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Regulatory Authorities Controlling Pharmacy Profession: A Review

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ABSTRACT

A new pharmaceutical entity can cost several millions of rupees or dollars to develop. Astonishingly, even a few month deferrals in taking it to the market can have notable impact on the pecuniary status of the company. One of the major activities of the regulatory specialist is to ensure that the label of the product and related information of the patient has correctly been established and even a small error in any of the regulatory activities can make the product to be ready for recall in addition to the loss of several millions of money which is eventually bound to give rise to fall in self assurance of financiers, health experts and the patients. aRegulatory Affairs is a comparatively new profession which developed from the desire of government to protect public health by controlling the safety and efficacy of products in areas including pharmaceutical, veterinary medicines, medical device, pesticides, agrochemical, cosmetics and complementary medicines, biologics and functional foods.

Keywords- Regulatory Affairs, cosmetics, agrochemical

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INTRODUCTION

What is Regulatory Affairs?

Regulatory Affairs is a comparatively new profession which developed from the desire of government to protect public health by controlling the safety and efficacy of products in areas including pharmaceutical, veterinary medicines, medical device, pesticides, agrochemical, cosmetics and complementary medicines, biologics and functional foods.

Regulatory Affairs in the Pharma industry may be defined as "The interface between the pharmaceutical company and the regulatory agencies across the world."

Goals of Regulatory Affairs as profession

- Protection of human health
- Ensuring safety, efficacy and quality of drugs
- Ensuring appropriateness and accuracy of product information.

Roles of Regulatory Affairs professionals

- Act as a liaison with regulatory agencies
- Preparation of organized and scientifically valid NDA, ANDA,INDA ,MAA,DMF submissions
- Ensure adherence and compliance with all the applicable cGMP, ICH, GCP, GLP guidelines, regulations and laws
- Providing expertise and regulatory intelligence in translating regulatory requirements into practical workable plans
- Advising the companies on regulatory aspects and climate that would affect their proposed activities.

The RA professional is the liaison between the company and worldwide regulatory agencies such as Central Drug Standard Control organization (CDSCO), US Food and Drug Administration (USFDA), Medicines and Healthcare Products Regulatory Agency, (MHRA), Therapeutic Goods Administration (TGA), European Medicines Agency (EMA).

Drug Regulatory Affairs is an emerging, rewarding field that embraces both scientific and legal aspects of drug development. Regulatory professionals are dedicated individuals who take pride in their contribution to improving the health and quality of life of people.

SIGNIFICANCE OF REGULATORY AFFAIRS:

A new pharmaceutical entity can cost several millions of rupees or dollars to develop. Astonishingly, even a few month deferrals in taking it to the market can have notable impact on the pecuniary status

of the company. One of the major activities of the regulatory specialist is to ensure that the label of the product and related information of the patient has correctly been established and even a small error in any of the regulatory activities can make the product to be ready for recall in addition to the loss of several millions of money which is eventually bound to give rise to fall in self assurance of financiers, health experts and the patients.

The regulatory affairs professional Responsibilities:

1. The regulatory professionals' job is to keep track of the ever changing regulations in all the regions in which the company desires to distribute its products.
2. They also give guidance on the legal and scientific restraints and requirements, and collect, evaluate the scientific data their research and development workmates are generating. They are accountable for the presentation of registration documents to regulatory agencies, and carry out all the following negotiations necessary to acquire and maintain marketing authorization for the products concerned.
3. They give tactical and technical advice at the highest level in their companies, right from the starting of the development of a product, making an important contribution both lucratively and scientifically to the success of a development program and the company as a whole.
4. Preparation of organized and scientifically reliable NDA(New drug application), ANDA(Abbreviated New Drug Application), INDA(Investigational New Drug Application), MAA(Marketing Authorization Application), DMF(Drug Master File) submissions.
5. Establish adherence and compliance with all the applicable cGMP (Good Manufacturing Practices), ICH (International Conference on Harmonization*)* .GCP (Good Clinical Practices), GLP (Good Laboratory Practices) guidelines, legislations and laws.
6. Providing proficiency and regulatory intelligence in translating regulatory requirements into practical feasible plans.
7. Suggesting the companies on regulatory aspects and climate that would affect their proposed activities.
8. Aside from the above main roles, there are assorted other roles which Regulatory Affairs professionals work.

Regulatory Affairs professional in Product Management:

The key role of RA professional is broader than registration of products; they direct companies both strategically and technically on the highest stage. Their role begins starting from development of a product, marketing and post marketing strategies. Their suggestions at all stages both in terms of legal and technical requirements help companies save a lot of time and money in developing the

product and marketing the same. Those countries that do not have their own regulations the World Health Organization (WHO) guidelines on health aspects and World Trade Organization (WTO) on trade regulations between nations are followed.

Regulatory Affairs Professional in Clinical Trials:

The RA professional is the primary liaison between the company and worldwide regulatory agencies such as US Food and Drug Administration (USFDA), Medicines and Healthcare Products Regulatory Agency (UKMCA), Therapeutic Goods Administration (TGA), European Medicines Agency (EMA), Central Drug Standard control organization (CDSCO), and Health Canada. He also promulgates and interprets the apparently endless mace of legislations, regulations and guidelines to the other departments of the organization. The RA personnel develops strategies to overcome delays and presents finding of clinical trials to the regulatory bodies so as to get quick approval thus reducing the time for approval of new molecules. The RA professional facilitates the collection, inspection and communication about the risks and advantages of health products to the regulatory authorities, medical and health systems and the public. Operationally Regulatory affairs professional is responsible for assuring that government obligation, market driven requirements and evolving scientific conventions are understood and addressed by various stakeholders.

Regulatory Affairs professional in R&D:

The regulatory affairs professional personnel work closely associated with marketing and Research to develop, innovative products that take advantage of new technological and regulatory developments to speed up time to market. With new products anticipated to add consequential revenues to the companies core, small decreases in time to market equate to large material gains in revenue and profit. Employing flexible clinical trial strategies, obtaining speedy approval from regulatory agencies and avoiding pitfalls in processes can expedite development of new products and help to reduce costly mistakes and time lags.

Regulatory affairs professional in Herbal Medicines:

After the Drugs and Cosmetics (Amendment) Act of 1964, the definition of Ayurveda, Siddha and Unani (ASU) medicines were introduced into the purview of the Act and all necessary provisions for Control of this class of drugs were introduced. According to the law license is mandatory for manufacture of ASU drugs but exempted for sale under license, suitable labeling and packaging are also necessary for marketing these products. GMP was implemented as Schedule T for manufacturing due course, plants of ASU drugs in Drugs and cosmetics act. In foreign countries for marketing approval and documentation to prove efficacy and safety is required before approval of herbal products.

Objectives of regulatory authorities can be classified under the following:

- To protect customers from monopoly power
- To promote social and macroeconomic objectives
- To promote competition

List of main regulatory authorities which guidelines are globally accepted and followed by the pharma and allied industries:

1. USFDA (united states food and drug administration)
2. TGA (therapeutics goods administration)
3. UKMCA (the medicines control agency)
4. ICH guidelines (international conference on harmonization)
5. WHO (world health organization)
6. FDA (food and drug administration)

WHY THERE IS NEED OF REGULATORY AUTHORITY IN PHARMA PROFESSION?

- Allows pharmacy practice to develop while protecting the safety of the patient and the public.
- Enhances the confidence of the public and patients by sending out a clear message that patient patient safety is paramount.
- Ensure that regestried professional are fit to safely deliver a wide range of service to public.
- Provide a framework for continuing professional development and, in due course, continuing fitness to practice.

Various countries drug regulatory bodies:s

S.NO	Country	Regulatory Body
1	India	Central Drugs Standard Control Organization (CDSCO)
2	USA	Food and Drug Administration (FDA)
3	UK	Medicines and Health care Products Regulatory Agency (MHRA)
4	Australia	Therapeutic Goods Administration (TGA)
5	Europe	Europe Medicines Evalution Agency (EMEA)

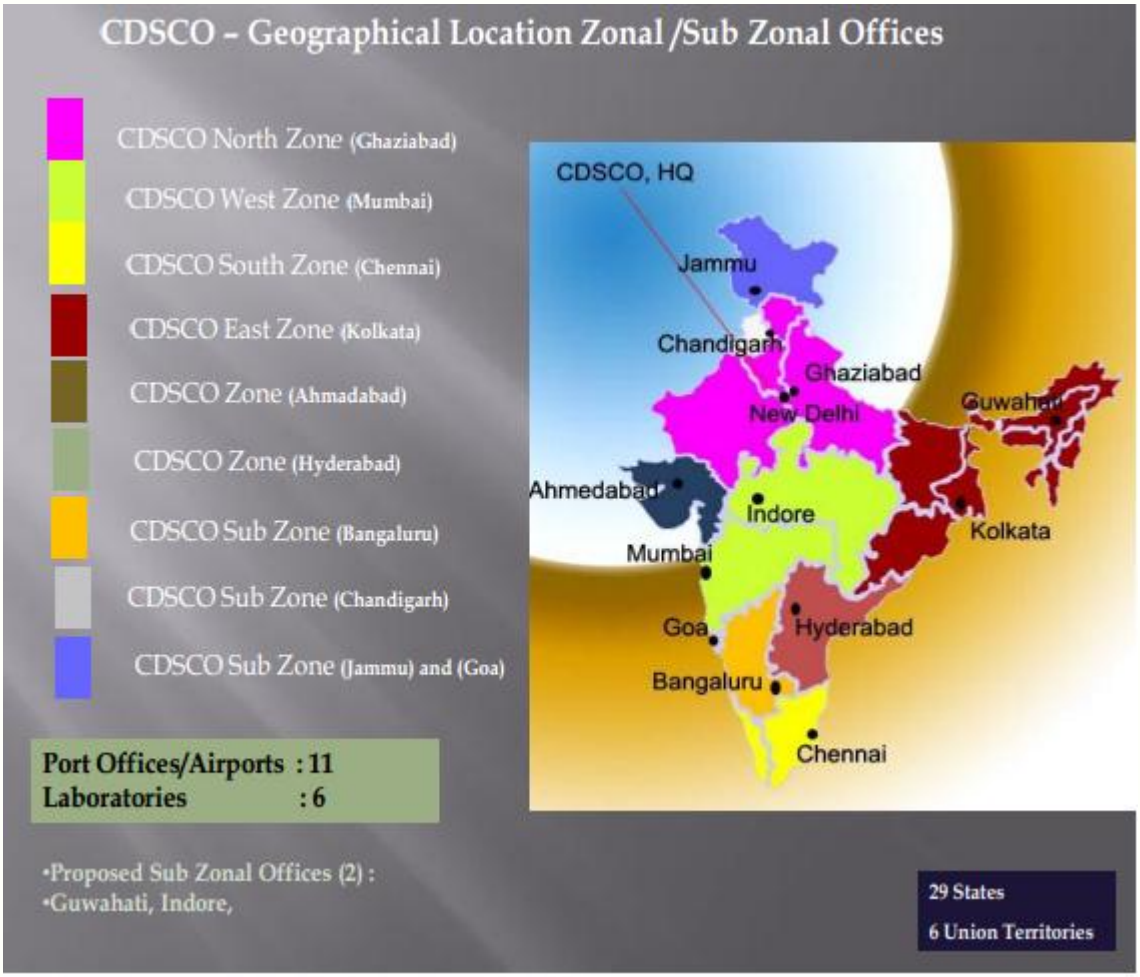
1. (CDSCO) CENTRAL DRUGS STANDARD CONTROL ORGANISATION

Introduction

The Central Drugs Standard Control Organization (CDSCO) is the Central Drug Authority for discharging functions assigned to the Central Government under the Drugs and Cosmetics Act. CDSCO has six zonal offices, four sub-zonal offices, 11 port offices and six laboratories under its control.

Major functions of CDSCO: 1. Regulatory control over the import of drugs, approval of new drugs and clinical trials, meetings of Drugs Consultative Committee (DCC) and Drugs Technical Advisory

Board (DTAB), approval of certain licenses as Central Licenses Approving Authority is exercised by the CDSCO hqrs.



Mission

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

Vision

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.

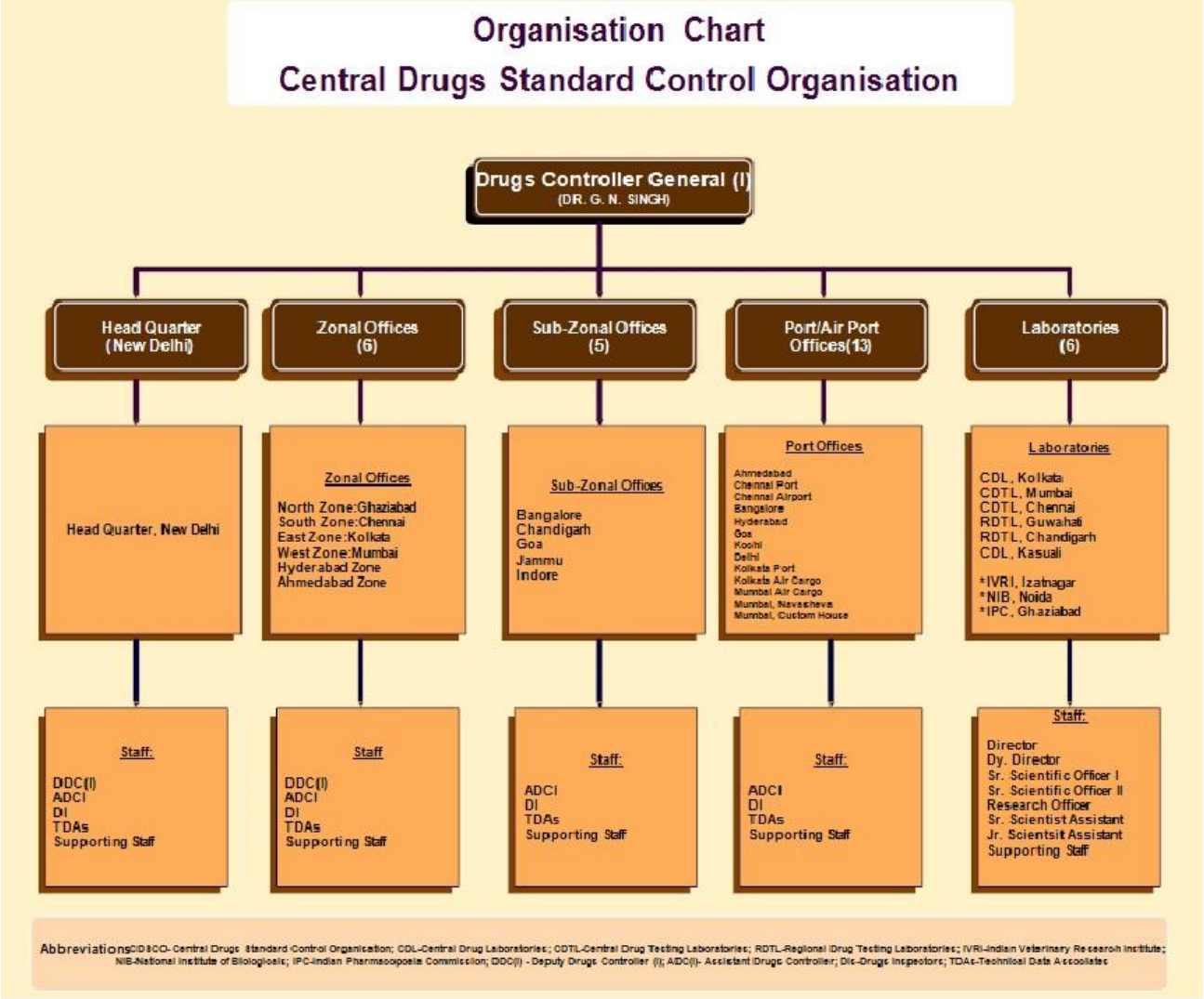
Values

- Independence
- Transparency
- Accountability
- Punctuality

- Courtesy
- Responsiveness
- Professionalism
- Impartiality
- Consistency
- Integrity
- Truthfulness and flexibility.

Functions

Under the Drug and Cosmetics Act, the regulation of manufacture, sale and distribution of Drugs is primarily the concern of the State authorities while the Central Authorities are responsible for approval of New Drugs, Clinical Trials in the country, laying down the standards for Drugs, control over the quality of imported Drugs, coordination of the activities of State Drug Control Organizations and providing expert advice with a view of bring about the uniformity in the enforcement of the Drugs and Cosmetics Act.



2. USFDA (UNITED STATE FOOD AND DRUG ADMINISTRATION)

Introduction

FDA ensures that the food we eat is safe and wholesome, that the cosmetics we use won't harm us, and that medicine, medical device, and radiation emitting consumer products such as microwave ovens are safe and effective. FDA also oversees food and drugs for pets and farm animals. Authorized by congress to enforce the federal food, drug, and cosmetic act and several other pubic health laws, the agency monitors the manufacture, import, transport, storage, and sale of $1trillion worth of goods annually, at a cost to tax payers of about $3 a person.

USFDA has over 9,000 employees, located in 167 U.S. cities .Among its staff FDA has chemists, microbiologists, and other scientists ,as well as investigators and inspectors who visit 16,000 facilities a year as part of their oversight of the businesses that FDA regulate.

How it works: Rule- making Process and Enforcement Strategy

- Public demands action

- Congress enacts general law
- FDA proposes science-based regulations to put the law into effect
- Regulations are notified, finalized and published in 21 Code of Federal Regulations (CFR)
- FDA assures compliance by enforcement and inspections that are targeted by risk assessment
- Industry has the ultimate responsibility to produce safe foods.

Important Aspects of the U.S. System

- FDA regulates interstate commerce
- Transparency
- Same standards for domestic and international
- Science-based regulations
- Consistency and predictability of implementation.

Responsibility

- Protecting the public health by assuring that foods are safe, wholesome, sanitary and properly labeled; human and veterinary drugs, and vaccines and other biological products and medical devices intended for human use are safe and effective
- Protecting the public from electronic product radiation
- Assuring cosmetics and dietary supplements are safe and properly labeled
- Regulating tobacco products
- Advancing the public health by helping to speed product innovations
- Helping the public get the accurate science-based information they need to use medicines, devices, and foods to improve their health
- FDA's responsibilities extend to the 50 United States, the District of Columbia, Puerto Rico, Guam, the Virgin Islands, American Samoa, and other U.S. territories and possessions.

Items regulated by FDA:

- Foods safety of all food products (except for most meat and poultry products, which are regulated by the U.S. Department of Agriculture)
  - labeling
  - bottled water
  - food additives
  - infant formulas
- Dietary Supplements
- Human Drugs

- product approvals.
- OTC and prescription drug labeling.
- drug manufacturing standards.
- Vaccines, Blood Products, and Other Biologics.
- product and manufacturing establishment licensing.
- safety of the nation's blood supply.
- research to establish product standards and develop improved testing methods.

- Medical Devices
  - from simple items like tongue depressors, to complex technologies such as heart pacemakers
  - premarket approval of new devices
  - manufacturing and performance standards
  - tracking reports of device malfunctioning and serious adverse reactions
- Electronic Products
  - products that give off radiation, such as microwave ovens and X-ray equipment
  - radiation safety performance standards for microwave ovens, television receivers, diagnostic
  - x-ray equipment, cabinet x-ray systems (such as baggage x-rays at airports), laser products, ultrasonic therapy equipment, mercury vapor lamps, and sunlamps
  - accrediting and inspecting mammography facilities
- Cosmetics
  - Safety
  - labeling
- Veterinary Products
  - livestock feeds
  - pet foods
  - veterinary drugs and devices
  - veterinary biologics not regulated by USDA are considered new animal drugs.

What FDA does not regulate?

FDA’s responsibilities are closely related to those of several other government agencies .often frustrating and confusing for consumers is determining the appropriate regulatory agencies to

contact. The following contact information is for government agencies that are function related to that of FDA.

- Advertising
- Alcohol
- Consumer product
- Drug of abuse
- Health insurance
- Pesticides
- Restaurants and glossary

3. MHRA (MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY)

Introduction

From 1 April 2003,the medicine and healthcare product regulatory agency (MHRA) replaced the Medical Device Agency(MDA) and the Medicines Control Agency (MCA).The MHRA in an executive agency of the Department of Health with trading funds status**.**

Aims of MHRA

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

Objectives of MHRA

1. Make an effective contribution to public health.
2. Provide authoritative and accessible information.
3. Influence international regulations.
4. Support industry and scientific innovation.
5. Minimize the cost of regulations.

The MHRA's activities

1. Assessing the safety, quality and efficacy of medicines, and authorizing their sale or supply in the UK for human use.
2. Overseeing the UK Notified Bodies that audit medical device manufacturers.

3. operating post-marketing surveillance and other systems for reporting, investigating and monitoring adverse reactions to medicines and adverse incidents involving medical 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.
4. Operating a proactive compliance programme for medical devices.
5. 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.
6. Regulating clinical trials of medicines and medical devices.
7. Monitoring and ensuring compliance with statutory obligations relating to medicines and medical devices through inspection, taking enforcement action where necessary.
8. Promoting good practice in the safe use of medicines and medical devices.
9. Managing the General Practice Research Database (GPRD) and the British Pharmacopoeia (BP) and contributing to the development of performance standards for medical devices.

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 process.

What MHRA regulates?

1. Medicine
2. Licensing of medicines
3. Medicines for children
4. Inspection and standards
5. Importing and exporting medicines
6. Best practice guidance on labeling and packaging of medicines
7. The safety of medicines.

The role of MHRA

1. Assess applications for marketing medicinal products

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

4. TGA (THERAPEUTICGOODSADMINISTRATION)

Introduction

The Therapeutic Goods Administration (TGA) is the regulatory body for therapeutic goods (including medicines, medical devices, gene technology, and blood products) in Australia. It is a Division of the Australian Department of Health established under the Therapeutic Goods Act 1989. The TGA is responsible for conducting assessment and monitoring activities to ensure that therapeutic goods available in Australia are of an acceptable standard and that access to therapeutic advances is in a timely manner. The Therapeutic Goods Administration (TGA) is a unit of the Australian Government Department of Health and Ageing, is responsible for administering the Act. This came into effect on 15 February 1991.

Objective of TGA

1. 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
2. Essentially therapeutic goods must be entered on the Australian Register of Therapeutic Goods (ARTG) before they can be supplied in Australia.

Role of the TGA

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

1. Pre-market evaluation and approval of registered products intended for supply in Australia;
2. Development, maintenance and monitoring of the systems for listing of medicines;
3. Licensing of manufacturers in accordance with international standards of GMPs
4. Post-market monitoring, through sampling, adverse event reporting, surveillance activities, and response to public inquiries;
5. The assessment of medicines for export.

TGA structure

The TGA's offices are grouped into three core groups - Market Authorization Group, Monitoring and Compliance Group and Regulatory Support Group

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

TGA Executive

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

The TGA Executive comprises:

1. TGA National Manager
2. Principal Medical Adviser,
3. Principal Legal Adviser,
4. Chief Regulatory Officer,
5. Chief Operating Officer

Committees

The TGA is supported in its work by a number of external expert advisory committees, including

1. Australian Drug Evaluation Committee (ADEC) - for prescription medicines
2. Adverse Drug Reactions Advisory Committee (ADRAC)
3. Medicines Evaluation Committee(MEC) - for over-the-counter medicines
4. Complementary Medicines Evaluation Committee(CMEC) - for complementary medicines
5. Therapeutic Devices Evaluation Committee (TDEC) - for medical devices.

Australian register of therapeutic goods (ARTG)

1. A 'therapeutic good' is broadly defined as a good which is represented in any way to be taken, for therapeutic use.
2. Therapeutic use means use in connection with
3. Preventing, diagnosing, curing a disease, ailment, defect or injury;
4. Inhibiting or modifying a physiological process;
5. Testing for pregnancy;
6. Replacement or modification of parts of the anatomy
7. The Australian Register of Therapeutic Goods (ARTG) was established under the Therapeutic Goods Act 1989.

8. The ARTG is a computer database of therapeutic goods. Therapeutic goods are divided broadly into two classes: medicines and medical devices.
9. 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.

The guidelines of TGA for

1. Listed Medicines
2. Registered Medicines
3. Complementary Medicines
4. OTC Medicine
5. Prescription Medicines
6. Medical devices
7. Blood and Tissues
8. Chemicals

5. (EMEA) Europe Medicines Evalution Agency

A centralized government body whose goal is to promote and protect human and animal health through overseeing the use of medications in European countries. The EMA, formerly called the European Agency for the Evaluation of Medicinal Products, is the European Union's equivalent to the U.S. Food and Drug Administration (FDA). The EMA is sometimes called the European Medicines Evaluation Agency or EMEA, although this is not its official name.

What is the EMEA?

The European regulatory system for medicines is complex for the simple reason that the Member States regulate medicine together. This means that there are national agencies in addition to one central regulatory body, the European Medicines Agency, created in 1995. The recent expansion of the European Union to a membership of 25, as well as plans for future enlargement, is a challenge to every aspect of integration, and pharmaceutical regulation is no exception. Consequently, the EMEA's main responsibility and mission is to coordinate the scientific resources of the 25 EU Member States, with a view to providing European citizens with high quality, safe, and effective medicines for humans and animals and, at the same time, to advance towards a single market for medicines.

Committees working parties and other groups

The European Medicines Agency (EMA) has seven scientific committees that carry out its scientific assessments. This page provides a general overview of how the committees operate. More details can be found on each committee's page.

- Committee for Medicinal Products for Human Use (CHMP)
- Pharmacovigilance Risk Assessment Committee (PRAC)
- Committee for Medicinal Products for Veterinary Use (CVMP)
- Committee for Orphan Medicinal Products (COMP)
- Committee on Herbal Medicinal Products (HMPC)
- Committee for Advanced Therapies (CAT)
- Paediatric Committee (PDCO)

The work of these committees is supported by Working parties and other groups.

What it regulates?

The European Medicines Agency's (EMA) main responsibility is the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use. The Agency is responsible for the scientific evaluation of applications for European Union (EU) marketing authorizations for human and veterinary medicines in the centralized procedure. Under the centralized procedure, pharmaceutical companies submit a single marketing authorization application to the EMA. Once granted by the European Commission, a centralized marketing authorization is valid in all European Union (EU) Member States, as well as in the European Economic Area (EEA) countries Iceland, Liechtenstein and Norway. By law, a company can only start to market a medicine once it has received a marketing authorization.

How it works?

The European Medicines Agency has a comprehensive body of **scientific evaluation practices** and respects the highest **scientific standards**. The Agency implements a **quality-assurance system** to continually review and strengthen the quality of its scientific work, which is underpinned by strict legal criteria.

All members of the Agency's Management Board, scientific committees and staff sign annual **declarations of interests** detailing their financial and professional relationship with the pharmaceutical industry.

The Agency has its own **legal personality**. It is partially funded from the European Union (EU) budget, but operates independently of institutions such as the European Commission and the European Parliament. The Agency is managed by its Executive Director, who is answerable to the Management Board. It is not managed by the European Commission.

Since its creation in 1995, the Agency has established key **operating principles and rules,** which have been adopted by its Management Board. It is also bound by EU legislation on issues such as public access to documents.

In accordance with its founding regulation, the Agency publishes the **decisions** of its scientific committees on this website, as well as main management documentation such as budgets, accounts and contracts.

Principles

The Agency conducts its activities in accordance with a set of guiding principles:

- Strongly committed to public and animal health.
- Independent recommendations based on scientific evidence, using state-of-the-art knowledge and expertise in our field.
- Support research and innovation to stimulate the development of better medicines.
- To assure continual improvement of our processes and procedures, in accordance with recognized quality standards.
- Adhere high standards of professional and personal integrity.

Inspections

The Agency is responsible for **coordinating inspections** requested by its committees in connection with the assessment of marketing authorization applications or referrals. These inspections may cover:

- good manufacturing practice (GMP)
- good clinical practice (GCP)
- good laboratory practice (GLP)
- pharmacovigilance (PhV).

Inspections aim to verify specific aspects of the clinical or laboratory testing of a medicine, its manufacture or control, or to ensure compliance with GMP, GCP, GLP or pharmacovigilance quality-assurance systems.

Inspections can also be performed in the context of the certificaton of vaccine antigen master files (VAMF) or plasma master files (PMF).

REFERANCES

1. Sachin Itkar, Dr. N. S. Vyawahare, “Drug Regulatory Affairs”, Nirali Prakashan.
2. Dr. B. S. Kuchekar, A. M. Khadatare, Sachin C. Itkar, “Forensic Pharmacy, Nirali Prakashan, 8th edition.

3. www.Google.com
4. www.cdsco.nic.in
5. http://www.cdscoonline.gov.in
6. www.fda.gov
7. www.mhra.org.uk
8. http://www.tga.gov.au
9. www.ema.europa.eu