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A review on regulatory affairs and regulatory requirements for new drug approval

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Abstract

Regulatory affairs in the pharmaceutical industry are essential as the sector grows rapidly; the demand for regulatory affairs experts is increasing. Regulatory affairs professionals to meet the industry's evolving needs in the face of global competition. Regulatory affairs are a profession that serves as the interface between pharmaceutical industries and government authorities worldwide. Developing a new drug is a lengthy process, spanning several years and encompassing discovery, toxicology studies, and clinical trials.Pharmaceutical drug regulatory affairs address the various registration criteria for pharmaceutical products.Due to the desire of Protecting public health worldwide is a top priority. A new profession called pharmacy was created. Developing a new drug is a complex and lengthy process that requires extensive research and development across multiple disciplines, including chemistry, manufacturing, controls, preclinical science, and clinical trials. This article will focus on the drug approval process in three major regions: the United States, Europe, and India.

Keywords: Regulatory affairs, Discovery, Preclinical.

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Introduction

Regulatory Affairs (RA) is a career opportunity that involves regulating industries such as pharmaceuticals, medical devices, veterinary medicine, cosmetics, and more" Regulatory Affairs combines the fields of science and management". Regulatory Affairs serves as a bridge between pharmaceutical companies and government authorities, ensuring the efficacy and safety of medicinal products and overseeing their registration process. Therefore, it is also known as 'Government Affairs. The regulatory affairs serve as a bridge between pharmaceutical companies and the country's health authorities. For any new pharmaceutical product entering the market, it typically requires about 10 to 15 years of development, involving significant time and financial investment. However, consider the current example of COVID-19, an infectious disease caused by the newly discovered coronavirus (SARS-CoV-2), which rapidly spread throughout the world. The regulatory framework is continually being improved and harmonized to ensure the goal of patient safety is achieved. Regulatory affairs are responsible for collecting, analyzing, interpreting, and communicating the risk versus benefit of healthcare products globally. Additionally, the term "regulatory affairs" carries a specific meaning within the healthcare sector. Drug regulatory affairs also play a key role in the clinical trials of drugs, which are conducted under the guidelines of the Drugs and Cosmetics Act of India..1The current pharmaceutical industry is well-structured, systematic, and adheres to international regulatory standards for the manufacturing of chemical and biological drugs for human and veterinary use, as well as medical devices, traditional herbal products, and cosmetics. These standards are set by national regulatory authorities, such as the FDA in the U.S. and the CDSCO in India. Those working in pharmaceutical regulatory roles are involved not only in the initial application phase for new or generic drugs, but also in the licensing and marketing stages, ensuring that all operations and products comply with required safety and efficacy standards Organizations such as the FDA also offer career opportunities for those interested in the field. As biotechnology continues to play a larger role in drug

development and the pharmaceutical industry, there is a growing demand for regulatory affairs positions in the biotech sector [2].

Importance of Regulatory Affair

Regulatory affairs activities are of considerable economic importance to a company. The development of a new drug can cost millions of euros, dollars, or pounds, and even a three-month delay in bringing it to market can have significant financial implications. The first point of contact between the corporation and the government agency is the regulatory affairs division. The regulatory affairs division informs the company about the government's perspective, influencing the company's strategic decisions. Regulatory affairs help ensure the drug enters the market on schedule, as even a slight delay can impact the company's financial health. Regulatory affairs help the company comply with all regulations and guidelines, thereby maximizing profits. A "right first time" approach is essential, as the time taken for a product to reach the market is critical to its success. Coordination of scientific efforts with regulatory requirements throughout the entire lifecycle of the product. Regulatory affairs professionals serve as the bridge between pharmaceutical industries and regulatory agencies worldwide.

Scope of Regulatory Affairs Professional in Industries:

Regulatory affairs experts are employed in enterprises, government regulatory authorities, and academia. The diverse range of regulatory professionals spans across these sectors:

- Pharmaceutical
- Medical devices
- In-vitro diagnostics
- Biologics and biotechnology
- Nutritional products
- Cosmetics
- Veterinary products

Objectives of Regulatory Affairs

The regulatory affairs department plays a crucial role in ensuring the safety and efficacy of drugs available to the public in the market.Regulatory affairs specialists manage and document internal regulatory processes, including audits, inspections, license renewals, and product registrations. They may also compile and prepare documentation for submission to regulatory agencies. Pharmaceutical legislations, Clinical trials Provides strategic and technical advice to R&D and production teamsand quality control division. Provide advice to internal colleague on legal and scientific requirements.4 They monitor and maintain records of all accepted applications, registration fees paid, DMFs (Drug Master Files), and other supporting documentation .The regulatory affairs department is also involved in shaping the marketing strategies for drug development. Before a drug or product can be commercially launched, regulatory affairs must approve the packaging and marketing materials.

Historical overview of regulatory affairs

The regulatory affairs department can be established based on government desires. And for regulating the severe adverse consequences in public health. Actually, regulatory affairs can act as interface between pharmaceutical industry and regulatory body. During the 1950s, several tragedies, including the sulfanilamide elixir, vaccine, and thalidomide incidents, led to a significant increase in legislation aimed at ensuring the quality, safety, and efficacy of drug products. As a result, there is a tightening of regulations governing Marketing Authorization (MA) and Good Manufacturing Practices (GMPs).

INDIA India's first patent law was introduced in 1856, and since then, numerous regulations have been developed and refined [5].

A) **1900-1960: Drug and cosmetic act, 1940:**

This act governs the manufacture, distribution, import, and sale of allopathic, homeopathic, Unani, and Siddha medications. Pure food and drug act 1906: Prevent false claim Poisonous act 1919: To control the cheap products and its flow in market processing of poisonous substance. The Pharmacy Act, 1948, as amended in 1985, provides the statutory framework for regulating and controlling the profession of pharmacy in India. Narcotic & psychotropic drugs act 1985:To regulate the narcotics & psychotropic drugs.

B) 1960-1980: The Indian pharmaceutical industry was not yet fully developed, with multinational corporations dominating the major market share and only a few Indian manufacturers in competition.United state of America (USA): This guidance provides recommendations to FDA staff and the industry on the content of 510(k) submissions and the decision-making process for determining the substantial equivalency of devices reviewed under the 510(k) program.6

1820 – United states pharmacopoeia committee established.

1901 –vaccines tragedy was happened.

1906 – Food and drug act.

1912 – Sherley amendment.

The Biological Control Act of 1902 was introduced as a consequence of the vaccine tragedy."

This legislation required licensing for the manufacturing and distribution of biological products, such as serums, vaccines, toxins, and viruses, and established labeling requirements that included the manufacturer's name, address, license number, product identification, and expiration date.

EUROPEAN UNION (EU): In the EU, the first regulation was introduced in 1950, and over the years, numerous regulations have been developed and evolved. In 1957, the European Economic Commission was formed, and in 1964, the Helsinki Declaration was established to prevent unethical and risky clinical trials.

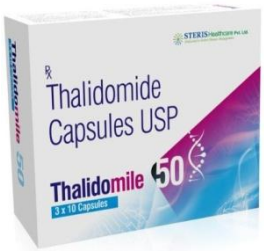
JAPAN: In Japan, two regulatory authorities oversee the use of medical devices: the PMDA and the Ministry of Health, Labour and Welfare (MHLW). The MHLW is responsible for regulatory decisions, including product approval guidelines and decisions made under the PMD Act (the Act on Ensuring the Quality, Efficacy, and Safety of Products, including pharmaceuticals and medical devices), as well as determining whether a product qualifies as a medical device

Recent Advancement In Regulatory

During the 1950s, numerous tragedies occurred due to misjudgments by personnel during manufacturing and the intentional adulteration of substances in pharmaceutical products, resulting in the deaths of patients. After numerous incidents, regulatory bodies introduced new laws and guidelines aimed at improving the quality, safety, and efficacy of products. This also led to stricter regulations for Marketing Authorization (MA) and Good Manufacturing Practices (GMPs). The standards of the pharmacy profession are set, and colleges are graded accordingly, providing students, parents, employers, and funding agencies with a valid and reliable assessment of the various pharmacy colleges in the country.

These are: The National Board of Accreditation (NBA), under the All India Council for Technical Education, and the National Assessment and Accreditation Council (NAAC), established by the University Grants Commission, are the key accrediting bodies [7].

Thalidomide Tragedy: The thalidomide tragedy was a series of events that occurred in the 1960s when it was discovered that the drug thalidomide caused severe birth defects in thousands of children. Thalidomide was a sedative widely prescribed in the 1950s and early 1960s to treat morning sickness in pregnant women.



REGULATORY AUTHORITIES: It can be created by government to oversee and enforces regulations recording occupational health & safety of medicinal products. Healthcare is my concern Medicines/ Pharmaceutical products for use by Humans/veterinarians and medical devices must be safe as well as effective for their intended use various territorial regulators have arisen to ensure this. Major regulatory bodies include the World Health Organization American Food; 1st Medicines Administration (USFDA).

WIPO-World intellectual property organization

WHO-world health organization

ICH-international council for harmonization

Role of Regulatory Affairs

- It is a distinct blend of science and management.
- It is the first point of contact between a pharmaceutical company and the regulatory authority.
- Ithelpsinknowinglegislationsimplementinglegislation sandgetapprovalforthelegislationslaid down by regulatory authorities.
- Stay updated on customer practices, guidelines, and international legislation
- Ensure that the company's products comply with current regulations.

Role of regulatory affairs started from product development to marketing, marketing to post marketing surveillance. Regulatory affairs should ensure the labeling and packing of drug products. The role of an RA professional goes beyond product registration; they provide both strategic and technical advice to companies at the highest level.

The role of regulatory affairs–Approval phase

Plan and manage agency meeting/ hearings: Early and successful interactions, including meetings and written communications, with the relevant regulatory authorities during the development of a drug, biologic, medical device, IVD, or combination product can significantly reduce both costs and time to approval. "Establishing a strong relationship is vital to ensuring that the governing health authority is well-informed and backs your planned development trajectory.

Clarify raised questions, plan response and strategies with bothered apartments:

When questions are raised by regulatory authorities, it's essential to clarify and address them promptly. Here's a step- by-step approach to plan a response and strategize with other departments: step 1; review and clarify the question. Step 2; assemble a response team. Step 3; develop a response strategy. Step 4; collaborate with other departments.

Negotiate approval and product information with agencies

Professionals in regulatory affairs facilitate the interaction between regulators (the government), the regulated (industry), and the market (consumers) to ensure that quality products reach the market, remain available, and prevent harmful products from being sold [8,9].

The Process of Drug Approval in India:

The process is carried out in three phases

First Phase

1) The applicant is presenting the IND (Investigational New Drug) application along with supporting informational studies to the CDSCO headquarters.
2) The information is thoroughly examined by the New Drug Division.
3) The IND committee then performs an in-depth review.
4) After reviewing the proper information from CDSCO, a recommendation is submitted to the DCGI.
5) Afterward, the IND application is approved.

Second Phase

1) A copy of the IND information is provided to the ethical committee along with the application.
2) The ethical committee then evaluates the IND application and submits a report
3) This procedure is carried out within 12 weeks.

Third Phase

1) Phase one involves the approval of the IND application; phase two requires a positive report from the ethical committee, and once that's received, phase three begins.
2) The third phase begins with the start of clinical trials.
3) Once completed, the application for new drug registration is given to CDSCO
4) The application is then reviewed by the DCGI at the final stage.
5) When the review is positive or finalized, the license is granted.

THEROLE OF REGULATOY AFFAIRS-POST APPROVAL PHASE

Compliance: regulatory compliance management is a systematic approach that helps organizations comply with voluntary compliance requirements, meet legal mandates, craft and implement policies and maintain continuous compliance to avoid regulatory penalties and ensure operational integrity.

Pharmacovigilance

It is well established that the regulatory affairs team in a pharmaceutical company ensures the safety and approval of new products. RA specialists handle pharmacovigilance activities, which became especially vital during the pandemic, including: establishing effective communication channel between HAs and pharma companies [10, 11].

Product information review: product information review is a critical process in regulatory affairs that ensures the accuracy, completeness, and consistency of product information. For pharmaceutical companies, this review is essential to ensure compliance with regulatory standards and to provide health care professions and patients with reliable information.

Renewals: renewals are a critical aspect of regulatory affairs ensuring that approved medicinal products remain compliant with regulatory requirements [12, 13]. Renewals involve the periodic review and update of a product's authorization, typically every 5-10 years.

Regulatory Affairs in Clinical Trials

The RA expert serves as the primary point of contact for the company with international regulatory bodies, including the US Food and Drug Administration (USFDA) and the Center for Devices and Radiological Health in the US. Clinical trial regulations are designed to guarantee that studies are carried out with the utmost safety and transparency. The RA staff implements strategies to avoid delays and ensures timely communication of clinical trial results to regulatory bodies, speeding up clearance and shortening the approval process for new molecules. The primary responsibilities of these professionals include offering regulatory consultation, developing drug strategies, preparing product dossiers, conducting gap analyses, submitting reports, communicating with regulatory agencies, and providing training in regulatory affairs. It should collect, analyses and communicate the obtained data to regulatory authorities for approval [14, 15].

- Granting the clinical trial license based upon the Pre-clinical studies
- Protocolassessmentwithregardstoriskbenefitsofinvestigationalproduct
- Pharmacovigilence(safety report analysis)
- Inspection.
- Evaluation of results.

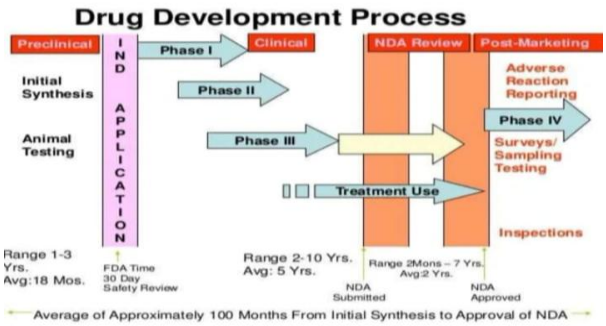
Various Phases in Clinical Trials

Phase I: Preliminary trials to evaluate safety and dosage. In Phase I trials, testing begins in human subjects, with a small group of 20-100 healthy volunteers typically being recruited.16,17During Phase I trials, dose-ranging, or dose escalation studies, are carried out to establish the safest and most effective dose and to pinpoint the level at which a compound is too toxic for administration.

Phase II: Extended trials to determine safety and efficacy After determining the dose or range of doses, the next goal is to evaluate if the drug produces any biological activity or effect Phase II trials, involving larger groups of 100-300 participants, aim to assess the drug's efficacy while continuing the safety evaluations from Phase I.

Phase III: Broad-scale studies to validate safety and efficacy. In Phase III studies, randomized, controlled multicenter trials are conducted on large patient groups (300-3,000 or more, depending on the condition), with the goal of providing a definitive evaluation of the drug's effectiveness relative to the current gold standard treatment.

Phase IV (**post-market surveillance**): Continuous assessment of product performance. Phase IV trials, also known as post-marketing surveillance trials, monitor the drug's performance after it reaches the market. After a drug is approved for sale, Phase IV trials encompass safety surveillance (pharmacovigilance) and ongoing technical support. The safety surveillance aims to identify rare or long-term adverse effects in a significantly larger patient population and extended time frame compared to Phase I-III clinical trials [18, 19].



REGULATORY AFFAIRS IN R&D: It should work to gather with research and development to and marketing to develop novel drug product by using latest technologies and regulatory development. By recruiting flexible clinical trial participants, obtaining quick regulatory approval, and avoiding process risks, the development of new products can be sped up while reducing expensive errors and time delays.13Working closely with marketing and R&D, the regulatory affairs team develops cutting-edge products that take advantage of the latest high-tech and regulatory developments to speed up market launch As new products are projected to drive significant revenue, even modest reductions in time to market can yield considerable improvements in revenue and profit.

Preclinical research: Investigations into pharmacology and toxicology.

Clinical trials: Composing papers, gathering supporting evidence, and interpreting mathematical data.

Manufacturing: The system includes rigorous safeguards to ensure the goods meet efficiency and cleanliness standards.

Functions of Regulatory affairs

- Establishing standards for drugs, cosmetics, diagnostics, and medical devices
- To manage the regulation of clinical trials in India.
- Responsibilities concerning the Drugs Technical Advisory Board (DTAB) and the Drug Consultative Committee (DCC).
- Keeping complete records of regulatory actions, submissions, approvals, and complaint resolutions.
- Maintaining proper documentation to facilitate regulatory submissions and audits
- Ensuring the implementation and maintenance of quality assurance systems and good manufacturing practices (GMP) to uphold product safety and consistency.
- Organizing and handling regulatory audits and inspections.
- To grant licenses for the manufacture of certain drug categories as the Central License Approving Authority, including blood banks, medical devices, r-DNA drugs, large volume parenterals, and vaccines & sera [20, 21].

Responsibilities Of Regulatory Affairs It is the regulatory affairs professional's job to monitor the continually changing legislation in all regions where the company aims to distribute its products [22, 23]. In addition, they advise on the legal and scientific limitations and requirements, and gather, organize, and assess the scientific data produced by their R&D colleagues. They provide strategic and technical advice at the highest levels within their companies, starting from the early stages of product development, making a significant contribution both commercially and scientifically to the success of the development program and the company as a whole. Making an important contribution both in terms of commercial success and scientific progress to the success of the development program and the company as a whole [24, 25].

A new pharmaceutical product can take up to 15 years to develop and launch, with many potential problems arising from both the scientific development process and the ever-changing regulatory environment.15By managing regulatory compliance, these professionals help the company avoid problems such as inadequate recordkeeping, faulty scientific reasoning, or subpar data presentation [26, 27].

Making sure their companies comply with all applicable policies and laws governing their business. Keep in touch with international legislation, guidelines and customer practices. Draft and review SOPs for regulatory affairs, ensuring the review of BMR, MFR, change control, and other essential documents. These professionals help the company avert issues related to poorly organized records, improper scientific reasoning, or weak data presentation. Regulatory requirements in most product areas also impose limitations on the claims that can be made in labeling or advertising [29].

Conclusion

Regulatory Affairs professionals widely believe that the New Approach to regulation will eventually apply to all healthcare products, as it is the best model for delivering new healthcare advancements to market in a reasonable timeframe while ensuring safety. With constant evolution and growth, the Regulatory Affairs department is one of the least affected during acquisitions, mergers, and economic downturns. Companies are increasingly growing their Regulatory Affairs departments. In the US, Europe, and India, drug approvals are considered to be the most challenging globally. The main objective of the regulations for medicinal products in the US, Europe, and India is to ensure public health safety. It is the responsibility of public regulatory authorities to ensure that pharmaceutical companies adhere to regulations. There are regulations that require drugs to be developed, tested, trialed, and manufactured according to guidelines to ensure their safety and protect patients' well-being.

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