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Review

Current Trends in Review of CTD Dossiers

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Abstract

Demonstration of safety and efficacy of the drug product for use in humans is essential before the drug product can be approved for import or manufacturing of new drug by the applicant by Regulatory authority in any country. Once preclinical and clinical trial data have been collected, a New Drug Application must be submitted to the regulatory authority for approval. Although the requirements for this submission have similarities around the world, until now, the applications have been different. Substantial documentation and data are required in these types of submissions, resulting in large, complex applications. Till date, applicants have used many different approaches in organizing the information and the differences in organization of data in each application has made reviewing more difficult and can also lead to omission of critical data or analyses. Thus, a common format of submission will help in overcoming these hurdles. Through the International Conference on Harmonization (ICH) process, the Common Technical Document (CTD) guidance's have been developed for Japan, European Union, and United States. ACTD have been developed for ASEAN countries for the registration pharmaceuticals for human use for ASEAN Regulatory Authorities. The ECTD is the electronic equivalent to the CTD. It has been developed by the ICH M2 Expert Working group. ICH-ECTD is an internationally driven standard designed to reduce cost in the administration, assessment and archiving of applications for marketing authorization of medicinal products for human use, to reduce the use of paper and streamline the assessment process making the system more efficient.

Keywords: ICH, CTD, ECTD.

INTRODUCTION

Regulatory affairs in pharmaceutical industry

Introduction to regulatory affairs

Regulatory affairs is a comparatively new profession which was 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 complimentary medicines. Regulatory affair also has a very specific meaning within the healthcare industries (pharmaceuticals, medical devices, Biologics and functional foods).

The companies responsible for the discovery, testing, manufacture and marketing of these products also want to ensure that they supply products that are safe and make a worthwhile contribution to public health and welfare. Most companies, whether they are major multinational pharmaceutical corporations or small, innovative biotechnology companies, have specialist departments of Regulatory Affairs professionals.

Regulatory Affairs regulate their business through designing appropriate laws and enforcing the same so that the drugs meeting the highest standards of quality are brought into the global trade. The Regulatory Affairs department is an important part of the organizational structure of pharmaceutical companies. Internally it liaises at the interphase of drug development, manufacturing, marketing and clinical research. Externally it is the key interface between the company and the regulatory authorities.

The Regulatory Affairs department will take part in the development of product marketing concepts and is usually required to approve packaging and advertising before it is used commercially. Many companies operating in the high-technology healthcare and related industries operate on a multinational basis and are very significant exporters. Their Regulatory Affairs department must be aware of the regulatory requirements in all the company's export markets. Regulatory Affairs contributes essentially to the overall success of drug development, both early at pre-marketing stages and at all times post-marketing.

The regulatory affairs professional

Regulatory Affairs professional[2] can play a key role in guiding drug development strategy in an increasingly global environment. Regulatory Affairs professionals are involved in product development from the beginning. The regulatory professional's job is to keep track of the ever-changing legislation in all the regions in which the company wishes to distribute its products.

Preparation of organized and scientifically valid NDA (New drug application), ANDA (Abbreviated New Drug Application), INDA (Investigational New Drug Application), MAA (*Marketing Authorization Application*), DMF (Drug Master File) submissions. Ensure adherence and compliance with all the applicable cGMP (Good Manufacturing Practices), ICH (I*nternational Conference on Harmonization)*, GCP (Good Clinical Practices), GLP (Good Laboratory Practices) guidelines, regulations and laws.

Regulatory professionals ensure that the information and data to be conveyed and discussed with the regulatory bodies are presented in the right way and form. They develop the regulatory strategy, arrange agency meetings, prepare and compile the questions and briefing documents; they attend the meetings and manage all communications with the agencies. At the last stage of product development regulatory professionals are responsible for the submission of the registration dossier e.g. Marketing Authorization Application (MAA) in the EU or New Drug Application (NDA) in the US. Managing variation applications, post approval changes and keeping record of annual update. Collaboration with Global and Regional Harmonization units for exchange of technical knowledge, developing guidelines as well as allotting mutual recognition status for technical documents, GMP status and product approval. Supporting manufacturer in defining drug development pathway during pre-NDA meeting and providing comments/confirming development pathway. Time to time meeting with pharmaceutical manufacturers association to discuss ongoing challenges, technical issues, guidelines/ guidance documents discussions and future development.

Importance of regulatory affairs

In today's competitive environment the reduction of time taken to reach the market is critical to a product's and hence the company's success. The proper conduct of its regulatory activities is therefore of considerable economic importance for the company. Inadequate reporting of data may prevent a timely positive evaluation of a marketing application. A new drug may have cost many millions of pounds, Euros or Dollars to develop and even a three month delay in bringing it to the market has considerable financial considerations. Even worse, failures to fully report all the available data or the release of product bearing incorrect labeling, may easily result in the need for a product recall. Either the occurrence may lead to the loss of several millions of units of sales, not to mention the resulting reduction in confidence of the investors, health professionals and patients. The regulation of medical products has been expanding since early 20th century. Regulatory agencies are being established in an ever increasing number of countries across the globe.Regulatory affairs (RA) professionals are employed in pharmaceutical industry, government, academic research and clinical institutions**.** Pharma regulatory affairs professionals play an essential role in ensuring all pharmaceutical products comply with regulations governing the industry.

The RA professional is the primary link between the company and worldwide regulatory agencies such as US Food and Drug Administration (USFDA), Medicines and Healthcare Products Regulatory Agency, United Kingdom, (MHRA), Therapeutic Goods Administration, (TGA) Australia, European Medicines Agency (EMA), Organization of Economic Collaboration and Development (OECD) and Health Canada.

During 1950s, multiple tragedies i.e. sulfanilamide elixir, vaccine tragedy and thalidomide tragedy have resulted in substantial increase of legislations for drug products quality, safety and efficacy. This has also resulted into stricter norms for Marketing Authorization (MA) and Good Manufacturing Practices (GMPs).

Drug Regulatory Affairs is a dynamic, rewarding field that embraces both scientific and legal aspects of drug development. DRA professionals are dedicated individuals who take pride in their contribution to improving the health and quality of life of peoples.

Importance of regulatory affairs

A new entity can cost several millions of rupees or dollars to progress. Surprisingly, even a few month deferrals in taking it to the market can have substantial impact on the monetary status of the company. One of the vital activities of the regulatory specialist is to ensure that the label of the product and related information of the patient has correctly been established and even a small mistake in any of the regulatory activities can make the product to be ready for recall in addition to the loss of several millions of money which is eventually bound to give rise to fall in self-assurance of financiers, health experts and finally the patients.

The regulatory professional Responsibilities

1. The regulatory professional's job is to keep track of the ever-changing legislation in all the regions in which the company wishes to distribute its products.
2. They also advise on the legal and scientific restraints and requirements, and collect, collate and evaluate the scientific data their research and development colleagues are generating. They are responsible for the presentation of registration documents to regulatory agencies,and carry out all the subsequent negotiations necessary to obtain and maintain marketing authorization for the products concerned.
3. They give strategic and technical advice at the highest level in their companies, right from the beginning of the development of a product, making an important contribution both commercially and scientifically to the success of a development program and the company as a whole.
4. 4.Preparation of organized and scientifically valid NDA(New drug application), ANDA(Abbreviated New Drug Application), INDA(Investigational New Drug Application), MAA(*Marketing Authorization Application),* DMF(Drug Master File) submissions.
5. Ensure adherence and compliance with all the applicable cGMP (Good Manufacturing Practices), ICH(*International Conference on Harmonization)*, GCP(Good Clinical Practices), GLP(Good Laboratory Practices) guidelines, regulations and laws
6. Providing expertise and regulatory intelligence in translating regulatory requirements into practical workable plans
7. Advising the companies on regulatory aspects and climate that would affect their proposed activities
8. Apart from the above main roles, there are various other roles which Regulatory Affairs professionals play.

Regulatory societies

- The Regulatory Affairs Professionals Society (RAPS)
- The Organization for Professionals in Regulatory Affairs (TOPRA)
- The Canadian Association of Professional Regulatory Affairs (CAPRA)

I. The Regulatory Affairs Professionals Society (RAPS) :

The Regulatory Affairs Professionals Society (RAPS) is the largest global organization of and for those involved with the regulation of healthcare and related products, including medical devices, pharmaceuticals, biologics and nutritional products. Founded in 1976, RAPS helped establish the regulatory profession and continues to actively support the professional and lead the profession as a neutral, non-lobbying nonprofit organization.

RAPS offers education and training, professional standards, publications, research, knowledge sharing, networking, career development opportunities and other valuable resources, including Regulatory Affairs Certification (RAC), the only post-academic professional credential to recognize regulatory excellence. RAPS is headquartered in suburban Washington, DC, with offices in Europe and Asia, and chapters and affiliates worldwide.

II. The Organization for Professionals in Regulatory Affairs (TOPRA)

TOPRA is the professional membership organization for individuals working in healthcare regulatory affairs. We work with our members internationally to enable and promote excellence across the healthcare regulatory profession. The members are individuals working in regulatory affairs all over the world. They come from a range of healthcare sectors including regulatory bodies, academia, regulatory affairs consultancies, the pharmaceutical and health technology industries, clinical research organizations and many others. TOPRA located at Bellerive House, 3 Muirfield Crescent, London E14 9SZ, United Kingdom.

III. The Canadian Association of Professional Regulatory Affairs (CAPRA)

The Canadian Association of Professionals in Regulatory Affairs (CAPRA) is a non-profit organization that serves the pharmaceutical, biologics, medical device, cosmetic and natural health product industries in Canada. The Canadian Association of Professionals in Regulatory Affairs (CAPRA) is an organization dedicated to providing its members with opportunities to enhance their professional development and maximize career opportunities. Whether you are a student, an entry-level associate or an experienced executive, a membership with CAPRA is a must.

Regulatory Issues in the Indian Pharmaceutical Industry

The principal regulatory bodies entrusted with the responsibility of ensuring the approval, production and marketing of quality drugs in India at reasonable prices are:

The Central Drug Standards and Control Organization (CDSCO), located under the aegis of the Ministry of Health and Family Welfare. The CDSCO prescribes standards and measures for ensuring the safety, efficacy and quality of drugs, cosmetics, diagnostics and devices in the country; regulates the market authorization of new drugs and clinical trials standards; supervises drug imports and approves licenses to manufacture the above-mentioned products.

The National Pharmaceutical Pricing Authority (NPPA), which was instituted in 1997 under the Department of Chemicals and Petrochemicals, which fixes or revises the prices of decontrolled bulk drugs and formulations at judicious intervals; periodically updates the list under price control through inclusion and exclusion of drugs in accordance with established guidelines; maintains data

on production, exports and imports and market share of pharmaceutical firms; and enforces and monitors the availability of medicines in addition to imparting inputs to Parliament in issues pertaining to drug pricing

In India, drug manufacturing, quality and marketing is regulated in accordance with the Drugs and Cosmetics Act of 1940 and Rules 1945. This act has witnessed several amendments over the last few decades. The Drugs Controller General of India (DCGI), who heads the Central Drugs Standards Control Organization (CDSCO), assumes responsibility for the amendments to the Acts and Rules. Other major related Acts and Rules include the Pharmacy Act of 1948, The Drugs and Magic Remedies Act of 1954 and Drug Prices Control Order (DPCO) 1995.

Some of the important schedules of the Drugs and Cosmetic Act includedealing with Schedule M: which, deals with Good Manufacturing Practices involving premises and plants and Schedule Y: which specifies guidelines for clinical trials, import and manufacture of new drugs.

In accordance with the Act of 1940, there exists a system of dual regulatory control or control at both Central and State government levels. The central regulatory authority undertakes approval of new drugs, clinical trials, standards setting, control over imported drugs and coordination of state bodies' activities. State authorities assume responsibility for issuing licenses and monitoring manufacture, distribution and sale of drugs and other related products

M4: The Common Technical Document

The agreement to assemble all the Quality, Safety and Efficacy information in a common format (called CTD - Common Technical Document) has revolutionised the regulatory review processes, led to harmonised electronic submission that, in turn, enabled implementation of good review practices. For industries, it has eliminated the need to reformat the information for submission to the different ICH regulatory authorities.

The CTD is organised into five modules. Module 1 is region specific and Modules 2, 3, 4 and 5 are intended to be common for all regions. In July 2003, the CTD became the mandatory format for new drug applications in the EU and Japan, and the strongly recommended format of choice for NDAs submitted to the FDA.

M4 (R3): Organisation Including the Granularity document that provides guidance on document location and paginations. The overall organisation of the CTD is presented here.

The CTD is organised into five modules

Module1 is for administrative information and prescribing information, and should contain documents that are specific to each region; for example, application forms or the proposed label for use in the region. Module 2 contains the CTD summaries and should begin with a general introduction to the drug, including its pharmacological class, mode of action and proposed clinical use. Module 2 should also provide the overall summary of the 'quality' information provided, the non-clinical overview and the clinical overview, as well as the non-clinical written summaries and the tabulated summaries, and the clinical summary. As a foundation for the aforementioned material, module 3 contains information on quality topics, module 4 contains the nonclinical study reports and module 5 contains the clinical study reports.

The organisation of summaries in module 2 is described in Guidelines for M4Q, M4S, M4E.

The Common Technical Document was agreed upon in November 2000 and re-edited with Numbering and Section Headers changes, September 2002.

M4 Q&As Document (R3)

In order to help users deal with issues which may arise during attempts to use the CTD, the ICH has supplied a Questions & Answers section on the ICH web site to answer most, if not all, questions anyone may have. If issues arise that are not answered on the web site, additional questions can be submitted for a formal response.

M4 Q (R1) Quality

Module 2: Quality Overall Summary (QOS)

Module 3: Quality

The section of the application covering chemical and pharmaceutical data including data for biological/ biotechnological products.

Re-edited with Numbering and Section Headers changes, September 2002

The Quality section of the Common Technical Document (M4Q) provides a harmonised structure and format for presenting CMC (Chemistry, Manufacturing and Controls) information in a registration dossier. The table of contents includes sections on Drug Substance and Drug Product. There are also sections for regional specific information as well as some appendices. Due to the fact that many CMC topics have not yet been the subject of ICH guidelines (e.g. drug substance synthesis, drug product manufacture, container closure), the content of M4Q is not totally harmonised. A new section on Pharmaceutical Development has been included to replace the Development Pharmaceutics Report (currently a part of the EU submission requirements). Also, a new CMC summary document, the Quality Overall Summary, has been developed.

M4S (R2)

Nonclinical Summaries and Organisation of Module 4

The non-clinical section of the application.

Re-edited with Numbering and Section Headers changes, September 2002

The CTD Safety (M4S) Guideline delineates the structure and format of the nonclinical summaries in Module 2 of the Common Technical Document, and provides the organisation of Module 4, the Nonclinical Study Reports. The Nonclinical Overview should present an integrated and critical assessment of the pharmacologic, pharmacokinetic, and toxicologic evaluation of the pharmaceutical, and generally should not exceed 30 pages. The Nonclinical Written Summaries (100 - 150 pages) are recommended to provide more extensive summaries and discussion of the nonclinical information on pharmacology, pharmacokinetics and toxicology. Thirty-four templates are provided for the preparation of the Nonclincal Tabulated Summaries, and 31 example tables are provided. Finally, the organisation of the Nonclinical Study Reports in Module 4 is described. Preparation of the nonclinical sections of the Common Technical Document according to the M4S Guideline results in a single harmonised dossier of the nonclinical information that is acceptable in all three ICH regions.

M4E (R1)
Module 2: Clinical Overview and Clinical Summary
Module 5: Clinical Study Reports
The clinical section of the Application.
Re-edited with Numbering and Section Headers changes, September 2002
CTD-Efficacy (M4E) describes the structure and format of the clinical data in an application, including summaries and detailed study reports. There are two high level clinical summaries in Module 2 of the CTD : the Clinical Overview, a short document that provides a critical assessment of the clinical data; and the Clinical Summary, a longer document that focuses on data summarisation and integration. Clinical Study Reports and raw data (where applicable) are included in Module 5 of the CTD.

M4E (R2)

Revision of M4E Guideline on Enhancing the Format and Structure of Benefit-Risk Information in ICH. This topic was endorsed by the ICH Steering Committee in April 2015. The M4E(R2) Concept Paper proposed a review and revision in some parts of the Section 2.5 Clinical Overview of the Module 2 of the Common Technical Document (CTD) (Section 2.5.1 and 2.5.6) to ensure the guideline is both harmonised and sensible in its entirety. The Common Technical Document (CTD) is a set of specification for application dossier for the registration of Medicines and designed to be used across Europe, Japan and the United States. It is an internationally agreed format for the preparation of applications regarding new drugs intended to be submitted to regional regulatory authorities in participating countries. It was developed by the European Medicines Agency (EMA, Europe), the Food and Drug Administration (FDA, US) and the Ministry of Health, Labour and Welfare (Japan). The CTD is maintained by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)
The Common Technical Document is divided into five modules:

1. Administrative and prescribing information
2. Overview and summary of modules 3 to 5
3. Quality (pharmaceutical documentation)
4. Preclinical (Pharmacology/Toxicology)
5. Clinical – efficacy (Clinical Trials)

Detailed subheadings for each Module are specified for all jurisdictions. The contents of Module 1 and certain subheadings of other Modules will differ, based on national requirements. After the United States, European Union and Japan, the CTD has been adopted by several other countries including Canada and Switzerland. The Electronic Common Technical Document (eCTD) is an interface for the pharmaceutical industry to agency transfer of regulatory information. The content is based on the Common Technical Document (CTD) format. It was developed by the International Conference on Harmonisation (ICH) Multidisciplinary Group 2 Expert Working Group (ICH M2 EWG). As of January 1, 2008, the U.S. Food and Drug Administration announced that the eCTD is the preferred format for electronic submissions.[1] To date, over 98,000 eCTD sequences have been submitted to the FDA.[2] Although the agency has not released an expected target date, the FDA revealed during the 2009 DIA Annual Meeting that it is looking at draft legislation to require eCTD. Pharmaceutical point of view.

The eCTD has five modules

1. Administrative information and prescribing information
2. Common technical document summaries
3. Quality
4. Nonclinical study reports
5. Clinical study reports here are two categories of modules:

- Regional module: 1 (different for each region; i.e., country)
- Common modules: 2–5 (common to all the regions)

The CTD defines the content only of the common modules. The contents of the Regional Module 1 are defined by each of the ICH regions (USA, Europe and Japan).

eCTD (data structure)
The eCTD is a message specification for the transfer of files and metadata from a submitter to a receiver. The primary technical components are:

- A high level folder structure (reqed)
- An XML "backbone" file which provides metadata about content files and lifecycle instructions for the receiving system
- An optional lower level folder structure (recommended folder names are provided in Appendix 4 of the eCTD specification)
- Associated document type definitions (DTDs) and stylesheets.

Each submission message constitutes one "sequence". A cumulative eCTD consists of one or more sequences. While a single sequence may be viewed with web browser and the ICH stylesheet provided, viewing a cumulative eCTD requires specialized eCTD viewers.

The top part of the directory structure is as follows:

In the 1980s, what is today the European Union began harmonising regulatory requirements. In 1989, Europe, Japan, and the United States began creating plans for harmonisation; ICH was created in April 1990 at a meeting in Brussels. The ICH has four major parts:

1. ICH Steering Committee
2. ICH Coordinators
3. ICH Secretariat
4. ICH Working Groups

The Steering Committee, made of six ICH Parties, governs the ICH, determining the policies and procedures, selecting topics for harmonisation and monitoring progress of harmonisation initiatives. The ICH consists of:

- European Commission
- European Federation of Pharmaceutical Industries and Associations (EFPIA)
- Ministry of Health, Labour and Welfare (Japan)
- Japan Pharmaceutical Manufacturers Association (JPMA)
- Food and Drug Administration (FDA)
- Pharmaceutical Research and Manufacturers of America (PhRMA)

The ICH Coordinators represents each ICH Party to the ICH Secretariat on a day-to-day basis.

The ICH Secretariat is primarily concerned with preparations for, and documentation of, meetings of the Steering Committee as well as coordination of preparations for Working Group (EWG, IWG, Informal WG) and Discussion Group meetings. The ICH Working Groups are created by the Steering Committee when a new topic is accepted for harmonisation, and is charged with developing a harmonised guideline that meets the objectives outlined in the Concept Paper and Business Plan. Face-to-face meetings of the EWG will normally only take place during the biannual SC meetings. Interim reports are made at each meeting of the SC. If consensus is reached the EWG will sign the Step 2 Experts Signoff sheet and submit it to the SC to request adoption. If there is no agreement in the EWG within the time frame the SC may extend the time frame, suspend or abandon the harmonization project.

Step 2: Confirmation of EWG consensus by the SC

Step 2 is reached when the SC agrees, based on the report of the EWG, that there is sufficient scientific consensus on the technical issues for the draft guideline. This text is signed off by the SC as Step 2 Final Document.]

Step 3: Regulatory consultation and discussion

The draft becomes subject of consultation in the three regions. It is published in the European Union (as draft CHMP or CVMP guideline), Japan (after translation by MHLW), and the USA (as draft guideline in the Federal Register) and everybody within these regions can comment on it. There is also an opportunity for companies, associations and authorities in non-ICH regions to comment on the draft, which is distributed by IFPMA and WHO. After obtaining all consultation results, the EWG will be resumed. A new rapporteur will be appointed from the regulatory party, preferably from the same region as the previous rapporteur. The same procedure described in Step 1 is used to address the consultation results into the Step 2 Final Document. The draft document to be generated as a result of the Step 3 phase is called

Step 4 Experts Document.

If industry and regulatory EWG members agree on the alterations as a result of the consultation, the Step 4 Experts Document is signed by the EWG regulatory experts only (Step 4 Experts Signoff) and submitted to the SC to request adoption as Step 4 of the ICH process.

Step 4: Adoption of an ICH harmonised tripartite guideline: Step 4 is reached when the SC agrees that there is sufficient scientific consensus on the technical issues. If one industry party has strong objections to the adoption of the guideline due to deviations of the revised draft from the original consensus the regulatory parties may agree that a revised document should be submitted for further consultation. In this case, the EWG discussion may be resumed. The Step 4 Final Document is signed off by the SC signatories for the regulatory parties of ICH as an ICH Harmonized Tripartite Guideline.

Step 5: Implementation

The ICH Harmonized Tripartite Guideline moves immediately to the final step of the process that is the regulatory implementation. This step is carried out according to the same national/regional procedures that apply to other regional regulatory guidelines and requirements, in the European Union, Japan, and the United States.

Although adherence to overall CTD structure is necessary, it should be noted that no guideline can cover all eventualities, and common sense and a clear focus on the needs of the regulatory authority assessor are the best guides to constructing an acceptable document. Therefore, applicants can modify the format at some of the subsection levels, if needed to provide the best possible presentation of the information, in order to facilitate the understanding and evaluation. This CTD guidance document is not applicable for the manufacture and sale of bulk drugs of a new drug approved in the country. In case of a new chemical entity, the approval of only API cannot be considered unless safety and efficacy of the finished formulation of the drug is evaluated and approved by this office.

GUIDELINES FOR PREPARATION OF CTD

CTD: OVERVIEW

The CTD is organized into five modules (Module 1, 2, 3, 4, and 5) and a diagrammatic representation of organization of the CTD

Module 1: General Information

This module should contain documents specific to India; for example, Form 44, Treasury challan fee or the proposed label for use in India.

Module 2: CTD Summaries

This module should begin with a general introduction to the pharmaceutical, including its pharmacologic class, mode of action, and proposed clinical use, not exceeding one page. Module 2 should contain 7 sections in the following order:

- CTD table of contents
- CTD introduction
- Quality overall summary
- Nonclinical overview
- Clinical overview
- Nonclinical written and tabulated summaries
- Clinical summary

Module 3: Quality

Information on Quality should be presented in the structured format as described in *Section 3.*

Module 4: Nonclinical Study Reports

The nonclinical study reports should be presented in the order described at *Section 4*.

Module 5: Clinical Study Reports

The human study reports and related information should be presented in the order described at *Section 5.*

DISCUSSIONS

Regulatory dossier

Introduction to regulatory

The regulation of medical products has been expanding since early 20th century. Regulatory agencies are being established in an ever increasing number of countries across the globe. Those that have established are reorganizing their systems and attempting to harmonize with organizations of other countries1. The pharmaceutical, biotechnology and medical devices are among the most highly regulated industries in the world. Regulatory affairs (RA) professionals are employed in pharmaceutical industry, government, academic research and clinical institutions. The Indian Pharmaceutical industry is one of the fastest growing industries in India, with a Compounded annual growth rate (CAGR) of over 13 % in last 5 years and it is expected to grow at a higher rate in coming 10 years. It is valued at $ 8.0 billion approximately and ranks 4th in terms of volume and 13th in terms of value globally. The clinical research industry, which provides opportunities for RA professionals, is also growing at an unparalleled rate. It has opened up new vistas of employment for a large number Of trained professionals. The clinical trials market worldwide is worth over USD 52 billion.

International regulatory environment

Good Manufacturing Practices has been in practice from Old Testament times (Laws of Kashrut). The Nuremberg Code, 1947 on Permissible Medical Experiments4 provided for basic principles to conduct medical experiments on human beings followed by Declaration of Helsinki (1964)5, Belmont Report of USA6 (1978) and WHO GCP7 (1995) and ICH GCP8 in 1996. In 1959, Canada instituted its QUAD regulations, which is the first recognizable drug GMP of modern era. It was followed by GMPs of USA in 1963 and that of UK in 1972.

Today 35 member countries along with 11 candidate countries and 4 international agencies have joined together to create the Pharmaceutical Inspection Cooperation Scheme (PIC/S) to promote a globally accepted GMP. The International Conference on Harmonization (ICH) was established in 1990 and has succeeded in harmonizing GMPs for manufacture of Active Pharmaceutical Ingredient (API), validation of analytical methodology, guidelines for Performance of stability studies, harmonization of pharmacopoeal monographs and test methods And other guidelines of working of GMP.

Responsibilities

The responsibilities of RA personnel in general can be summarized into three

(i) Ensuring that their companies comply with all of the regulations and laws pertaining to their Business,

(ii) Working with federal, state and local regulatory agencies and personnel on specific issues affecting their business
(iii) Advising companies on the regulatory aspects and climate that would affect their proposed

Skills

As regulatory affairs professional, they are often responsible for tracking changes in Regulatory guidelines as they may occur. In order to do this, they must take the initiative to keep Current on all changes in regulations. For example, they have to check the FDA Web site and They can learn about new guidelines from different sources like peers, print releases of regulatory authorities and by attending conferences. All changes in regulations must be documented in the manner required by the company.

Regulatory affairs in product management

The key role of RA professional is broader than registration of products, they advise companies both strategically and technically at the highest level. Their role begins right from development of a product to making, marketing and post marketing strategies. Their advice at all stages both in terms of legal and technical requirements help companies save a lot of time and money in developing the product and marketing the same. For countries that do not have theiron regulations the World Health Organization guidelines on health matters16 and World Trade Organization on trade regulations between nations is followed.

Regulatory affairs in clinical trials

- The RA professional is the primary link between the company and worldwide regulatory agencies such as US Food and Drug Administration (USFDA &Center for Devices and Radiological Health)18, 10 , Medicines and Healthcare Products Regulatory Agency, United Kingdom, (UKMCA)19, Therapeutic Goods Administration, Australia20 European Medicines Agency21 , Organization of Economic Collaboration and Development (OECD) and Health Canada14, 23. He also communicates and interprets the seemingly endless mace of laws, regulations and guidelines to the other departments of the company.
- The RA personnel develops strategies to overcome delays and presents finding of clinical trials to the regulatory bodies so as to get quick clearance thus reducing the time for approval of new molecules. At its core, the RA professional facilitates the collection, analysis and communication about the risks and benefits of health products to the regulatory agencies, medical and health systems and the public. Operationally RA is responsible for assuring that government obligation, market driven demands and evolving scientific conventions are understood and addressed by various stakeholders.

CONCLUSION

Any medicinal agent to be marketed in the United Kingdom has to follow the guidelines and regulations framed by MHRA, a regulatory authority which approves the drug products. The objective of this review article is to highlight information regarding the requirements, the different types of submissions for the registration of a medicinal product in a market in the UK. It also includes all the details about the fee for the application and the time period for the approval of the application after the submission of the application. By knowing the requirements of the MHRA guidelines and regulations, it is easy for a product to get into the UK market. This regulatory dossiers of USA is a guideline of the agreed upon common format for the preparation of a well-structured Common Technical Dossier (CTD) applications that will be submitted to regulatory authorities for the registration of pharmaceuticals for human use. This guideline describes a CTD format that will significantly reduce the time and resources needed to compile applications for registration and in the future, will ease the preparation of electronic documental submissions.ICH-ECTD is an internationally driven standard designed to reduce cost in the administration, assessment and archiving of applications for marketing authorization of medicinal products for human use, to reduce the use of paper and streamline the assessment process making the system more efficient. Unlike CTD the ECTD is not mandatory in Europe (highly recommended).

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