COMMON TECHNICAL DOCUMENT

CONTENTS:

INTRODUCTION

- The Common Technical Document 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.
- The FDA characterized the CTD as “An information package of clinical ,non-clinical, manufacturing, technical data in the same format and with the same content, that would be submitted for registering new drugs in all three ICH regions i.e.; US, European Union and Japan.

Objective

- To increase international harmonization of technical requirements to ensure that safe, effective, and high quality medicines are developed and registered in the most efficient and cost-effective manner.
- Activities have been undertaken to promote public health, prevent unnecessary duplication

ORIGIN OF CTD…

CTD

CTD IS A JOINT EFFORT OF 3 REGULATORY AGENCIES:

1. European Medicines Agency (EMEA, Europe),

2. Food and Drug Administration (FDA, USA) and

3. Ministry of Health, Labour and Welfare (MHLW,Japan).

CTD is maintained by ICH through EWG.

It has been adopted by several other countries
including Canada and Switzerland.

- Any guideline which is given by ICH passes through different steps.
- These different steps are called STATUS of that GUIDELINE.

STATUS	FUNCTIONALITY
Step 1	Development of Consensus
Step 2	Text released for consultation
Step 3	Consultation outside ICH
Step 4	ICH guideline finalized
Step 5	Implementation

Status of CTD
STEP 4 STATUS ACHIEVED IN NOV.2000 IN 5TH ICH CONFERENCE IN SANDIEGO..
STEP 5 STATUS ACHIEVED IN MAY.2001 IN ICH MEETING IN TOKYO.
GUIDANCE MADE AVAILABLE TO INDUSTRY IN OCTOBER 16,2001 BY FDA.

Significance

- 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.

IS CTD MANDATORY FOR ALL TYPE OF SUBMISSIONS?

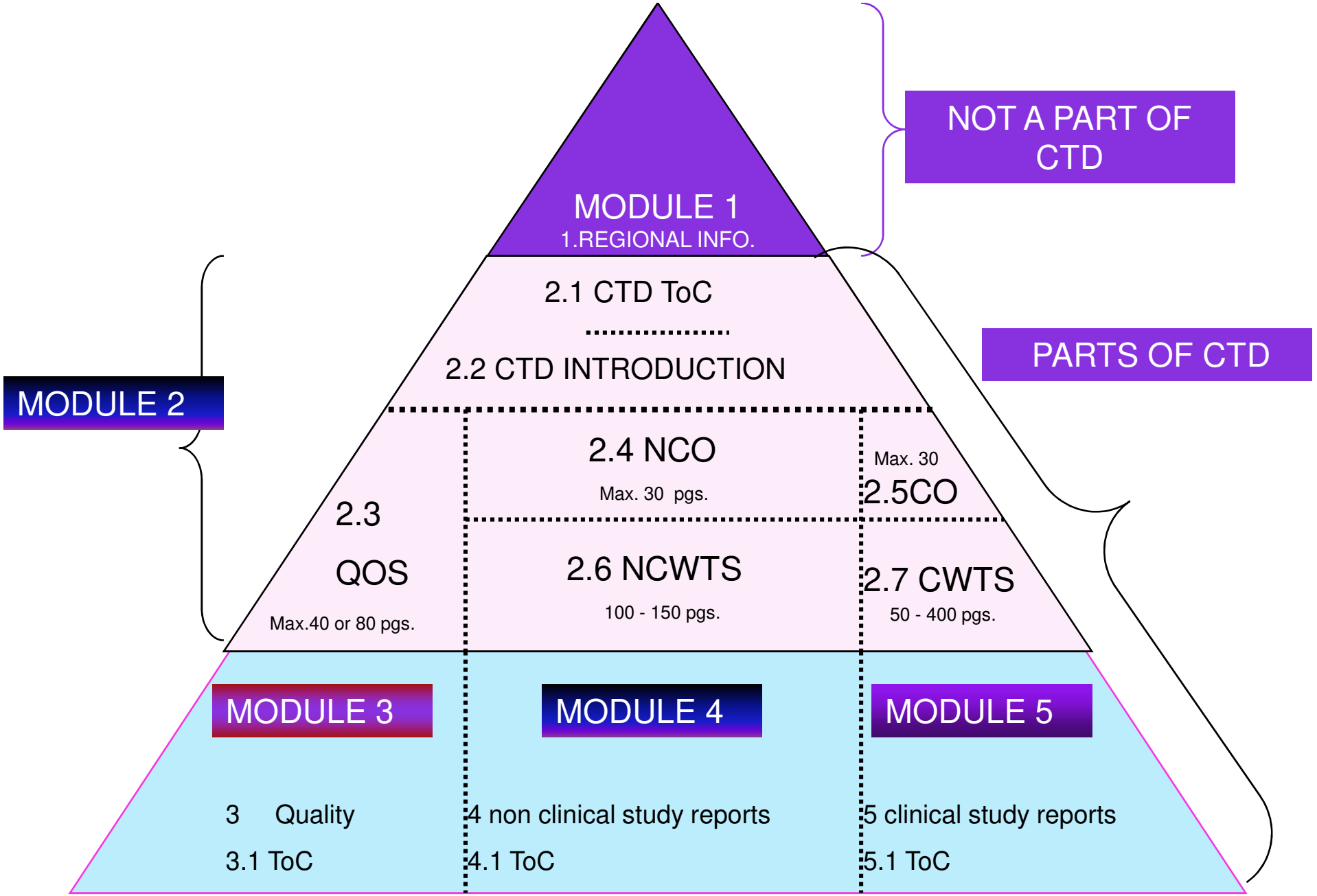
CTD is mandatory for all Import and/or manufacture and marketing approval of new drugs (New chemical entity, new indication, new dosage forms, new route of administration etc.)

- As a finished pharmaceutical product, for first time submission and for subsequent applications until 4 years.
- Modified release formulations (even after 4 years of approval by CDSCO)
- Fixed Dose Combinations under item (a) of Appendix VI of Schedule Y of Drugs and Cosmetics Rules 1945.

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

ORGANISATION OF CTD

- It should be organized into 5 modules.
  - Module-1→Administrative&prescribing information.
  - Module-2→Overview&summery of modules 3-5.
  - Module-3→Quality(pharmaceutical documentation).
  - Module-4→Safety toxicology studies.
  - Module-5→Efficacy clinical studies.
- Module-1 is region specific.
- Module-2,3,4&5 are intended to be common for all regions.


NOT A PART OF CTD
MODULE 1
1.REGIONAL INFO.
PARTS OF CTD
MODULE 2
2.1 CTD ToC
2.2 CTD INTRODUCTION
2.4 NCO
Max. 30 pgs.
Max. 30
2.5CO
2.3
QOS
Max.40 or 80 pgs.
2.6 NCWTS
100 - 150 pgs.
2.7 CWTS
50 - 400 pgs.
MODULE 3
MODULE 4
MODULE 5
3 Quality
3.1 ToC
4 non clinical study reports
4.1 ToC
5 clinical study reports
5.1 ToC

MODULE-1:

- This module should contain documents specific to each region.
- Ex: Application forms regarding the prescribing information, proposed label.
- This module is not part of the CTD.
- The content & format of this module can be specified by the relevant regulatory authorities.

MODULE-2:

- It should begin with a general introduction to the pharmaceutical, including it's pharmacological class, mode of action& proposed clinical use. In general, the information should not exceed one page.
- Module-2 should contain 7 sections in the fallowing order:

1) CTD table of contents.
2) CTD introduction.
3) Quality& overall summery.
4) Non-clinical overview.
5) Clinical overview.
6) Non-clinical written& tabulated summaries.
7) Clinical summary.

- The individual organization of these summaries is described in three separate documents.
  a) M4 Q→ The CTD Quality.
  b) M4S → The CTD Safety.
  c) M4 E → The CTD Efficacy.

a) M4 Q:

The Quality section of the CTD provides a harmonized structure and format for presenting CMC (Chemistry, Manufacturing, Controls) information in a registration dossier.

- The table of contents include sections on Drug substances & Drug products.

- Due to the fact that many CMC topics have not yet been the subject of ICH guidelines

  (Ex: Drug product manufacture, Drug substance synthesis), the content of CTD-Q is not totally harmonized.

b) ***M4-S:***

CTD for the Registration of pharmaceuticals for human use → Safety.

- Module-2 → Non-clinical overview & Non-clinical summary.
- Module-4 → Non-clinical study reports.

- M4 S describes the structure and format of the non-clinical data in module-2 of the CTD.
- It also provide the organisation of module-4 i.e.; the non-clinical study reports.
- Non-clinical overview→ should present an integrated and critical assessment of the pharmacological, pharmacokinetic & toxicological evaluation of the pharmaceuticals.(should not exceed 30 pages)
- The non-clinical written summaries (100-150 pages) are to provide more extensive summaries and discussion of non-clinical information on pharmacology, pharmacokinetics & toxicology.

c) ***M4-E:***

The CTD For the Registration of pharmaceuticals for human use .

- Module -2 → Clinical overview & clinical summery.
- Module-5 → clinical study reports.
- M4 E 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:

1. **Clinical overview:** A short document that provides a critical assessment of the clinical data.
2. **Clinical summary:** A longer document that focuses on data summarization and integration.

MODULE-3:(Quality)

- Information on Quality should be presented in the structured format .
- This is described in the guidance M4-Q.
- Literature References

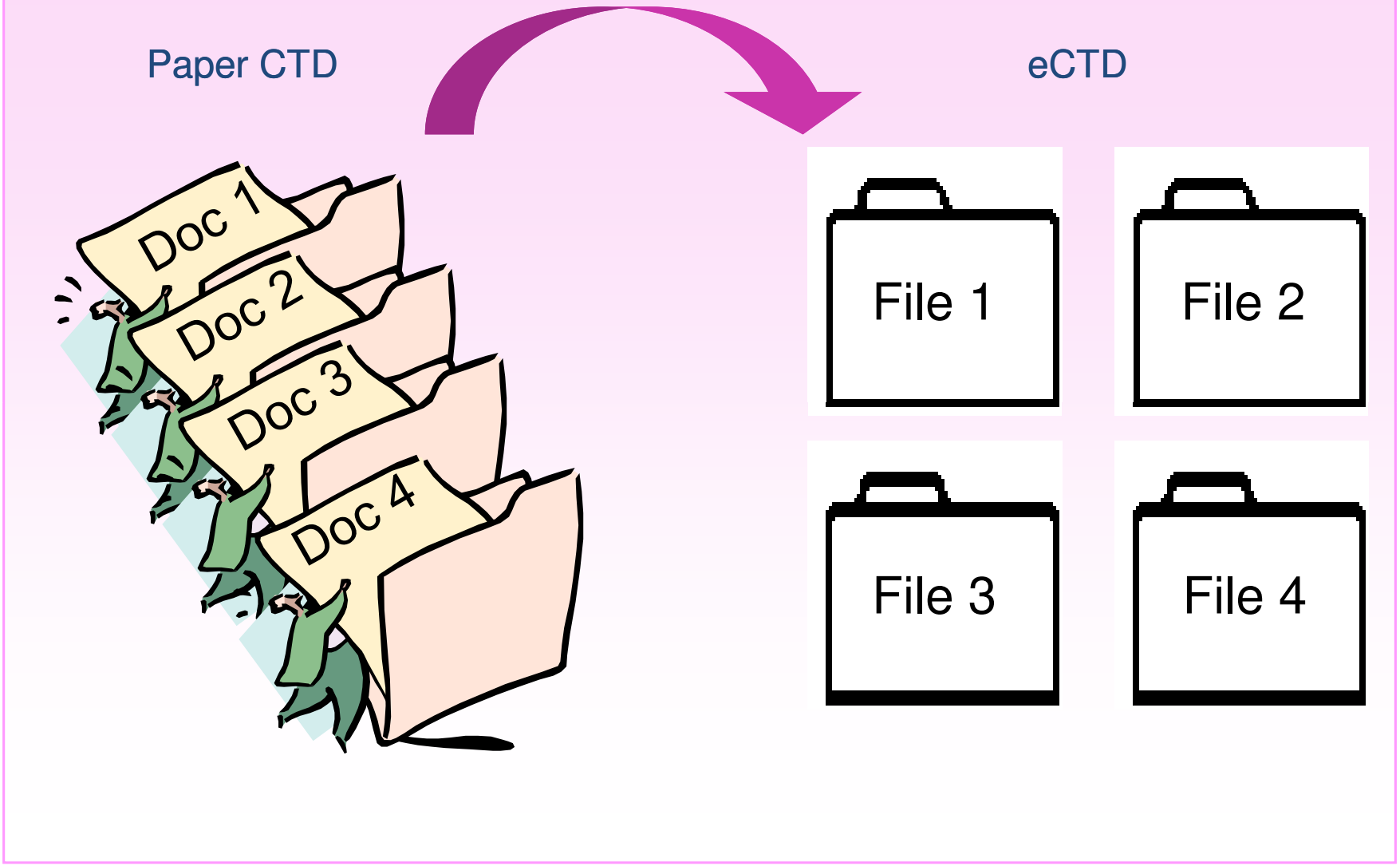
MODULE-4:

- In this explains the non-clinical study reports.
- The non-clinical study reports should be presented in the order described in the guidance M4- S.
- Literature References.

MODULE-5:

- In this explains the clinical study reports.
- The human study reports and related information should be presented in the order described in the guidance M4- E.
- Literature References.

Type of Study	Study Identifier	Location of Study Report	Objective (s) of the Study	Study Design and Type of Control	Test Product(s); Dosage Regimen & Route	No. of Subjects	Healthy Subjects or Diagnosis of Patients	Duration of Treatment	Study Status; Type of Report
BA	001	Vol 3, Sec. 1.1, p. 103	Absolute BA IV vs Tablet	Cross-over	Tablet, 50mg single dose, oral. 10 mg IV	20	Healthy Subjects	Single dose	Complete: Abbreviated
BE	002	Vol 4, Sec. 1.2, p. 254	Compare clinical study and to-be-marketed formulation	Cross-over	Two tablet formulations, 50 mg, oral	32	Healthy Subjects	Single dose	Complete: Abbreviated
PK	1010	Vol 6, Sec. 3.3, p. 29	Define PK	Cross-over	Tablet, 50mg single dose, oral	50	Renal Insufficiency	Single dose	Complete: Full
PD	020	Vol 6, Sec. 4.2, p. 147	Bridging study between regions	Randomised placebo-controlled	Tablet, 50mg, multiple dose, oral, every 8 hrs	24 (12 drug, 12 placebo)	Patients with primary hypertension	2 weeks	Ongoing; Interim
Efficacy	035	Vol 10, Sec. 5.1, p. 1250	Long term: Efficacy & Safety; Population PK analysis	Randomised active-controlled	Tablet, 50mg, oral, every 8 hrs	300 (152 test drug, 148 active control)	Patients with primary hypertension	48 weeks	Complete; Full


Paper CTD
eCTD
Doc 1
Doc 2
Doc 3
Doc 4
File 1
File 2
File 3
File 4

eCTD:electronic CTD

- Developed by M2 EWG (Multidisciplinary 2 Expert Working Group) of ICH.

Industry <-----> Message <------> Agency

Paper submission
has been replaced
by electronic
submission

Characteristics of eCTD:-

1. Files Referenced in the XML Backbone(s)

   (Extensible Markup Language)

REASONS:

1. It manages the large data for the entire submission and for each document within the submission.
2. This XML backbone allows the eCTD submission to be viewed via a web browser and can be loaded on a Web server.

2. The file formats that can be included in the eCTD are Portable Document Format (PDF) and XML.

   However other formats can be used for graphs and images.

   JPEG

   PNG

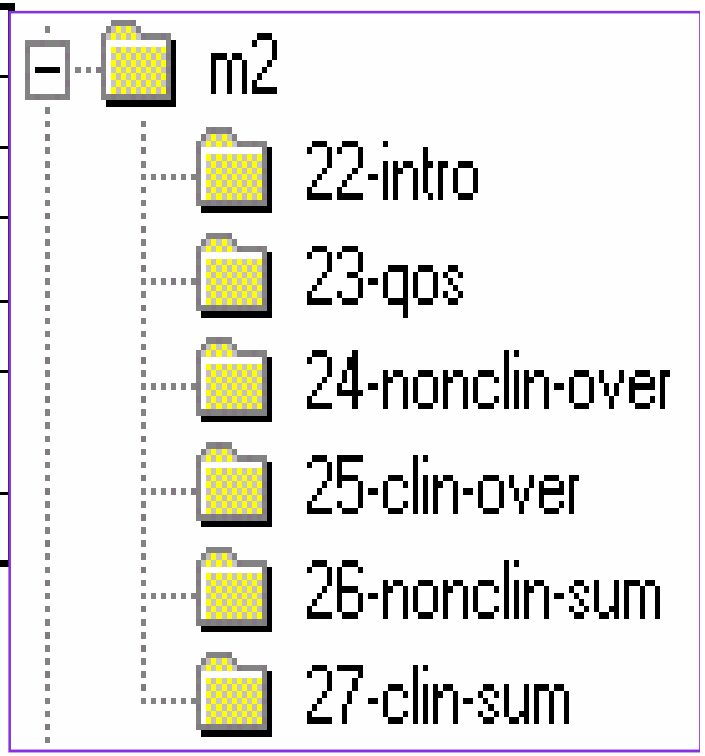
   GIF

   -may be used for higher resolution.

Nomenclature for files and eCTD submission.

EXAMPLE:- MODULE 2 FILE NOMENCLATURE AND eCTD submission

Description	**File Name**
2.2 introduction	*22-intro*
2.3 Quality overall summary	*23-qos*
2.4 Non clinical Overview	*24-nonclin-over*
2.5 Clinical Overview	*25-clin-over*
2.6 Non clinical Written and Tabulated Summaries	*26-nonclin-sum*
2.7 Clinical summary	*27-clin-sum*



CONCLUSION

- There is now a common format for the submission of Marketing Authorizations Applications across the three ICH regions - Europe, Japan and the USA. This should facilitate pharmaceutical companies to make simultaneous filings in the ICH regions as it will eliminate the extensive work previously required to convert, for example, a US dossier to an EU dossier and vice versa.

REFERENCES

- Guidelines on common technical document (CTD) 28.10.2010, central drugs standard control organization (CDCSO).
- www.wikipedia. Com
- www.ICH.org
- www.fda.gov/cder/regulatory/ersr/ectd.htm
- http://esubmission.eudra.org/