviser,
- Principal Legal Adviser,
- Chief Regulatory Officer,
- Chief Operating Officer

2. Market Authorization Group (MAG)

- The Market Authorization Group is responsible for undertaking evaluations of applications to approve new therapeutic products for supply in Australia. The MAG makes decisions whether to approve or reject market authorization of medicines, medical devices and blood and tissues that are imported, exported, manufactured and supplied in Australia.

3. Monitoring and Compliance Group (MCG)

- The Monitoring and Compliance Group is responsible for ongoing monitoring of therapeutic products approved for supply in Australia to ensure they meet the necessary standards throughout their lifecycle.

4. Regulatory Support Group

- Provides regulatory support services to the TGA, this includes the legal, finance, information technology and information management, communications, parliamentary and human resource management services.

5. Office of Regulatory Integrity(ORI)

- The Office of Regulatory Integrity (ORI) provides an independent and objective review and advisory service to provide assurance to the National Manager of the TGA that the TGA's financial and operational controls are operating in an efficient, effective and appropriate manner and that its regulatory controls are operating in an efficient, effective and appropriate manner and are consistent with relevant legislative requirements.

Australian Government
Department of Health
Therapeutic Goods Administration

Australian register of therapeutic goods (ARTG)

A 'therapeutic good' is broadly defined as a good which is represented in any way to be taken, for therapeutic use.

Therapeutic use means use in connection with

- Preventing, diagnosing, curing a disease, ailment, defect or injury;
- Inhibiting or modifying a physiological process;
- Testing for pregnancy;
- Replacement or modification of parts of the anatomy

- **TheAustralian Register of Therapeutic Goods** (ARTG) was established under the Therapeutic Goods Act 1989.

- **The ARTG is a computer database of therapeutic goods**. Therapeutic goods are divided broadly into **two classes: medicines and medical devices.**

- Unless exempt, medicines must be **entered as either 'registered' or 'listed'** medicines and medical devices must be included before they may be supplied in or exported from Australia.

- **AUST R** medicines are assessed for safety, quality and effectiveness and higher risk medication.
- They include all prescription medicines.
- Many over-the-counter products such as those for pain relief, coughs and colds and antiseptic creams.

- **AUST L** medicines are much lower risk self-medication products

- They are used for **minor health problems** and are reviewed for safety and quality. They include sunscreens and many **vitamin, mineral, herbal and homoeopathic products**

- Listed and Registered medicines are differentiated on the product label by the designation, 'AUST L' or 'AUST R' respectively, followed by a unique number.

Assessment criteria

Whether a product is listed or registered in the ARTG depends largely on three things:

- The ingredients;
- The dosage form of the product; and,
- The promotional or therapeutic claims made for the product.

In assessing the level of 'Risk', factors such as

- strength of a product
- side effects,
- toxicity, and
- the seriousness of the medical condition for which the product is intended to be used.

MHRA

(MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY)

MHRA
Regulating Medicines and Medical Devices

➢ What is MHRA?

The MHRA was **set up in April 2003** from a merger of the Medicines Control Agency and the Medical Devices Agency. The MHRA is the **government agency** which is **responsible for ensuring that medicines and medical devices work, and are acceptably safe**.

MHRA
Regulating Medicines and Medical Devices

Aims of MHRA

- **Protecting** public health through regulation, with acceptable benefit-risk profiles for medicines and devices.
- **Promoting** public health by helping people who use these products to understand their risks and benefits.
- **Improving** public health by encouraging and facilitating developments in products that will benefit people.

Objectives of MHRA

- Safeguard public health through MHRA's primary role in ensuring that the products MHRA regulate meet required standards, that they work and are acceptably safe;
- Carry out communication role through the provision of accurate, timely and authoritative information to healthcare professionals, patients and the public;
- Support research, ensuring through the application of Better Regulation principles that regulation does not stifle innovation;
- Influence the shape of the future regulatory framework through use of our effective European and International relationships;
- Run an organisation with a skilled and equipped workforce that is fit for the future

The MHRA's activitie

- **Assessing the safety, quality and efficacy** of medicines, and authorising their sale or supply in the UK for human use.

- Overseeing the UK Notified Bodies that **audit** medical device manufacturers.

- O**perating post-marketing surveillance** and other systems for reporting, investigating and monitoring adverse reactions to medicines and adverse incidents involving medicinal devices and taking any necessary action to safeguard public health, for example through safety warnings, removing or restricting the availability of products or improving designs.

- **Operating a proactive compliance programme**

- **Operating a quality surveillance system** to sample and test medicines and to address quality defects, monitoring the safety and quality of imported unlicensed medicines and investigating

- **Internet sales** and potential counterfeiting of medicines.

- **Regulating clinical trials** of medicines and medicinal devices.

- **Monitoring and ensuring** compliance with statutory obligations relating to medicines and medicinal devices through inspection, taking, enforcement action where necessary.

- **Promoting good practice** in the safe use of medicines and medical devices.

- **Managing** the General Practice Research Database **(GPRD)** and the British Pharmacopoeia **(BP)** and contributing to the development of performance standards for medical devices.

- **Offering scientific, technical and regulatory advices** on medicines and medical devices.

- **Providing** the public and professions with **authoritative information** to enable informed dialogue on treatment choices.

MHRA's structure:

Corporate governance

1. **The Agency Board** is made up of a non-executive Chairman, six non-executive members and the Agency's Chief Executive Officer who is responsible for service delivery and resources.
2. **The Executive Board** consisting of the Agency's directors takes overall responsibility for day-to-day management, strategic decision-making, line management, and all financial, policy, operational and resource management issues.
3. **The Risk and Audit Committee** provides independent feedback to the Chief Executive and the Management Board on the effectiveness of risk management processe

What MHRA regulates?

- **Medicine**
- ✓Licencing of medicines
- ✓Medicines for children
- ✓Inspection and standards
- ✓Importing and exporting medicines
- ✓Best practice guidance on labelling and packaging of medicines
- ✓The safety of medicines

The role of MHRA

- Assess applications for marketing medicinal products
- Assess applications to undertaken clinical trials
- Inspect the manufacturers and wholesalers of medicines-licensing
- Undertake post-marketing surveillance including:
  - Pharmacovigilance
  - Quality defect monitoring
  - Sampling and testing
  - Product recalls.

- Issue certificates to companies wishing to export their medicinal products to countries outside the EU.

- Enforce the statutory requirements covering medicines control and good clinical practice guidelines.

- Publish quality standards for drug substances through the "British Phaarmacopoeia"

Central Drugs Standard Control Organization (CDSCO)

Central Drugs Standard Control Organization

What is CDSCO....??

- It is the National Drug Regulatory Authority of the Government of India works under **Directorate General of Health Services, Ministry of Health & Family Welfare, Government** of India is the National Regulatory Authority (NRA) of India.

- Central Drugs Standard Control Organization (CDSCO) exercises regulatory control over the quality of drugs, cosmetics and notified medical devices in the country.

- CDSCO has six zonal offices, four sub-zonal offices, thirteen port offices and seven laboratories under its control.

Central Drugs Standard Control Organization

- It is the Central Drug Authority for discharging functions assigned to the Central Government under the Drugs and Cosmetics Act.
- **Ministry responsible:** Ministry of Family & Health Welfare
- **Minster responsible :** Dr. Harsh Vardhan
- **Drug Controller General of India:** Dr. V. G. Somani

Central Drugs Standard Control Organization

Vision:

- To protect and promote health in India

Mission:

- To safeguard and enhance the public health by assuring the safety, efficacy and quality of drugs, cosmetics and medical devices

Values:

- To achieve the mission and mandate of the CDSCO we will strive to act with transparency, accountability, punctuality, courtesy, openness, responsiveness, professionalism, impartiality, consistency, integrity and truthfulness

Strategies:

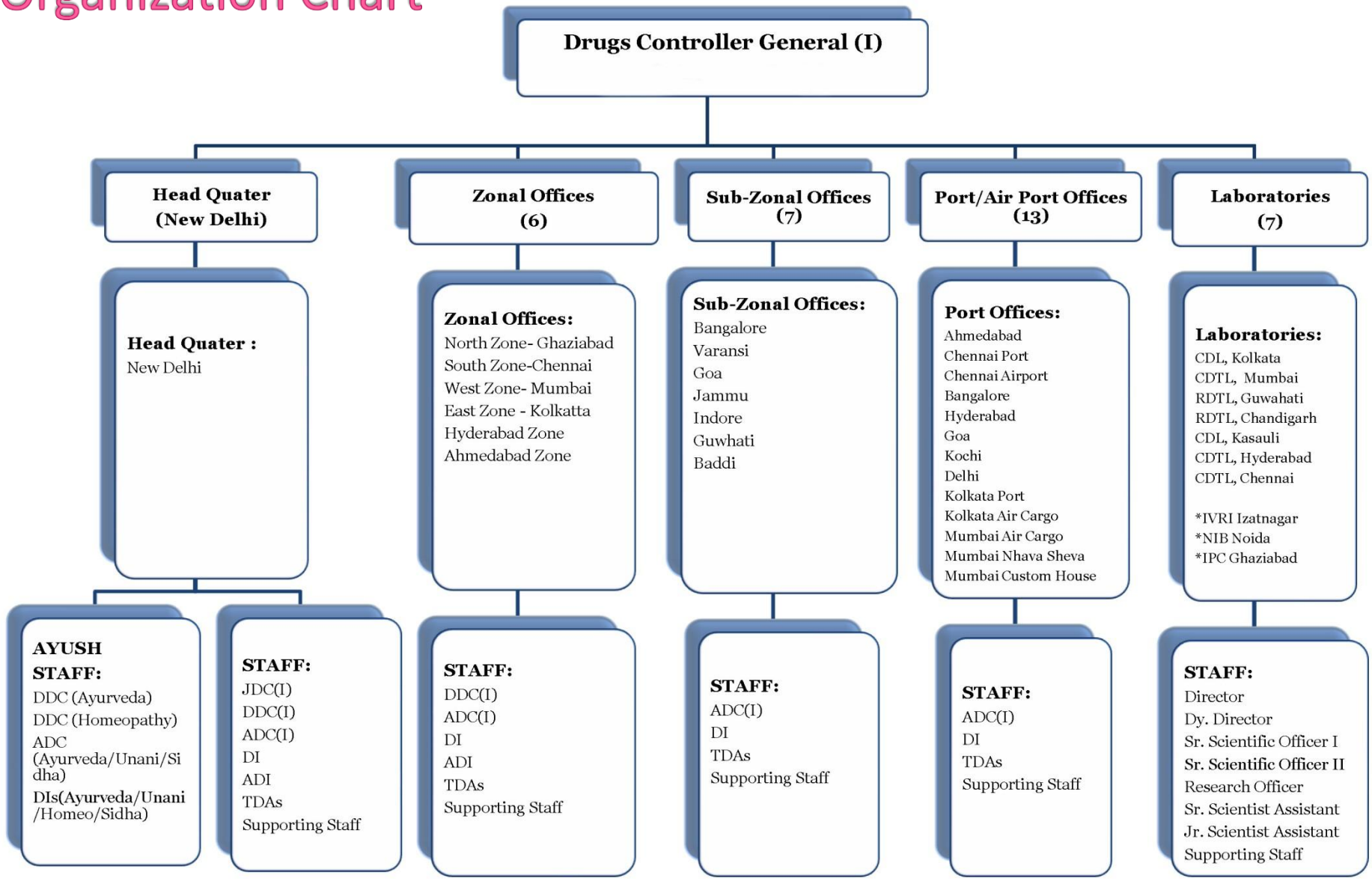
- Initiate in framing of rules, regulations and guidance documents to match the contemporary issues in compliance with the requirements of Drugs & Cosmetics Act 1940 and Rules 1945.
- Facilitate in Uniform implementation of the provisions of the Drugs & Cosmetics Act 1940 and Rules 1945.
- Function as Central license Approving Authority under the provisions of Drugs and Cosmetics Act 1940 and Rules 1945.
- Collaboration with other similar International agencies.
- Providing training to the Indian regulatory personnel.

Central Drugs Standard Control Organization

Functions of CDSCO

- Approval of new drugs and clinical trials
- Import Registration and Licensing
- License approving of Blood Banks, LVPs, Vaccines, r-DNA products & some Medical Devices (CLAA Scheme)
- Amendment to D &C Act and Rules
- Banning of drugs and cosmetics
- Grant of Test License, Personal License, NOCs for Export
- Testing of New Drugs
- Oversight and market Survillance through Inspectorate of Centre Over and above the State Authority

Organization Chart



CDCO and D&C Act

- The Drugs & Cosmetics Act,1940 and rules 1945 have entrusted various responsibilities to central & state regulators for regulation of drugs & cosmetics.

- Under the Drugs and Cosmetics Act, CDSCO is responsible for **(Functions)**
  - Approval of Drugs,
  - Conduct of Clinical Trials,
  - Laying down the standards for Drugs,
  - Control over the quality of imported Drugs
  - Coordination of the activities of State Drug Control Organizations

CONCLUSION:

- The Regulatory systems for medicines must continue to ensure that the medicines having highest possible level of confidence in their overall safety and quality.

- The current systems of regulation of medicines allows consumers to have faith in the quality, safety and efficacy of medicines.

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THANK YOU