

# **MAJOR BODIES REGULATING INDIA PHARMACEUTICAL SECTOR**

RASMITA JENA

ASSISTANT PROFESSOR

SoPLS, CUTM

- Drug Regulatory Affair is a function which regulates the pharmaceutical science in order to facilitate trade / business in and outside the country of origin for public interest.
- Effective drug regulation is required to ensure the safety, efficacy and quality of drugs.
- The drug regulation mainly consists of:
  1. Drug Regulatory Bodies
  2. Drug Laws
  3. Quality Control
  4. Drug Information Centers etc.

## Why RA in Pharmaceuticals?

- The Pharmaceutical sector has been ever growing and with globalization, the race to lead to be first is no more restricted by boundaries. Companies success lies in the “time taken” by the product to reach the market.
- The companies responsible for the discovery, testing, manufacture and marketing of these products also want to ensure that they supply products that are safe and make a worthwhile contribution to public health and welfare.
- On an average it takes 15-20 years for a new drug development, and it cost around \$800-1000 million.

- The process of drug regulation consists of :
  - Drug laws
  - Drug agencies
  - Drug board
  - Quality control
  - Drug information centers

## **DRUG REGULATORY AGENCIES IN INDIA:**

India has emerged as one of the leading markets for pharmaceutical products. Increase in the private healthcare infrastructure, widening rural markets, and inclusion of newer technologies have placed healthcare as an independent sector in India. With privatization of healthcare, the medical devices sector is growing too.

In order to regulate the import, manufacture, distribution and sale of drugs and cosmetics, the Drugs and Cosmetics Act, 1940 (“D&C, Act”) was introduced in India in 1940. However, no separate regulation has been enacted for regulating the import, manufacture, distribution or sale of medical devices in India till date by the Government of India.

Drugs and Health is in concurrent list of Indian Constitution. It is governed by both Centre and State Governments under the Drugs & Cosmetics Act, 1940.

## Organizational Structure

Ministry of Health

CDSCO

Drugs Controller General India (DCGI)

Deputy Drugs Controller [India]

Assistant Drugs Controller [India]

Medical Device Division

Diagnostic Division

Drug Inspectors

Technical Data  
Associates

Drug Inspectors

Technical Data  
Associates

## **MAIN BODIES:-**

Central Drug Standard Control Organization (CDSCO)

Ministry of Health & Family Welfare (MHFW)

Indian Council of Medical Research (ICMR)

Indian Pharmaceutical Association (IPA)

Drug Technical Advisory Board (DTAB)

Central Drug Testing Laboratory (CDTL)

Indian Pharmacopoeia Commission (IPC)

National Pharmaceutical Pricing Authority (NPPA)

Functions undertaken by Central Government Statutory function laying down standards of drugs, cosmetics, diagnostics and devices. Laying down regulatory measures, amendments to Acts and Rules. To regulate market authorization of new drugs. To regulate clinical research in India to approve licenses to manufacture certain categories of drugs as Central Licence Approving Authority i.e. for Blood Banks, Large Volume Parenteral and Vaccines & Sera. To regulate the standards of imported drugs. Work relating to the Drugs Technical Advisory Board (DTAB) and Drugs Consultative Committee (DCC). Testing of drugs by Central Drugs Labs. Publication of Indian Pharmacopoeia.

## I. CDSCO-

In India, the Central Drugs Standard Control Organization ('CDSCO') is the main regulatory body currently regulating import, sale and manufacture of medical devices which have been notified as drugs by virtue of Section 3(b) (IV) of the D&C Act. The CDSCO lays down standards of drugs, cosmetics, diagnostics and devices and issues licenses to drug manufacturers and importers. It also lays down regulatory measures, amendments to Acts and Rules and regulates market authorization of new drugs, clinical research in India and standards of imported drugs etc.

Headquartered in New Delhi, the CDSCO is India's main regulatory body for pharmaceuticals and medical devices and Within the CDSCO, the Drug Controller General of India (DCGI) is responsible for the regulation of pharmaceuticals and medical devices. The DCGI is advised by the Drug Technical Advisory Board (DTAB) and the Drug Consultative Committee (DCC). Licensing and classification of medical devices are handled by the Central Licensing Approval Authority (CLAA). The CLAA is also responsible for setting and enforcing safety standards, appointing notified bodies to oversee conformity assessment, conducting post-market surveillance and issuing warnings and recalls for adverse events.



- 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.
- **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

The CDSCO establishes safety, efficacy, and quality standards for pharmaceuticals and medical devices. It publishes and updates the Indian Pharmacopeia, a list of regulated pharmaceuticals and devices. For all drug and device applications, the CDSCO appoints notified bodies to perform conformity assessment procedures, including testing, in order to ensure compliance with their standards. The CDSCO is also divided into several zonal offices which do pre-licensing and post-licensing inspections, post-market surveillance, and recalls when necessary.

In addition to its regulatory functions, the CDSCO offers technical guidance, trains regulatory officials and analysts, and monitors adverse events. The CDSCO works with the World Health Organization to promote Good Manufacturing Practice (GMP) and international regulatory harmony.

# 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

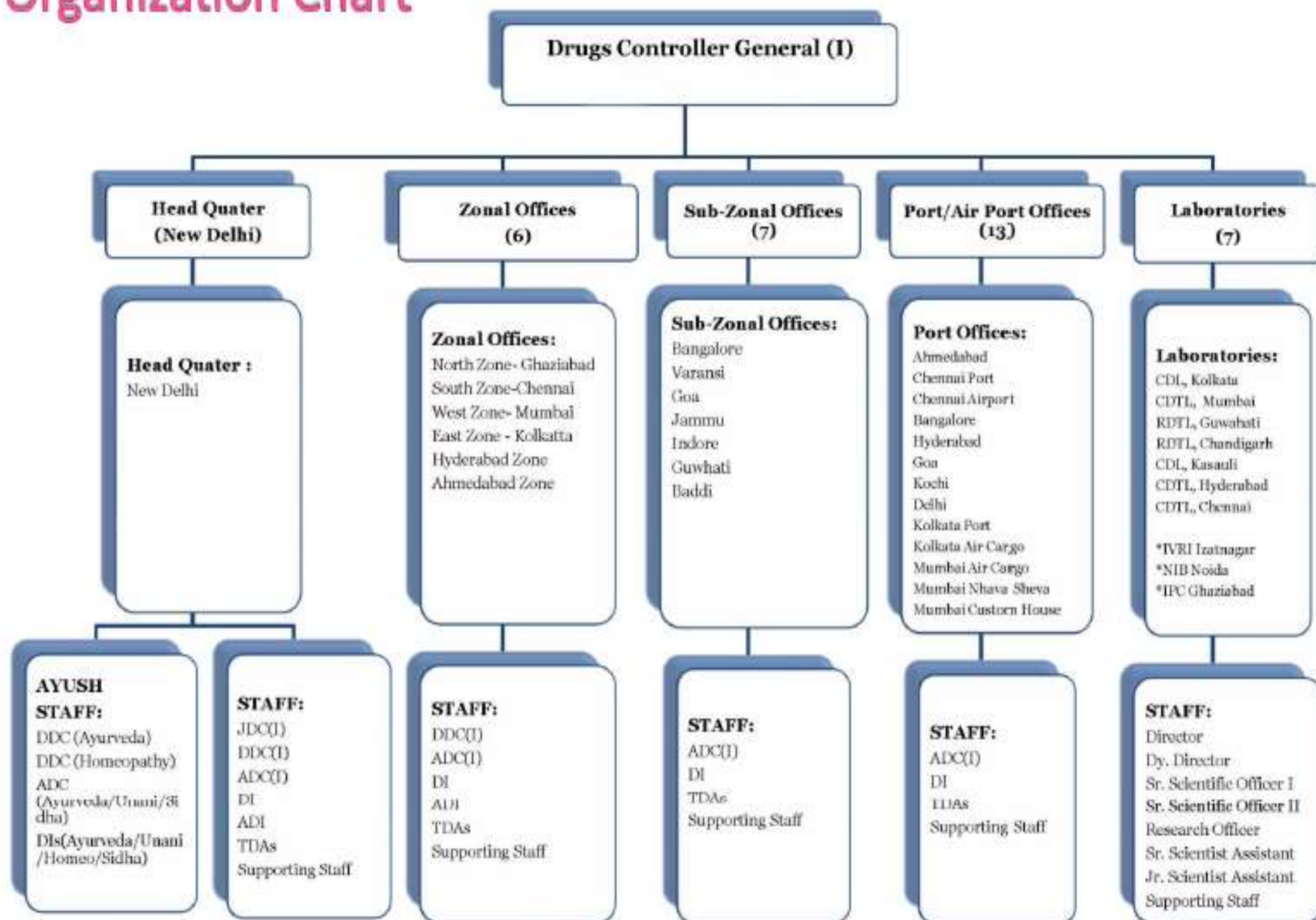
Testing of New Drugs

Oversight and market Surveillance through Inspectorate of Centre Over and above the State Authority

# 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
  - 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

# Organization Chart



**2. National Institute of Health and Family Welfare (NIHFW)**-NIHFW is an Apex Technical Institute, funded by Ministry of Health and Family Welfare, for promotion of health and family welfare programmers in the country through education, training, research, evaluation, consultancy and specialized services. The NIHFW was established on March 9, 1977 by a merger of the National Institute of Health Administration and Education (NIHAE) with the National Institute of Family Planning (NIFP).

\*List of Governing Body Members of NIHFW

18 members

1 Chairman (ex-officio)

1 Vice Chairman (ex-officio)

9 Member (ex-officio)

6 Member

1 Member Secretary (ex-officio)

## **ACTIVITIES AND RESPONSIBILITIES:**

Measuring weight of children to assess the nutritional status. Assessment of diseases like level of anaemia. Testing of food material like cooking salt for level iodine. To release fund on the advice of the Ministry. It is responsible for all governmental programs relating to family planning in India.

### **3. DRUG TECHNICAL ADVISORY BOARD (DTAB):**

The Central Government constitute a Board (to be called the Drugs Technical Advisory Board) to advise the Central Government and the State Governments on technical matters arising out of the administration of D&C, Act 1940.

List of Governing Body Members of NIHFV:

18 Members

10 ex-officio Members

5 Nominated Members

5 Elected Members

**ACTIVITIES AND RESPONSIBILITIES:**

It advises matter related to Drugs. The nominated and elected members of the Board shall hold office for three years, but shall be eligible for re-nomination and re-election. The Board may, subject to the previous approval of the Central Government, make bye-laws fixing a quorum and regulating its own procedure.



**4. CENTRAL DRUG TESTING LABORATORY (CDTL)** The central drug laboratory, Kolkata is national statutory laboratory of the government of India for quality control of drug and cosmetic and established under the D&C act, 1940. Oldest quality control laboratory of the drug control authorities in India. Function under the director general of Health Services in the Ministry of Health and Family Welfare.

**COMPOSITION:** Indian Pharmacopoeia Commission (IPC)

General Body 19 Members

Governing Body 10 Members

Scientific Body 23 Experts

CIPL Lab IPC Secretariat Indian Pharmacopoeia was prepared by Indian Pharmacopoeia Commission (IPC)

**ACTIVITIES AND RESPONSIBILITIES:**

Development of comprehensive monographs. Accord priority to monographs of drugs included in the national Essential Drug List and their dosage forms. Preparation of monograph for products that have normally been in the market for not less than 2 years. Collaborate with pharmacopoeias like the BP, USP, JP and International Pharmacopoeia with a view to harmonizing with global standards.

# Drug Regulatory Authority

- The drug regulatory authority (DRA) is the agency that develops and implements most of the legislation and regulations on pharmaceuticals.
- Its main task is to ensure the quality, safety and efficacy of drugs, and the accuracy of product information.
- This is done by making certain rules that the manufacture, procurement, import, export, distribution, supply and sale of drugs, product promotion and advertising, and clinical trials are carried out according to specified standards.

## **Functions of Regulatory Authority:**

- Product registration (drug evaluation and authorization, and monitoring of drug efficacy and safety).
- Regulation of drug manufacturing, importation, and distribution.
- Regulation & Control of drug promotion and information.
- Adverse drug reaction (ADR) monitoring.
- Licensing of premises, persons and practices.
- Main goal of drug regulation is to guarantee the safety, efficacy and quality of drugs.

# Role of regulatory affair department

- Raw material department
- Research and development
- Production
- Finished product
- Quality control
- Quality assurance
- Packaging

# WHO(World Health Organization)

- WHO is the directing and coordinating authority for health within the United Nations system (see more on web site: <http://www.who.int/en/>).
- 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.
- In the 21st century, health is a shared responsibility, involving equitable access to essential care and collective defence against transnational health threats

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- 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.

- The headquarter is at Geneva, Switzerland.
- Six regional offices are :
  - Regional Office for South-East Asia: - at New Delhi
  - Regional Office for Africa: - at Congo
  - Regional Office for the America: - at Washington, USA
  - Regional Office for Europe: - at Copenhagen, Denmark
  - Regional Office for the Eastern Mediterranean: - at Cairo, Egypt
  - Regional Office for the Western Pacific: - at Manila, Philippines

# 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.
- To act as the directing & coordinating authority on international health work.
- To assist governments, upon request, in strengthening health services.
- To furnish appropriate technical assistance & in emergencies, necessary aid upon the request of governance.
- To stimulate & advance work to eradicate epidemic, endemic & other diseases.
- To promote & conduct research in the field of Health.
- To establish & revise as necessary international nomenclature of diseases, of causes of death & public health practices.
- To develop, establish & promote international standards of food, biological, pharmaceutical products.
- To provide information ,counsel & assistance in the field of Health.
- To promote improved standards of teaching & training in the Health, medical & related professions.
- To establish & maintain effective co-operation with the United Nations, specialized agencies, governmental health administration & professional groups

- WHO's role in drug regulation is fourfold.
- First, issuing necessary norms and standards through its
  - Expert Committees (such as WHO Expert Committee on Specifications for Pharmaceutical Preparations and
  - WHO Expert Committee on Biological Standardization)
  - Expert Committee like bodies (such as International Nonproprietary Names Expert Group and International Working Group for Drug Statistics Methodology issuing Anatomical, Therapeutic and Chemical or ATC codes Daily Defined Doses or DDDs for drug utilization research).
- Second, supporting regulatory capacity building leading to implementation of drug regulation on national level and its harmonization on regional and Global level.
- This activity involves assessment of regulatory activities on country level and various technical training courses (such as GMP and GCP, how to assess generic medicines, bioequivalence, safety monitoring and Pharmacovigilance, quality assurance and quality control) and customized technical assistance (in cooperation with numerous WHO collaborating centers and other partners) to the countries.

- Third, in selected areas of essential products, ensuring the quality, safety and efficacy of limited high public health value essential medicines (such as anti-retrovirals to treat HIV/AIDS, or medicines to treat malaria) and vaccines (used in national vaccination programs) through “prequalification”.
- De facto prequalification, although primarily meant for UN procurement and international donors, is a regulatory activity mimicking medicines registration (marketing authorization) in its all elements to ensure that products prequalified meet all international standards for quality, safety and efficacy.
- Prequalification program has also a very strong capacity building element built into it.
- Fourth, WHO plays a very important role in facilitating exchange of regulatory information for which it has developed a number of tools.

- Since 1980 WHO convenes every second year International Conference of Drug Regulatory Authorities (ICDRA) and publishes their proceedings.
- These conferences provide drug regulatory authorities of WHO Member States with a forum to meet and discuss ways to strengthen collaboration.
- The ICDRAs have been instrumental in guiding through its recommendations regulatory authorities, WHO and interested stakeholders and in determining priorities for action in national and international regulation of medicines, vaccines, biomedicines and herbals.

- WHO manages also a system for regular exchange of information between Member States on the safety and efficacy of pharmaceutical products, using a network of designated national drug information officers.
- WHO ensures the prompt transmission to national health authorities of new information on serious adverse effects of pharmaceutical products and it also responds to individual requests for information.
- These goals are achieved by the regular publication of regulatory information in the WHO Pharmaceuticals Newsletter (<http://www.who.int/medicines/publications/newsletter/en/index.html>) and by the dissemination of one-page Drug Alerts on an ad hoc basis.

- Relevant restrictive regulatory decisions are ultimately compiled in the United Nations Consolidated List of Products Whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely Restricted or not Approved by Governments
- WHO publishes updates to this list: Pharmaceuticals: Restrictions in use and availability. WHO publishes also quarterly WHO Drug Information (<http://www.who.int/druginformation/>) journal which provides an overview of topics of current relevance relating to drug development, safety and regulation.
- Latest lists of proposed and recommended International Nonproprietary Names (INN) for Pharmaceutical Substances are also published in this journal.

- WHO cooperates very actively with national regulatory authorities of all of its Member States.
- It tries to facilitate spreading best practices and experience.
- Through its observer role in the international Conference of Harmonization (ICH) WHO is liaising between ICH and non-ICH countries trying to ensure that information exchange between highly industrialized and less resourced countries is taking place.

# USFDA

- 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:
  - 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



## 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 and Foods
- Labelling
- Drugs and Veterinary products.
- Product approvals
- OTC and prescription drug labelling
- Drug manufacturing standards
- 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

# WHAT USFDA DOES NOT REGULATES?

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

# TGA (Therapeutic Good Administration Australia)

## HISTORY

- The Evolution of Therapeutic goods Administration in Australia can be broadly segmented into following periods.
- 1)The period until 1938 -During this period there was an increasing number of medicines appearing in an unregulated market, with many products regarded as 'quack' medicine.
- 2)1939-1961:NHMRC developing a more uniform national approach to labeling and standards need for independent laboratory testing. The government moved to regulate the standards for medicines for good quality. The National Biological Standards Laboratory was established to independently test medicines on the Australian market and regulate their manufacture.
- 3)1962-1988: Pre-market assessment of quality, safety and efficacy evolved and finally was integrated into National system of integration of therapeutic good regulation and establishment of TGA.
- 4)1989-2007:The national system TGA continued to mature into an internationally harmonized regulatory system with increasing globalization.

## **INTRODUCTION OF TGA:**

- The Therapeutic Goods Administration (TGA) is a unit of the Australian Government Department of Health and Ageing.
- The TGA monitoring activities to ensure therapeutic goods available in Australia are of an acceptable standard.
- The Australian community expects that medicines and medical devices in the marketplace are safe and of high quality, and of a standard at least equal to that of comparable countries.
- The regulatory framework within which the TGA operates is based on a risk management approach. It is designed to ensure public health and safety.
- It is beneficial for both consumers and industry.
- In undertaking its responsibility, the TGA has developed a constructive partnership with industry at the same time freeing industry from any unnecessary regulatory burden and minimizing the cost of medicines.

# TGA STRUCTRE

- The TGA Regulatory offices are grouped into –
  - 1. Market Authorization Group
  - 2. Monitoring and Compliance Group
  - 3. Regulatory Support Group
- **TGA Executive:** The TGA Executive has overall responsibility for the management of the TGA's regulatory activities.
- **Market Authorization Group:** The Market Authorization Group is responsible for the evaluation and authorization of therapeutic goods to ensure they meet appropriate standards of quality, safety and efficacy.

- **Monitoring and Compliance Group:** The Monitoring and Compliance Group is responsible for monitoring of therapeutic goods on the Australian market to ensure that they comply with required standards of quality, safety, efficacy .
- **Regulatory Support Group:** The Regulatory Support Group provides the business systems and support services that help the TGA to undertake its regulatory responsibilities.
  - Office of Regulatory Integrity
  - The Office of Regulatory Integrity functions as an internal auditor of regulatory activity and advises the TGA Executive on the appropriate operations.

# Therapeutic Goods Act 1989

- Therapeutic Goods Act 1989, is to provide a national framework for the regulation of therapeutic goods in Australia to ensure the Quality, Safety and Efficacy of medicines Ensure the quality, safety and performance of medical devices.
- The Act is a Commonwealth Act that provides a uniform national system of controls over therapeutic goods.
- facilitating trade between the States/Territories and benefiting for both consumers and industry.
- Essentially therapeutic goods must be entered on the Australian Register of Therapeutic Goods (ARTG) before they can be supplied in Australia.
- The ARTG is a computer database of information about therapeutic goods for human use approved for supply in, or exported from Australia.



- It also details the requirements for listing or registering medicines in the Australian Register of Therapeutic Goods.
- The act sets out the legal requirement for the import , export, and supply of medicines in Australia.
- The Therapeutic Goods Act sets out requirements for manufacturing, advertising and labeling of medicines in Australia.
- It also establishes controls relating to the advertising of therapeutic goods which aim to minimize the risk of misuse of such products arising out of, for example, misrepresentation or misunderstanding about the uses of the goods.
- It offers the advantage for consumers and healthcare professionals to be able to have confidence in the standard of ready-made proprietary therapeutic goods which they use or prescribe.

## **Does the Act apply to your product?**

- You will need to comply with the Act if your product is a 'therapeutic good'. 'Therapeutic goods' may be:
  - Medicines, or
  - Medical devices
  - Some products will be classified as a medicine or as a food or cosmetic depending on how that particular product fits with the criteria set out in the Act.

## **What are 'therapeutic goods'?**

- A 'therapeutic good' is broadly defined as a good which is represented in any way to be, or is likely to be taken to be, for therapeutic use under section 7 of the Act.
- Therapeutic good is a product for use in humans that is used in, or in connection with:-
  - Preventing, diagnosing, curing a disease, defect or injury OR
  - Influencing, inhibiting or modifying a physiological process OR
  - Testing the susceptibility of persons to a disease OR
  - Influencing, controlling or preventing conception OR
  - Testing for pregnancy

# Regulation of Medicines

- The Therapeutic Goods Administration overall control the of supply of medicines in Australia is exercised through following main processes:
  1. Pre-market evaluation and approval of medicines intended for supply in Australia.
  2. Licensing of manufacturers in accordance with international standards under Good Manufacturing Practice.
  3. Post-market monitoring, through sampling, adverse event reporting, surveillance activities, and response to public inquiries.
  4. maintenance and monitoring of the systems for registering and listing of medicines

## Pre-Market Assessment

- Drugs are required to undergo an assessment before it can be listed or registered.
- Number of factors are taken into consideration including:
  - The toxicity of the ingredients.
  - The dosage form of the medicine
  - whether the medicine is indicated for a serious form of a disease, or disorder, or for the treatment, cure, prevention of a disease or disorder
  - whether the drug is likely to result in significant side effects, including interactions with other medicines; and
  - The degree of control over a medicine is directly related to the risk level of that medicine. Therefore, registered medicines are required to undergo a more rigorous assessment than listed medicines

## **Manufacturing Requirements**

- Australian manufacturers of medicines must be licensed under the Therapeutic Goods Act 1989. Their manufacturing processes must comply with principles of Good Manufacturing Practice. The aim of licensing is to protect public health by ensuring that medicines meet definable standards of quality assurance and are manufactured in conditions which are clean and free of contaminants.
- Licensing of Manufacturers Applications for a manufacturing license are assessed through an inspection of the manufacturing premises. Auditors from the TGA conduct audits of manufacturing premises and a license is issued only after all the requirements have been met. Audits are conducted before a license is issued, And at regular intervals after the license has been granted generally every 15 to 24 months.

# **Medicines and Healthcare products Regulatory Agency (MHRA)**

- The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.
- The MHRA now also looks after blood and blood products, working with UK blood services, healthcare providers, and other relevant organizations to improve blood quality and safety.
- The MHRA regulates a wide range of materials from medicines and medical devices to blood and therapeutic products/services that are derived from tissue engineering.

## History

- The agency was formed on 1 April 2003 with the merger of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA).
- It is an Executive Agency of the Department of Health.
- **Roles of the MHRA:**
  - Operate post-marketing surveillance for reporting investigating and monitoring of adverse drug reactions to medicines and incidents with medical devices.
  - Assessment and authorization of medicinal products for sale and supply in U.K.
  - Investigate internet sales and potential counterfeiting of medicines, and prosecute where necessary.
  - Regulate clinical trials of medicines and medical devices.
  - Monitor and ensure compliance with statutory obligations relating to medicines and medical devices.
  - Promote safe use of medicines and devices.
  - Manage the General Practice Research database and the British Pharmacopeia.

# Regulatory Program

- Assess application for authorization to market products for human use and either grant authorizations to market each product or reject such applications.
- Assess applications to undertaken clinical trials and grant, or refuse, permission.
- Inspect the manufacturers and wholesalers of medicines for human use and either grant manufacturing and wholesale licenses or refuse such licenses.
- Undertaken post marketing surveillance including
  - Pharmacovigilance
  - Quality defect monitoring
  - Sampling and testing
  - Product recalls



# Monitoring of Safety and Quality Standards

- The MHRA monitors safety and quality standards by:-
  - Regular inspections of good and safe practice, including ;
  - Medicines manufacture and supply
  - Medicines distribution and storage
  - Clinical trials
  - Auditing of clinical inspecting system for devices
  - Laboratories testing medicines
  - Auditing Notified Bodies

# Dealing with faulty Medicines

- The MHRA's Defective Medicines Report Centre (DMRC) issues alerts to healthcare professionals, hospitals, GP surgeries, and wholesalers to tell them when a medicine is being recalled or when there are concerns about the quality that will affect its safety or effectiveness.
  - **Class 1** requires immediate recall, because the product poses a serious or life threatening risk to health .
  - **Class 2** specifies a recall within 48 hours, because the defect could harm the patient but is not life threatening.
  - **Class 3** requires action to be taken within 5 days because the defect is unlikely to harm patients and is being carried out for reasons other than patient safety.
  - **Class 4** alerts advise caution to be exercised when using the product, but indicate that the product poses no threat to patient safety.

## **MHRA Governance**

- The Agency Board is made up of a non-executive Chairman, six non-executive members and the Agency's Chief Executive Officer.
- The Agency's Chief Executive is responsible for service delivery and resources.
- The Executive Board, consisting of the Agency's directors.
- The Agency Board is chaired by the MHRA Chairman, and consists of six non-executive directors and the Chief Executive Officer.
- The executive Board's primary responsibility are to ensure:-
  - The strategic direction set by the Agency Board is implemented and reflected in the day to day operations of the Agency.
  - Principles of good governance are followed.
  - The Agency is well managed financially.
  - Appropriate human resources(HR) policies are followed.
  - Reporting to the Agency Board on the operations of the Agency.

# Medicines Control Council (MCC)

- South Africa has developed a medicines regulatory authority with internationally recognized standing.
- The Medicines Control Council (MCC) is a statutory body that was established in terms of the Medicines and Related Substances Control Act, 101 of 1965, to oversee the regulation of medicines in South Africa.

## History

- More than 20 000 medicines have been approved.
- More than 220 meetings have been held to decide on the registration of medicines.
- The South African Pharmacy Council has licensed 300 wholesalers and distributors.
- The Medicines Control Council approves more than 280 clinical trials annually

## **Regulatory Program**

- The Medicines Control Council applies standards laid down by the Medicines and Related Substances Control Act, (Act 101 of 1965) which governs the manufacture, distribution, sale, and marketing of medicines.
- The prescribing and dispensing of medicines is controlled.
- The Council has eleven technical committees, with 146 members from various institutions in the country.
- The MCC operates through external experts who are members of Council Committee structures. Most experts evaluate data sets submitted by the pharmaceutical industry for purposes of registration.
- The office of the Registrar provides administrative and technical support to Council and its activities. The Registrar is also an executive secretary to Council.

- The staff complement of Medicines Regulatory Affairs includes doctors, pharmacists, veterinarians, other scientists and administrative staff.
- The skills of Council and its committees are written into law and include expertise in toxicology and medicine safety, clinical pharmacology, biotechnology, pharmaceuticals, internal medicine, virology, pharmaceutical chemistry, neonatology, pediatrics, immunology, veterinary science, complementary medicines and law.

## Guidelines

- Good Manufacturing Practices:-
  - Guidelines on inspections involving the GMP inspectors
  - Isolator technology
  - Penicillin manufacturing
  - Radiopharmaceutical manufacturing
  - Aerosol manufacturing
  - Guidelines for preparation of site master file

## Conclusion

- The Regulatory system for complementary medicines must continue to ensure that the medicines having highest possible level of confidence in their overall safety and quality.
- The current system of regulation of complementary medicines allows consumers to have faith in the quality, safety and efficacy of medicines.

## **(ANVISA) (Agencia Nacional de Vigilancia Sanitaria) Brazilian Health Surveillance Agency**

- ANVISA is regulatory body of BRAZIL. Brazil is biggest country of South America. Some of the small countries nearby Brazil are following the rules according to ANVISA.
- ANVISA means “Agencia Nacional de Vigilancia Sanitaria”. This abbreviation is in Portuguese language.
- In English, it means “National Health Surveillance Agency” or sometimes it is written as “Brazilian Health Surveillance Agency”.
- ANVISA is established on 26th January, 1999. Thus it does not have long historical backgrounds.



- The National Health Surveillance Agency was established in 1999 by president Fernando Henrique Cardoso. Linked to the Ministry of Health, the agency coordinates:
  - The National Sanitary Surveillance System
  - The National Program of Blood and Blood Products
  - The National Program of Prevention and Control of Hospital Infections

### **Anvisa's Mission**

- "To protect and promote health, ensuring the hygiene and safety of products and services and taking part in developing access to it."
  - Values
  - Transparency
  - Knowledge (as a springboard for action)
  - Co-operation

# Vision

- The National Health Surveillance Agency was established by Law 9.782, of January 26, 1999. The Agency is designated an autonomous agency operating under a special regime.
- This means that ANVISA is an independently administered, financially-autonomous regulatory agency, with security of tenure for its directors during the period of their mandates. The Agency is managed by a Collegiate Board of Directors, comprised of five members.
- Within the structure of Federal Public Administration, the Agency is linked to the Ministry of Health, under a Management Contract. The agency incorporated additional attributions:
- Coordination of the National Sanitary Surveillance System (SNVS), the National Program of Blood and Blood Products and the National Program of Prevention and Control of Hospital.
- Infections; monitoring of drug prices and prices of medical devices; attributions pertaining to regulation, control and inspection of smoking products; technical support in granting of patents by the National Institute of Industrial Property.

## **ANVISA is responsible for :**

- monitoring drug prices
- prices of medical devices
- control and inspection of smoking products
- technical support in granting of patents by the National Institute of Industrial Property.
- protection of the health of the population by exercising sanitary control over production
- marketing of products and services subject to sanitary surveillance, controlling ports, airports and borders
- linked to the Brazilian Ministry of Foreign Affairs and foreign institutions over matters concerning international aspects of sanitary surveillance.

# ANVISA is a part of NSSS

- National System of Sanitary Surveillance (NSSS) is an organization of Brazil whose responsibility is:
  - To keep a watch over certain professional activities
  - To put a stop to charlatanism
  - To inspect ships, cemeteries and places where food was on sale to the public.

## **OFFICES OF ANVISA:**

- Advisory Council
- Office of Ombudsman

## **ADVISORY COUNCIL:**

- It monitors and follows up the development of activities carried out by ANVISA.
- Council comprise of Representatives from
  - Public Administration Institutions
  - Organized Civil Society
  - Scientific Community
- The main function of advisory council is to provide information upon request by any citizen, patient, industrialist or health professional on any topics.
- Unlike other well known regulatory bodies, ANVISA does not have specific offices for each topic to provide specific information only. It has a general functioning common Advisory council.

## **OFFICE OF OMBUDSMAN:**

- It is an independent body for direct communication of Citizens or Institutes to attend the Complaints.
- It is characterized by impartiality and transparency.
- It has no direct or indirect linking with ANVISA. It is regulated directly under the Brazilian ministry of health.
- It Start action against complaints within 2 days, if appropriate.

## **Regulations by ANVISA:**

- Blood and blood products
- Cosmetics
- Drugs
- Generic Drugs
- Food
- Health services o International Affairs
- Market regulations
- Medical devices
- Pharmacovigilance
- Ports, airports and borders
- Sanitizing o Tobacco
- Toxicology o REBLAS – Brazilian network of Analytical Laboratory Products

# REGISTRATION OF NEW DRUG:

- Registration procedure of new drug is divided in mainly 3 parts as follows...

1. **Pre-registration measures** (Protocol for Clinical study )

2. Registration

- Documents to be submitted
- Protocol for the new drug
- Protocol for import of new drug

3. Post-registration

- Alteration in Registration, Renewal of Registration

Thus, these three parts can be considered similar to IND, NDA and Supplementary NDA as per US FDA.

# **I. Pre-registration measures**

- In case of a new national drug product, the protocols of the clinical studies and the results or current status of the studies in compliance with the legislation in force has to be submitted.
- In case of a new imported drug product that will undergo phase III clinical studies in Brazil, the study protocol and the results or current status of the studies in compliance with the legislation in force has to be submitted.
- Whenever phase III will take place with a new product manufactured in the country, pre-notification for the production of pilot batch according to the GUIDE FOR THE NOTIFICATION OF PILOT BATCHES OF MEDICINES has to be submitted.



## II. Registration:

### 1. Documents to be submitted

- Registration petition forms
- Proof of payment of Sanitary Surveillance Inspection
- copy of the company's Operation License
- Technical Responsibility Certificate by the Regional Pharmacy Council
- Copy of the notification protocol of pilot batch production
- Good Manufacturing Practices certificate (GMP) emitted by ANVISA

### 2. Protocol for the new drug: General data: package insert text, label etc...

- Expiry date by Stability studies
- All Toxicity study reports
- Clinical trial data with statistical treatments
- For Combination – Maximum 3 is allowed for oral or injectable preparations. Four combinations are allowed only if the fourth ingredient is caffeine.
- Physico-Chemical parameters of drug
- Synthesis route (all reagent, solvent, condition)
- Pharmacodynamic parameters
- Pharmacokinetic parameters
- Production Report (Batch size, methods and equipments used)
- Q.C. of raw material and finished products

### 3. Protocol for the import of new drug :

- GMP of importing country or Inspection by ANVISA.
- Documentation is allowed in Portuguese, English or Spanish language.
- Label, Package Insert must be in Portuguese (Brazilian) language
- Official Documents like certificates given by importing country, if it is in foreign language that must be translated with Legal translator only.
- In some cases, applicator wants to import Bulk drug from foreign and then Pack the product in Brazil. In such cases, Expiry Date must be counted from Manufacturing date in foreign, and not the packaging date in Brazil

### III. Post-registration measures:

- Any registration changes shall follow the procedures specified in the GUIDE FOR MAKING POST-REGISTRATION ALTERATIONS AND INCLUSIONS IN MEDICINES.
- ANVISA may undertake a control analysis of commercialized batches in official laboratories in order to monitor the quality and conformity of the drug with the drug registered. Whenever necessary, ANVISA may request that the companies train their technicians in order to enable them to undertake this monitoring.
- In-vitro Diagnostic product: ANVISA had classified in vitro diagnostic product into 4 classes as follows...
  - Group A - Materials, devices, accessories and inputs for support of in vitro diagnostic products.
  - Group B - for diagnosis of non-transmissible diseases.
  - Group C - for diagnosis of infectious-contagious diseases, except those classified in Group D.
  - Group D - for diagnosis of infectious-contagious diseases, sexually transmissible diseases or diseases spread by blood and blood products, as well as identification of blood groups, transfusion or preparation of blood products

## **Documents required for Registration**

- Application form, Fee payment receipt.
- Copy of License or Permit for Manufacturing.
- Label on the package of product, Instruction for Use
- Technical Report.
- If imported, proof of Registration at competent health agency of importing country

## **OTHER FUNCTIONS OF ANVISA:**

- Brazilian Network of Analytical Laboratories. It is the laboratory network and every analysis and clinical studies must be performing at any one of the REBLAS center approved by ANVISA.
- Along with Drugs and Cosmetics, ANVISA have also regulation on...
  - Medical devices
  - Food
  - Tobacco products
  - Toxic products
  - Pharmacovigilance

## Travelers Information:

- This section is covered under a specific part of ANVISA related to Airport and Border regulation. Any new visitor of Brazil has to take Vaccine against YELLOW FEVER at least 10 days before his arrival to Brazil. And on arrival he has to show “International Certificate of Vaccination (ICV)”.
- If he had taken Vaccine against yellow fever, before 10 years, then he has to take it again a booster dose.
- Anvisa's Public Health Care Centers and Vaccination Rooms (in Portuguese) are ready to provide the vaccine and to issue the International Certificate of Vaccination (ICV), which is yellow.

## **RECENT TRENDS OF ANVISA:**

- Launched the project to prevent the resistance against Antibiotic drugs.
- The site is among the ten best in two categories of the iBest Awards. ANVISA's site is among the ten finalists in two categories i.e. "Government" and "Health and Well-being".
- Launched the project to prevent the resistance against Antibiotic drugs.

## **INDIAN PHARMA IN BRAZILIAN MARKET:**

### **Prominent product exporters:**

- Zydus Cadila
- Torrent Pharmaceuticals
- Dr. Reddys Labs
- Ranbaxy Pharmaceuticals
- Intas Pharmaceuticals
- Sun Pharmaceuticals

### **Major Drugs exported:**

- Losartan Potassium
- Zolpidem tartarate
- Alprazolam
- Enalapril Maleate
- Nortryptiline
- Carbamazepine
- Clonazepam
- Fluconazole
- Fluoxetine, etc.







