AN OVERVIEW OF REGULATORY AFFAIRS IN PHARMACEUTICAL INDUSTRIES

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Abstract: Pharmaceutical drug regulatory affairs cowl extraordinary registration parameter of pharmaceutical product. As it's miles the new career which changed into developed from the favored of everywhere in the international to protect the general public fitness through providing correct excellent of drugs such as safety and efficacy within the region of now not handiest pharmacy however also inside the area of the veterinary medicinal drug, scientific tool, pesticides, pesticides, agrochemical, beauty and complementary medication. It also made the interface among the pharmaceutical company and the regulatory organizations. it is also liable for keeping the appropriateness and accuracy of the product data. And its principal role to behave as a liaison with regulatory groups, supplying information and regulatory intelligence in translating regulatory requirement into sensible practicable plan, advising the corporation on regulatory aspects and climate that might affect their proposed activities. Regulatory affairs in the pharmaceutical industry play an essential position because the Pharmaceutical area is rising very hastily and there's a need of regulatory affairs specialists to provide the current desires of industries for the worldwide opposition. A regulatory affair is a profession which acts as the interface among pharmaceutical industries and authorities internationally. The goal of the regulatory affairs professional is the protection of human health, ensuring safety, efficacy, and quality of drugs, making sure appropriateness and accuracy of product facts. This gift article discusses the evolution of Regulatory Affairs, its role inside the pharmaceutical enterprise and its involvement for the implementation of regulatory suggestions which improve the increase of the industry.

Keywords: Regulatory Affairs, Pharmaceutical industries, regulatory bodies.

Introduction: The modern Pharmaceutical enterprise is well prepared, systematic and compliant to international regulatory standards for manufacturing of Chemical and biological tablets for human and veterinary intake in addition to scientific gadgets, conventional herbal merchandise and cosmetics. Stringent GMPs are being accompanied for blood and its by-product in addition to controlled production for classic herbal drug treatments, Cosmetics, food and dietary products which became in any other case otherwise a century before. Each regulatory gadget had confronted certain occasions which brought about modern-day well-defined managed regulatory framework. This has resulted into systematic manufacturing and advertising of secure, efficacious and qualitative pills. With the boom of enterprise, the legislation from each area have come to be increasingly complex and created a need for regulatory specialists.[1]

Regulatory Affairs (RA), also known as Goverment Affairs, is a profession inside regulated industries, including pharmaceuticals, clinical gadgets and so on. RA profession at its heart is all about gathering, studying and speaking the dangers and advantages of health care products to regulatory organizations and public all around the international.

A technological know-how of growing new gear, requirements and procedures to evaluate the protection, efficacy, satisfactory and overall performance of regulated products.

All drugs must meet 3 standards: be of true high-quality, safe and effective. The judgments approximately medicines fine, protection and efficacy ought to be based on stable technology. Regulatory Affairs additionally has a completely particular which means inside the healthcare industries (prescribed drugs, scientific gadgets, Biologics and practical meals. The success of regulatory method relies upon on interpretation, application, and communication inside out of doors the corporations. Drug Regulatory Affairs Regulatory Affairs is a brand-new career that is initiated from governments to defend public health, with the aid of controlling the protection and efficacy of products in areas together with prescribed drugs, veterinary drug treatments, medical gadgets, insecticides, agrochemicals, cosmetics and complementary medicines. The corporations manufacture and marketing these merchandises should ensure that they supply fine products to public for his or her fitness and welfare. Now maximum of the agencies have expert departments of Regulatory Affairs experts. Regulatory Affairs departments are developing inside companies & is constantly evolving and developing and is the only that's least impacted in the course of the purchase and Merger, and also during recession. global harmonization in standards has caused constant technique in regulatory submissions and as a result its evaluation. This department is responsible for understanding the regulatory necessities for purchasing new prevalent merchandise approved.[2]

A regulatory affair (RA) is a career which acts because the interface between the pharmaceutical industry and drug regulatory government internationally. it's far mainly involved inside the registration of drug products in the respective international locations prior to their marketing.

The modern Pharmaceutical industry is well prepared, systematic and compliant to global regulatory standards for the producing of Chemical and organic drugs for human and veterinary intake in addition to scientific gadgets, conventional natural products and cosmetics. The Regulatory Affairs department is an important part of the organizational shape of pharmaceutical companies. Internally it liaises on the interface of drug improvement, manufacturing, advertising and marketing and clinical studies. Regulatory Affairs is actively concerned in each degree of improvement of latest medicine and the publish-advertising sports with authorized medicinal merchandise.[3]

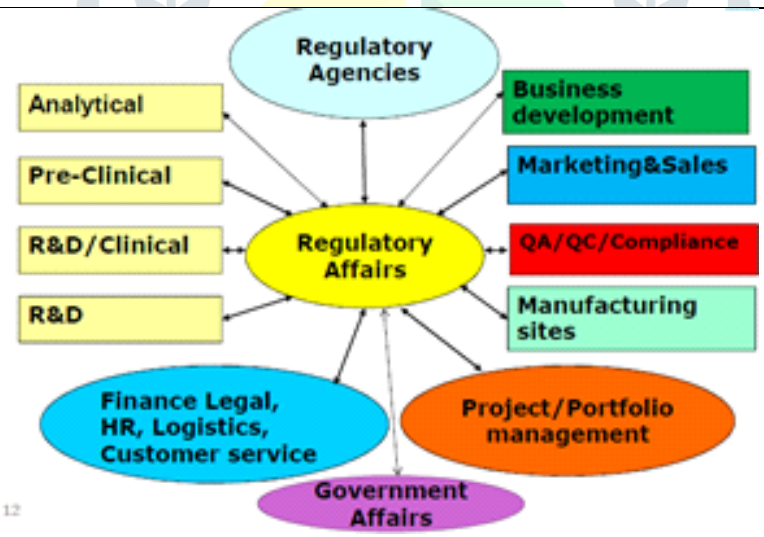

Figure 1: Roles or interactions of RA

The success of regulatory strategy is less dependent on the regulations than on how they are interpreted, applied, and communicated within companies and to outside constituents[4]. Pharma regulatory affairs professionals play an essential role in ensuring all pharmaceutical products comply with regulations governing the industry. Those working in pharma regulatory affairs jobs not only work in the initial application phase for a new or generic drug, but also in the licensing and marketing stages – making sure all operations and products meet required safety and efficacy standards. Professionals must combine knowledge of the business, legal and pharmaceutical industries to determine if regulations are being followed and, in many cases, form the link between pharma companies and regulatory authorities, such as the Food and Drugs Agency (FDA) and the European Union[5].

Objectives of The Regulatory Affairs: The present study describes a brief review of various regulatory bodies of major developed and developing countries around the world and the scope and challenges of such pharmaceutical regulatory organizations in delivery of safe and effective healthcare products.

The main objective of regulatory affairs is to provide the basis for the assurance of high quality of food products which can increase consumer's interest for ensuring the efficacy, quality, and safety.

1. Roles of Regulatory Affairs Professional in Health Authorities as well as Pharmaceutical Industry.

2. Pharmaceutical Legislations.

3. Clinical Trials.

4. Roles of Regulatory Affairs Professional in Health Authorities as well as Pharmaceutical Industry.

5. Regulatory Affairs Network in Pharmaceutical Industry.

6. Indian Pharmaceutical Industry & Drug Regulations development in different Era.

7. Major Rules and Act of India.

8. Drug Regulatory Affairs and Global, Regional and National Regulatory Network.

Historical Overview of Pharmaceutical Industries And Regulatory Affairs: During 1950s, multiple tragedies i.e., sulfanilamide elixir, vaccine tragedy and thalidomide tragedy have resulted in substantial increase of legislations for drug products quality, safety and efficacy. This has also resulted into stricter norms for Marketing Authorization (MA) and Good Manufacturing Practices (GMPs). To understand the chronological development of the modern era of pharmaceutical industry and regulatory framework, we will glance through the historical evolution of regulations in USA, Europe and India. Let us see what happened in USA, Europe and India.

United States of America (USA):

During the early Eighteenth century, chemical manufacturing factories had started establishing and the first large scale manufacturing of glycerin started during 1818-1840. However, with regard to medicines, it was being compounded by Pharmacists and Doctors at Pharmacy laboratories. Crude drugs i.e., opium was extracted from natural plants by compounding pharmacists and progressed further for identifying and isolating active ingredients from the crude drug.

In the USA, the root of modern pharmaceutical industry was borne during Mexican- American war 1846-1848. The American troops had suffered due to import of spurious medication for Malaria, Cholera, Dysentery, Yellow Fever and that had brought federal government into action for creation of Custom Laboratories. The first law which controlled import of medicines was Import Drugs Act of 1848. As per this law, it was mandatory to inspect imported drugs for quality and purity at the entry of port. To define the quality and purity of drug, federal government recognized United States Pharmacopoeia (USP) as an official compendium. Note that though United States Pharmacopoeia Committee (USPC) was established in 1820, it was non-government body till Import Drugs Act of 1848. It was formed with the objective of creating system for standards, quality control and national formulary.

At the start of the nineteenth century, new legislations for medicines control started coming into effect due to multiple tragedies worldwide. This was the era when ancient traditions of manufacturing and distribution of drugs evolved into the modern highly organized pharmaceutical industry and controlled system of Drug Regulatory Affairs (DRA).

Almost five decades after issuance of Import Drugs Act of 1848, vaccines tragedy happened in 1901. During this era, City and State Health Departments use to maintain stables and vaccine preparation facilities unlike the private industry today. Legislations mandating exclusive manufacturing facility for vaccines enacted post two events of death due to immunization failure. The diphtheria antitoxin developed by City Health Department of St. Louis was contaminated by tetanus causing bacteria. This was ended up with the death of 14 children in November 1901.

Simultaneously, smallpox vaccine administered was found contaminated and resulted into nine more death in Camden, New Jersey (Figure 2).

The Biologics Control Act of 1902 was the result of the vaccine tragedy. This legislation mandated manufacturing and distribution licensing of biological products i.e., serum, vaccine, toxin, viruses as well as defined labeling in terms of manufacturer's name, address, license number, identification of product and expiry date.

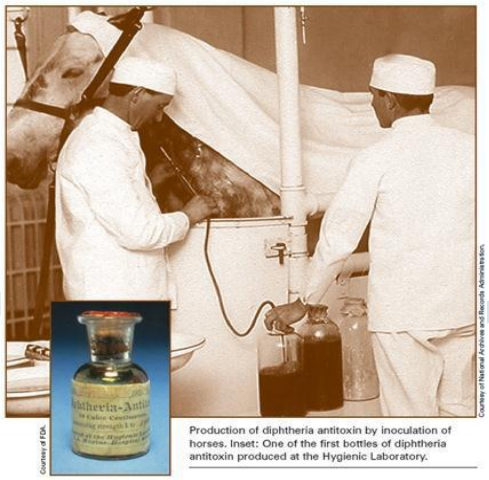

Figure 2: Vaccine Preparations at City Health Department.

Proceeding further from Import Drugs Act of 1848 to The Biologics Control Act of 1902, federal government took steps for controlling adulteration or misbranding of foods, drugs, medicines, liquors. This law prohibited interstate transportation of adulterated food and drugs. With this law toxic colors and preservatives like borax, sulphuric acid, formaldehyde, copper and sulphate were banned for usage in food and drugs. The Food and Drugs Act of 1906 is best known as Wiley Act, named by Dr. Harvey W. Wiley. This law made mandatory labelling of ingredients and its content for drugs i.e., alcohol, cocaine, heroin, morphine, opium. This was the first wide ranging, national legislation on food and medicines safety (Figure 3).

Figure 3: Dr. Harvey W. Wiley (last third from right) with chemistry department staff.

The Federal Food and Drugs Act 1906 was starting point for eventual creation of Food and Drug Administration (FDA). Originally The Bureau of Chemistry was used to regulate food safety, however in 1927, it was reorganized into the Bureau of Chemistry and Soils and Food, Drug and Insecticide Administration. In 1930, the current Food and Drug Administration (FDA) came into effect after shortening of earlier organization. Since the root of FDA was born in 1906, FDA still celebrates 1906 as its establishment year.

From the above act, regulatory control on food and drug has increased drastically. However, Sulfanilamide Elixir tragedy raised concern about the safety of drug products. In 1938, more than 100 people were died due to diethylene glycol (highly toxic solvent) utilized for mixing Sulfanilamide drug. Consequently, the law was enacted as Food, Drug and Cosmetic Act of 1938 to oversee safety of medicine. With this law, pre-marketing approval of all new drugs was made mandatory and proof for scientific safety study was asked by FDA. This law also mandated the directions for safe use (Figure 4).

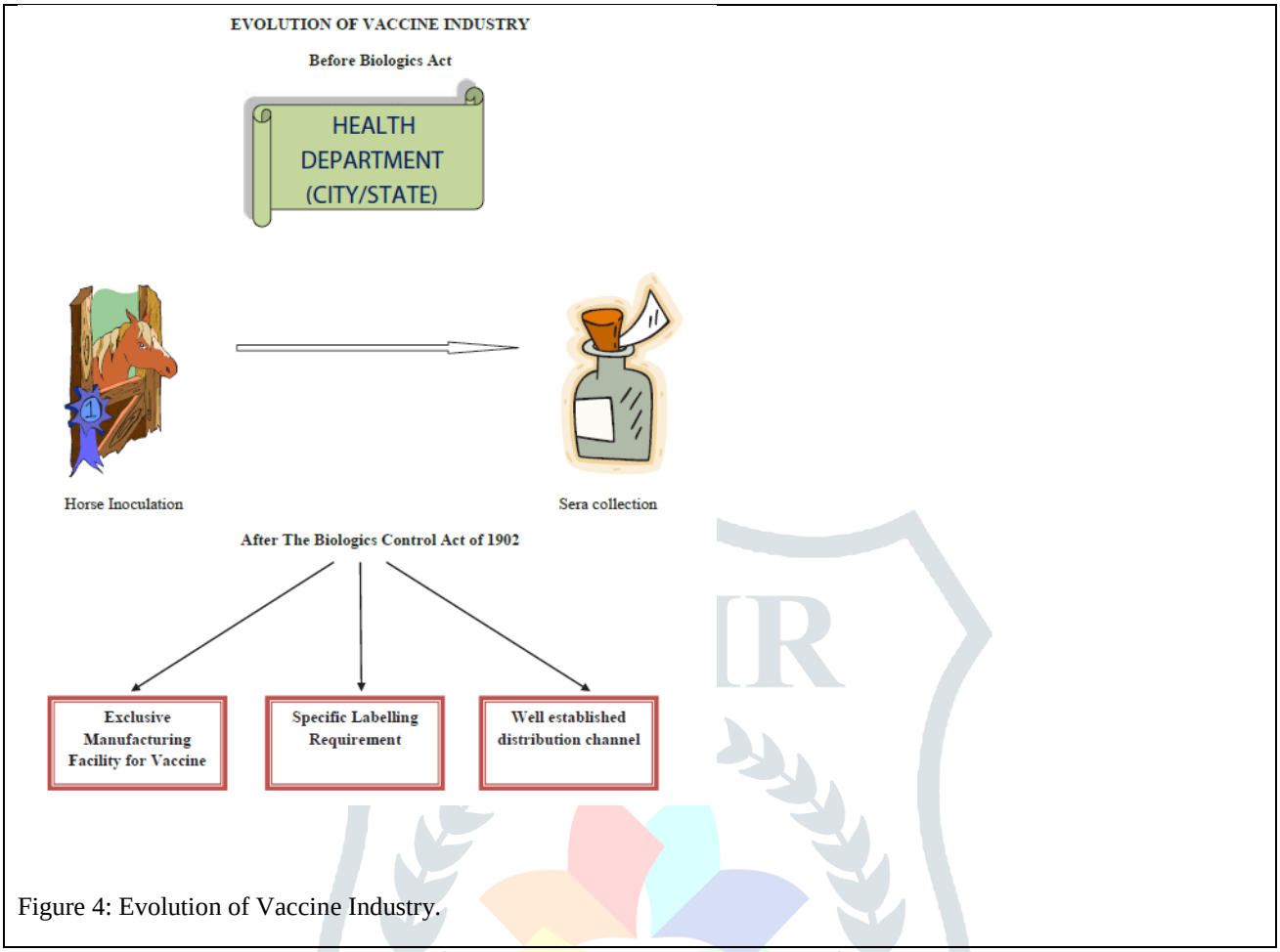

Figure 4: Evolution of Vaccine Industry.

European union (EU)

In European Countries, the healthcare regulations have developed with main objective of keeping unsafe products out of marketplace. In addition to Quality, Safety and Efficacy, few other factors were responsible for well defined legislation as well as highly advanced pharmaceutical industry.

Ethical considerations: To avoid unethical and unsafe clinical trials and have safe and proper treatment of human subjects, the Helsinki Declaration has been set in 1964.

Economic issues: First health insurance system was developed in later half of 20th century. This has resulted in to pricing transparency due to the fact that cost of medicines was transferred from customer to private and public health insurance system.

Unsafe products usage: In European Countries, major revolution of drug regulations started post Thalidomide tragedy. In late 1950s, a German company was marketing new sedative pills throughout Europe that supposedly helped reduced nausea in pregnant women. While taking this drug during early pregnancy, it created teratogenic effect which resulted into birth defects in almost 10000 children. The babies born to women in Germany and England were without hands, feet, toes or fingers like flippers growing out of their shoulders and trunk.

Until Thalidomide tragedy, the drugs were being sold by notification to health authority and NO safety, efficacy or quality data were required to be submitted prior marketing. However, this has changed with the formation of European Economic Commission (EEC) in 1957 (Currently known as European Union-EU).

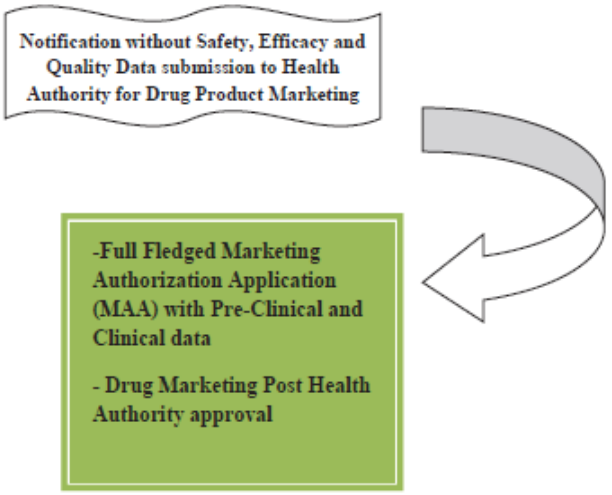

Figure 5: Gradual development of Marketing Approval System.

The first directive passed by European Economic Commission was 65/65/EEC mandating that no medicines can be marketed in European Communities until and unless it is not approved by at least one competent authority within Europe. The objective of this legislation was to have standard common marketing approval for medicines process within European Economic Commission. At the same time, few more directives specific to the category of products i.e. radiopharmaceuticals, immunological and homeopathic medicines as well as classification, labeling and promotion directives were came into effect.

Early 1990s in UK, Creutzfeldt-Jacob disease cases were started increasing. This is a human equivalent Bovine Spongiform Encephalopathy (BSE), commonly known as "mad cow disease". It was suspected that this disease was due to consumption of Bovine Spongiform Encephalopathy (BSE) infected beef. Based on this incidence, the legislation pertaining to Bovine Spongiform Encephalopathy (BSE) and Transmissible Spongiform Encephalopathy (TSE) free use of materials have come into place. It is applicable to ingredients derived from bovine materials i.e., lactose, magnesium stearate, gelatin.

Free availability of information: Positive and negative news/ information about medicine is available almost to everyone due to wide spread use of media and World Wide Web (internet) network. To ensure public's confidence in healthcare system, regulations pertaining to quality, safety, efficacy and clear instructions for use came into effect.

Products and technology innovation: Development of new products such as biologics, blood and blood related products, and *in-vitro* diagnostics needed new legislations. It has led to the development of "concertation procedure" in 1987, where member states agreed to assess common Marketing Authorization Application (MAA).

Demands for products safety: Regulatory authority demands safety data to support Marketing Authorization (MA) as well as monitoring of safety data throughout the products post authorization cycle. New legislations have started coming in place due to public demand of improved quality of life as well as improved survival rate and longevity.

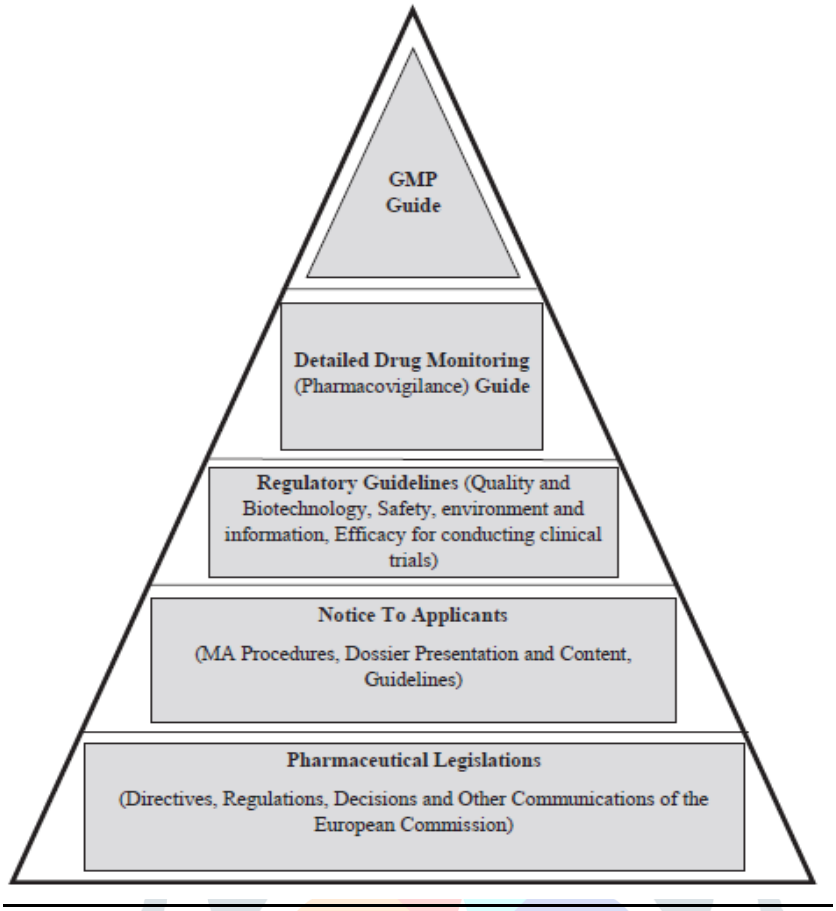

Figure 5: The Rules Governing Medicinal Products in the European Union.

Changes in market structure: Healthcare regulations were required due to creation of single EU market by removing trade barrier. In this scenario, regulatory framework was varied from one country to another. Hence common regulatory framework was required. Since the market was open, the quality concern for imported products was arise and led to the development of new regulations.

Decisions and other communication of European commission: Decisions are the measures, intended to bind individual pharmaceutical manufacturers /member states. EU also published non-binding recommendations and opinions and express committee view.

Post thalidomide tragedy, directives and regulations are kept on expanding and today the scope has widened for medical devices, traditional herbal medicines, cosmetics, food & dietary products.

India:

The drug industry in India was at very primitive stage till 20th Century. Most of the drugs were imported from foreign countries. Post First World War, the demand for drugs had increased tremendously and that led to the cheap & substandard drugs into the market, as like in USA post Mexican American war.

a) 1900-1960: To control cheap drugs in market, Government passed the Poisons Act 1919. This Act regulates possession of substance or sale of substances as specified as poison. It also specifies the safe custody of the poisons, labeling and packaging of poisons, maximum quantity to be sold and inspection as well as examination of the poison sold by vendor during the year.

The Poisons Act was followed by The Dangerous Drugs Act 1930. This act regulates the opium plant cultivation, manufacture and possession of opium, its import, export, transship and sell of opium.

The Narcotics and Psychotropic Substances Act was passed in 1985 which revoked the Dangerous Drugs Act 1930 and Opium Act, 1878. Following acts & rules were passed during this era:

• **Drugs and Cosmetics Act, 1940:** Regulate the import, manufacture, distribute and sale of drugs. This act covers allopathic, homeopathic, Unani and Siddha drugs.

• **Drugs and Cosmetics Rules, 1945:** The rules under the Drugs and Cosmetics Act regulate only manufacture of Ayurvedic drugs for sale, and not for consumption, use or possession.

• **Pharmacy Act, 1948:** This law was amended lastly in 1986 and it regulates the pharmacy profession of India.

• **Drugs and Magic Remedies (Objectionable Advertisements) Rules, 1955:** These rules control the drug advertisement in India.

• **Drugs Prices Control Order, 1955 (DPCO) (under the essential commodities Act):** DPCO was further amended in 1995. Under this rule, government may review and fix maximum sale price for bulk drugs as well as formulation.

b) 1960-1970: The market share was dominated by multinational companies and very few Indian manufacturers were present. The Indian Pharmaceutical industry was in an early stage of growth. Focus for pure research and development was very little due to lack of patent protection. Due to very high import dependency on drugs, the cost of drugs was very high as well as market availability was comparatively low.

c) 1970-1980: Government took control for the medicines regulation and issued few acts and rules.

• **Indian Patent Act 1970:** It serves as the basis for patent protection in India. Based on this, only process and method of manufacture of Drug substance was allowed to get the patent. Product patent was not allowed under this act. Indian Patent Act of 1970 came into force from April 20, 1972. This new act replaced the Indian Patents and Designs Act of 1911.

• **Drug prices capped:** Drug Prices Control Order (DPCO) was introduced to control the high price against consumers.

• **Local companies begin to make an impact:** Since the product patent was allowed by Indian Patent Act 1970; local companies began manufacturing products/ drugs using different manufacturing process by reverse engineering. Due to these new drugs were available cheaply as well as many more substitute drugs were available in the market against costly imported new drugs. This has resulted in 1) increase the exports to countries like Russia, Africa, China, and South America. 2) Export of Bulk drug post patent expiry.

d) 1980-1990: The industry has started investing in API process development and created production infrastructure. Government has also issued export incentives. The Narcotic Drugs and Psychotropic Substances Act, 1985 was issued which regulates the operation of narcotic drugs and substances.

e) 1990-2000: The pharmaceutical industry has observed a rapid expansion of domestic market and during same era globalization happened. The companies have entered into research activity.

India joined Paris Cooperation Treaty (PCT) in 1999 and implemented product patent effective from Jan 1, 2005.

f) 2000-2010: This period is considered to be the Innovation and Research era. During these years, innovative research activity, patenting of the drugs formula, process, indication as well as merger of companies was started.

• **Patent Amendment Act 2005:** With this act, provision for Black Box Application made, as per that if patent application is filed before Jan 1, 2005, then under the transit provision of Trade Related aspects of Intellectual Property Rights (TRIPS), manufacturer can market this product post 2005 without infringing product patent, if manufacturer has made significant investment in manufacturing of the product, produced and marketed on or before Jan 1, 2005.

• **Compulsory Licenses:** Such licenses can be granted for manufacture and export of the drug products "to any country having insufficient or no manufacturing capacity, for the said product, to address public health problems".

Herbal preparations having medicinal values can be patented under new amended law.

Major regulatory changes in terms of marketing authorization process as well guidelines have come into effect. Few to name are as below:

• **Drugs and Cosmetics (First Amendment) Rules, 2011:** It mandates registration of Clinical Research Organization (CRO) for conducting Clinical Trials (CT). Schedule Y1 suggests requirements and guidelines for registration of Clinical Research Organizations.

• **Clinical Trial Registry- India (CTRI):** It has been set up by the ICMR's (Indian Council of Medical Research) National Institute of Medical Statistics (NIMS). India has developed on-line registry system and mandated registration of CRO before the enrolment of first patient for clinical trials. CRO needs to disclose mandatory items as mentioned under WHO International Clinical Trials Registry Platform (ICTRP) dataset.

• **Pharmacovigilance Programme of India (PvPI):** The Central Drugs Standard Control Organization (CDSCO) has launched Pharmacovigilance programme to assure drugs safety to Indian patients. This will help monitoring adverse drug reactions to Indian patients, as well as monitoring of benefit-risk ratio.

• **Guidance documents:** CDSCO has issued guidance for Industry for Fixed Dose Combinations (FDCs) registration as well as Guidance for preparation of Common Technical Document for Import/manufacture and Marketing Approval of New drugs for Human Use (New Drug Application-NDA).

With this CDSCO has implemented system for preliminary scrutiny at the time of application receipt for marketing approval of Fixed Dose Combinations (FDCs).[6]

Recent Advancement In Regulatory Affairs: During the 1950s, many tragedies happened due to the misjudgment of the personnel during manufacture and some intentional addition of adulteration of substances into the pharmaceutical product, which has lead to the death of the patients. After so many incidents, the regulatory bodies introduced the new laws and guidelines which improve the quality, safety and efficacy of the products. This has also resulted in stricter norms for Marketing Authorization (MA) and Good Manufacturing Practices (GMPs).[7]

That is the tragedies of **SULPHANILAMIDE ELIXIR, VACCINE TRAGEDY & THALIDOMIDE TRAGEDY.**

Figure 6: Thalidomide and Sulfanilamide Tragrdy

FDA launched in 1906 as Bureau of chemistry, served simply to police claims made about food and drugs ingredients. At that time no formal government approval required to market new drugs. The disasters provoked a

public outcry that led to the passage of the 1983 Food Drug & Cosmetics Act, which gave the FDA power to monitor the safety of new drug.

Beginning of the 1980 the European Union erupted to systematized the regulation of healthcare products in the member states. The postulation of regulating medicines was genuine in most member countries besides indistinguishable rules to the US model, but many countries did not have at all notable medical device regulation. coexistent the EU had been evolving the notion of New Approach Directives where at most extensive notion were registered into the law and the large amplitude of the technological allocate authorized to abidance with acceptable standards (which are more easily upgradable).

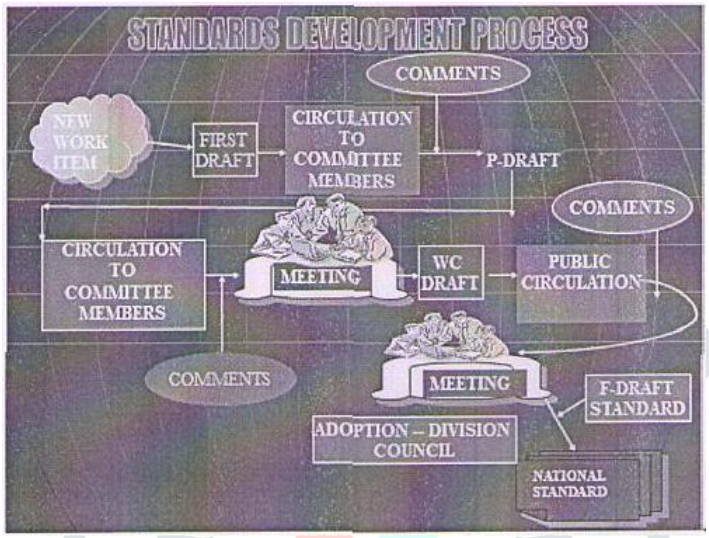

Figure 7: Standard development process

1) The Europeans pulled the revolutionary strategies of petition the New Approach Directive to Medical Devices and beyond performing so assembled the initial notable abstracts promote in healthcare regulation being almost the century.

2) The European Model for medical device has mostly take on by the Global Harmonization Task Force as long as the intercontinental arrangement revolution.

3) Besides regulatory affairs professional, they are habitually in control for tracing alters in regulatory guide lines as they mayhappen.

4) For the purpose of this, they should take hold of the ingenuity to maintain latest on all alterations in regulations. For example, they have to check the PDA Web site and read professional journals.

5) They can study about recently introduced guidelines from individual sources like peers, print liberated from regulatory authorities and be present at convocations.

6) All alterations in regulations necessarily registered in the way demanded by the company. Changes must also be clarify and commune to suitable persons in the company.

7) Management be allowed at that time regulate what alterations in company approaches and action may be needed to remain in submission.

8) They are also incorporated with harmonizing and executing the alterations which claims for greatly responsiveness so that alterations proposed are fluently received by the company's management and the regulatory bodies. They have a vital endowment to make in company's victory both economically andscientifically.

Regulatory Strategy:

• Planning of regulatory affairs

• Planning of addressing critical development issues, which is dynamic and changes during the process

• Plan of how to register a product in the global market (to be in line with corporate, business and strategy of RA unit and projects)

• Plan how to balance time & cost & human resources Strategy is only as good as the analysis behind it.

• To ensure that a dossier results in a SmPC (Summary for the prescribers Package leaflet Information for the patient) that results in sales

• To ensure that the regulators are the first supportive customers for the product

• Networking, regulatory intelligence

• The integration of regulatory into the discovery and development process[8]

Regulatory Bodies in The World: Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue guidelines for drug development, licensing, registration, manufacturing, marketing and labeling of pharmaceutical products.

Table 1: Different regulatory bodies of countries

Country	**Regulatory Body**
USA	Food and Drug Administration (FDA)
UK	Medicines and Healthcare Products Regulatory Agency (MHRA)
Australia	Therapeutic Goods Administration (TGA)
India	Central Drug Standard Control Organization (CDSCO)
Canada	Health Canada
Europe	European Medicines Agency (EMEA)
Japan	Ministry of Health, Labour & Welfare (MHLW)
Italy	Italian Pharmaceutical Agency
Thailand	Ministry of Public Health

International Organizations:

World Health Organization (WHO)
Pan American Health Organization (PAHO)
World Trade Organization (WTO)
International Conference on Harmonization (ICH)
World Intellectual Property Organization (WIPO)

Table 2: Different regulatory bodies in World[9]

Regulatory Affair Proffesion: It takes many years for bringing a new drug to the market; it is therefore essential that the process should be managed effectively from beginning to end in order to meet the regulatory requirements and permit a favorable evaluation of Quality, efficacy and safety in the shortest possible time[10]. The drug regulatory affairs (DRA) professional plays an important role in each phase of this process, from developing effective regulatory strategies following the discovery of a new molecule up to the planning post-marketing activities.

The main role of the DRA professional within a pharmaceutical Industry is to secure approval of drug submissions from Health Therapeutic Products Program and to ensure regulatory compliance of marketed and investigational drugs with the Food and Drug Act and Regulations and Guidelines/Policies.

For this position, the DRA professional must possess a proficient scientific background and have a thorough knowledge of Domestic regulations as well as international regulations. Because the regulatory environment is evolving rapidly toward global harmonization (several ICH guidelines have now been adopted by TPP) and mutual recognition between different health authorities across the world, it is a major challenge for the DRA professional to keep abreast of policy changes and determine how these changes affect the approval process. Consequently, the importance of DRA in the development and approval of new drugs has increased significantly over the last decade.

Whether a submission is filed to the TPP for the conduct of a clinical trial (Investigational New Drug Submission, or IND), for the approval to market a new drug (New Drug Submission, or NDS), for a new indication or dosage form for a marketed drug (Supplemental NDS, or S/NDS), or for the maintenance of a marketed drug's regulatory status, the submission's preparation entails the close collaboration of a multidisciplinary team. The DRA professional must actively participate in discussions and coordinate team activities to obtain all the necessary documentation as per the current TPP policies and then assess it for completeness and accuracy. Therefore, the effective DRA professional must exhibit the organizational and interpersonal skills of a "team player" and also be thorough and detail-oriented.

possess excellent writing and communication skills and be an effective negotiator. This is to ensure that the requests or comments generated during the submissions review process are promptly and satisfactorily answered and to negotiate the most favorable labeling (Product Monograph) consistent with the sponsor's business objectives.

The scope of responsibilities is wide and may vary significantly according to the organizational structure of the pharmaceutical company. The responsibilities of some DRA professionals may focus exclusively on pharmacovigilance activities or on the electronic representation of information (electronic submissions). The common point, however, is that the DRA professional is the primary liaison between the sponsor and the TPP. In this capacity, the individual must possess excellent writing and communication skills and be an effective negotiator. This is to ensure that the requests or comments generated during the submissions review process are promptly and

satisfactorily answered and to negotiate the most favorable labeling (Product Monograph) consistent with the sponsor's business objectives[11].

In line with today's growing technological developments, knowledge of several computer applications is essential to effectively fulfill the job requirements. DRA is a dynamic, rewarding field that embraces both scientific and legal aspects of drug development. DRA professionals are dedicated individuals who take pride in their contribution to improving the health and quality of life of peoples[12].

Responsibility of Regulatory Affairs Professional's: The Regulatory Affairs professional's job is to keep track of the ever-changing legislation in all the regions in which the company wishes to distribute its products. They also advise on the legal and scientific restraints and requirements, and collect, collate, and evaluate the scientific data that their research and development colleagues are generating[13]. They are responsible for the presentation of registration documents to regulatory agencies, and carry out all the subsequent negotiations necessary to maintain marketing authorization for the products concerned. They give strategic and technical advice at the highest level in their companies, right from the beginning of the development of a product, making an important contribution both commercially and scientifically to the success of a development program and the company as a whole[14].

It may take anything up to 15 years to develop and launch a new pharmaceutical product and many problems may arise in the process of scientific development and because of a changing regulatory environment[15]. Regulatory affairs (RA) professionals help the company avoid problems caused by badly kept records, inappropriate scientific thinking or poor presentation of data. In most product areas where regulatory requirements are imposed, restrictions are also placed upon the claims which can be made for the product on labelling or in advertising[16].

List of responsibilities of Regulatory Affairs Department:

1. Keep in touch with international legislation, guidelines and customer practices

2. Keep up to the date with a company's product range

3. Ensure that a company's products comply with the current regulations.

4. The Regulatory Affairs professional's job is to keep track of the ever-changing legislation in all the regions in which the company wishes to distribute its products. They also advise on the legal and scientific restraints and requirements, and collect, collate, and evaluate the scientific data that their research and development colleagues are generating[17].

5. Formulate regulatory strategy for all appropriate regulatory submissions for domestic, international and/or contract projects.

6. Coordinate, prepare and review all appropriate documents for example dossier and submit them to regulatory authorities within a specified time frame in conjugation with the organization.

7. Prepare and review of SOPs related to RA. Review of BMR, MFR, change control and other relevant documents[18].

8. Monitor the progress of all registration submission.

9. Maintain approved applications and the record of registration fees paid against submission of DMF's and other documents.

10. Respond to queries as they arise, and ensure that registration/ approval are granted without delay[19].

11. Impart training to R&D, Pilot plant, ADl and RA. Team members on current regulatory requirements.

12. Advising their companies on the regulatory aspects and climate that would affect proposed activities. i.e., describing the "regulatory climate" around issues such as the promotion of prescription drugs and Sarbanes-Oxley compliance.

13. Manage review audit reports and compliance, regulatory and customer inspections[20].

14. Regulatory Affairs professionals help the company avoid problems caused by badly kept records, inappropriate scientific thinking or poor presentation of data. In most product areas where regulatory requirements are imposed, restrictions are also placed upon the claims

which can be made for the product on labelling or in advertising.

15. Have a duty to provide physicians and other healthcare professionals with accurate and complete information about the quality, safety and effectiveness of the product.

Challenges to regulatory affairs profession:

Regulatory affairs include complete dynamics:

- Multi –dimensional
- Knowledge in science and technology
- Prolific communication skill
- Deal with people with diverse background, skills, culture, and personalities
- Deal with conflicting loyalties, motivations, social and ethicals, responsibilities

Case in point: submission of a dossier During submission of a dossier a regulatory affair would be:

- Guided by various regulatory guidance
- Receiving input from various department within the firm about process capabilities and product attribute specification
- Receiving advice from peers about easy way to get approvals
- Receiving motivation from the management through incentives for achieving speedy approvals.[21]

Role Of Regulatory Affairs In Pharmaceutical Industries: Regulatory Affairs professionals provides tactical and practical guidance to R&D, Production, QC department etc. Just aid the drawn of the progress of a product, making main benefaction both together economically and scientifically to the triumph of a evolution scheme and company as a entirely. It takes time of about up to 15 years to evaluate and to put a new pharmaceutical product and many issues may stand up in the process of scientific progress and because of an altering regulatory habitat. Regulatory professionals help out the company to keep out of issues originated by immaterial documentation, unsuitable scientific reasoning or impoverished presentation of records.

The roles of regulatory affairs professional is to act as cooperation with regulatory agencies:

1. To audit on constantly changing constitution.

2. Adapted documents to regulatory agencies.

3. To give tactical and practical advice to R&D, Production, QC Department.

4. Preparation of well ordered and Ensure fidelity and complaisance with all the applicable CGMP, ICH, GCP, GLP guidelines regulations and laws.[22]

This department is responsible for knowing the regulatory requirements for getting new products approved. They know what commitments the company has made to the regulatory agencies where the product has been approved. They also submit annual reports and supplements to the agencies. Regulatory Affairs typically communicates with one of the Centers (e.g., Center for Drug Evaluation and Research) at the FDA headquarters, rather than the FDA local district offices. Gimps do not directly apply to Regulatory Affairs; however, they must understand and evaluate changes to drug manufacturing and testing activities to determine if and when the FDA must be notified. Regulatory Affairs is a comparatively new profession which has developed from the desire of

governments to protect public health, by controlling the safety and efficacy of products in areas including pharmaceuticals, veterinary medicines, medical devices, pesticides, agrochemicals, cosmetics and complementary medicine. 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. Regulatory Affairs professionals, with their detailed knowledge of the regulations and guidelines, are frequently called in to advice on such matters.

Regulatory Affairs In Product Management:

The key role of RA professional is broader than registration of products, they advise companies both strategically and technically at the highest level. Their role begins right from development of a product to making, marketing and post marketing strategies. Their advice 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. For countries that do not have their own regulations the World Health Organization guidelines on health matters and World Trade Organization on trade regulations between nations is followed.

Regulatory Affairs In Clinical Trials:

The RA professional is the primary link between the company and worldwide regulatory agencies such as US Food and Drug Administration (USFDA & Center for Devices and Radiological Health) Medicines and Healthcare Products Regulatory Agency, United Kingdom (UKMCA), Therapeutic Goods Administration, Australia European Medicines Agency, Organization of Economic Collaboration and Development (OECD) and Health Canada. He also communicates and interprets the seemingly endless mace of laws, regulations and guidelines to the other departments of the company. The RA personnel develops strategies to overcome delays and presents finding of clinical trials to the regulatory bodies so as to get quick clearance thus reducing the time for approval of new molecules. At its core, the RA professional facilitates the collection, analysis and communication about the risks and benefits of health products to the regulatory agencies, medical and health systems and the public. Operationally RA is responsible for assuring that government obligation, market driven demands and evolving scientific conventions are understood and addressed by various stakeholders.

Regulatory Affairs In Research & Development:

The regulatory affairs personnel work hand in hand with marketing and R&D to develop, innovative products that take advantage of new technological and regulatory developments to accelerate time to market. With new products expected to add significant revenues to the company's bottom lines, small decreases in time to market equate to large material gains in revenue and profit. Employing adaptive clinical trial strategies, obtaining quick approval from regulatory authorities and avoiding pitfalls in processes can accelerate development of new products and help to reduce costly errors and time lags.[23]

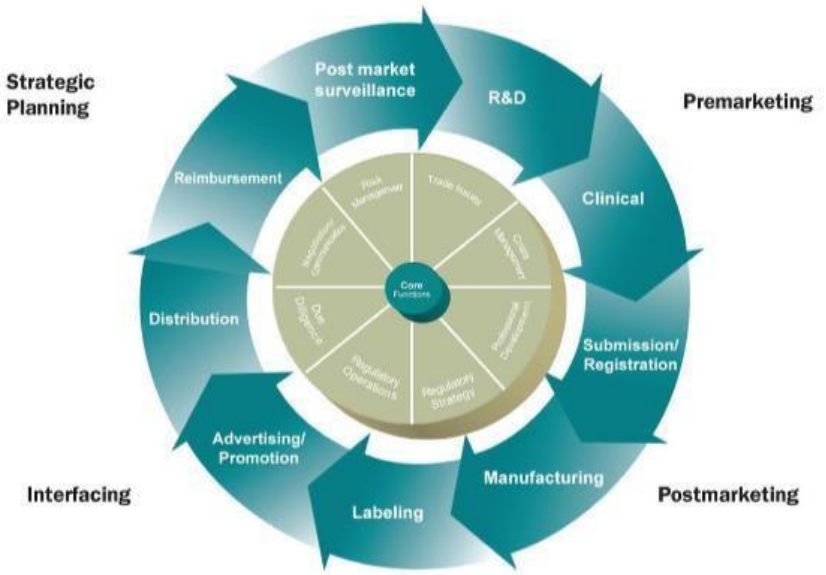

Figure 8: RA Profession: Integral to the healthcare products lifecycle

The other various roles within regulatory affairs:

- Project management
- Submission management
- Maintenance management
- CMC specialist
- Pre-clinical/Clinical specialist
- Labeling expert
- Regulatory intelligence
- Global versus local Regulatory Affairs[24]

Conclusion: Regulatory Affairs branch is usually evolving and developing and is the one that is least impacted in the course of the acquisition and merger, and also during the recession. Regulatory Affairs departments are developing inside organizations. due to the changing assets important to fulfil the regulatory requirements, a few organizations additionally select to outsource or out assignment regulatory affairs to external

carrier providers. In nowadays aggressive surroundings, the reduction of the time taken to reach the market is essential to a product and as a result the enterprise's success. The right implementation of regulatory pointers and laws will enhance the economic increase of the organization and also improves the protection of the humans.

RA is a dynamic, profitable subject that consists of each clinical and prison components of drug development. DRA experts are devoted folks who take satisfaction in their contribution to improving the fitness and pleasant of life of peoples. RA as career is broader than registration of merchandise, they advise organizations each strategically and technically at the highest level. Their function begins proper from improvement of a product to creating, advertising and marketing and submit marketing. Regulatory Affairs experts assist the agency avoid issues due to badly saved information, beside the point clinical questioning or many more.

Many in the Regulatory Affairs profession trust the new technique to regulation will finally be followed for all healthcare products as it represents the great version for turning in new healthcare advances to marketplace in an inexpensive time with suitable protection.

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