eCTD Implementation in China
- technology, processes, standards & organization

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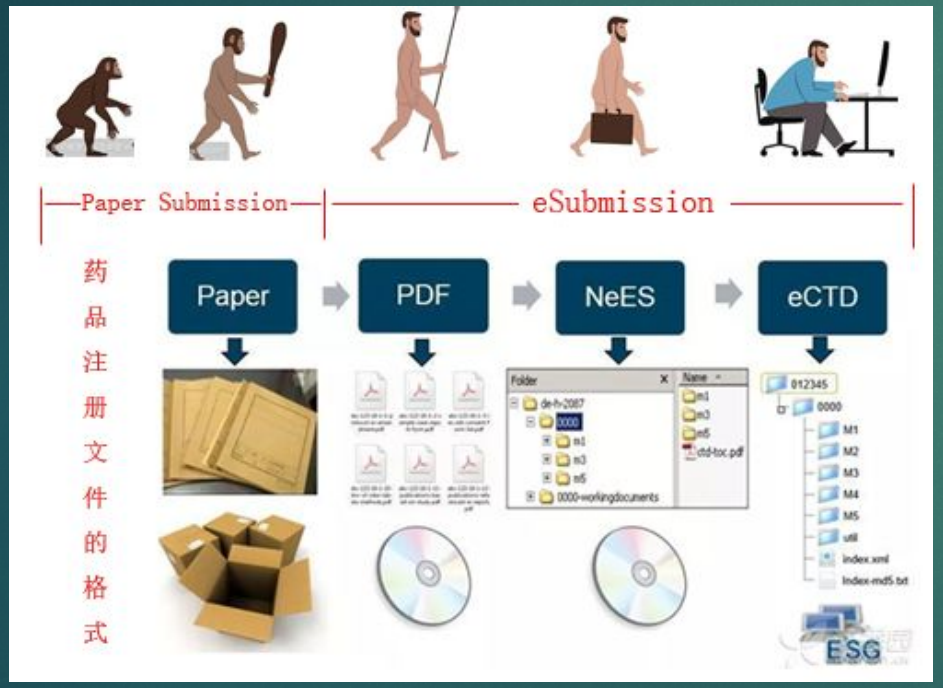
PhUSE Beijing Single Day Event, May-17, 2019

Ways of Submission



- **Paper Submission**
  - ✓ Still a way of filling drug registration documents in most countries and regions today
- **eCTD Submission**
  - ✓ A PDF file package with XML structure combining a large number of PDF files organically
  - ✓ Life cycle management embedded in the registration files by defining the properties of the PDF file

eCTD Submission Workflow

CD & Gateway

Sponsor

Regulatory Authoring

Submission documents authoring & QC

eCTD Publishing

Modification & publishing
Validation & adjustment
Submission

Portal

Server

Documents receiving & validation

HA

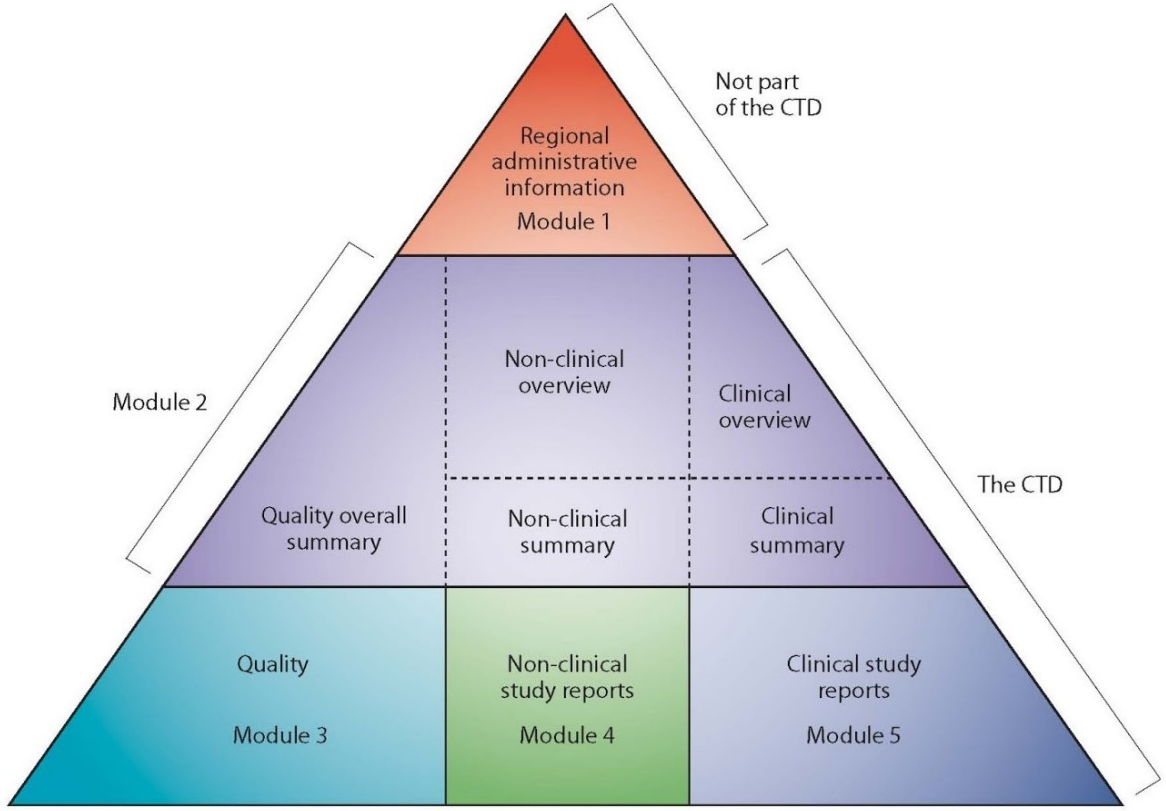
Review & Approval

Documents review
Questions & feedback
Approval

e-Document Management Systems

HA eCTD Document Management Systems

CTD Triangle



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.

Global Action

2003	• EU & Japan mandate CTD • US strongly recommend CTD for NDAs
2008	• eCTD v3.2.2 released • US mandated eCTD format for all eSubmissions
2010	• EU mandated eCTD for Centralized Procedures
2017	• US mandated eCTD for all submissions
2019	• Planning and preparation for the implementation of eCTD 4.0

China HA Action

2017

- Draft version of eCTD structure and guideline released

July 2018

- Vendor confirmed by HA

March 2019

- eCTD technical conformance guidelines released for public comments

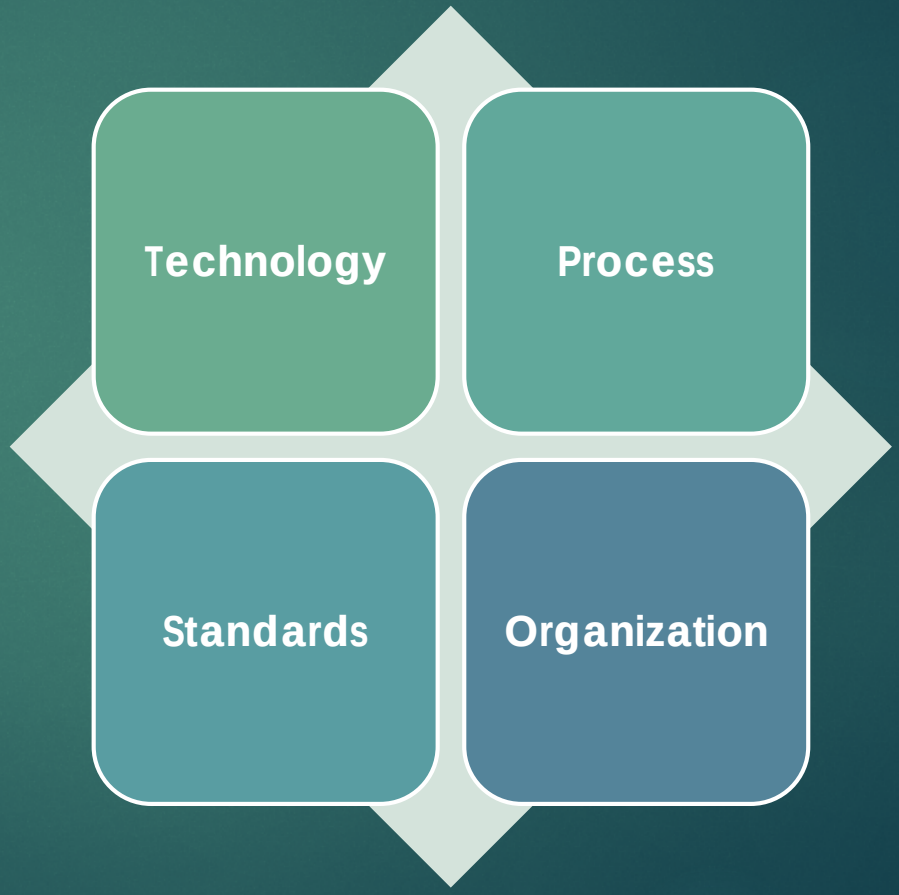
China HA Action

- On July 02, 2018, the Chinese National Medical Products Administration's (NMPA) Center for Drug Evaluation (CDE) selected **Shanghai Baosight Software** Co., Ltd. in a tender to establish the eCTD data management system, and **LORENZ** was chosen by Baosight as **software provider** in this project.

  https://www.lorenz.cc/News/press-releases/press-release.cfm?ID=235

Business Impact to China Sponsors

- eCTD submission is a fundamental change to the way clinical development line functions work today
- Preparation for eCTD submission may focus on four main areas



Technology

- **Vendor selection**
  - ✓ Extedo, **Lorenz**, DXC, Global Submit, Collietech, etc.
  - ✓ Simultaneous update in line with CDE for technical updates
- **Regional files**
  - ✓ cn-regional.xsd for defining eCTD cover letter and M1 heading
  - ✓ cn-regional.xsl for defining eCTD M1 stylesheet

Technology

- **STF file-tags (valid-values.xml v5)**
  - ✓ Organizes study information into meaningful, standardized headings
  - ✓ Allows reviewer to quickly understand what has been submitted
  - ✓ Helps guide reviewer to specific documents they are looking for
  - ✓ Provides consistency over the lifecycle of the regulatory application

  Examples

File	Tag
SDTM	data-tabulation-dataset-sdtm
ADaM	analysis-dataset-adam
define.xml	data-tabulation-data-definition
acrf	annotated-crf

Technology

- **Controlled vocabularies enable interoperability**
  - ✓ One of the essential components of eCTD v4.0 which will ultimately enable a clear, unambiguous communications between systems sending and receiving XML messages
  - ✓ Will be governed by multiple entities – ICH, regional authorities such as FDA and other designated third-party organizations

Technology

- **Naming convention**
  - ✓ Underscore “_” is allowed to use in file naming or folder naming

- **Application number**
  - ✓ E.g., **x201912345**,
  - ✓ (**x**=NDA, **y**=ANDA, **I**=IND) + (**year** in 4 digits) + (**serial number** in 5 digits)

Process

- **Trainings in place**
  - ✓ eCTD overview
  - ✓ eCTD naming convention
  - ✓ CRT publishing process
  - ✓ **eCTD folder structure for study datasets**
  - ✓ **eCTD technical rejection criteria for study data**
  - ✓ eCTD review and QC

Process

(eCTD technical rejection criteria for study data)

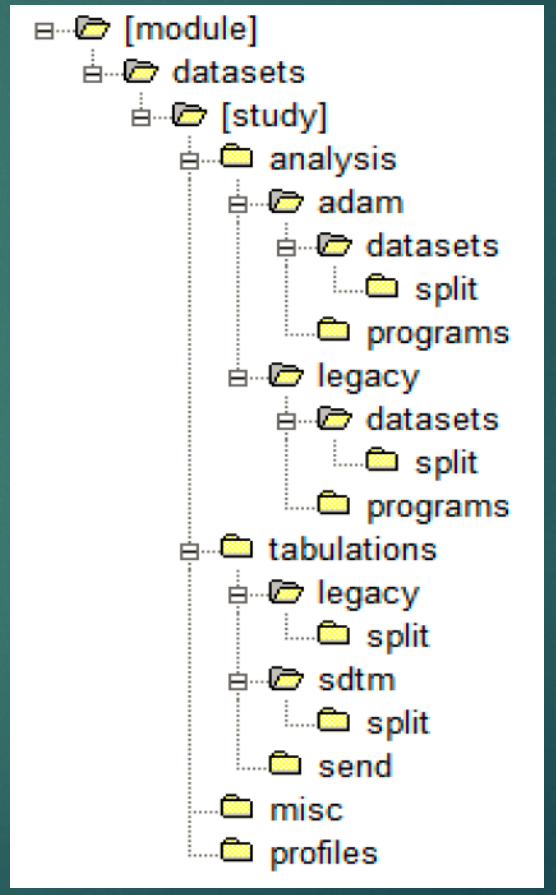
- The FDA **may refuse to file (RTF) for NDAs and BLAs, or refuse to receive (RTR) for ANDAs**, an electronic submission that does not have study data in conformance to the required standards specified in the FDA Data Standards Catalog.

High	Medium
• TS dataset must be present • DM dataset and define.xml must be present in M4; DM & ADSL dataset, define.xml must be present in M5	• The correct STF file-tags must be used for all standardized datasets • For each study no more than one dataset of the same name should be submitted as new

Process

(eCTD folder structure for study datasets)

- **FDA Study Data Technical Conformance Guide, Section 7.1 eCTD Specifications**
  - ✓ Figure 1: Folder Structure for Study Datasets
  - ✓ Table 2: Study Dataset and File Folder Structure and Description



Standards

- **ICH Guidelines (Chinese translated version)**
  - ✓ eCTD Specification v3.2.2
  - ✓ ICH The eCTD Backbone File Specification for Study Tagging Files
  - ✓ ICH Specification for Submission Formats for eCTD
  - ✓ ICH eCTD IWG Question and Answer and Specification Change Request Document
  - ✓ ICH E3 Structure and Content of Clinical Study Report

Organization

- **Involvement from multiple line functions**
  - ✓ Regulatory Affairs
  - ✓ CMC
  - ✓ Clinical Development, DMPK
  - ✓ Trial Management & Operation
  - ✓ Statistician, Data Management, Programming
  - ✓ ...
- **Cross-functional ready for eCTD**
- **All of documents should be uploaded and finalized in e-Document Management System**

Once eCTD, always eCTD