

CTD

INTRODUCTION

- 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.
- Globalization of the pharmaceutical industry has created the need to harmonize the recommendations for the development of new pharmaceuticals, as well as the regulatory requirements of various countries.
- Common format of submission will help in overcoming the 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.
- Most countries have adopted the CTD format. Hence, CDSCO has also decided to adopt CTD format for technical requirements for registration of pharmaceutical products for human use.



WHAT IS CTD ?

- The CTD is a set of specifications of a dossier (Record/Documents) for the registration of medicines.
- It is designed to be used across Europe, Japan and the United States.

WHAT IS CTD & WHAT ISN'T CTD.

CTD IS

A common application for preparing marketing authorizations in the three ICH regions.

A guideline that merely indicates an appropriate format for the data have been acquired.

CTD NOT

A statements of data required for applications.

A guideline that intended to indicate what studies are required.

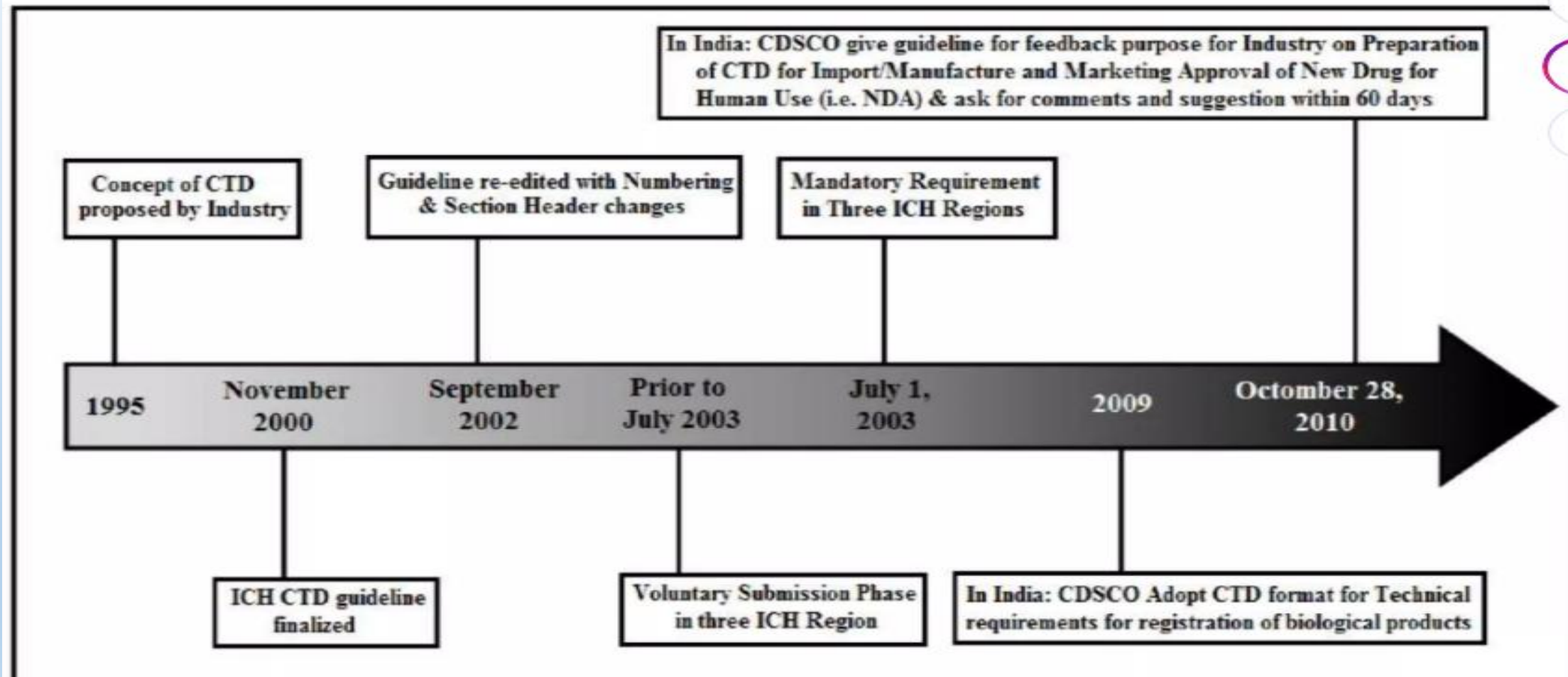
EVOLUTION OF CTD

- **In ICH Region**
- 1995: Concept of CTD proposed by Industry.
- November 2000: ICH CTD guideline finalized.
- September 2002: Guideline re-edited with Numbering & Section Header changes.
- Prior to July 2003: Voluntary Submission Phase in three ICH Region.
- 1 July 2003: Mandatory Requirement in three ICH Regions.

CONT.

- **In India**
- 2009: CDSCO Adopt CTD format for Technical requirements for registration of biological products.
- October 28, 2010: CDSCO give guideline for feedback purpose for Industry on Preparation of CTD for Import/Manufacture and Marketing Approval of New Drug for Human Use (i.e. NDA) & ask for comments and suggestion within 60 days.

THE EVOLUTION OF THE COMMON TECHNICAL DOCUMENT IS ILLUSTRATED IN FIGURE - 1



OBJECTIVE OF ICH TO PREPARE THE CTD



- The primary objective of the ICH is to avoid duplicative animal and human testing and to reach a common understanding of the technical requirements to support the registration process in the three ICH regions.
- These objectives are achieved through harmonized guidelines and result in a more economical use of human, animal and material resources, as well as the elimination of unnecessary delays in the global development and availability of new medicines.
- Maintaining safeguards on quality, safety and efficacy, and regulatory obligations to protect public health. With the development of the Common Technical Document (CTD), the ICH hopes to accomplish many of its objectives.

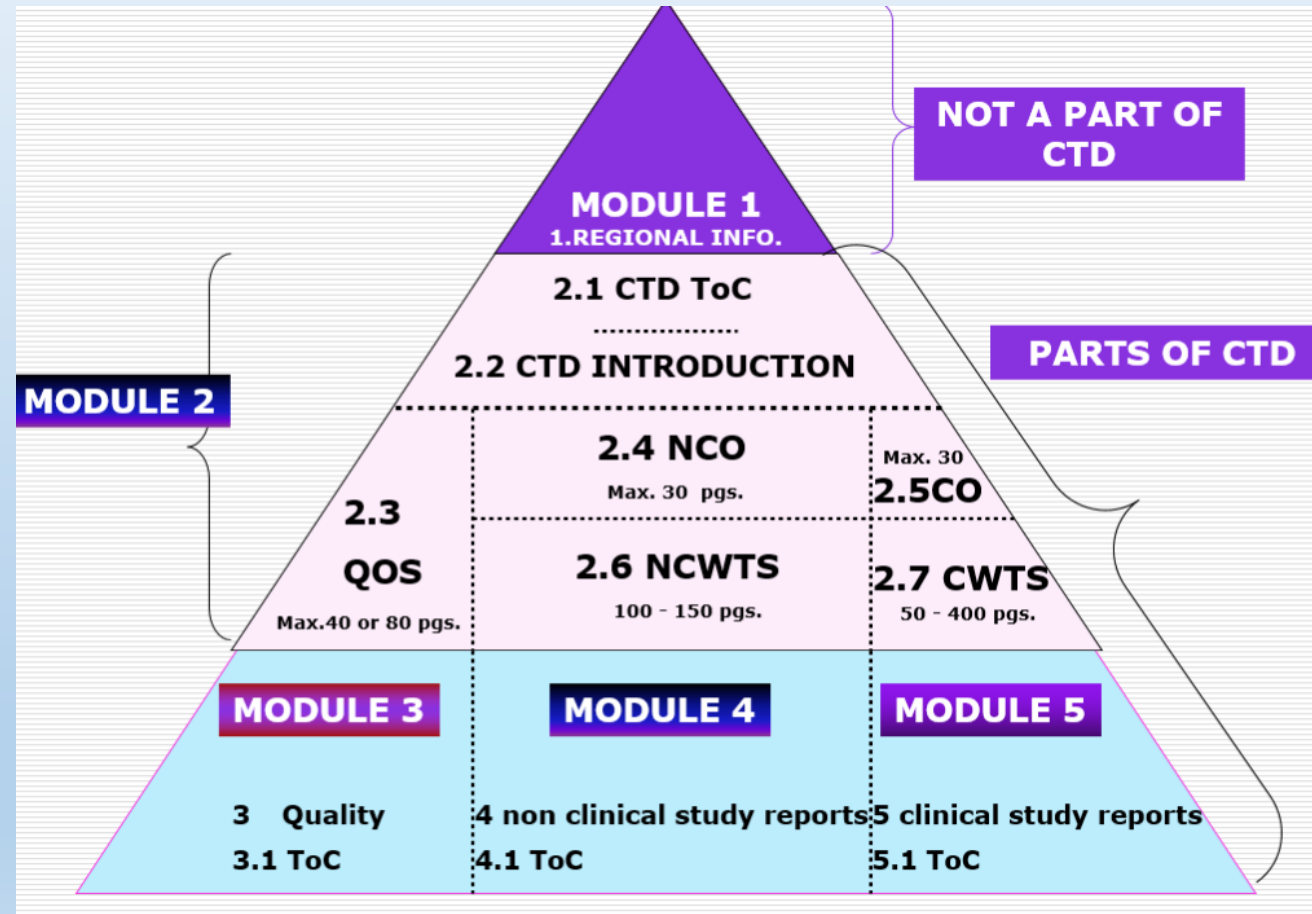
CTD STRUCTURE

- 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)

COMPONENTS OF THE CTD

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

CTD TRIANGLE



MODULAR ORGANIZATION OF CTD

- The CTD is organized into five modules:
- **MODULE 1: Regional Administrative Information**
- Module 1 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. The content and format of this module can be specified by the relevant regulatory authorities.
- **In India:** 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: Overview and summary of modules 3 to 5**
- 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 nonclinical overview and the clinical overview, as well as the non-clinical written summaries and the tabulated summaries, and the clinical summary.
- **In India:** 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 3: Quality (Pharmaceutical Documentation)**
- The Quality section of the Common Technical Document (M4Q) provides a harmonized 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.

- **MODULE 4: Safety (Toxicology Studies – Non Clinical Study Report)**
- 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 organization 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.

- **MODULE 5: Efficacy (Clinical Study Report)**
- 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 summarization and integration.
- Clinical Study Reports and raw data (where applicable) are included in Module 5 of the CTD.

ADVANTAGES OF CTD

- The main aim behind implementing a common format of submission is to make the reviewing of each application more easy and also to avoid omission of critical data or analyses. Omissions of such data can result in unnecessary delays in approvals.
- A common format for the technical documentation will significantly reduce time and resources needed to compile applications for registration of human pharmaceuticals and will ease the preparation of electronic submission.
- Implementation of CTD is expected to significantly reduce time and resources needed by industry to compile application for global registration.¹
- CTD not only help in raising the Indian standard but also will help to bring a proper structure to the whole process of filling an application.
- In addition, exchange of regulatory information between regulatory authorities will also be simplified.

SILENT BENEFITS OF CTD

- Global harmonization of applications.
- Provides standards to prepare submission-ready documents in the IND phases.
- Standardization assists project management and information management.
- Facilitates life cycle management.
- Facilitates drug development planning.