



An overview on Drug Regulatory Affairs

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ABSTRACT: Regulatory affairs in pharmaceutical industry aim at the protection of human health. People and government spent money on drugs because of the role they can play in saving lives, restoring health, preventing diseases and stopping epidemics. But, in order to do so, drug must be safe, effective and of good quality. Since the purpose of drug is to diagnose, prevent or treat diseases or ailments in humans, they are products intimately linked with the advances in research and regulation. The pharmaceutical industry, while pursuing an international market, is obliged to comply with national regulations. So, in this review article, an overview of new drug approval process in India, Regulatory approval and submission procedure in USA. Regulatory agencies and organizations play a vital role to meet the requirements of legal procedures related to drug development process in a country. Every country has its own regulatory authority, which is responsible to regulate the new drug approval of manufacturing and sale.

Keywords: Regulatory Affairs professionals, Regulatory agencies, New drug approval in India and USA.

I. INTRODUCTIONS:

A new molecule can cost several millions of rupees or dollars to progress and any blunder causes greater impact on company's status. As medicines play a vital role in human's life there must be regulations for medicines ensuring Quality, Safety and Efficacy of drugs. The regulatory affairs professional is the only one who is completely responsible for holding products in compliance and maintaining all the records. One of the vital activities of the regulatory specialist is to ensure that all the information regarding medicines has been correctly established to the patient covering labelling also. Even a small mistake in any of the activities related to regulatory can make the product to be recall in addition to loss of several millions of the money.¹ The current Pharmaceutical Industry is well organized, systematic and compliant to

international regulatory standards for manufacturing of Chemical and Biological drugs for human and veterinary consumption as well as medical devices, traditional herbal products and cosmetics.² Drug development to materialistically is highly controlled. Every drug before acquire market approval must undergo meticulous inspection and clinical trials to make sure its safety, efficacy and quality. These standards are bring by regulatory authorities of their corresponding countries like as FDA in US and DCA in India etc. Regulation influences all strands of the pharmaceutical world, from maverick pioneers and pharmaceutical companies to regulatory and managerial bodies and patients also. Regulatory department is pivotal interface between company, products and regulatory authorities whose positive or negative vantage point to strengthen the discernment of the regulatory authority into the industry, for good or for bad. So, the better the scientific exactitude, the greater will be the chances for a product to come to the market within the expected **time (1)**

IMPORTANCE OF REGULATORY AFFAIR

In today's competitive environment the reduction of the time taken to reach the market is critical to a product's and hence the company's success. The proper conduct of its Regulatory Affairs activities is therefore of considerable economic importance for the company. A new drug may have cost many millions of Euros or dollars, pounds, to develop and even a three- month delay in bringing it to the market has considerable financial considerations. Even worse, failures to fully report all the available data or the release product bearing incorrect labelling, may easily result in the need for a product recall. Either occurrence may lead to the loss of several millions of units of sales, not to mention the resulting reduction in confidence of the investors, health professionals and patients. The Regulatory Affairs department is very often the first point of contact between the government authorities and the company.⁽²⁾ The first point of contact between

the corporation and the government agency is the regulatory affairs division. Aids in coordinating research efforts with regulatory requirements. Maximize resource efficiency for the company(3)

Approval of New Drug in India

When a company in India wants to manufacture/import a new drug it has to apply to seek permission from the licensing authority (DCGI) by filing in Form 44 also submitting the data as given in Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945. In order to prove its efficacy and safety in Indian population it has to conduct clinical trials in accordance with the guidelines specified in Schedule Y and submit the report of such clinical trials in specified format. But a provision is there in Rule - 122A of Drugs and Cosmetics Act 1940 and Rules 1945 that the licensing authority may waive certain trails if he considers that in the interest public health he may grant permission for import of new drugs basing on the data of the trials done in other countries. Similarly there is another provision in Rule - 122A which says that the clinical trials may be waived in the case of new drugs which are approved and being used for several years in other countries. Section 2.4 (a) of Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945 says for those drug substances which are discovered in India all phases of clinical trials are required. Section 2.4 (b) of Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945 says that for those drug substances which are discovered in countries other than India; the applicant should submit the data available from other countries and the licensing authority may require him to repeat all the studies or permit him to proceed from Phase III clinical trials. Section 2.8 of Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945 says that the licensing authority may require pharmacokinetic studies (Bioequivalence studies) first to show that the data generated in Indian population is equal to data generated abroad and then require him to proceed with Phase III trials. In summary, the exact requirements of Clinical trials may change from case to case and depend on the extent to which licensing authority is satisfied about its safety and efficacy. The process of approval of new drug in India is a very complicated process, which should meet necessary requirements along with NDA to FDA. The need of the present work is to study and document the requirements for the process of

approval of new drug in India with emphasis on clinical trials as per Drugs Control department Government of India.(4)

REGULATORY APPROVAL & SUBMISSION PROCEDURE IN USA:-

The FDA Drug and Biologic Approval Process: In 1820, the new era of USA drug regulation was started with the establishment of U.S. Pharmacopoeia. In 1906, Congress passed the original Food and Drugs Act, which require that drugs must meet official standards of strength and purity. However, in 1937, due to sulphanilamide tragedy, the Federal Food, Drug and Cosmetic Act (of 1938) was enacted and added new provisions that new drugs must be shown safe before marketing. Further, in 1962, the Kefauver-Harris Amendment Act was passed which require that manufacturers must prove that drug is safe and effective (for the claims made in labeling). The Food and Drug Administration is responsible for protecting and promoting public health. Like general drug approval process, FDA's new drug approval process is also accomplished in two phases: clinical trials (CT) and new drug application (NDA) approval. FDA approval process begins only after submission of investigational new drug (IND) application. The IND application should provide high quality preclinical data to justify the testing of the drug in humans. Almost 85% of drugs are subjected to clinical trials, for which IND applications are filed. The next step is phase I, phase II and phase III clinical trials. A new drug application (NDA) can be filed only when the drug successfully passes all three phases of clinical trials and includes all animal and human data, data analyses, pharmacokinetics of drug and its manufacturing and proposed labeling. The preclinical, clinical reports and risk-benefit analysis (product's beneficial effects outweigh its possible harmful effects) are reviewed at the Center for Drug Evaluation and Research by a team of scientists. Generally approval of an NDA is granted within two years (on an average), however, this process can be completed from two months to several years. The innovating company is allowed to market the drug after the approval of an NDA and is considered to be in Phase IV trials. In this phase, new areas, uses or new populations, long-term effects, and how participants respond to different dosages are explored. Figure 1 represents the new drug approval process of FDA.



In order for pharmaceutical and biotech companies to market their drugs and biologics, companies must receive FDA approval, a rigorous, expensive, and time consuming process that can take over a decade to complete. Of 5000 compounds discovered in the pre-clinical stage, only about 5 will make it through the entire FDA approval process. Therefore, companies have to cover not only the cost of successful development of a single drug, but of many drugs that never make it to market in The Phases in the FDA Approval Process¹⁰Pre-Clinical PhaseIn the pre-clinical or drug discovery phase of the approval process, researchers look for potential new compounds to treat targeted diseases. Once a compound has been identified and refined to a formula that can be tolerated by humans, its toxicology is tested in animals and living tissue. The process takes roughly three and a half years.(4)

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.

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. (5)

Country Regulatory Authority

India :(CDSO) Central Drugs Standard Control organisation

Europe :(EDQM)European Directorate for Quality of Medicines,

(EMEA) European Medicines Evaluation Agencies.

UK:(MHRA) Medicines and Health care products Regulatory Agency.

Australia:(TGA) Therapeutic Goods Administration.

Japan:(MHLW) Japanese Ministry of health, Labour and Welfare.

Canada :(HC) Health Canada

Brazil :(ANVISA) Agency Nacional de Vigilância Sanitaria

South Africa:(MCC) Medicines Control Council.

USA :(FDA) Food and Drug Administration(6)

Skills & Attributes required for making a good RA Skills:

- Influence IT Literate
- Work independently
- Persuade Accuracy
- An effective negotiator
- Present Quality
- Excellent writing and communication skills(6)
- Listen actively
- Interpret and consolidate data
- Strong follow-ups and convincing ability
- Technical sound knowledge(7)

NEED OF REGULATORY AFFAIRS IN THE PHARMACY CURRICULUM

India is growing very rapidly in pharmaceutical sector; there is a need of regulatory affairs professionals to cater the current needs of industries for the global competition. Regulatory affairs professionals are the link between pharmaceutical industries and worldwide regulatory agencies. They are required to be well versed in the laws, regulations, guidelines and guidance of the regulatory agencies. There is a growing need to incorporate the current requirements of pharmaceutical industries in the standard curriculum of pharmacy colleges to prepare the students with the latest developments to serve the industries .(8)

Historical Overview of Pharmaceutical Industry

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). (9)

The drug industry in India was at very primitive stage till 20th century. Most of the drugs were imported from foreign countries.

a) 1900-1960:

Government passed the Poisons Act , 1919 to check and hold the control on cheap drugs available in market. This Act helps in the administered possession of substance or sale of substances as specified as poison. It also stated the sale and protected custody of the poisons, packaging and labeling 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 which includes the regulation of cultivation, manufacturing possession and trade of opium. In 1985, Dangerous Drugs Act 1930 and Opium Act 1878 was revoked by passing of the Narcotics and Psychotropic Substances Act.

b) 1960-1970:

The Indian Pharmaceutical industry was not mature enough and major market share was dominated by MNC and very few Indian manufacturers were in competition. Focus on pure research and development was very little because of deficiency of patent protection. The low

availability and high drug price is because majority shares depend upon the high drug import

c) **1970-1980** :Government took control for the medicines regulation and issued few ach andrules

□ **Indian Patent Act 1970** (which came in force on 20 Aprs 1972 and replaced Indian Patents and Designs Act of 1911) : It serves as the basis for patent protection in India . Under this Act product patent was not allowed but the process and method of manufacturing of Drugsubstance was allowed to get the parent

□ **Drug price capped:-** Drug Prices Control Order (DPCC) was introduced to con the high priceagainst consumers .

d) **1980-1990:**

The Indian industry has started investing in process development of APL and created production infrastructure for the same .

e) **1990-2000 :**

A rapid expansion in domestic market has observed in pharmaceutical industry. The companies have started entering into Research and Development

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 .(13)

REGULATORY AFFAIRS IN R&D

The affairs personals work in collaboration with the R&D and FR&D to develop, innovative products that meetthe new technology and the regulatory developments to accelerate time to market. The new products are expected to increase the revenues of the organization; losses due to delayed marketing will eventually get nullified with the large materials gains in revenue and profit over time. Employing adaptive clinical trial strategies to obtain the quick approval from regulatory authorities and avoiding the pitfalls in processes can accelerate development of new products and helps to reduce the expensive errors and time lags.

Regulatory affairs in Clinical Trials

Regulatory affairs professionals are the primary link between the company and worldwide regulatory agencies such as official bodies (US FDA, CDSCO, MCCA, TGA etc.). These professional's work is to furnish timely reports of the new data which is obtained in the trails and help in the approval process of the new products as according to the local regulating bodies in their respective states.

Role of Regulatory affairs in Product Development

The drug products are highly regulated channels compared to the others. These regulations are generally maintained and handled by the regulatory bodies, these bodies generally give advice on the product development based on the IND/NDA guidelines once after the approval process completes these bodies generally focus on the drug post market properties and also on the Pharmacovigilance aspects of the drug product, and it also reminds the drug Renewal period.

Regulatory affairs in Product Management

The general role of the Regulatory Affairs is broader than the registration of products, they advise companies both strategically and technically at the highest level. Their role begins right from development of a product, marketing, and post marketing strategies. Their advice at all stages both in terms of legal and technical requirements help companies to save a lot of time and money in the developing the new products.(10)

SCOPE OF REGULATORY AFFAIRS PROFESSIONAL IN INDUSTRIES

Regulatory affairs professionals are employed in industry, government regulatory authorities and academics. The wide range of regulatory professionals includes in these areas:

- Pharmaceuticals
- Medical devices
- In-vitro diagnostics
- Biologics and biotechnology
- Nutritional Products
- Cosmetics
- Veterinary Products(11)

II. CONCLUSION

Regulatory Affairs department is constantly evolving and growing in the word . it also work for acuracy of the dose of drug .Regulatory Affairs departments are growing within companies. Due to the changing resources necessary to fulfill the regulatory requirements, some companies also choose to outsource or out task regulatory affairs to external service providers. In today's competitive environment the reduction of the time taken to reach the market is critical to a product's and hence the company's success. The proper conduct of its Regulatory Affairs activities is therefore of considerable economic importance

for the company. Regulatory Affairs has many years history for the sale of dangerous drug

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