IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

CRITICAL EVALUATION OF DIFFERENT COMPONENTS USED IN THE DOSSIER OF A PHARMACEUTICAL PRODUCT

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Abstract: A Pharmaceutical Dossier is collection of data on new drug for their approval. Any pharmaceutical preparation intended for human use must go through the process of analysing and evaluating the pharmaceutical drug dossier, which includes comprehensive information on administrative, quality, non-clinical, and clinical data. The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH TR) maintains the Common Technical Document (CTD). The CTD was created to offer a standard dossier filing format for the registration of novel drug products between the United States, Japan, and European nations. Administrative and prescription information, an overview and summary of Modules 3–5, quality (pharmaceutical documentation), preclinical (pharmacology and toxicology), and clinical (effectiveness and safety), are the five modules of the CTD. Various registration requirements across the global market are the barriers to the efficient and successful filing of an application for a new drug product. There are certain limitation which leads to the modification of the process like maintenance of data of each module of single drug for years. For the evaluation process, a lot of time was required. This led ICH to create an electronic version of CTD known as the "Common Technical Document" (eCTD). The applicant may submit the Common Technical Document (CTD) electronically to the regulator in accordance with the Electronic Common Technical Document (eCTD). Nowadays, this process is streamlined by modifying the usage of tools like different software for regulatory submission.

***Key words*:** Dossier, CTD, eCTD, ICH, Regulatory submission, Quality, Non-clinical study, Clinical study, Drug regulatory authorities

INTRODUCTION

The term "registration dossier" refers to a collection of documents about a medical product's safety, efficacy, and quality information that are submitted to a regulatory body for review; if the submission is approved, the product will be granted marketing authorisation. (1)

A pharmaceutical product's "registration dossier" is a document that includes all technical data (administrative, quality, nonclinical, and clinical) of a pharmaceutical product that is to be approved, registered, and marketed in a country; it is more commonly known as a new drug application (NDA) in the United States or

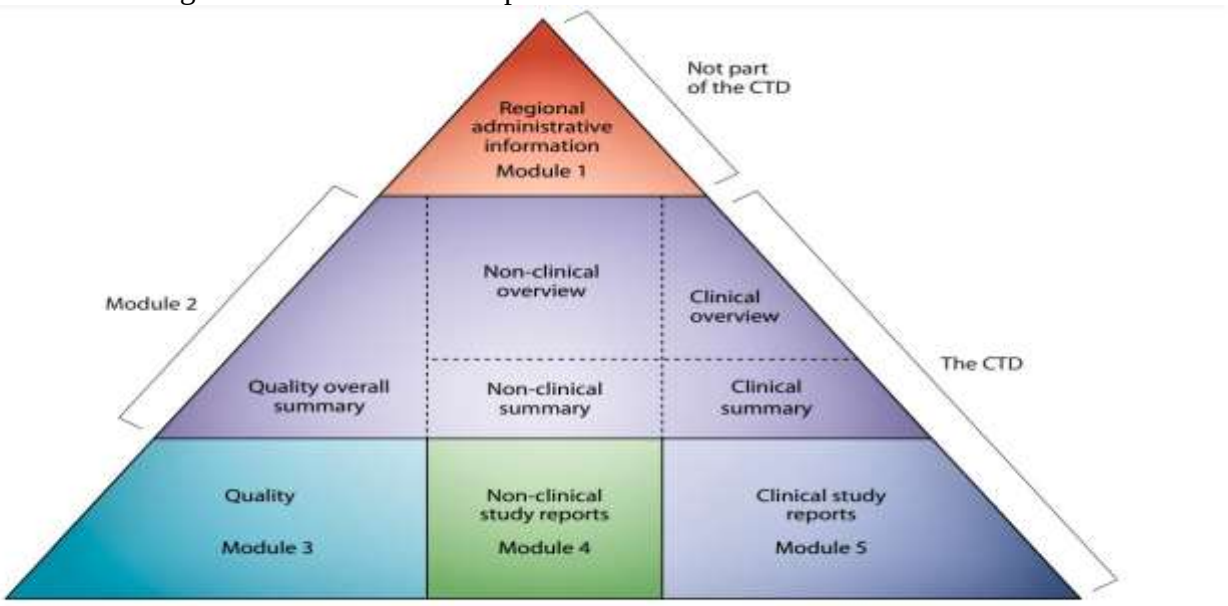
a marketing authorisation application (MAA) in the European Union (EU) and other countries just as a registration dossier.After the common technical document (CTD) guideline was released, the international conference on harmonisation (ICH) procedure significantly standardised how documents are registered. The CTD guideline's suggested format for registration applications has gained widespread acceptance among regulatory bodies inside and outside of the ICH Regions. Therefore, a dossier is a file document that must be provided in accordance with the parameters of the market authorisation and drug approval process. (1)

It is a thorough scientific document used by various health authorities to grant a medicine global license permission or market authorisation. Its production, processing, compilation, and field dispatch by a regulatory affairs department rely on numerous interconnected operations; the authorisation and filling process in emerging markets will vary by location. (2)

The pharmaceutical industry's globalisation has made it necessary to standardise guidelines for the creation of novel drugs as well as national regulatory needs. Therefore, a standard submission structure will aid in getting past these obstacles. The CTD guidelines have been produced for the United States, Japan, and the European Union through the ICH process. The majority of nations have embraced the CTD format. (3)

Common Technical Document

An internationally accepted method for preparing applications for novel medications that are meant to be presented to regional regulatory bodies in participating nations is the common technical document (CTD). Beginning at the World Health Organisation International Conference of Drug Regulatory Authorities (ICDRA) in Paris in 1989, it was created by the European Medicines Agency (EMA, Europe), the Food and Drug Administration (FDA, US), and the Ministry of Health, Labour, and Welfare (Japan). The International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is responsible for maintaining the CTD. Following the United States, the European Union, and Japan, Canada and Switzerland were among the other nations to adopt the CTD. (4)



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

figure 1: CTD triangle

Evolution of CTD [1]

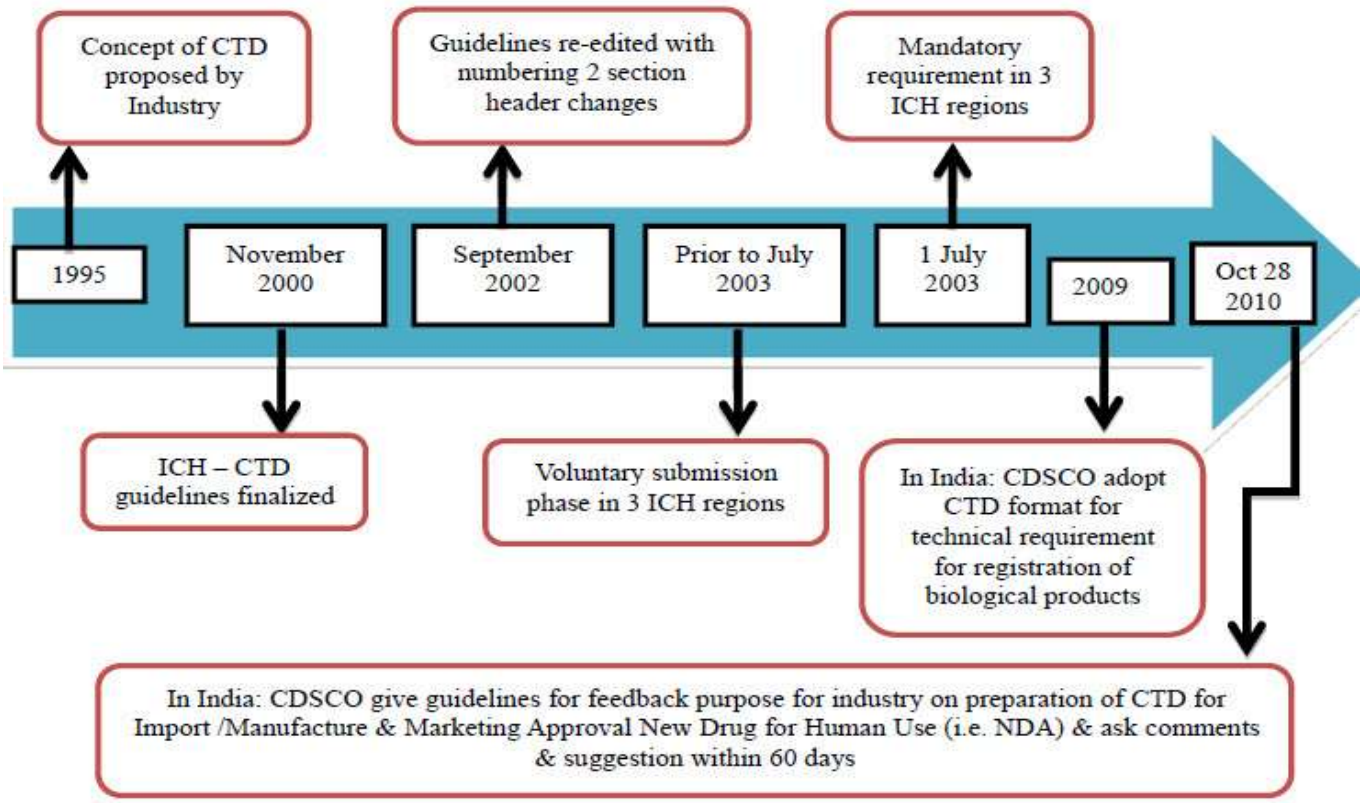


figure 2: evaluation of CTD

Module 1: Administrative Information

Module 1 is dedicated to administrative and prescribing information; it includes documents specific to each location, such as application forms or the suggested label for usage in that area. The relevant regulatory bodies have the authority to specify the format and content of this module. [5]

table 1: content of administrative information

SR.	CONTENT
1.	**APPLICATION INFORMATION**
1.1	Application letter
1.2	Registration form
1.3	Certificate of incorporation
1.4	Power of attorney
1.5	Notarized declaration of applicant
1.6	Power of attorney/ contract manufacturing agreement
1.7	Certificate of pharmaceutical product
1.8	Certificate of good manufacturing practice
1.9	Manufacturing authorization

1.10	Evidence of trademark registration
1.11	Superintendent pharmacist's annual licence to practice
1.12	Certificate of registration and retention of premises
1.13	Evidence of previous marketing authorization
1.14	Invitation letter for GMP inspection
1.15	Copy of certificate of suitability of European pharmacopoeia
1.16	Letter of access for APIMF
1.17	Biowaiver request in relation to conducting BCS- based bioavailability study
1.18	Biowaiver request in relation to conducting additional strength bioavailability study
2.	**Product information**
2.1	Summary of product characteristics (SmPM)
2.2	Labelling
2.3	Package Insert
3.	**Regional summaries**
3.1	Bioequivalence trial information form
3.2	Quality information summary
4.	**Electronic review documents**
5.	**Samples**

Module 2: Common Technical Document (CTD) Summaries

Module 2, which includes the CTD summaries, starts with a broad overview of the medication, covering its pharmacological class, mechanism of action, and suggested clinical application. Additionally, module 2 offers the clinical summary, the non-clinical and clinical overviews, the non-clinical written summaries, the tabulated summaries, and the overall summary of the "quality" information supplied. Module 2 provides an overview of Module 3. [5]

table 2: content of CTD summaries

MODULE 2: COMMON TECHNICAL DOCUMENT (CTD) SUMMARIES	
2.1	**CTD table of contents (Module 2-5)**
2.2	**CTD introduction**
2.3	**Quality overall summary-product dossier (QOS-PD)**
2.3.S	**Drug substance (S)**
2.3.S.1	General information
2.3.S.2	Manufacture
2.3.S.3	Characterization
2.3.S.4	Control of API
2.3.S.5	Reference standards or materials
2.3.S.6	Container closure system
2.3.S.7	Stability
2.3.P	**Finished pharmaceutical product**
2.3.P.1	Description and composition of the drug product
2.3.P.2	Pharmaceutical development
2.3.P.3	Manufacture
2.3.P.4	Control of excipients
2.3.P.5	Control of the drug product
2.3.P.6	Reference standards or materials
2.3.P.7	Container closure system

2.3.P.8	Stability
2.3.A	Appendices
2.3.A.1	Facilities and equipment
2.3.A.2	Adventitious agents safety evaluation
2.3.A.3	Novel excipients
2.3.R	Regional information
2.3.R.1	Production documentation
2.3.R.1.1	Executed production documents
2.3.R.1.2	Master production documents
2.3.R.2	Analytical procedures and validation information
2.4	Non clinical overview
2.4.1	Overview of the nonclinical testing strategy
2.4.2	Pharmacology
2.4.3	Pharmacokinetics
2.4.4	Toxicology
2.4.5	Integrated overview and conclusions
2.4.6	List of literature references
2.5	Clinical overview
2.5.1	Product development rationale
2.5.2	Overview of biopharmaceutics
2.5.3	Overview of clinical pharmacology
2.5.4	Overview of efficacy
2.5.5	Overview of safety
2.5.6	Benefits and risks conclusions
2.5.7	Literature references
2.6	**Non clinical summary**
2.6.1	Summary of pharmacological properties
2.6.2	Summary of pharmacokinetics properties
2.6.3	Summary of toxicology
2.7	**Clinical summary**
2.7.1	Summary of bio-pharmaceutics
2.7.2	Summary of clinical pharmacology
2.7.3	Summary of clinical efficacy
2.7.4	Summary of clinical safety

Module 3: Quality

The quality section of the dossier, which is necessary for the drug product to be registered in the regulatory countries, includes comprehensive information about the chemistry, production, and control of the drug product. Table of contents, body of data, drug substance, general information it contains, nomenclature, structure, and general API qualities constitute the quality section. [6]

table 3: content of module 3

MODULE 3: QUALITY	
3.1	**Table of contents**
3.2	**Body of data**
3.2. S	**Drug substance**
3.2. S.1	**General information**
3.2. S.1.1	Nomenclature
3.2. S.1.2	Structure
3.2. S.1.3	General properties
3.2. S.2	**Manufacture**
3.2.S.2.1	Manufacturer(s)

3.2. S.2.2	Description of manufacturing process and process controls
3.2.S.2.3	Control of materials
3.2.S.2.4	Controls of critical steps and intermediates
3.2.S.2.5	Process validation and/or evaluation
3.2.S.2.6	Manufacturing process development
3.2. S.3	**Characterization**
3.2.S.3.1	Elucidation of structure and other characteristics
3.2.S.3.2	Impurities
3.2.S.4	**Control of the API**
3.2.S.4.1	Specification
3.2.S.4.2	Analytical procedures
3.2.S.4.3	Validation of analytical procedures
3.2.S.4.4	Batch analyses
3.2.S.4.5	Justification of specification
3.2.S.5	**Reference standards or materials**
3.2.S.6	**Container closure system**
3.2.S.7	**Stability**
3.2.S.7.1	Stability summary and conclusions
3.2.S.7.2	Post-approval stability protocol and stability commitment
3.2.S.7.3	Stability data
3.2.P	**Drug product (or finished pharmaceutical product (FPP))**
3.2.P.1	**Description and composition of the drug product**
3.2.P.2	**Pharmaceutical development**
3.2.P.2.1	Components of the FPP
3.2.P.2.1.1	Active pharmaceutical ingredient
3.2.P.2.1.2	Excipients
3.2.P.2.2	Finished pharmaceutical product
3.2.P.2.2.1	Formulation development
3.2.P.2.2.2	Overages
3.2.P.2.2.3	Physicochemical and biological properties
3.2.P.2.3	Manufacturing process development
3.2.P.2.4	Container closure system
3.2.P.2.5	Microbiological attributes
3.2.P.2.6	Compatibility
3.2.P.3	**Manufacture**
3.2.P.3.1	Manufacturer(s)
3.2.P.3.2	Batch formula
3.2.P.3.3	Description of manufacturing process and process controls
3.2.P.3.4	Controls of critical steps and intermediates
3.2.P.3.5	Process validation and/or evaluation
3.2.P.4	**Control of excipients**
3.2.P.4.1	Specification
3.2.P.4.2	Analytical procedures
3.2.P.4.3	Validation of analytical procedures and COA'S of excipients
3.2.P.4.4	Justification of specifications
3.2.P.4.5	Excipients of human or animal origin
3.2.P.4.6	Novel excipients
3.2.P.5	**Control of FPP**
3.2.P.5.1	Specification(s)
3.2.P.5.2	Analytical procedures

3.2.P.5.3	Validation of analytical procedures
3.2.P.5.4	Batch analyses
3.2.P.5.5	Characterization of impurities
3.2.P.5.6	Justification of specification(s)
3.2.P.6	**Reference standards or materials**
3.2.P.7	**Container closure system**
3.2.P.8	**Stability**
3.2.P.8.1	Stability summary and conclusion
3.2.P.8.2	Post-approval stability protocol and stability commitment
3.2.P.8.3	Stability data
3.2.A	**Appendices**
3.2.A.1	Facilities and equipment's
3.2.A.2	Adventitious agents safety evaluation
3.2.A.3	Novel excipients
3.2.R	**Regional information**
3.2.R.1	Production documentation
3.2.R.1.1	Executed production documents
3.2.R.1.2	Master production documents
3.2.R.2	Analytical procedures and validation information
3.3	Literature references

Module 4: Non-Clinical Study (Pharmacology/Toxicology)

The non-clinical report that should be part of the dossier is this one. This module's content and the topic it will cover have previously been discussed. The primary headings that the dossier must contain are

4.1 Table of contents of module 4
4.2 Study reports
4.2.1 Pharmacology
4.2.2 Pharmacokinetics
4.2.3 Toxicology
4.3 Literature references used in module 4.

This module's clinical section requires the completion of pharmacokinetic, pharmacodynamic, and biopharmaceutics studies, which guarantee the safety and efficacy of the therapeutic product. The report also includes the case report form for each individual patient. [6]

table 4: content of module 4

MODULE 4: NONCLINICAL STUDY REPORTS	
4.1	**Table of contents**
4.2	**Study reports**
4.2.1	**Pharmacology**
4.2.1.1	Primary pharmacodynamics
4.2.1.2	Secondary pharmacodynamics

4.2.1.3	Safety pharmacology
4.2.1.4	Pharmacodynamic interactions
4.2.2	**Pharmacokinetics**
4.2.2.1	Analytical methods and validation reports
4.2.2.2	Absorption
4.2.2.3	Distribution
4.2.2.4	Metabolism
4.2.2.5	Excretion
4.2.2.6	Pharmacokinetic interactions (non-clinical)
4.2.2.7	Other pharmacokinetic studies
4.2.3	**Toxicology**
4.2.3.1	Single-dose toxicity
4.2.3.2	Repeat-dose toxicity
4.2.3.3	Genotoxicity (in vitro, in vitro, toxic kinetics evaluation)
4.2.3.4	Carcinogenicity (long, short- or medium-term studies)
4.2.3.5	Reproductive and developmental toxicity
4.2.3.6	Local tolerance
4.2.3.7	Other toxicity studies
4.3	**Literature references**

Module 5: Clinical – Efficacy And Safety (Clinical Trials)

A systematic study carried out on human participants to assess a drug's pharmacokinetics, safety, and/or effectiveness is called a clinical study. It include researching the drug's effects, adverse effects, dose recommendations, and total therapeutic benefit in a monitored and controlled setting. After preclinical testing in lab settings and animal models, clinical studies are a crucial phase in the drug development process. These studies offer vital information that helps guide clinical decision-making, evaluate the drug's effectiveness in humans, and support regulatory applications.[6]

table 5: content of module 5

MODULE 5: CLINICAL STUDY REPORTS	
5.1	**Table of contents**
5.2	**Tabular listing of clinical studies**
5.3	**Clinical study reports**

5.3.1	Reports of bio-pharmaceutical studies (bio-availability study reports, comparative bio-availability, and bio-equivalence study reports, in vitro and in vivo correlation study report, reports of bio-analytical and analytical methods)
5.3.2	Reports of studies pertinent to pharmaco-kinetics using human bio- materials
5.3.3	Reports of human pharmaco-kinetic studies
5.3.4	Reports of human pharmaco-dynamic studies
5.3.5	Reports of efficacy and safety studies
5.3.6	Reports of post-marketing experience
5.3.7	Case reports forms and individual patient listings
5.4	**Literature references**

Advantages of CTD

1. Eliminating extra crucial data or analysis missions and simplifying the assessment of each application are the primary objectives of adopting a standard submission format. This information may be omitted, which could result in needless delays in approvals.
2. By establishing a standard format for technical documentation, applications for human pharmaceutical registration can be prepared more quickly and with fewer resources. It will also be simpler to prepare electronic submissions.[7].
3. To streamline regulatory evaluations and correspondence with the application, a similar document will be utilised.
4. The industry's time and resource requirements for gathering worldwide registration applications are anticipated to be greatly reduced with the use of CTD. [8]

CTD's Silent Benefits

1. Harmonisation of applications worldwide.
2. Provides instructions for creating documents that are ready for submission throughout the IND phases.
3. Data and project management are facilitated by standardization.
4. Facilitates life cycle management.
5. Supports drug development planning. [8]

eCTD (Electronic Common Technical Document)

Over one lakh pages may be included in the paper CTD. For regulatory bodies, sorting through and reviewing this massive amount of data is quite challenging. A lot of time will be needed for the review process. Additionally, it becomes quite time-consuming to identify a certain topic of CTD during its examination because the reviewer must physically seek that file. [9]

Pharmaceutical product regulatory information is submitted to regulatory bodies using a standard format called the electronic common technical document (eCTD). It is a standardised format for electronic submission that makes it easier to submit, review, and archive regulatory papers in an organised and consistent way. [9]

Clinical study reports, nonclinical study reports, quality data, administrative and regional information, and other pertinent paperwork are among the modules into which the eCTD arranges the submission. Each module includes particular kinds of information on the drug product, including labelling, safety and efficacy data, and manufacturing procedures.[10]

By offering a uniform framework for arranging and displaying data, the eCTD format enhances the regulatory review process's effectiveness and uniformity. The submitted information may be evaluated more quickly and effectively since it makes it simple for regulatory bodies to navigate and access the required data.(11)

The electronic form of CTD is called an electronic common technical document, or eCTD. To develop an XML backbone, eCTD requires specialised software.

eCTD Submission Checklist

Training and assistance for eCTD software provided by the supplier Compiling and eCTD (11)

eCTD hyperlinking

eCTD quality control Use a CD/DVD or an electronic gateway to submit your eCTD. (11)

eCTD Structure

The USFDA strongly advises using eCTD for filing NDAS, BLAS, DMFS, and INDs. The European Union also made electronic CTD filing mandatory for all proceedings starting in 2010. (11)

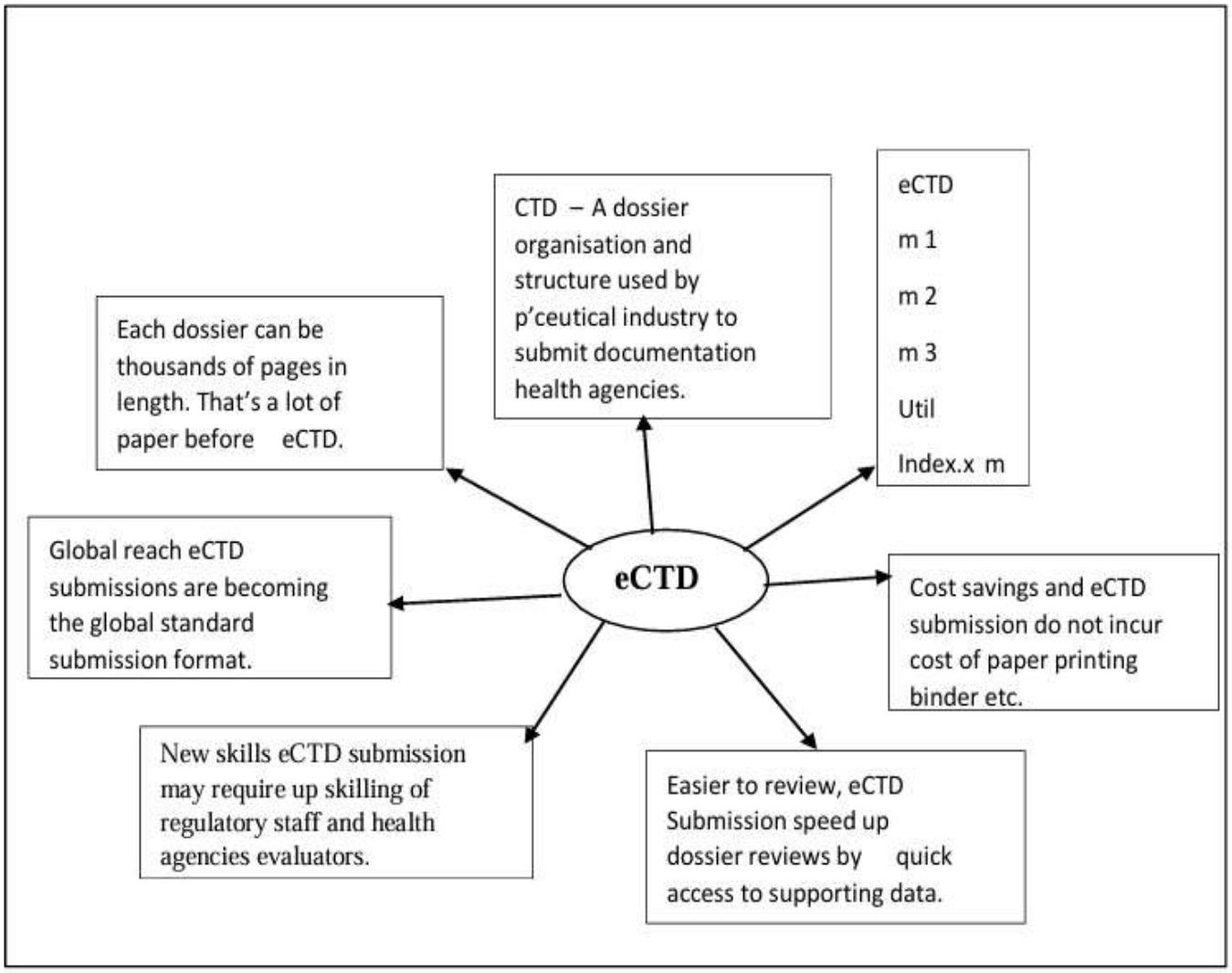


figure 4: overview of eCTD submission. (12)

eCTD Advantages

The use and expenses related to creating and maintaining paper dossiers are decreased when the eCTD dossier takes over as the only authoritative regulatory repository. improved capacity for managing, planning, and organizing submitted content. A quicker approval process, shorter response times to agency requests, and easier interactions with agency reviewers are all possible. allows teams of document authors, reviewers, publishers, and outside partners to work together more easily. [13,14]

There are five modules in eCTD as mentioned here

1. Region-specific information.
2. Summary documents.
3. Information related to quality.
4. Non-clinical study reports.
5. Clinical study reports (CSRs).

Comparison oF CTD and eCTD [15]

table 6: comparison of CTD and eCTD

Sr. No	Paper CTD [Common Technical Document]	eCTD [Electronic Common Technical Document]
1	Electronically entered volumes, tabs, and slip sheets were subsequently printed on paper.	Electronically filed with e-documents in folders.
2	A4 paper must be used.	A4 or US letter size documents are acceptable.
3	TOCs and volume are used to navigate the CTD.	XML backbone for eCTD navigation.

Tools used in eCTD Submission [15]

table 6: tools used in eCTD submission

TOOLS	DESCRIPTION	BENEFITS OF REVIEW TOOLS
JMP	Statistical software that makes it simple for reviewers to view data, do analyses, create graphs, and open data files (such as xpt and xls).	1) Capable of collecting and evaluating both standardised and non-standardized data 2) If someone has an account, sharing analysis with them is simple.
JMP Clinical	Desktop software that provides pre-clinical, clinical, and post-market data discovery, analysis, and reporting	1)Can combine data-sets across the application to gives a more integrated view of the submission data 2)Reviewers like the graphic patient profiles to view data across all domains on a timeline

JReview	An online review tool that lets users examine, tabulate, and visualise safety and efficacy information	1)Can ingest and analyse no standardized and standardized data 2)Can share analyses with other users that have accounts 3) The ability to display data across all domains on a timeline in the form of graphic patient profiles is appealing to reviewers. 4)Standard analysis catalog for clinical review continues to expand
MedDRA-Based Adverse Events Diagnostics (MAED)	examines clinical trial data using a number of exploratory adverse event analysis.	1) Can use standardized and no standardized data 2)Provides the ability to perform custom queries
Statistical Analysis Software (SAS), including SAS Analysis Panels	SAS - software suite developed by the SAS Institute for advanced analytics SAS Analysis Panels – scripts developed to perform standard analyses for clinical reviewers.	The MedDRA at a Glance output offers a view of the MedDRA hierarchy that is currently unavailable from any other tool.
Janus Non-clinical	Janus Non-clinical	Janus Non-clinical

Software used in eCTD Submission

1)**Lorenz life sciences**

Offering adaptable Regulatory Information Management systems that suit all work settings, Lorenz Life Sciences is a market leader in software solutions for the life sciences industry. [15]

2)Take solutions

TAKE Solutions provides domain-intensive services in supply chain management and life sciences. TAKE provides customers with a distinctive blend of full-service clinical, regulatory, and safety services supported by specialised technological know-how in the rapidly expanding life sciences sector. They offer a wide range of services, supported by knowledge gained via exclusive industry networks and forums, including clinical trials, regulatory filings, and post-marketing safety. TAKE provides clients with successful results through the use of best-in-class systems and procedures, a team of top Life Sciences professionals, and customised, sector-specific technology and analytics. Large and small innovative biopharmaceutical firms as well as generics manufacturers are among their global clientele. [16]

3)PharmaREADY

A web-based platform for creating and publishing dossiers, Navitas Life Sciences pharmaREADY eCTD was created to satisfy the ICH eCTD standard while enabling the use of best practice procedures. It satisfies the needs of life science organisations, where the main business drivers are affordability, convenience of use, regulatory compliance, and ease of installation.
The pharmaREADY eCTD product's functionality is the result of a thorough comprehension of the conditions necessary to satisfy and uphold FDA 21 CFR Part 11 and other international standards. PharmaREADY eCTD

offers smooth visibility into the complete regulatory document management lifecycle, from document creation to regulatory submissions. It can be purchased as a stand-alone product or readily integrated with other PharmaREADY products, such as PharmaREADY DMS and PharmaREADY PPS. [17,18]

pharmaREADY eCTD is an end-to-end web-based eCTD product providing
Submission roadmap / structure creation
Document assembly
Work in progress / Final preview
Internal review
Sequential / Parallel approval cycles
Compilation
Publishing
Seamless collaboration between all key stake holders of a drug submission including author / assembler, reviewer, approver and publisher

Key pharmaREADY eCTD features include

- Intuitive electronic content assembly processes.
- Integrated document management and publishing features.
- Support for all major regional templates (i.e. US, EU, CA, CH, SFDA, MCC, TGA)
- Submission lifecycle management and consolidated submission reviews
- Role-based document authoring and access management for multi-user electronic submission, authoring and publishing.
- Automatic creation of a validated, submission-ready package that includes the index XML backbone, regional XML backbone, and associated Leaf documents.
- Module 1 – Regional templates for US, Europe, Canada, Australia, South Africa, Saudi FDA, Swiss Medic readily available – Facilitates easy cloning for other regions.
- CTD Module 2 to Module 5 can be independently assembled based on the submission type and module requirements.
- Drastically reduce assembly / document-CTD section association time, effort and cost.
- Create standardized submission dossiers across different product applications.

pharmaREADY eDMS meets the needs of these types of Life Sciences organizations including

- PharmaceuticalBiotech
- Contract Manufacturers
- Medical Device
- Generics
- Animal Health
- Clinical Research Organizations

PharmaREADY DMS handles the complete content lifecycle process and provides you with the means to safely handle a variety of business documents, such as submission dossiers and papers pertaining to regulated compliance. The Navitas Life Sciences team leverages its extensive experience as technology specialists and life sciences professionals to a product vision that aims to lessen the load of business issues faced by life sciences organisations. [17,18]

Comparison table for CTD and eCTD in different countries [19]

Sr. no.	Points to be address	USA	EUROPE	JAPAN	CHINA	ICH	INDIA	WHO

1	Regulatory authority	Food and drug administration	European medicines agency	Ministry of health labour and welfare	State food and drug administration	n/a	Central drug standard and control organisation	n/a
2	Types of application	3types: NDA, ANDA, BLA	MAA	3types: NDA, ANDA, BLA	5types: NDA, ANDA Supplemental import drug application renewal	MAA	MAA	n/a
3	Types of registration procedure	The application is directly submit to FDA	4 types of registration procedure: CP, DCP, MRP, NP	Japan new drug application procedure(J-NDA)	2 types: standard review procedure, special review procedure	n/a	n/a	n/a
4	Technical data about drug substance or API called	Drug master file	Active substance master file	Japanese master file	Chinese master file	n/a	Drug master file	APIMF
5	eCTD	eCTD mandatory for all types of application	eCTD not fully mandatory but NeeS is submitted along with paper submission till 2009	eCTD is not fully mandatory	NeeS mandatory from sept. 2012. SFDA accept only eCTD from 3 January 2015	mandatory	eCTD not mandatory	Not mandatory
6	Administrative and prescribing information	FDA form 356h	Volume 2B notice to applicant	Application approval form	Chinese specific application form	n/a	Form 44	Application information form
7	Drug product labelling	Package inserts are provided	Summery of product labelling	Draft package inserts	---	---	Proposed draft label and cartoons provided in module 1	WHO public assesment report

8	Reference drug for label and cartoon	Similar to reference listed drug given in orange book	Mock ups and specimens of label sent with application appropriate	Japan reference drug	----	---	---	---
9	Information about clinical investigator	Provided in module5	Module 2	Module1	---	---	Module1	---
10	Biowaiver request for BA/BE	Module1	Module1	Module1	---	---	Module1	Module1
11	Executed batch records for manufacturing and packaging	Single batch records provided in module 3.2 R	Three executed batch records	Single executed batch records	---	---	---	---
12	Batch size for manufacturing and control	100000 units	100000 units	Not specified	---	---	---	---
13	Process validation	Not required	required	required	---	---	required	---
14	Letter of access	Not mentioned	Letter of access for ASMF provided	---	---	Not mentioned	Not mentioned	Provided by APIMF's

Conclusion

The Common Technical Document (CTD) format has become the global standard for submitting regulatory documents for pharmaceutical products. The CTD format provides a harmonized structure for organizing and presenting data, facilitating the review process for regulatory authorities. The electronic Common Technical Document (eCTD) has further enhanced the efficiency of the submission process, enabling faster and more accurate review of regulatory documents. Software solutions such as PharmaReady, Take Solution, and Lorenz Life Science have streamlined the dossier preparation process, ensuring compliance with regulatory requirements. A comparison of CTD and eCTD requirements across different countries reveals variations in implementation

and acceptance. However, the overall trend towards harmonization and electronic submission is clear. As the regulatory landscape continues to evolve, it is essential for pharmaceutical companies to stay up-to-date with the latest requirements and best practices for dossier preparation. By leveraging software solutions and adopting a harmonized approach to regulatory submissions, companies can ensure timely and successful approval of their medicinal products.

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