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A Review on MHRA and USFDA Agencies

[1]Vaibhav Ravindra Waghchaure, [2] Ankur Sanjay Sonawane, [3]Yogesh Vijay Taro, [4]Abhijeet Gagdish Bargude, [5]Assist. Prof. Manisha Raut

[1]Final year B. Pharmacy, Wakla, Tal. Vaijapur, Dist. Sambhajinagar.
[2,3, 4]Final Year B Pharmacy
[5]Shree Mahavir institute of pharmacy Nashik.

Abstract

Regulatory Affairs (RA), also known as government affairs, is a relatively new profession that arose from governments' desire to protect public health by regulating the safety and efficacy of products such as pharmaceuticals, medical devices, pesticides, veterinary medicines, cosmetics, agrochemicals, and complementary medicines. Pharmaceutical regulatory affairs is concerned with the registration of pharmaceutical goods. All regulatory elements and guidelines connected to product filing are summarized in this evaluation. This study covers the whole CTD and eCTD submission process, as well as the modules that go with it. It also focuses on the key regulatory bodies across the world. Various roles of DRA departments, drug regulatory affairs professionals, the importance of drug affairs in pharmacy curriculum, emerging trends affecting regulatory strategy, regulatory affairs in product management, clinical trials, R&D and the drug approval process in the US, EU, and ROW market trends are discussed.

Key words: Regulatory affairs, MHRA, USFDA, pharmacovigilance, R&D, CTD.

Introduction

Drug development to commercialization is highly regulated. Every drug before getting market approval must undergo rigorous scrutiny and clinical trials to ensure its safety, efficacy and quality. These standards are set by regulatory authorities of their respective countries such as FDA in US and DCA in India etc. Regulation affects all aspects of the pharmaceutical world, from independent innovators and pharmaceutical companies to regulatory and administrative bodies and patients also. Regulatory department in pharmaceutical

Industry is crucial link between company, products and regulatory authorities whose positive or negative standpoint foster the insight of the regulatory authority into the industry, for good or for bad. So, the better the scientific precision, the greater will be the chances for a product to come to the market within the expected time.

Regulatory importance is growing very rapidly in the pharmaceutical sector; need of PRA professionals to cater to the current needs of industries globally is increasing. Pharmaceutical industry is in immense need of professionals capable of handling issues related to regulatory affairs in a comprehensive manner. MNCs abroad are looking to India as their preferred destination for drug development, research activities and contract research organizations. A regulatory affair is a dynamic, rewarding field that embraces both scientific and legal aspects of drug development; plays a lead and pivotal role in drug development and research activities. There is a need to incorporate the current requirements of pharmaceutical updates incorporated by the regulatory bodies. 4

Regulation involves extensive evaluation of a particular drug product to ensure protection of public health, promotion of the product, Drug registration, marketing authorization, import and distribution, pharmacovigilance.

Regulatory Affairs is a comparatively new profession which has developed from the desire of governments to protect public health, by controlling the safety and efficacy of products in areas including pharmaceuticals, veterinary medicines, medical devices, pesticides, agrochemicals, cosmetics and complementary medicines.

MHRA

The Medicines and Healthcare products Regulatory Agency (MHRA) is an executive agency of the Department of Health and Social Care in the United Kingdom which is responsible for ensuring that medicines and medical devices work and are acceptably safe.

The MHRA was formed In 2003 with the merger of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA). In April 2013, it merged with the National Institute for Biological Standards and Control (NIBSC) and was rebranded, with the MHRA identity being used solely for the regulatory centre within the group. The agency employs more than 1,200 people in London, York and South Mimms, Hertfordshire.

In 1999, the Medicines Control Agency (MCA) took over control of the General Practice Research Database (GPRD) from the Office for National Statistics. The Medicines Control Agency (MCA) and the Medical Devices Agency (MDA) merged in 2003 to form MHRA. In April 2012, the GPRD was rebranded as the Clinical Practice Research Datalink (CPRD). In April 2013, MHRA merged with the National Institute for Biological Standards and Control (NIBSC) and was rebranded, with the MHRA identity being used for the parent organisation and one of the centres within the group. At the same time, CPRD was made a separate centre of the MHRA.[2]

On vaccines

On 2 December 2020, the MHRA became the first global medicines regulator to approve an RNA vaccine when it gave conditional and temporary authorization to supply for use of the Pfizer–BioNTech COVID-19 vaccine codenamed BNT162b2[15][16][17] (later branded as Comirnaty).[18][19] This approval enabled the start of the UK's COVID-19 vaccination programme. The regulator's public assessment report for the vaccine was published in 15 December. [20]

The MHRA went on to give conditional and temporary authorization to supply of further vaccines: AZD1222 from Oxford University and AstraZeneca on 30 December,[21] mRNA-1273 from Moderna on 8 January 2021,[22] and a single-dose vaccine from Janssen on 28 May 2021.[23] The approval of

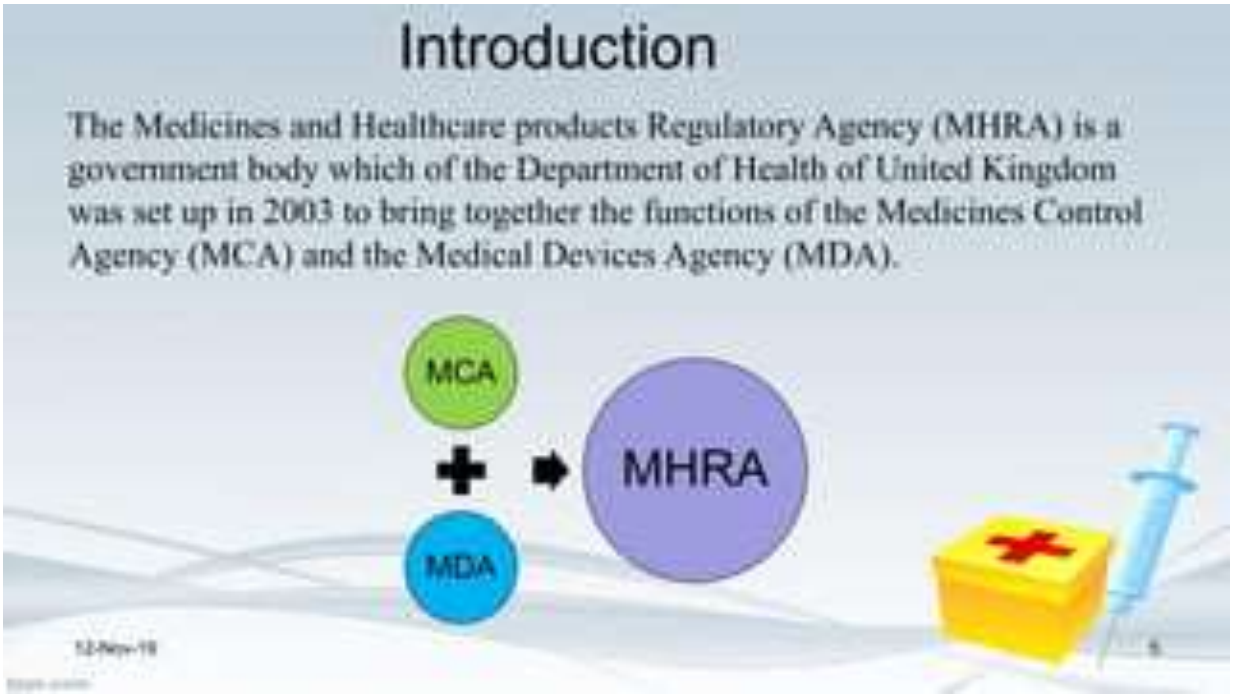
the Pfizer-BioNTech vaccine was extended to young people aged 12–15 in June 2021,[24] 5–11 in December 2021,[25] and from six months in December 2022.[26]

The status of the Oxford / AstraZeneca vaccine was upgraded to conditional marketing authorisation on 24 June 2021.[21] The MHRA confirmed in September 2021 that supplementary "booster" doses of these vaccines would be safe and effective, but stated that the Joint Committee on Vaccination and Immunisation had the task of advising if and when they should be used in this way.[27] Later that month, the MHRA said the Moderna vaccine could also be given as a booster dose.[28]

In August and September 2022, the MHRA approved the first bivalent COVID-19 booster vaccines.[29][30]

On tests

In January 2021, the MHRA expressed concern to the UK government over plans to deploy lateral flow tests in schools in England, stating that they had not authorised daily use of the tests due to concerns that negative results may give false reassurance.The government suspended the scheme the following week, citing risks arising from high prevalence of the virus and higher rates of transmission of a new variant.



Roles

Operate post-marketing surveillance – in particular the Yellow Card Scheme – for reporting, investigating and monitoring of adverse drug reactions to medicines and incidents with medical devices.

Assess and authorise of medicinal products for sale and supply in the UK.

Oversee the Notified Bodies that ensure medical device manufacturers comply with regulatory requirements before putting devices on the market.

Operate a quality surveillance system to sample and test medicines to address quality defects and to monitor the safety and quality of unlicensed products.

Investigate internet sales and potential counterfeiting of medicines, and prosecute where necessary.

Regulate clinical trials of medicines and medical devices.

Monitor and ensure compliance with statutory obligations relating to medicines and medical devices.

Promote safe use of medicines and devices.

Manage the Clinical Practice Research Datalink and the British Pharmacopoeia.

USFDA

The United States Food and Drug Administration (FDA or US FDA) is a federal agency of the Department of Health and Human Services. The FDA is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, caffeine products, dietary supplements, prescription and over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), cosmetics, animal foods & feed[3] and veterinary products.

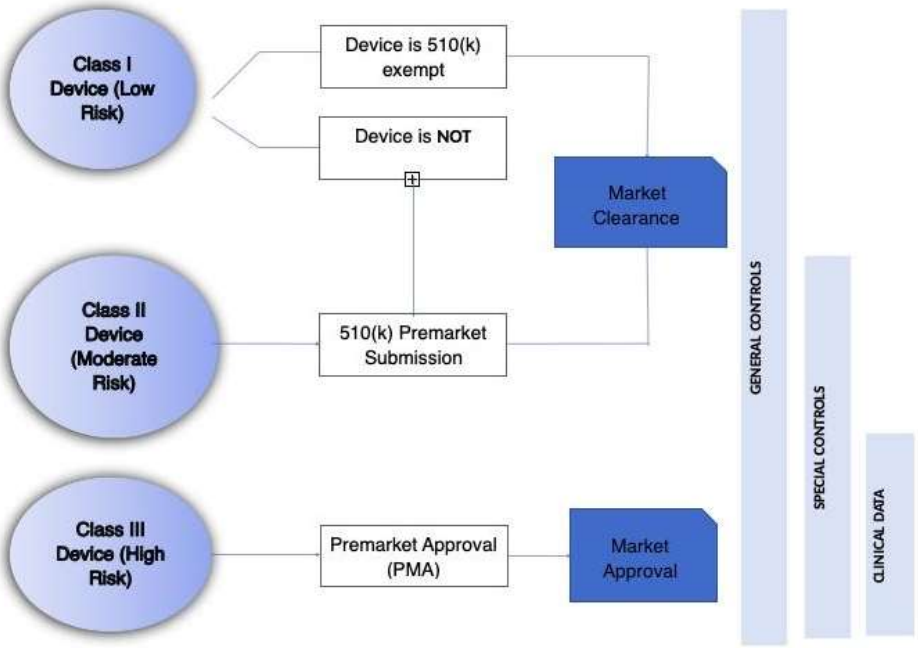
The FDA's primary focus is enforcement of the Federal Food, Drug, and Cosmetic Act (FD&C), but the agency also enforces other laws, notably Section 361 of the Public Health Service Act, as well as associated regulations. Much of this regulatory-enforcement work is not directly related to food or drugs, but involves such things as regulating lasers, cellular phones, and condoms, as well as control of disease in contexts varying from household pets to human sperm donated for use in assisted reproduction.

The FDA is led by the Commissioner of Food and Drugs, appointed by the President with the advice and consent of the Senate. The Commissioner reports to the Secretary of Health and Human Services. Robert Califf is the current commissioner, as of 17 February 2022.[4]

The FDA has its headquarters in unincorporated White Oak, Maryland.[5] The agency also has 223 field offices and 13 laboratories located throughout the 50 states, the United States Virgin Islands, and Puerto Rico.[6] In 2008, the FDA began to post employees to foreign countries, including China, India, Costa Rica, Chile, Belgium, and the United Kingdom.[7]

Since 1990, the FDA has had employees and facilities on 130 acres (53 hectares) of the White Oak Federal Research Center in the White Oak area of Silver Spring, Maryland.[5][11] In 2001, the General Services Administration (GSA) began new construction on the campus to consolidate the FDA's 25 existing operations in the Washington metropolitan area, its headquarters in Rockville, and several fragmented office buildings. The first building, the Life Sciences Laboratory, was dedicated and opened with 104 employees in December 2003. As of December 2018, the FDA campus has a population of 10,987 employees housed in approximately 3,800,000 square feet (350,000 square metres) of space, divided into ten office and four laboratory buildings. The campus houses the Office of the Commissioner (OC), the Office of Regulatory Affairs (ORA), the Center for Drug Evaluation and Research (CDER), the Center for Devices and Radiological Health (CDRH), the Center for Biologics Evaluation and Research (CBER) and offices for the Center for Veterinary Medicine (CVM).[5]

With the passing of the FDA Reauthorization Act of 2017, the FDA is projecting a 64% increase in employees to 18,000 over the next 15 years, and would like to add approximately 1,600,000 square feet (150,000 square metres) of office and special use space to their existing facilities. The National Capital Planning Commission approved a new master plan for this expansion in December 2018,[12] and construction is expected to be completed by 2035, dependent on GSA appropriations.[13]



Office of Regulatory Affairs

The Office of Regulatory Affairs is considered the agency's "eyes and ears," conducting the vast majority of the FDA's work in the field. Its employees, known as Consumer Safety Officers, or more commonly known simply as investigators, inspect production and warehousing facilities, investigate complaints, illnesses, or outbreaks, and review documentation in the case of medical devices, drugs, biological products, and other items where it may be difficult to conduct a physical examination or take a physical sample of the product. The Office of Regulatory Affairs is divided into five regions, which are further divided into 20 districts. Districts are based roughly on the geographic divisions of the Federal court system. Each district comprises a main district office and a number of Resident Posts, which are FDA remote offices that serve a particular geographic area. ORA also includes the Agency's network of regulatory laboratories, which analyze any physical samples taken. Though samples are usually food-related, some laboratories are equipped to analyze drugs, cosmetics, and radiation-emitting devices.

The Office" of Criminal Investigations was established in 1991 to investigate criminal cases. To do so, OCI employs approximately 200 Special Agents nationwide who, unlike ORA Investigators, are armed, have badges, and do not focus on technical aspects of the regulated industries. Rather, OCI agents pursue and develop cases when individuals and companies commit criminal actions, such as fraudulent claims or knowingly and willfully shipping known adulterated goods in interstate commerce. In many cases, OCI pursues cases involving violations of Title 18 of the United States Code (e.g., conspiracy, false statements, wire fraud, mail fraud), in addition to prohibited acts as defined in Chapter III of the FD&C Act. OCI Special Agents often come from other criminal investigations backgrounds, and frequently work closely with the Federal Bureau of Investigation, Assistant Attorney General, and even Interpol. OCI receives cases from a variety of sources—including ORA, local agencies, and the FBI, and works with ORA Investigators to help develop the technical and science-based aspects of a case.[14

Up until the 20th century, there were few federal laws regulating the contents and sale of domestically produced food and pharmaceuticals, with one exception being the short-lived Vaccine Act of 1813.[88] The history of the FDA can be traced to the latter part of the 19th century and the Division of Chemistry of the U.S. Department of Agriculture,[89] which was itself derived from the Copyright and Patent Clause. Under Harvey Washington Wiley, appointed chief chemist in 1883, the Division began conducting research into the adulteration and misbranding of food and drugs on the American market.[89] Wiley's advocacy came at a time when the public had become aroused to hazards in the marketplace by muckraking journalists like Upton Sinclair, and became part of a general trend for increased federal regulations in matters pertinent to public safety during the Progressive Era.[90] The Biologics Control Act of 1902 was put in place after a diphtheria antitoxin derived from tetanus-contaminated serum caused the deaths of thirteen children in St. Louis, Missouri. The serum was originally collected from a horse named Jim who had contracted tetanus.[91]

What makes a good Regulatory Affairs professional?

While biotechnology degrees are becoming increasingly essential, the bulk of regulatory practitioners have a research background, generally in biological sciences or pharmacy. Some people desire to acquire a law degree to go along with their other qualifications. It's critical to be able to deal with data from a range of study disciplines and to grasp new concepts and technological expertise quickly. Analyzing questions and giving written and oral evidence before a jury of experts, which may include scientists, pharmacists, physicians, and government attorneys, needs a deep understanding of both legal and technical issues.

Extreme vigilance is essential while suggesting and implementing the strategy and tactics required to obtain marketing approval in a manner that pleases the authorities in order to protect the company's best interests. Great attention must be exercised if the company's condition is to be presented to the authorities in the best possible light. It must be accomplished without obscuring the data, allowing regulators to make an informed and genuine conclusion regarding the product's safety, efficacy, and consistency.

Regulatory practitioners must constantly use prudence in their job. A strong leader possesses two qualities: integrity and the drive to encourage others. The characteristics of trust and confidence are essential. Project management skills assist them in reaching their ambitious goals. They will participate in multidisciplinary teams and, if required, lead them. They are capable of performing under pressure while inspiring and encouraging others to do the same [7].

Regulatory Affairs in R and D

The affairs team partners with R&D and FR&D to develop novel solutions that address evolving technological and regulatory trends in order to minimise time to market. The new products are expected to increase sales; losses from delayed marketing will be compensated by considerable commodity income and benefit increases over time.

By getting quick approval from regulatory bodies and avoiding difficulties in the process, adaptive clinical trial techniques can assist to speed up the introduction of new medications and eliminate costly blunders and time lags. Professionals in regulatory affairs engage with marketing and R&D to develop cutting-edge technologies that take advantage of new technical and regulatory improvements while reducing time to market.

Small reductions in time to market result in significant gains in commodity sales and profitability, with new products expected to contribute significantly to the company's bottom line. Adaptive clinical trial strategies, quick regulatory approval, and avoiding procedural hazards will all assist to accelerate the introduction of new medications while decreasing costly errors and time delays [8].

Regulatory affairs in Clinical Trials

Regulatory affairs professionals act as the primary contact between an organisation and worldwide regulatory organisations such as official bodies (US FDA, CDSCO, MCCA, TGA, etc.). Their role is to offer quick evaluations of new data gathered during trials and to help in the approval of new medications as necessary by local regulatory bodies in their respective states.

The RA team devises strategies to prevent delays and communicates clinical trial data to regulatory authorities in order to gain quick approval and reduce the time it takes for novel compounds to be authorised. The capacity of the RA professional to acquire, evaluate, and disseminate knowledge regarding the risks and benefits of health products helps regulatory authorities, medical and educational services, and the general public. RA's operational tasks include ensuring that all parties are aware of and comply with government requirements, market-driven needs, and developing research conventions [9].

Regulatory affairs in Product management

Drug goods are tightly regulated in compared to other channels. These rules are usually maintained and managed by regulatory bodies; these bodies generally guide substance formulation based on IND/NDA standards until the approval Phase is complete; once the approval process is complete, these bodies focus on the medication post-market properties as well as the Pharmacovigilance characteristics of the drug product; and it frequently reminds the drug.

The entire job of Regulatory Affairs goes beyond substance registration; they also give strategic and technology guidance to firms at the highest levels. They play a significant role in everything from product development to promotion and post-marketing efforts. Their guidance at all stages of the development process, both in terms of regulatory and technological requirements, saves time and money for enterprises [10].

Importance of Regulatory Affairs

In today's fast-paced environment, a product's and hence a company's success is dependent on minimising the time it takes to reach a consumer. As a result, the Regulatory Affairs activities of the firm must be effectively handled. Inadequate data reporting can stymie a timely constructive evaluation of a marketing application. A new drug might have cost millions of Euros or pounds to develop, and even a three-month delay in bringing it to market can be costly.

A product reca"l might be forced if all available data is not recorded or if a product is released with improper labelling. Any occurrence might result in a revenue loss of millions of dollars, as well as a loss of investor, healthcare provider, and patient confidence. Regulatory Affairs is frequently a company's initial point of contact with government regulators [2].

Global market: Pharma market broadly divided into two types Regulated market and Semi- regulated market

Regulated Market

EU (UK, Germany, France, Ireland, Sweden etc.), US, Japan, Canada, Australia, New Zealand, South Africa.

Semi-regulated Market (ROW Countries)

- African Countries: Algeria, Zambia, Ethiopia, Ghana, Kenya, Mozambique, Malawi, Nigeria, Namibia, Sierra, Leone, Tanzania, Zimbabwe etc.
- Asia: Sri Lanka, India, Bangladesh, And And ASEAN: having groups of 10 Countries – Vietnam, Malaysia, Philippines, Singapore, Thailand, Indonesia, Laos, Cambodia, Brunei Darussalam, Myanmar.
- Latin America: Brazil, Panama, Peru, Mexico, Argentina, Guatemala, Chile, Dominican Republic.
- Middle East countries: also called Gulf Co-operation Council countries i. e. Kuwait, Bahrain, Qatar, Oman, Saudi Arabia, and UAE.
- Common Wealth of independent States (CIS): Ukraine, Russia, OFSU (America, Azerbaijan, Belarus, Georgia, Kazakhstan, Kirghizstan, Turkmenistan etc [11].

U. S. FDA (United States Food and Drug Administration)

FDA mission

The Food and Drug Administration is liable for protecting the public health by ensuring the safety, efficacy, and security of Human and veterinary drugs, medical devices, and biological products and by ensuring the safekeeping of our nation's food supply, cosmetics and products that emit radiation.

FDA also plays a crucial role in the regulation of manufacturing, marketing, and distribution of tobacco products to protect public health and to reduce tobacco use by minor's i. e the person under the age of full legal responsibility. FDA also focuses on to improve the public health by providing more effective use, safer, and more affordable medical products. This can be achieved by using accurate science based information [15].

FDA Approved Product

The Food and Drug Administration of the United States has approved and regulated the following products: Bottled water is used in diet supplements, food additives, infant formulae, and other food items (although U.S Department of Agriculture plays a lead role in a regulating aspect of some meat, poultry, and eggs products). Prescription drugs (including brand-name and generic), biologics, and nonprescription (over-the-counter) medicines are examples of medications. Vaccines for people- blood and blood derivatives, products for cellular and gene therapy allergens in tissues and tissue products. Medical equipment, such as: Objects as basic as tongue depressors and bedpans, heart pacemaker and dental devices are example of complex technologies. Prosthetics and surgical implants. Radiation-

Emitting electronic products include: X-ray equipment microwave ovens, items with lasers, ultrasonic therapy apparatus, vapor lamp made of mercury, the sunlamps. Cosmetics, for example: Colorants used in cosmetics and other personal care products such as skin moisturizers and cleansers, nail polish, and perfume. Veterinary medicines, such as: Pet food is fed to animals. Veterinary pharmaceuticals and applications. Products containing tobacco, such as: Roll your own tobacco, cigarettes, tobacco that does not produce smoke.

Drug approval process in US

Vaccines for individuals, including blood and blood derivatives, cellular and gene therapy products, and allergens in tissues and organs The United States has some of the world's strictest drug approval standards. Drug approval criteria in the United States are stringent. Many individuals consider nations to be the most difficult in the world. The adoption of the United States Drug Act in 1820 marked the start of a new era in drug regulation in the United States. It was decided to construct the United States Pharmacopoeia. Congress approved the first Food and Drug Act in 1906, mandating medications to satisfy official strength and purity requirements. Create products. However, due to the great depression in1937, the Federal food, Drug, ad Cosmetics Act (of 1938) and Sulfanilamide Tragedy was enacted, which included new Requirement for the approval of new drugs (medicines).Demonstrated to be safe before marketing.

Vaccines for individuals, including blood and blood derivatives, cellular and gene therapy products, and allergens in tissues and organs The FDA's new medication approval procedure includes two stages: United Clinical Trials (CT) and New Drug Application (NDA) approval. A new drug application regulates the new medication product. NDA (Non- Disclosure Agreement) (National Defense Authorization Act). Such applications have been accepted for analysis in eCTD at this time. The approval procedure begins once an investigational new drug (IND) application is submitted to the FDA. The Drug Laws and Regulations in the United States The United States Pharmacopoeia (USP) was founded in 1820 to provide a standard for medication strength and purity [16].

The Food and Drugs Act (1906) Is a major landmark in the history of US drug law. It stipulates that drugs must satisfy certain criteria. Food, Drug, and Cosmetics Acts of 1938: After that, it was enacted. To demonstrate the safety of a medication before it is approved, the sulfanilamide tragedy occurred.it has been advertised.

In 1962, the Kefauver-Harris Amendment was passed. Following the thalidomide tragedy, it was moved. It is necessary for medication manufacturers to show that their product is both safe and dependable. Every company should send out a bad message. The FDA has received the communication. The Orphan Drug Act of 1973 allows for tax deductions for medications judged to be uncommon. Companies are working on developing orphan medicines. It is concerned with arrests made under the 1992 Generic Drug Enforcement Act. The generic drug control Act deals with convictions related to ANDA authorization (1902). There are several changes to the FDA Modernization Act of 1997 (FDAMA). The Food, Drug, and Cosmetics Act governs the manufacturing and distribution of food, medicines, and cosmetics. User fees are being calculated, and the approval process is being accelerated.

Investigational New Drug Application (INDA)

An FDA application is filed prior to human inspection. It goes through the chemistry, manufacturing, and quality assurance in great depth. The following information must be provided in the IND application: (1) Toxicology and Pharmacology Research in Animals. (2) Clinical investigators and procedures. (3) Data about the manufacturing process. After submitting the IND, the sponsor must wait 30 days. Count down the days before the start of any clinical trials. The Food and Drug Administration (FDA) has the authority to verify the IND for safety throughout this period to guarantee that it is secure. The criteria for the content and form of an IND application are laid forth in Section 312 of the 21 code of federal regulations. If you wish to perform a clinical review, you need submit a "Investigator New Project" application. Fill out the "Drug Application" form in the sequence listed below [17].

- 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 New Drug Application must be submitted in order to market a new medicine (drug) in the United States. An NDA contains all of the information provided in the IND, as well as the results of clinical trials showing safety and efficacy. The FDA will begin the review process 60 days after the application, providing a non-disclosure agreement in NDA format and contents for a set of two. The application is divided into two sections: (1) archival copy and (2) review.

Archival Copy: it includes copies of tabulations and clinical trial case report forms, and it acts as a reference source for FDA reviewers looking for details not included in the review copy.

Review Copy: Each technical section is bound separately in each folder as a review copy. Each technical section should include the following: 2.1) Index, 2.2) FDA form 356 h (copy). 2.3) A duplicate of the cover letter 2.4) Authorization letters 2.5) A copy of the application summery is required.

The FDA will meet with the sponsor at least twice: once at the conclusion of phase 2 clinical trials and again before an NDA is filed, referred to as a pre-NDA meeting. The analysis committee will look into it. The study's finding and decide whether or not to accept the proposal the application [18].

Abbreviated New Drug Application (ANDA)

ANDA is used for goods with the same or similar active components, dose type, and strength, as well as the same or similar administration and usage routes. As well as choosing a product that has been proved to be safe and dependable. When a product's patent expires and the firm wants to sell it in order to advertise its replica, this is true. These drugs are known as generics, and they must meet bio and pharmacological comparable standards. The Office of Drug Evaluation and Research of the Center for Drug Evaluation and Research receives an ANDA. In the Generic Drugs category, it has been examined and approved [19].

Supplemental New Drug Application (SNDA) [20]

After the NDA or ANDA has been granted, any substantial modifications in the conditions mentioned in the applications must be acknowledged by filing a New NDA or ANDA. The CDER must approve a supplemental NDA or ANDA that includes modifications like as packaging or ingredients. This category contains new-uses approvals of previously approved medications, which are a better breakthrough than new-uses approvals of previously approved drugs since they require fewer resources to examine. For the first time, approvals are required.

Common technical documents (CTD)

The common technical documents (CTD) are a collection of application requirements for the registration of medicine and design that may be utilized throughout Europe, the United States (US), and Japan. It is an international accepted format for constructing an application for a novel medication intended to be presented to regional regulatory bodies in the participating country.

CTD is a collaborative effort of three regulatory agencies: 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). The CTD was kept up to date by the International Council on Harmonization (ICH) of technical requirements for pharmacological approval for human use. CTD is a globally recognized format for organizing technical requirements for submission to regulatory authorities .

Objectives of CTD

- The main objective is to reduce the time required and resources used to compile applications.
- It will help to the preparation of electronic submissions of application.
- To facilitate simultaneous submission in three regions.
- It will help to exchange of regulatory information and consequently ensure faster availability of new medicine

The CTD triangle. The Common Technical Document is organized into five modules. Module e 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

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

The format should be clearly readable and understandable manner e.g. font size should be 12, font should be in Times New Roman and page layout for EU and Japan – A4 paper and for U.S.A. – 8.5 x 11. The margin for the left hand should be large enough and the information should be not be out of sight and uncertain after binding.

- The common technical document are details and surely acceptable by the regulatory authority.
- The document can be easily review by the reviewer.
- The submitted document should be dated and signed.
- The document should be properly labelled as per the regulatory guidelines of the country.
- Documents that can be required should be submitted as per the checklist to avoid rejection of the application or queries which in turn speed up the review process and approval.
- The justification for certain tests should be properly mentioned and supportive documents should be attached.
- Once dossier is prepared before sending it has to checked and verified for any mistakes.
- In the report of the clinical study as per module 5 CRF, all the study reports should be attached with the documents.
- Some of the authorized countries ask for the validation certificates.
- If there are changes in any batch that should be mentioned and justify.

Module -1 administrative and prescribing information

It is the region specific not the part of CTD. It gives administrative as well as prescribing information. This document is specific to each region e.g. application form, proposed label use for on the region. General information regarding the module 1

- Gives general information about covering letter and content of comprehensive table
- Gives administrative information such as, short information about the applicant company. Gives the correctly completed and signed the application in the form 44 and treasury challan. It gives legal and critical documents as like copy of clinical trial/ BE., there is no objection letters issued by the CDSCO, Batch release certificate that can be issued by national Regulatory Authorities. E.g. for the production and marketing of finished product, in addition to the above-mentioned documents. Such as Copy of existing manufacturing license in Form 25 / 28, Copy of Form-29, Certificate of Analysis, Coordinates related to the application.
- Provides general information on finished drug products.
- Provides regulatory status in different countries.
- Provides internal price of the finished drug product followed in the countries
- It can also provide a brief information of the manufacturer’s research activities.
- It can also provide a brief information manufacturer’s business activity in national as well as international market.
- Provides details regarding involvement of the experts
- It gives information about sample of drug product and promotional materials.

Non-clinical overview

In the non-clinical overview there is Implications of nonclinical findings for the safe use of the pharmaceutical

- Introduction and GLP statement
- Overview of the Non-Clinical Testing Strategy
- Pharmacology.
- Pharmacokinetics.
- Toxicology

- Integrated Overview and Conclusions
- List of Literature References

Clinical overview

In the clinical overview there is an overview of the clinical data were analysed.it also provides a brief overview of the new clinical findings. Analyses the benefits and risks of the medicinal products in its intended use [21].

- Product Development Rationale.
- Overview of Biopharmaceutics.
- Overview of Clinical Pharmacology
- Overview of Efficacy
- Overview of Safety
- Benefits and Risks Conclusions
- Literature References

Non-clinical summaries

The non-clinical summary can be written and tabulated format. It includes Summary of pharmacokinetic, pharmacological and toxicology studies with in-vivo/In-vitro, species, route and duration and effect related to appropriate age and gender.

Clinical summaries

This section is intended to provides a detailed, factual summarization of all of the clinical information in the CTD this include information provided in clinical study reports, information obtained from any analyses for which full reports have been included in Module 5 and post-marketing data for products that have been marketed in other regions [22].

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] Kumar S, Panwar R. US-J of R D in, 2013 undefined. Regulatory affairs in the pharmacy curriculum. Ijrdpl.com [Internet].2021; 2(6): 690–8.

[3] Vanaja K, Rani RHS. Design of experiments: Concept and applications of plackett burman design. Clin Res Regul Aff [Internet]. Jan 2007; 24(1): 1–23.

[4] Wood KL. The medical dictionary for drug regulatory affairs (MEDDRA) project. Pharmacoepidemiol Drug Saf. 1994; 3(1): 7–13.

[5] safety KW-P, drug, undefined. The medical dictionary for drug regulatory affairs (MEDDRA) project. Wiley Online Libr [Internet].1994;

[6] Roshan K. (GJRA) JA-GJFRA, 2018 undefined. ROLE OF REGULATORY AFFAIRS IN PHARMACEUTICAL COMPANY: AN OVERVIEW. Wwjournals.org [Internet].2018.

[7] Drago D, Yap M. Regulatory OE-CR and, undefined. Increasing the odds of effective drug development: Elevating regulatory affairs professionals to strategic partners. Taylor Fr [Internet]. 2016.

[8] Affairs BK-IJ of DR, 2013 undefined. Overview of Drug Regulatory Affairs and Regulatory Profession. Researchgate.net [Internet]. 2013; 2013(1): 1–4.

[9] Information MX-CMD. Undefined. Overview of Medical Device Regulatory Affair Professional's Training Abroad and its Implication for China. En.cnki.com.cn [Internet]. 2009.

[10] 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.

[11] Sutar M, Gawhane D. of CT-IJ. Undefined. Drug Regulatory Approval Process an Comparative Requirement of Common Technical Documents (CTD) in Europe, USA and India in Coordination with Drug …. Sites.google.com [Internet].2013.

[12] Dalal K, Ganguly B. diagnostic AG-J of clinical and, 2016 undefined. Assessment of rationality of fixed dose combinations approved in CDSCO list. Ncbi.nlm.nih.gov [Internet]. 2016.

[13] Evangeline L, Mounica N. VR-TP. Undefined. Regulatory process and ethics for clinical trials in India (CDSCO). Researchgate.net [Internet]. 2017.

[14] 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.

[15] Kumar V. Comparative Study of the Regulatory Guidelines for Clinical Trials in Regulated and Semi-Regulated Countries. 2016.

[16] Zivin JA. Acute stroke therapy with tissue plasminogen activator (tPA) since it was approved by the U.S. Food and Drug Administration (FDA). Ann Neurol. 2009 Jul; 66(1): 6–10.

[17] Drago D, Yap M, Ekmekci O. Increasing the odds of effective drug development: Elevating regulatory affairs professionals to strategic partners. Clin Res Regul Aff. 1 Oct 2016; 33(2–4): 59–65.

[18] 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.

[19] 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.

[20] 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.

[21] PharmaTutor YV-, undefined. Regulatory Affair: Link between company and Government Authority. Pharmatutorjournal.com [Internet]. 2014.

[22] Barber CM. VP Regulatoy, Quality Assurance, Medical & Clinical Affairs. FASEB J. Apr 2010; 24(S1).

[23] 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.

[24] Cartwright AC. The electronic common technical document: From design to submission. Int J Pharm Med. 2006; 20(3): 149–58.