JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

Requirements of Common Technical Document Preparation -A Technical Drive

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ABSTRACT:

The CTD is a harmonized registration dossier which can be submitted into Europe, USA, Japan, Canada and Australia. CTD is used for Drug products for human use, Biotechnological products, Herbal products and drug filing. CTD is mainly consists of five modules. Central Drugs Standard Control Organization (CDSCO), India has also decided to adopt CTD format for technical requirements for registration of pharmaceutical products for human use. Implementation of CTD is expected to significantly reduce time and resources needed by industry to compile applications for global registration.

Keywords: CTD, CDSCO, ICH, DCGI, NDA

Article history:
Received 19 Mar 2014
Accepted 14 April 2014
Available online 13 May 2014

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INTRODUCTION:

Drug approval is the goal of the long process of drug development. Once preclinical and clinical trial data have been collected a New Drug Application must be submitted to the regulatory authority for approval. Every drug, before receiving approval for marketing in India, or indeed many other countries, must undergo rigorous scientific testing and scrutiny to ensure that it is safe and effective for its intended use. Drug development starts with *in vivo* animal studies that primarily evaluate the pharmacology and potential toxicities of a product. Once these studies are complete, the sponsor of a drug submits an Investigational New Drug application (IND) for review. The IND contains the preclinical data and proposed plans for study in a human population. The information submitted in an IND is reviewed in the India by DCGI – CDSCO and a decision is made whether to allow a sponsor to begin clinical trials in humans.[1]

CTD- five modules

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.

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. Safety (toxicology studies)
5. Efficacy (clinical studies)

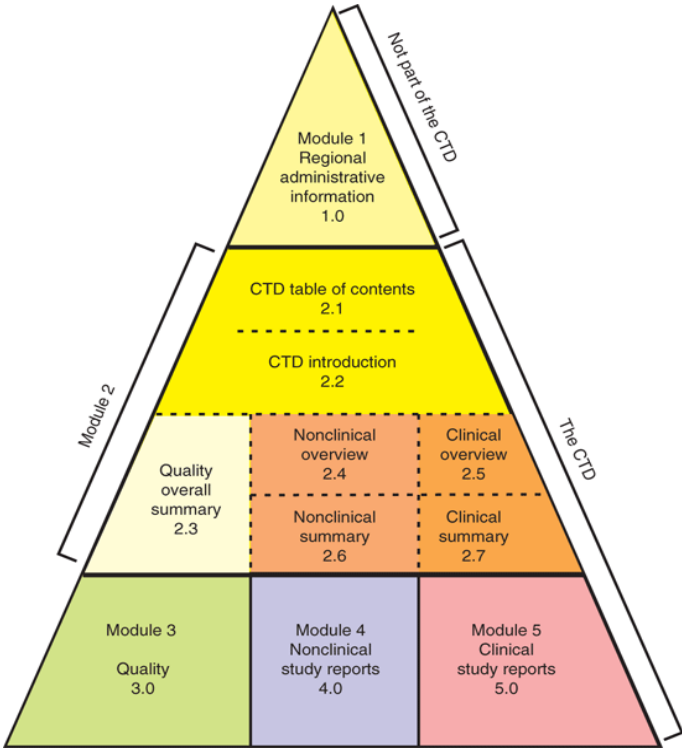
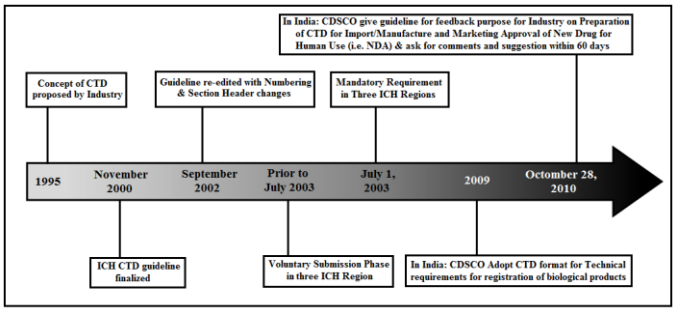


FIGURE 1: ICH CTD MODULE [2]

EVALUATION OF COMMON TECHNICAL DOCUMENTS

Efforts over the past 15–20 years by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) have resulted in a unified dossier for drug applications, the Common Technical Document for the registration of Pharmaceuticals for Human Use (CTD). [4]



General Requirements:

- Front type: Times new roman
- Front size: 12
- Paper size: A4

SIGNIFICANCE OF CTD: [1]

- Avoid generating and compiling different registration dossiers.
- Common format will significantly reduce the time and resources.
- Facilitates simultaneous submission in three regions.
- Facilitates exchange of information among regulatory authorities.
- Faster availability of new medicines.

TECHNICAL DATA OF COMMON TECHNICAL DOCUMENT:

Table 1: Administrative Information and Prescribing Information [5]

MODULE 1 REGIONAL ADMINISTRATIVE INFORMATION	
SECTION	**REQUIRMENTS**
1.1	**Covering letter**
	Comprehensive Table of content
1.2	**Application form (properly filled and signed by the qualified responsible)**
1.3	**Product Information**
	Summary of Product Characteristics (SPC)
	Labeling Information
	Patient Information Leaflet (PIL)
	Arabic Leaflet
	English Leaflet
	Artworks (Mock-ups)
	Samples (two original finished samples)
	Marketing authorisation holder, Contact persons, Company
	Orphan medicinal product designation
1.4	**Information on the Experts**
	Quality information
	Non-clinical information
	Clinical information
1.5	**Environmental Risk Assessment**
	Non-Genetically Modified Organism (Non-GMO)certificate
	Clinical Package Insert and Patient Information Leaflet amendments / updates
	Amendments in Medicines Register Details
1.6	**Pharmacovigilance**
	Pharmacovigilance system
	Risk Management Plan
1.7	**Certificates**
	Original legalized valid Certificate of a Pharmaceutical Product (CPP)
	Copy of valid GMP certificates for the manufacturing site(s)

	Certificate of Analysis - Drug Substance (At least 3 batches)
	Certificate of Analysis - Finished Product (At least 3 batches)
	Alcohol-content declaration
	Pork - free declaration
	TSE/BSE free certificate
	API certificate of suitability
	GMP certificate for the API source
	API Acknowledgment letter
	certificate for a Vaccine Antigen Master File (VAMF)
	certificate for a Plasma Master File (PMF)
	Relation-ship letters & Technical agreement between parties involved in contract manufacturing and/or marketing
	manufacturing site(s) registration certificate(s)
	Composition certificate with active ingredient(s), inactive ingredient(s) quantities per unit dose and functions
	The diluents and colouring agents in the product formula
	Patent letter with copy of the patent reference
	Registration and Marketing status in other countries(with copies of registration certificates)
1.8	**Pricing**
	Original legalized Price Certificate

Table 2: Common Technical Document Summaries

MODULE 2: COMMON TECHNICAL DOCUMENT SUMMARIES	
SR. NO	**CONTENTS**
2.1	CTD Table of Contents
2.2	CTD Introduction
2.3	Quality Overall Summary
2.4	Nonclinical Overview
2.5	Clinical Overview
2.6	Nonclinical Written and Tabulated Summary
	• Pharmacology
	• Pharmacokinetics
	• Toxicology
2.7	Clinical Summary
	Bio pharmaceutics and Associated Analytical Methods
	• Clinical Pharmacology Studies
	• Clinical Efficacy
	• Clinical Safety
	• Synopses of Individual Studies

Table 3: Quality [6]

MODULE 3: QUALITY	
SR NO.	**CONTENTS**
3.1	**Table of contents of Module 3**
3.2	**Body of data**
3.2.S	**DRUG SUBSTANCE**
	General information
	Nomenclature
	Structure
3.2.S.2	**Manufacture**
	Manufacturer(s)
	Description of Process and Process Controls
	Control of Materials
	Control of Critical Steps and Intermediates
	Manufacturing Process Development
3.2.S.3	**Characterization**
	Elucidation of Structure and Other Characteristics
	Impurities
3.2.S.4	**Control of Drug Substance**
	Specifications
	Analytical Procedures
	Validation of Analytical Procedures
	Batch Analyses
	Justification of Specification
3.2.S.5	**Reference Standards or Materials**
3.2.S.6	**Container/Closure Systems**
3.2.S.7	**Stability**
	Stability Summary and Conclusions
	Post -approval Stability Protocol and Commitment
	Stability Data
3.2.P	**DRUG PRODUCT**
3.2.P.1	**Description and Composition of the Drug Product**
3.2.P.2	**Pharmaceutical Development**
	Components of the Drug Product
	Excipients
	Drug Product
	Formulation Development
	Overages

	Physiochemical and Biological Properties
	Manufacturing Process Development
	Container Closure System
	Microbiological Attributes
	Compatibility
3.2.P.3	**Manufacture**
	Batch Formula
	Description of Manufacturing Process and Process Controls
	Controls of Critical Steps and Intermediates
	Process Validation and/or Evaluation
3.2.P.4	**Control of Excipients**
	Specifications
	Analytical Procedures
	Validation of Analytical Procedures
	Excipients of Human or Animal Origin
	Novel Excipients
3.2.P.5	**Control of Drug Product**
	Analytical Procedures
	Validation of Analytical Procedures
	Batch Analyses
	Characterization of Impurities
3.2.P.6	**Reference Standards or Materials**
3.2.P.7	**Container/Closure System**
3.2.P.8	**Stability**
	Stability Summary and Conclusions
	Post-Approval Stability Protocol and Stability Commitments
3.2.A	**Appendices**
	Facilities and Equipment
	Adventitious Agents Safety Evaluation
	Excipients
3.2.R	**Regional Information**
	Alcohol Content Declaration
	Porcine/Pork-content/origin
	The diluents and colouring agents in the product formula
3.3	**Literature References**

Table 4: Nonclinical Study Reports [7]

MODULE 4: NONCLINICAL STUDY REPORTS	
SR. NO.	**CONTENTS**
4.1	**TABLE OF CONTENTS OF MODULE 4**
4.2	**STUDY REPORTS**
4.2.1	**Pharmacology**
	Primary Pharmacodynamic
	Secondary Pharmacodynamic
	Safety Pharmacology
	Pharmacodynamic Interactions
4.2.2	**Pharmacokinetics**
4.2.3	**Toxicology**
	Single-Dose Toxicity
	Repeat- Dose Toxicity
	Genotoxicity
	Carcinogenicity
	Reproductive and Developmental Toxicity
	Local Tolerance
	Other Toxicity studies
4.3	**LITERATURE REFERENCES**

Table 5: clinical Study Reports [8]

MODULE 5: CLINICAL STUDY REPORTS	
SR. NO.	**CONTENTS**
5.1	**TABLE OF CONTENTS OF MODULE 5**
5.2	**TABULAR LISTING OF ALL CLINICAL STUDIES**
5.3	**CLINICAL STUDY REPORTS**
5.3.1	Reports of Bio-pharmaceutics studies
	Bioavailability (BA) Study Reports
	Bioequivalence (BE) Study Reports
	In vitro/In vivo Correlation (IV/IVC) study reports
	Reports of Bio-analytical and Analytical Methods for Human Studies
5.3.2	Reports of studies pertinent to pharmacokinetics using human biomaterials
	Plasma Protein Binding Study Reports
	Reports of Hepatic Metabolism and Drug Interaction Studies
	Reports of Studies Using other Human Biomaterials
5.3.3	Reports of human pharmacokinetic studies
	Healthy Subject PK and Tolerability
	Patient PK and Initial Tolerability
	Intrinsic Factor PK Study Reports
	Extrinsic Factor PK Study Reports
5.3.4	Reports of human Pharmacodynamic studies

	Healthy Subject Pharmacodynamic (PD) and PK/PD Study Reports
	Patient PD and PK/PD Study Reports
5.3.5	Reports of efficacy and safety studies
	Study Reports of Controlled Clinical Studies
	Study Reports of Un-Controlled Clinical Studies
5.3.6	Reports of post-registration experience
5.3.7	Samples of case reports forms and individual patient listings
5.4	**LITERATURE REFERENCES**

ACKNOWLEDGEMENT :

The authors are thankful to Dr. K. Pundarikakshudu, Principal of L. J. Institute of Pharmacy, Ahmedabad, India for providing all the facilities to carry out the work.

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