IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

REVIEW ON REGULATORY AFFAIRS IN PHARMACEUTICAL INDUSTRIES.

1Saklen Harun Sayyad, 2Siddhi Sanjay Sharma, 3Vishakha R. Nagare, 4Madhuri Ravindra Damale, 5Ram Vijay Kothwal

1Pursuing B.Pharmacy, 2Pursuing B.Pharmacy, 3M.Pharma , 4Pursuing B.Pharmacy, 5Pursuing B.Pharmacy

1Savitribai Phule Pune University,

2Savitribai Phule Pune University,

3Savitribai Phule Pune University,

4Savitribai Phule Pune University,

5Savitribai Phule Pune University

Abstract: Governments' desire to safeguard public health led to the creation of the relatively new field of regulatory affairs (RA), also known as government affairs. RA regulates the efficacy and safety of goods like pharmaceuticals, medical devices, pesticides, veterinary medicines, cosmetics, agrochemicals, and complementary medicines. The registration of pharmaceutical items is a subject of pharmaceutical regulatory affairs. Different registration criteria for pharmaceutical products are covered by pharmaceutical drug regulatory affairs. As a result of the desire of people all over the world to protect the public health, a new profession called pharmacy was created. This profession covers not only the field of pharmacy, but also veterinary medicine, medical devices, insecticides, pesticides, agrochemicals, cosmetics, and complementary medicine.

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

Introduction: A job in regulatory affairs (RA) involves working in regulated fields such pharmaceuticals, medical devices, veterinary medicine, cosmetics, and other related fields. Gathering, analyzing, documenting, and disseminating risk assessments and benefits of healthcare goods to regulatory agencies and the general public around the world are the fundamental responsibilities of the regulatory affairs profession. All medications must be of the highest quality possible and be safe and effective. The scientific and legal components of the New Drug Application (NDA), Investigated New Drug Application (INDA), and Market Authorization processes are all included in the dynamic field of regulatory affairs [1].

For industrialized nations primarily, pharmaceuticals constitute a significant source of wealth. It is believed that the top ten pharmaceutical companies in the world, which focus primarily on the selling of new patented pharmaceuticals, sell more than USD 0.5 trillion worth of drugs annually [2]. The supply and sale of

pharmaceuticals, both generic and newly developed medications, are subject to intense competition on a global scale.

Most businesses have specialized departments of Regulatory Affairs personnel, regardless of whether they are large, multinational pharmaceutical corporations or tiny, creative biotechnology enterprises [3].

Fig.1 Drug Regulatory Affairs

The Regulatory Affairs Department's function:-

The pharmaceutical industry's regulatory affairs (RA) division is in charge of securing approval for new pharmaceutical drugs and ensuring that approval is upheld for as long as the company chooses. Regulatory affairs practitioners, often known as regulatory professionals, are in charge of the following areas: ensuring that their companies follow all relevant rules and laws. A regulatory affairs specialist is in charge of acting as a point of contact for regulatory bodies. Prepare well-organized paperwork to ensure compliance with all relevant CGMP, ICH, GCP, and GLP regulations, legislation, and laws. They help translate regulatory standards into workable, realistic plans by bringing their experience and regulatory knowledge to the table.

Regulatory affairs specialists offer strategic and technological direction to R&D, Production, and Quality Control departments, among others, from the very beginning of a product's development. As a result, they significantly advance a development initiative and the company as a whole from a financial and scientific standpoint. The development and launch of a new pharmaceutical product might take up to 15 years, during which time several challenges may appear as a result of technological breakthroughs and shifting regulatory frameworks. Regulatory experts assist the business in avoiding issues brought on by inaccurate records, flawed statistical reasoning, or weak proof presentation [4].

Fig.2 Experts in regulatory affairs

Regulatory affairs experts work for numerous departments, including

Preclinical investigation:-

1. Preclinical investigation

Preclinical research evaluated potential medication candidates using pharmacology and toxicology testing.

2. Medical studies

Clinical research includes the collection of data, the interpretation of mathematical results, and the production of papers.

3. Production

There are many measures in place to guarantee that the products are efficient and clean.

4. Quality control involves inspecting all materials for quality, potency, safety, and purity.

5. Quality control

includes managing tasks including processing complaints, auditing, defect audits, and defect auditing.

REGULATORY AFFAIRS PROFESSION:-

To meet regulatory requirements and enable a favorable evaluation of efficacy and safety in the shortest amount of time possible, it is crucial that the process be managed effectively from beginning to end in the pharmaceutical research and development process of bringing a new drug to market, which takes many years [5]. Every stage of this process, from designing regulatory strategies after the discovery of a new chemical entity to organizing post-marketing operations, involves the professional in drug regulatory affairs (DRA).

The DRA professional is required to have a strong scientific background (B.Sc, M.Sc, Ph.D., M.D., B. Pharm, M.Pharm, or Pharm.D.) and in-depth understanding of both Indian and international legislation [6].

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

- Keep abreast of global laws, customs, and consumer behavior.
- keep abreast of a company's product line.
- The Regulatory Affairs professional's role is to stay on top of the constantly evolving regulations in all of the countries where the organization wants to sell its goods. They will provide legal and technical guidance, as well as gather, collate, and review the scientific evidence generated by their research and development colleagues.
- Plan, organize, and review all pertinent paperwork, including dossiers, in cooperation with the agency, then submit it to the appropriate regulatory bodies on time.
- Create a regulatory plan and include all required submissions for contract, international, and domestic projects.
- Observe applications that are approved and registration costs that are assessed in return for DMFs and other documentation.

Keeping abreast of the constantly evolving regulations in every nation where the company intends to market its goods is the responsibility of the Regulatory Affairs specialist. Experts in regulatory affairs are in charge of submitting registration documents to regulatory bodies and conducting all required negotiations to maintain the products' availability on the market. From the start of a product's development, they provide technological and strategic support at the highest levels of their organizations, making a significant financial and clinical contribution to the success of the development effort and the company as a whole [7].

PROFEESSION CHALLENGE TO REGULATORY AFFAIRS

Complete dynamics are included in regulatory affairs:-

- Multi-dimensionality.
- Scientific and technological knowledge.
- Prolific communication skills .
- Ability to work with individuals of different backgrounds.
- Abilities, cultures, and personalities, and the ability to resolve conflicts between competing interests, motivations, social and ethical obligations.

Drug approval process in India:-

The Indian parliament passed the Drug and Cosmetic Act 1940 and Rules 1945 to control the import, production, distribution, and manufacturing of drugs and cosmetics. The Drugs Controller General (DCGI) (CDSCO) is in charge of the Central Drugs Standard Control Organization. In 1988, the Indian government created Schedule Y by amending the 1945 Drug and Cosmetics Rules.

Businesses in India who wish to research, develop, or import new medications are required to submit Form 44 to the licensing body (DCGI) along with the information required by Schedule Y of the Drugs and Cosmetics Act 1940 and Rules 1945. It must carry out clinical trials in compliance with Schedule Y's requirements and provide the findings in the Schedule Y-outlined way to demonstrate the product's safety and effectiveness in the Indian community [8].

The state of the medication in other nations determines the necessity of local clinical trials in India. Phase III studies are often anticipated if the drug has received approval in other nations. Phase I studies are only allowed in India if there is international data available. DCGI will approve the conduct of Phase 1 studies in India if the medication is very important for addressing a health concern in India, such TB or malaria.

The Bioavailability and Bioequivalence Testing (BABE) should adhere to the established parameters. Comprehensive information about the drug's commercial status in other nations is required, in addition to safety and effectiveness data. It is also necessary to seek documentation pertaining to the medication, samples and testing procedures, product monographs, and labeling.

Approval of a clinical trial in India usually takes three months. Clinical trials can be registered with the Clinical Studies Registry of India (CTRI), which maintains records of the participants and the studies themselves. The following regulations are provided under the 1945 Drugs and Cosmetics Laws:

The 1945 Drugs and Cosmetics Rules had the following clauses:

- 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:-

- The filing of a proposal for a clinical trial with the aim of evaluating a product's efficacy and safety**.**
- Requirements for new medications to be approved.
- After approval, biological goods can be improved with data on cost, efficacy, and protection.
- The preparation of superior data in order to approve a pharmaceutical proposal for new drug approval. The majority of countries have embraced the CTD format. Consequently, CDSCO has consented to utilize the CTD format for technical parameters when registering prescription products for human consumption.

FDA (Food and Drug Administration):-

FDA mission:-

The Food and Drug Administration is responsible for safeguarding the nation's food supply, cosmetics, and radiation-emitting goods in addition to assuring the efficacy, security, and safety of pharmaceuticals for humans and animals, medical equipment, and biological products.

Additionally, the FDA is essential in regulating the production, promotion, and distribution of tobacco products in order to safeguard the public's health and lower tobacco use among minors, or those under the legal drinking age. The FDA also strives to enhance public health by offering medical goods that are safer, easier to use, and more reasonably priced. Accurate science-based information may be used to accomplish this [9].

FDA Approved Product:-

The following goods have been authorized and regulated by the US Food and Drug Administration: While the US Department of Agriculture is primarily responsible for regulating certain meat, poultry, and egg products, bottled water is also utilized in baby formula, diet supplements, and other food goods. Medications include nonprescription (over-the-counter) items, biologics, and prescription (both name-brand and generic) pharmaceuticals. Human vaccinations against allergens found in tissues and tissue products, blood and blood derivatives, and items used in cellular and gene therapy. Medical equipment includes simple items like tongue depressors and bedpans as well as sophisticated items like cardiac pacemakers and dental systems. implants used in surgery and prosthetics.

Electronic devices that emit radiation include sunlamps, microwave ovens, laser-equipped objects, ultrasonic treatment equipment, mercury vapor lamps, and X-ray equipment. Cosmetics: Colorants found in makeup and other personal care items including cleansers and moisturizers for the skin, nail varnish, and cologne. Animals are provided pet food and veterinary medications. Veterinary medications and their uses. Items that include tobacco, such cigarettes, roll-your-own tobacco, and smokeless tobacco.

Investigational New Drug Application (INDA):-

Before a human inspector gets involved, an FDA application is filed. It covers production, quality assurance, and chemistry in great detail. The IND application has to have the following data: (1) Pharmacology and Toxicology Studies on Animals. (2) Clinical researchers as well as protocols. (3) Information on the production procedure. 30 days must pass after the sponsor submits the IND. Recount the days that remain until any clinical trials begin. During this time, the Food and Drug Administration (FDA) is able to confirm the IND's security and safety by checking it. Section 312 of the 21 Code of Federal Regulations specifies the requirements for the format and substance of an IND

application. You must submit an application for a "Investigator New Project" if you would want to conduct a clinical review. Complete the "Drug Application" form according to the steps outlined below [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):-

To be marketed as a novel medication (drug) in the US, a novel Drug Application has to be filed. All of the data in the IND is included in an NDA, along with the outcomes of efficacious and safe clinical studies. The FDA will provide a non-disclosure agreement in NDA format and contents for a set of two, and start the review process sixty days following the application. There are two sections to the application:

(1) Archival copy.

(2) Review.

Archival Copy: It serves as a reference source for FDA reviewers seeking information not included in the review copy and contains copies of tabulations and clinical trial case report forms.

Review Copy: Each technical section is bound separately in each folder as a review copy. 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) A copy of the application summery is required.

The sponsor and the FDA will have at least two meetings: one after phase 2 clinical trials are completed, and the other before an NDA is filed, which is known as a pre-NDA meeting. The committee for analysis will investigate. the results of the investigation and choose whether or not to approve the application proposal [11].

Abbreviated New Drug Application (ANDA):-

ANDA is used for products that have comparable active ingredients, dosage forms, and strengths, as well as comparable administration and usage methods. In addition to selecting a product that has been demonstrated to be trustworthy and safe.

This is true when a product's patent expires and the company wants to sell it to promote its copy. Known as generics, these medications have to fulfill equivalent bio and pharmacological requirements. An ANDA is given to the Center for Drug Evaluation and Research's Office of Drug Evaluation and Research. It has been reviewed and given the all-clear in the Generic Drugs category [12].

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

Any significant changes to the terms included in the applications must be recognized by submitting a new NDA or ANDA after the original one has been approved. A supplementary NDA or ANDA containing changes to the ingredients or packaging requires approval from the CDER. Since they take less time and resources to review than new-uses approvals of already approved treatments, new-uses approvals of previously approved medications fall under this category and represent a superior advancement. It's the first time that permissions are needed.

Common technical documents (CTD):-

A set of application standards for the registration of designs and medicines that may be used in Japan, the US, and Europe is known as the Common Technical Documents (CTD). It is a globally recognized method for creating a new drug application that is meant to be submitted to local regulatory agencies in the participating countries.

The European Medicines Agency (EMA), the Food and Drug Administration (FDA), and the Ministry of Health, Labor, and Welfare in the United States (MHLW, Japan) are the three regulatory bodies that work together on CTD. The International Council on Harmonization (ICH) of technical standards for pharmacological approval for human use maintained the CTD current. Technical requirements can be arranged using the widely used CTD format before being submitted to regulatory bodies [14].

Goals of CTD:

- The primary aim is to minimize the amount of time and resources needed for application compilation.
- It will aid in the preparation of electronic application submissions.
- To enable concurrent submission in three areas.
- It will facilitate the sharing of regulatory data, resulting in expedited access to novel medications.

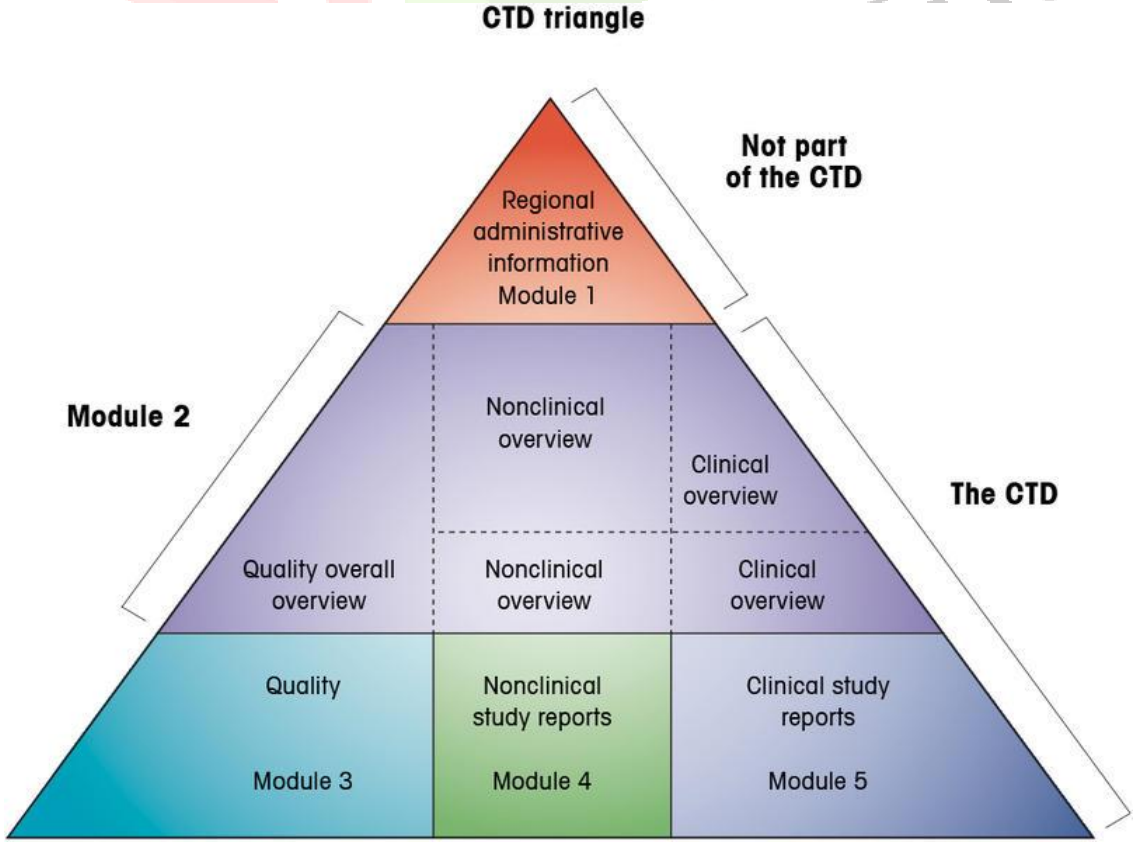

Fig.3 The triangle of CTD. There are five modules in the Common Technical Document. Modules 2, 3, 4, and 5 are meant to be universal for all locations, but Module E1 is region-specific.

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

- Module 1: administrative and prescribing information.
- Module 2: common technical documents CTD summaries.
- Module 3: Quality data.
- Module 4: Nonclinical study reports.
- Module 5: Clinical study reports.

Electronic common technical document (eCTD):-

The CTD's electronic counterpart is called the eCTD. "The eCTD is defined as an interface for industry to agency transfer of regulatory information while at the same time taking into consideration the facilitation of the creation, review, lifecycle management, and archiving of the electronic submission," states the official regulatory position. The major international authorities have approved the standard and several of the modules. All upcoming contributions for the application must be made in eCTD format after the initial submission is delivered in that format.

From a technological point of view, the eCTD is an organized collection of shared folders on a CD or DVD that hold PDFs and SAS (Statistical Analysis Software) files. It can also be supplied via agency online portals. An XML (Extensible Markup Language) file that represents the submission's structure serves as the foundation of the eCTD. It also contains connections to other files and additional metadata, such as check sum details. It is an electronic format known as "Electronic Common Technical Documents," in which data and documents are electronically submitted via software to the appropriate regulatory agency. It is an electronic document that was put together by an agency or pharmaceutical firm in accordance with European laws and regulations in order to request any changes or marketing.

The application, supplements, reports, master formulas, etc. are all submitted through eCTD. The largest obstacle is using the eCTD format correctly in the application, which is understandable. When the document does not follow the proper format, the application and promoter may encounter issues because the application need to be rejected [15].

Benefits of eCTD:-

The eCTD need to be simple to distribute and evaluate, make better use of available resources, and cause the corporation less expense and strain. A well-structured, searchable, and self-validating electronic table of contents is essential for the eCTD.

Beginning on January 1, 2008, eCTD will be implemented by the FDA. After that, it will become the norm for electronic submissions for CDER. From 2007 to 2008, the FDA mandated that all electronic submissions be in the eCTD format. Paper copies are still welcomed, though. From 72 ANDA submissions to the FDA in 2006 to 1550 submissions in 2009, this is a significant rise. maintaining the massive amount of data related to the complete submission, including details about the manufacturer, documents, IDs, and organization sending and receiving the information [16].

Common format for eCTD:-

- Narrative: Portable Document Format (PDF) [Calibri 12].
- Structure: Extensible Markup Language (XML).
- 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:-

In order to provide students, parents, employers, and funding agencies with an accurate and trustworthy ranking of the many pharmacy colleges in the nation, the Indian government has established a few autonomous committees to assess the standards of the pharmacy profession and grade the institutions appropriately.In [17]

One of these is the

(1)National Board of Accreditation (NBA), which operates under the All India Council for Technical Education's auspices.

(2) University Grants Commission's National Assessment and Accreditation Council (NAAC).

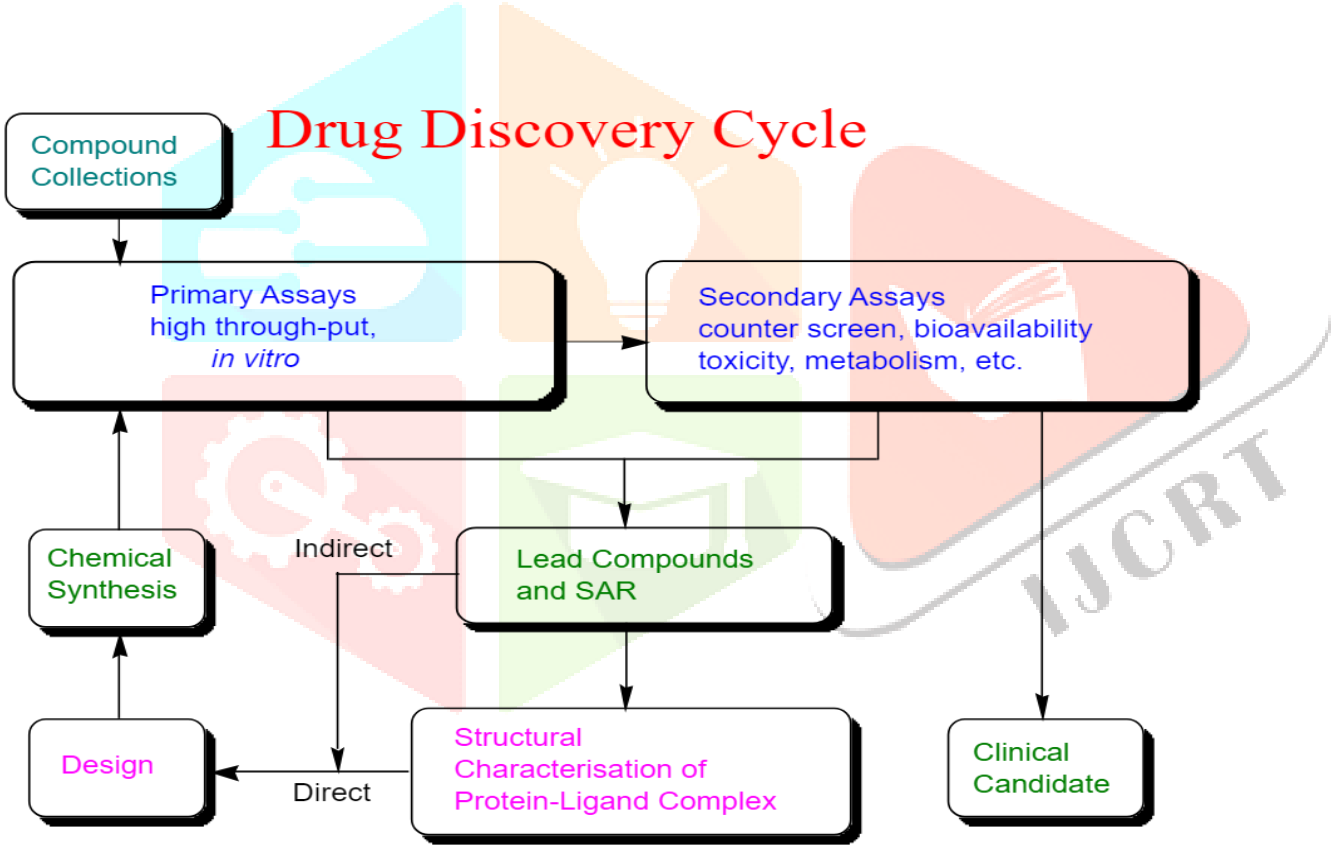

Fig.4 Drug Discovery Cycle

Conclusion:-

The department of regulatory affairs is the one least affected by acquisitions, mergers, and recessions because it is always changing and expanding. Within businesses, regulatory affairs sections are expanding. Some businesses also decide to outsource or outtask regulatory issues to outside service providers due to the fluctuating resources required to meet regulatory standards. In the current competitive landscape, a product's and the company's success depends on how quickly it can reach the market. Enforcing laws and regulations correctly would not only increase public safety but also boost the company's economic success.One of the sectors of the global economy with the strictest regulations is the pharmaceutical one. Globally, regulatory governing bodies, or authorities, have been established to guarantee that pharmaceuticals intended for human consumption meet international standards pertaining to safety, efficacy, and quality.

Reference:-

1. Writing SG-L-M. undefined. Good regulatory practice and the role (s) of a regulatory affairs professional. Taylor Fr [Internet]. Dec 2013; 22(4): 279–81.
2. Kontoghiorghe, C.N.; Andreou, N.; Constantinou, K.; Kontoghiorghes, G.J. World health dilemmas: Orphan and rare diseases,orphan drugs and orphan patients. World J. Methodol. 2014, 4, 163–188.
3. International regulatory affair updates 2005 available at http://www.iraup.com/about.php
4. Wood KL. The medical dictionary for drug regulatory affairs (MEDDRA) project. Pharmacoepidemiol Drug Saf. 1994; 3(1): 7–13.
5. http://www.medindia.net/indian_health_act/drugs-andcosmetics-act-1940 introduction
6. Topra brought by dimension associates availableathttp://www.topra.org/careers/whatregulatoryaffairs.
7. Roshan K. (GJRA) JA-GJFRA, 2018 undefined. ROLE OF REGULATORY AFFAIRS IN PHARMACEUTICAL COMPANY: AN OVERVIEW. wwjournals.org [Internet].2018.
8. Deep A, Khurana G, Research JK. Trials C. undefined. Comparison of Basic Regulatory Requirements for Generic Drug Products Registration in CIS and Latin American Countries. ingentaconnect.com [Internet]. 2012.
9. Kumar V. Comparative Study of the Regulatory Guidelines for Clinical Trials in Regulated and Semi-Regulated Countries. 2016.
10. Drago D, Yap M, Ekmekci O. Increasing the odds of effective drug development: Elevating regulatory affairs professionals to strategic partners. Clin Res RegulAff. 1 Oct 2016; 33(2–4): 59–65.
11. Reynolds I, Rising J, AC-J internal, undefined. Assessing the safety and effectiveness of devices after US Food and Drug Administration approval: FDA-mandated postapproval studies. jamanetwork.com [Internet]. 2014.
12. Kane R, Farrell A, Sridhara R, Research RP-CC, undefined. United States Food and Drug Administration approval summary: bortezomib for the treatment of progressive multiple myeloma after one prior therapy. AACR [Internet]. 2006
13. Downing N, Shah N, Aminawung J, Jama AP-, undefined. Postmarket safety events among novel therapeutics approved by the US Food and Drug Administration between 2001 and 2010. jamanetwork.com [Internet]. 2017; 317(18): 1854–63.
14. Mahaparale S, Desai B. Role and overview of drug regulatory affairs in pharmaceutical industry with implementation of CTD and ECTD. Sonali al World J Pharm Res [Internet]. 2018; 7.
15. Suchanek A, Ostermann H. The Electronic Common Technical Document (eCTD): An International Pro/Con Analysis of the Pharmaceutical Product Electronic Submission Process. Drug Inf J. Jan 2012; 46(1): 124–39.
16. Cartwright AC. The electronic common technical document: From design to submission. Int J Pharm Med. 2006; 20(3): 149–58
17. AN OVERVIEW OF REGULATORY AFFAIRS IN PHARMACEUTICAL INDUSTRY by Rajesh L. DumpalaDr. Reddy's Laboratorieshttps://www.researchgate.net/publication/343684866