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BRIEF REVIEW ON CTD AND e-CTD AS PER USFDA AND EMA

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ABSTRACT

The Common Technical Document (CTD) used to be designed to supply a frequent layout between Europe, USA, and Japan for the technical documentation covered in a software for the registration of a human pharmaceutical product. "The widespread structure for submitting submissions, modifications, supplements, and reports to the Centre for Drug Evaluation and Research (CDER) and the Centre for Biologics Evaluation and Research (CBER) of the FDA is recognised as digital Common Technical Document (eCTD).

KEYWORDS: Common technical document, Electronic technical document, ICH, FDA, ANDA.

INTRODUCTION

The construct of electronic regulatory submissions isn't new, and has been evolving in America and Europe since the late 1980 before the implementation of the Common Technical Document (CTD) in 2002, every of the 3 major restrictive regions (EU, USA, and Japan) had its own set of pointers and format for the submission of a restrictive written account to get selling approval for a brand-new drug or a variation to the licensing of an existing drug. In 2000, representatives from the EU Medicines Agency (EMA), the USA authority, and therefore the Ministry of Health, Labour, And Welfare in Japan developed a collection of pointers shaping the structure and content of the written account for an application for the registration of a brand-new drugs that would be used across all 3 regions.[1] eCTD (electronic Common Technical Document) is a standard format of submitting Regulatory information (such as applications, supplements, and reports) to the concerned Health Authorities (HAs). It provides a harmonized solution to implement the Common Technical Document (CTD) electronically.

An eCTD consists of individual documents in PDF format which are arranged in a hierarchical form as per the CTD structure. It also has an XML backbone which cross-links required documents and provides information regarding the submission. The purpose of introducing eCTD was to reduce the burden on the reviewers of the has. It also simplifies the process of submission as all the Regulatory authorities use it as a standard format. This module-based regulatory application format was developed by the International Conference on Harmonization (ICH M2 EWG). In 2008 the FDA (Food and Drug Administration) made eCTD format compulsory for all electronic submissions by FDA in 2008.[2]

Significance

It provides appropriate format data which is easy to understand and helps in evaluation of data.

CTD is relevant to all types of products.

It is extra format that helps in simpler evaluation for reviewer also.

CTD additionally helps in simultaneous submission of archives for approval in 3 regions and helps trade of regulatory information. Moreover, it allows electronic submissions and faster availability of new drug treatments to patient populations.[3]

RESULTS

ORGANISATION OF THE COMMON TECHNICAL DOCUMENT IN US

The Common Technical Document is prepared into 5 modules. Module 1 is location specific. Modules 2, 3, 4, and 5 are supposed to be frequent for all regions. Conformance with this guideline should ensure that these four modules are furnished in a layout proper to the regulatory authorities.

Module 1: Administrative Information and Prescribing Information

This module contain documents unique to every region; for example, application types or the proposed label for use in the region. The content material and layout of this module can be precise by means of the applicable regulatory authorities.

Module 2: Common Technical Document Summaries

Module 2 should begin with a general introduction to the pharmaceutical, such as its pharmacologic class, mode of action, and proposed clinical use. In general, the Introduction need to no longer exceed one page.

Module 2 should contain 7 sections.

1. CTD Table of Contents
2. CTD Introduction
3. Quality Overall Summary
4. Nonclinical Overview
5. Clinical Overview
6. Nonclinical Written and Tabulated Summaries
7. Clinical Summary

The organisation of these summaries is described in Guidelines for M4Q, M4S, and M4E.[4]

Module 3: Quality

Information on Quality should be presented in the structured format described in the M4Q guidance.

Module 4: Nonclinical Study Reports

The nonclinical study reports should be presented in the order described in the M4S guidance.

Module 5: Clinical Study Reports

The human study reports and related information should be presented in the order described in the M4E guidance.[4]

Organisation of the common technical document in EU

The Common Technical Documentation organized into five modules. Module one is space specific. Modules 2, 3, 4, and five area unit meant to be frequent for all regions. Conformity with this guideline make certain that these four modules area unit equipped in an exceedingly format applicable to the restrictive authorities.

Module 1: Administrative Information and Prescribing Information

Module have to be compelled to documents specific to every region; for instance, application forms or the planned label to be used within the region. The content material and format of this module is specific by suggests that of the applicable regulative authorities.

Module 2: Common Technical Document Summaries

Module a pair of got to begin with an established introduction to the pharmaceutical, alongside its pharmacological category, mode of action, and projected clinical use. In general, the Introduction should not exceed one page.

Module 2 should contain 7 sections in the following order.

1. CTD Table of Contents
2. CTD Introduction
3. Quality Overall Summary
4. Nonclinical Overview
5. Clinical Overview
6. Nonclinical Written and Tabulated Summaries
7. Clinical Summary

The organisation of these summaries is described in Guidelines for M4Q, M4S, and M4E.

Module 3: Quality information on Quality should be given within the structured format represented in Guideline M4Q.

Module 4: Nonclinical Study Reports The nonclinical study reports should to be given within the order represented in Guideline M4S.

Module 5: Clinical Study Reports The human study reports and connected information should be given within the order represented in Guideline M4E.[5]

The primary technical components are.

- A high-level folder structure (required)
- An Extensible Mark-up Language (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 respective modules of the eCTD specification below)
- Associated document type definitions (DTDs) and style sheets that support the presentation and navigation.[1]

ORGANISATION OF THE ELECTRONIC COMMON TECHNICAL DOCUMENT IN US

It contains 5 modules.

Module 1: Administrative and prescribing information

It includes, however is not restricted to body, labelling, REMS and message documents. The topic matter for every document should be allotted to all times low level of the hierarchy printed within the associated food and drug administration technical specification comprehensive table of contents headings and hierarchy.

Module 2: Summaries

Module 3: Quality

Module 4: Nonclinical

The organization of Module 4 is the same for all applications and related submissions. The guidance provided below addresses general considerations for the submission contents.

Module 5: Clinical

The organization of Module 5 is the same for all applications and related submissions. The guidance provided below addresses general considerations for the submission contents (i.e., the physical files and folders) and the contents of the message.[6]

ORGANISATION OF THE ELECTRONIC COMMON TECHNICAL DOCUMENT IN EU.

Modules of eCTD

The eCTD has five modules in two categories. There are.

1. Regional module which includes only Module 1-Administrative information and prescribing information -not harmonized -different for each region; i.e., country, defined by each of the ICH regions (USA, Europe and Japan).[7]

2. Common modules: which includes module 2 –5(Harmonized -common to all the regions).

- ✓ Module 2 -Common technical document summaries
- ✓ Module 3 -Quality
- ✓ Module 4 -Nonclinical study reports
- ✓ Module 5 -Clinical study reports

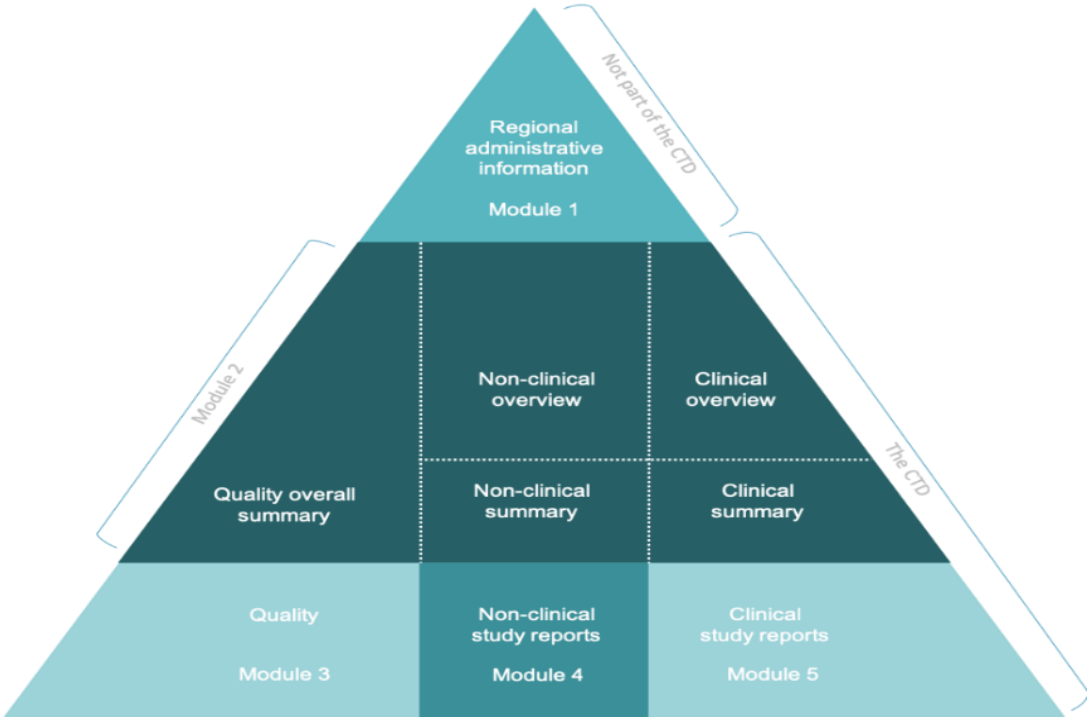

Figure showing Electronic common technical document.

e-CTD submissions are accepted for the following applications.

- Investigational New Drug (INDs)
- New Drug Applications (NDAs)
- Abbreviated New Drug Applications (ANDAs)
- Biologics License Applications (BLAs)
- All the applications following the submission of the above-stated applications
- All the Master Files (MFs) which are part of any above-mentioned applications

DISCUSSION

Comparison of CTD and eCTD in USA and EU.

Table 1: Comparison of CTD and eCTD in USA and EU.[8]

SR.NO	Point to be address	USA	EU
1	Regulatory authority	Food and Drug Administration	European Medicines Agency
2	Types of Application	3 types: NDA ANDA BLA	MAA
3	Types of registration procedure	The application is directly submit to the FDA or through any approved contact agent	4 types of registration procedure: CP, DCP, MRP and NP

4	Technical data about drug substance or API	Drug master file	Active substance Master File
5	eCTD	eCTD mandatory for all types of application	eCTD not fully mandatory but Nees is submitted along with paper submission till 2009
6	Drug product labelling	Package inserts are provided	Summary Of product Labelling
7	Information about clinical investigator	Provided in module 5	Module 1
8	Certificate of suitability	Not applicable	Latest certificate of suitability
9	Batch size for manufacturing and control	100000 units	100000 units
10	Bio-waiver request for BA/BE	Module 1	Module 1

CONCLUSION

The study provides evidence of importance of the CTD comparison with eCTD & the global regulatory challenges faced by the CTD and eCTD. It is clear that CTD, has helped many countries like US and EUROPE not only develop their own registration processes but to participate more and more in the development of new ICH guidelines.

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