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REVIEW ON REGULATORY AFFAIRS IN PHARMACEUTICAL INDUSTRIES

Ms. Pratibha Nivrutti Nyaharkar,Mr.Shivprasad Deokar,Dr. Kawade Rajendra M.

Nandkumar Shinde College of Pharmacy Vijapur , Maharashtra : 423701

Abstract-

The relatively new area of regulatory affairs (RA), usually referred to as government affairs, was created as a result of governments' need to protect public health. Pharmaceuticals, medical equipment, insecticides, veterinary medications, cosmetics, agrochemicals, and complementary therapies are among the products whose efficacy and safety are governed by RA.Pharmaceutical regulatory affairs is in charge of registering pharmaceutical products. Pharmaceutical drug regulatory affairs handle several registration requirements for pharmaceutical products. The desire of people everywhere to safeguard public health led to the creation of a new profession known as pharmacy.In addition to pharmacy, this profession deals with veterinary care, medical devices, pesticides, insectic ides, agrochemicals, cosmetics, and complementary medicine.

Keywords: Regulatory affairs, pharmaceutical products, Medicines, Agrochemicals.

Introduction –

Working in regulated industries like pharmaceuticals, medical devices, veterinary medicine, cosmetics, and other r elated sectors is part of a regulatory affairs (RA) career. The core duties of the regulatory affairs profession include obtaining, evaluating, recording, and communicating risk assessments and advantages of healthcare products to re gulatory bodies and the global public.Every medication needs to be safe, effective, and of the best quality available. The dynamic field of regulatory affairs encompasses the legal and scientific aspects of the market authorization, investigated new drug application, and new drug application (NDA) processes [1]. Pharmaceuticals are largely a major source of income for developed countries. The top ten pharmaceutical corpora tions in the world,which mostly concentrate on selling newly patented medications, are thought to sell almost USD 0.5 trillion worth of drugs a year [2].Globally, there is fierce competition for the supply and sale of pharmaceutica ls, including both innovative and gener ic drugs. Whether they are small, innovative biotechnology companies or big, international pharmaceutical conglo merates, the majority of businesses have dedicated departments of Regulatory Affairs staff [3].

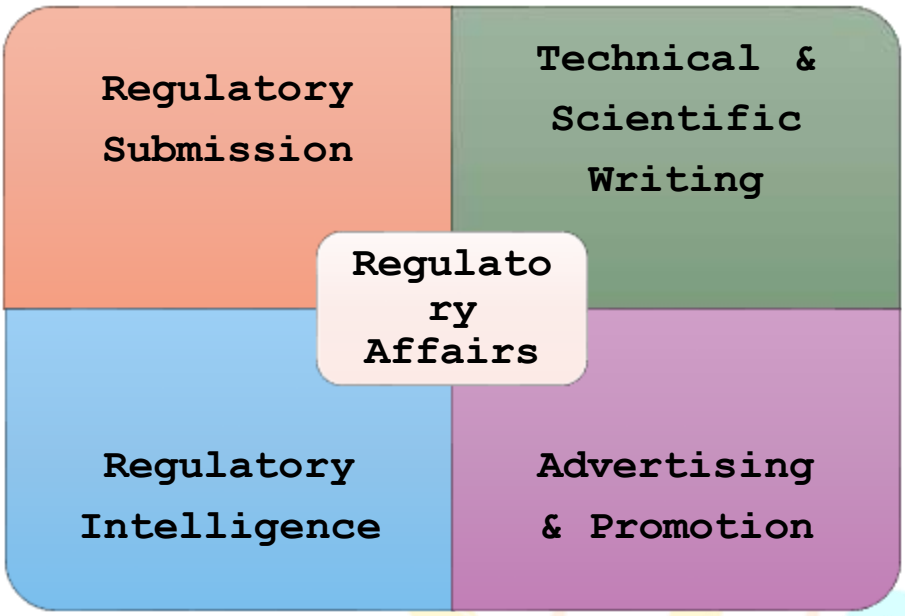

Fig. 1 Drug Regulatory Affairs

The Regulatory Affairs Department's function: -

Securing permission for new pharmaceutical medications and making sure that approval is maintained for as long as the corporation wants are the responsibilities of the regulatory affairs (RA) section of the pharmaceutical industry. Regulatory professionals, also referred to as regulatory affairs practitioners, are responsible for making sure that their organizations abide by all applicable laws and regulations. Serving as a point of contact for regulatory authorities is the responsibility of a regulatory affairs professional. To guarantee adherence to all pertinent CGMP, ICH, GCP, and GLP rules, laws, and regulations, provide well-organized documentation. By contributing their experience and regulatory knowledge, they assist in converting regulatory criteria into feasible, practical plans.

From the outset of a product's development, regulatory affairs specialists provide strategic and technological guidance to departments such as R&D, production, and quality control. From a financial and scientific perspective, they greatly progress development endeavors and the business overall. A new pharmaceutical product's development and introduction could take up to 15 years, during which time a number of obstacles could arise due to evolving regulatory frameworks and technology advancements. Regulatory specialists help the company steer clear of problems caused by imprecise documentation, faulty statistical analysis, or inadequate proof presentation [4].

Fig. 2 Experts in Regulatory Affairs

Regulatory affairs experts work for numerous departments, including Preclinical investigation: -

1.Preclinical research Pharmacological and toxicological testing were used in preclinical research to assess possibl e drug candidates.

2. Research in medicine Data collection, mathematical result interpretation, and paper preparation are all included in clinical research.

3. Manufacturing To ensure that the products are effective and hygienic, numerous precautions are taken.

4. Quality control includes examining every substance for purity, safety, potency, and quality.

5. Managing duties such as handling complaints, auditing, and defect auditing is part of quality control.

REGULATORY AFFAIRS PROFESSION: -

The pharmaceutical research and development process of bringing a new drug to market takes many years, and it is essential that the process be managed effectively from start to finish in order to meet regulatory requirements and enable a favorable evaluation of efficacy and safety in the shortest amount of time possible [5]. Drug regulatory a ffairs (DRA) professionals are involved at every step of this process, from planning postmarketing operations to d eveloping regulatory strategies following the discovery of a new chemical entity. A solid scientific foundation (B. Sc., M.Sc., Ph.D., M.D., B. Pharm., M.Pharm., or Pharm.D.) and a thorough comprehension of both Indian and int ernational laws are prerequisites for the DRA professional [6].

The following is a list of what the Regulatory Affairs Department does:

- Regulatory affairs professionals are responsible for keeping up with the ever-changing legislation in all of the nations where the company wishes to sell its products.
- They also keep up with worldwide laws, customs, and consumer behavior.
- In addition to gathering, compiling, and reviewing the scientific information produced by their research and development colleagues, they will offer legal and technical advice.
- Collaborate with the agency to plan, arrange, and review all relevant documentation, including dossiers, and then promptly submit it to the relevant regulatory organizations.
- Make a regulatory strategy that includes all necessary submissions for domestic and contract projects.
- Track approved applications and registration fees that are charged in exchange for DMFs and other paperwork.

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PROFEESSION CHALLENGE TO REGULATORY AFFAIRS:

- Multiple dimensions.
- Knowledge of science and technology.
- Excellent communication abilities.
- The capacity to collaborate with people from diverse backgrounds.
- Capabilities, cultures, and personalities, as well as the capacity to reconcile conflicting motives, interests, and social and ethical commitments.

Drug approval process in India: -

To regulate the import, manufacture, distribution, and manufacturing of pharmaceuticals and cosmetics, the Indian parliament approved the Drug and Cosmetic Act 1940 and Rules 1945. The Central Drugs Standard Control Organization is overseen by the Drugs Controller General (DCGI) (CDSCO). The 1945 Drug and Cosmetics Rules were amended by the Indian government in 1988 to create Schedule Y.
In India, companies that want to study, create, or import new drugs must submit Form 44 to the licensing body (DCGI) together with the data needed by Schedule Y of the Drug and Cosmetics Act 1940 and Regulations 1945.To prove the product's efficacy and safety in the Indian community, it must conduct clinical trials in accordance with Schedule Y's specifications and present the results in the manner specified by Schedule Y [8].

The need for local clinical trials in India is determined by the condition of the drug in other countries. If the medication has been approved in other countries, phase III studies are frequently expected. Only when foreign data is available are phase I studies permitted in India. Phase 1 research in India will be authorized by DCGI if the drug is crucial for treating an Indian health issue, such as malaria or tuberculosis.

The specified parameters for the Bioavailability and Bioequivalence Testing (BABE) should be followed. In addit ion to safety and efficacy data, detailed information regarding the drug's commercial status in other countries is ne eded. Additionally, documentation about the drug, samples and testing methods, product monographs, andlabeling must be sought.In India, it typically takes three months for a clinical experiment to be approved.

The Clinical Trials Registry of India (CTRI),which keeps track of the participants
and the studies' own records, is where clinical trials can be registered.

The 1945 Drugs and Cosmetics Laws establish the following guidelines:

- Rule 122 – A: Request for New Drug Import Approval
- Rule 122-B: application for permission to import a new medication that is not on Schedule C or C1
- Permission to import or export fixed dosage combinations (Rule 122-D).
- Rule 122 – DA: Request for approval to perform clinical trials for a new drug or an investigational new drug.
- DAB: Compensation in the event of injuries or death during clinical trials (Rule 122).

Stages of Approval: -

- Submitting a clinical trial proposal in order to assess the safety and effectiveness of a product.
- Conditions for the approval of new drugs.
- Following approval, information on the cost, effectiveness, and protection of biological products can be used to improve them.
- To approve a pharmaceutical application for a novel drug, superior data must be prepared.
- The CTD format has been adopted by most nations.
- Therefore, when registering prescription drugs for human consumption, CDSCO has agreed to use the CTD format for technical characteristics.

FDA (Food and Drug Administration): -

FDA mission-

In addition to ensuring the effectiveness, security, and safety of medications for humans and animals, medical equi pment, and biological products, the Food and Drug Administration is in charge of protecting the country's food su pply, cosmetics, and radiation-
emitting devices. In order to protect the public's health and reduce tobacco use among minors, or those who are no t yet of legal drinking age, the FDA also plays a crucial role in regulating the manufacture, marketing, and distribu tion of tobacco products. By providing safer, more user-
friendly, and more affordable medical products, the FDA also aims to improve public health. This can be achieved with accurate science-based knowledge [9].

FDA Approved Product: -

The US Food and Drug Administration has approved and regulated the following products: Bottled water is used i n baby formula, diet supplements, and other food products, although the US Department of Agriculture is mostly i n charge of regulating specific meat, poultry, and egg products. Prescription (name-
brand and generic) pharmaceuticals, biologics, and over the
counter (nonprescription) goods are all considered medications. Immunizations for humans against allergens prese

nt in blood and blood derivatives, tissues and tissue products, and materials utilized in gene and cellular therapy. Medical equipment ranges from basic devices like bedpans and tongue depressors to more complex ones like dent al systems and cardiac pacemakers. Implants for prostheses and surgery.

Sunlamps, microwave ovens, laserequipped items, ultrasonic treatment equipment, mercury vapor lamps, and Xra y equipment are examples of electronic devices that release radiation. Cosmetics: Colorants used in paint and oth er personal hygiene products, such as skin cleansers and moisturizers, nail polish, and cologne. Pet food and veter inary drugs are given to the animals. The applications of veterinary drugs. Products that contain tobacco, includin g smokeless tobacco, roll-your-own tobacco, and cigarettes.

Investigational New Drug Application (INDA): -

An FDA application is submitted before a human inspector steps in. It goes into extensive detail about chemistry, production, and quality control. The following information must be included in the IND application:

(1) Research on Animal Pharmacology and Toxicology.

(2) Both protocols and clinical researchers.

(3) Details on the manufacturing process.

After the sponsor submits the IND, 30 days must elapse. Count the number of days left until any clinical trials start. The Food and Drug Administration (FDA) can verify the IND's security and safety during this period by examining it. The standards for the structure and content of an IND application are outlined in Section 312 of the 21 Code of Federal Regulations.Applying for a "Investigator New Project" is required if you wish to perform a clinical review. Follow the instructions below to fill out the "Drug Application" form [10].

- FDA Form 1571
- Tables of contents
- Statement of intent and investigational strategy
- Sponsor's brochure
- Protocols are a set of rules that govern how
- Data on chemistry, manufacturing, and control.

- Data on pharmacology and toxicology.
- Previous people/human experience.
- Additional information

New Drug Application (NDA): -

A novel drug application must be submitted in order for a medication to be sold as a novel drug in the United Stat es. An NDA contains all of the information in the IND as well as the findings of safe and effective clinical trials. F or a set of two, the FDA will give a non-
disclosure agreement in NDA format and contents, and the review procedure will begin sixty days after the applica tion.

These are the two sections of the application: -

(1) Archival copy.

(2) Review

Archival Copy: It includes copies of tabulations and clinical trial case report forms and acts as a reference for FD A reviewers looking for material not included in the review copy.

Review Copy: A separate review copy of each technical component is bound in its own folder. The following sho uld be included in every technical section:

Each technical section Should include the following:

1) Index
2) FDA form 356 h (copy)
3) A duplicate of the cover letter
4) Authorization letters
5) ßA copy of the application summery is required

At least two meetings will be held between the sponsor and the FDA: one following the conclusion of phase 2 clini cal trials and another known as a pre-
NDA meeting that takes place prior to the filing of an NDA. After reviewing the investigation's findings, the analy sis committee will decide whether to accept the application proposal [11].

Abbreviated New Drug Application (ANDA): -

Products with similar active components, dosage forms, and strengths—
as well as similar administration and usage techniques—
are referred to by ANDA. Along with picking a product that has been proven to be secure and reliable. This is the case when a business wishes to sell a product to promote its copy after its patent expires. These drugs, also referre d to as generics, must meet comparable pharmacological and biochemical standards. The Office of Drug Evaluatio n and Research within the Center for DrugEvaluation and Research receives an ANDA. After review, it was appro ved for use in the Generic Drugs category [12].

Supplemental New Drug Application (SNDA) (13): -

Once the initial NDA or ANDA has been approved, any substantial modifications to the provisions contained in th e applications must be acknowledged by submitting a new one. The CDER must approve a supplemental NDA or ANDA that includes modifications to the ingredients or packaging. New-use
approvals of previously approved pharmaceuticals fall under this category and are a superior advancement since t hey require less time and resources to analyze than new-use
approvals of previously approved treatments. This is the first time that authorization is required.

Common technical documents (CTD):

The Common Technical Documents (CTD)are a set of application requirements for the registration of designs and medications that are permitted for use in the US, Europe, and Japan. It is a widely accepted process for developing a new medication application intended for submission to regional regulatory bodies in the participating nations. The three regulatory agencies that collaborate on CTD are the Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Ministry of Health, Labor, and Welfare in the United States (MHLW, Japan). The CTD was kept up to date by the International Council on Harmonization (ICH) of Technical Standards for Pharmacological Approval for Human Use. Before submitting to regulatory agencies, technical needs might be organized using the popular CTD format. (14)

Goal of CTD: -

Reducing the time and resources required for application compilation is the main goal.

It will speed up access to new drugs by facilitating the exchange of regulatory data.

To provide three places for simultaneous submission.

It will help in getting ready to submit applications electronically.

CTD triangle

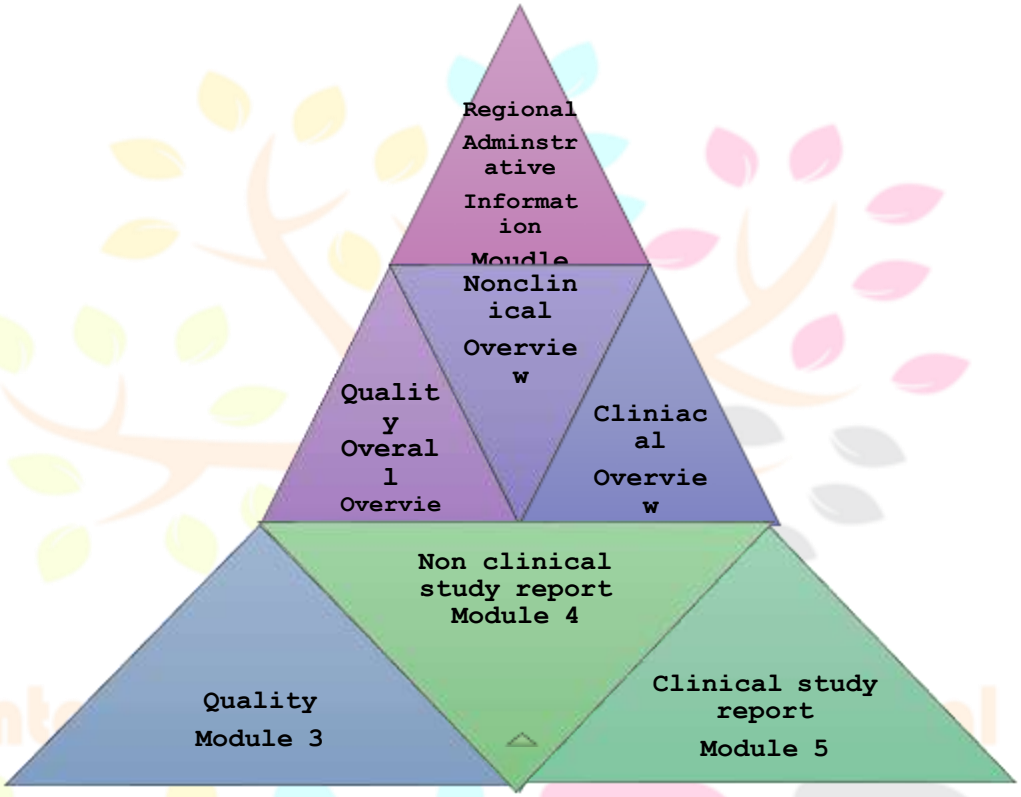

Fig. 3 The triangle of CTD. There are five module in the common Technical Document .Module 2,3,4& 5are meant to be universal for all location ,but Module E1is region specific.

Modules of CTD It can be organized into 5 Modules: -

Module 1: prescription and administrative data.

Module 2: CTD summaries of common technical publications.

Module 3: Data quality.

Module 4: Reports on nonclinical studies.

Module 5: Reports from clinical studies

Electronic common technical document (eCTD): -

The eCTD is the electronic equivalent of the CTD. "The eCTD is defined as an interface for industry to agency transfer of regulatory information while at the same time taking into consideration **the fa**cilitation of the creatio n, review, lifecycle management, and archiving of the electronic submission," according to the official regulatory stance. The standard and a number of its modules have been adopted by the main international bodies. Following t he delivery of the initial submission in eCTD format, all further additions to the application must be made in that f ormat as well.

Technically speaking, the eCTD is a well-organized set of shared folders that contain SAS (Statistical Analysis Software) and PDF files on a CD or DVD. Additionally, it can be provided through agency web portals. The eCTD is based on an XML (Extensible Markup Language) file that represents the structure of the submission. It also inc ludes other metadata, like checksum details
and links to other files. It is an electronic format called "Electronic Common Technical Documents," where docu ments and data are sent to the relevant regulatory body electronically through software.In order to seek any adjust ments or marketing,an agency or pharmaceutical company created this electronic document in compliance with E uropean rules and regulations.

eCTD is used to send the application, reports, master formulae, supplements, etc. It seems sensible
that the biggest challenge is correctly utilizing the eCTD **format** in the program. The application and promoter ma y face difficulties if the document does not adhere to the correct format, as the application must be denied [15].

Benefits eCTD: -

The eCTD must be easy to implement and assess, optimize the use of existing resources, and.
result in reduced stress and expense for the company. The eCTD requires an electronic table
of contents that are self-validating, searchable, and well-
structured. The FDA will start implementing eCTD in January,1,2008. Electronic submissions for CDER will t hen be the standard.The FDA required all electronic submissions to be in the.
eCTD format from 2007 to 2008. However, paper copies are still appreciated. The number of ANDA submissions to the FDA increased significantly from 72 in 2006 to 1550 in 2009. Preserving the vast quantity of information p ertaining to the entire submission, such as the manufacturer's details, papers, identification, and the sending and re ceiving organization.

Common format for eCTD: -

- Story: [Calibri 12] Portable Document Format (PDF).
- Extensible Markup Language (XML) is the structure.
- Graphic: Use PDF, whenever PDF is not supporting, use Joint Photographic Experts Group (JPEG), Portable Network
- Graphics (PNG), Scalable Vector Graphics (SVG) and Graphic Interchange Format (GIF).
- Font size 9 and 10 are suggested for tables.

RECENT ADVANCEMENT IN DRUG REGULATORY AFFAIRS: -

TheIndian government has set up a few independent committee to evaluate the standards of the pharmacy professi on and assign a suitable grade to the numerous pharmacy colleges in the country. This is done in order to give stu dents, parents, employers, and funding agencies an accurate and reliable ranking of the institutions. In [17]One of these is the

1) The AllIndia Council for Technical Education is the parent organization of the National Boad of Accreditation (NBA).

(2) The National Assessment and Accreditation Council (NAAC)

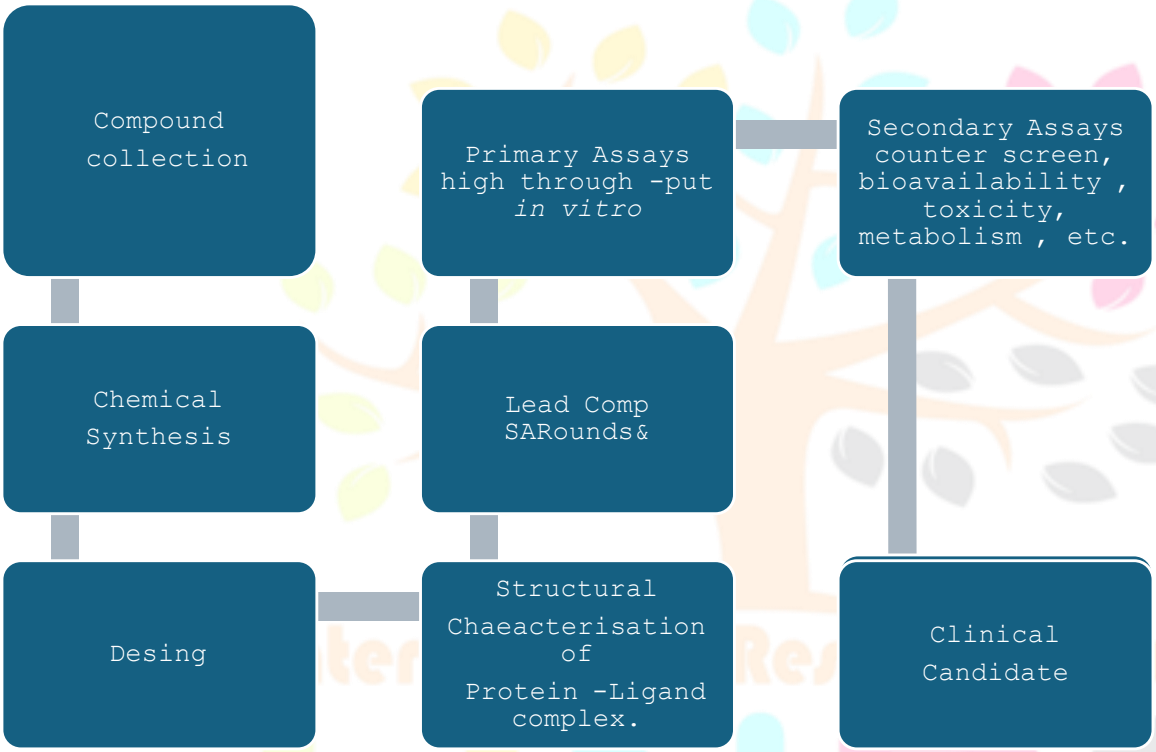

Fig.4 Drug Discovery Cycle

Conclusion: -

Due to its constant expansion and change, the department of regulatory affairs is the one least impacted by mergers , acquisitions, and recessions. Regulatory affairs departments are growing throughout companies. Due to the varyi ng resources needed to achieve regulatory standards, some companies also choose to outsource or out task regulatory difficulties to outside service providers. In the current competitive environment, the speed at whic h a product may reach the market determines its success as well as that of the firm. In addition to improving publi c safety, properly enforcing laws and regulations would increase the company's financial success.
The pharmaceutical industry is one of the most heavily regulated areas of the global economy. To ensure that drugs meant for human consumption fulfill international criteria pertaining to safety, efficacy, and quality, regulatory bodies, or agencies, have been established globally.

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