Marketing Authorisation

Learning objectives

Students will be able to:

1. Explain the purpose of marketing authorization in the pharmaceutical industry.
2. Outline the formatting and organizational principles of the Common Technical Document (CTD) and its role in streamlining the documentation process for marketing authorization.
3. Describe the composition of the registration commission in Algeria and the specific steps involved in the registration process.

Table of content

1. Introduction

Marketing authorization or registration is a crucial step in the process of bringing pharmaceutical products to market. It represents the formal approval from regulatory authorities that a particular drug or medical product meets the required safety, quality, and efficacy standards for public use. The Common Technical Document serves as a standardized format for compiling essential information and data to support this authorization. It is like a common language for the pharmaceutical world.

Before the CTD: Different regions had their own rules for new drug submissions. Imagine a puzzle with missing pieces; it was complicated.

Collaborative Solution: In 2000, experts from three major regions (EU, USA, and Japan) teamed up to simplify the process.

CTD's Goal: The CTD aimed to create a common template, like a universal language, for drug documentation.

Benefits: It reduces the time and effort needed for drug approvals, streamlines communication, and eases electronic submissions.

Global Adoption: These guidelines became a global standard for drug submissions.

Going Digital: As technology advances, the paper CTD is evolving into the eCTD, keeping up with the digital age.

2. General principles

To maintain clarity and transparency, the Common Technical Document (CTD) follows specific formatting guidelines:

- The ICH M4 guidance advises that documents should be designed for both A4 paper (EU and Japan) and 8.5 × 11" paper (USA).
- Narrative text in the CTD should use Times New Roman, 12-point font for consistency.
- Define acronyms and abbreviations the first time they appear in each module to prevent confusion.
- Literature references should be cited at the end of each module following the Uniform Requirements for Manuscripts Submitted to Biomedical Journals.

- All documents in the CTD should start numbering from page 1. However, for individual literature references, you can rely on existing journal page numbering.
- There's no need to display page numbers as '1 of n', where 'n' is the total number of pages in the document.
- Every page in a document must have a unique header or footer briefly identifying its subject matter. This typically includes an abbreviation of the full section number and title (e.g., 2.7 Clinical Summary).

These guidelines aim to ensure that the CTD's format is consistent, clear, and universally understandable, promoting efficiency and precision in pharmaceutical documentation.

3. Overall organisation of the CTD

The Common Technical Document (CTD) is organised according to the ICH M4 guidelines and includes a granularity section that provides guidance on document location and pagination within the CTD dossier. The CTD dossier is divided into five main modules (see Figure 1).

Module 1: Regional administrative information
Module 2: Overviews and Summaries of Modules 3–5
Module 3: Quality (pharmaceutical documentation)
Module 4: Non-clinical reports (pharmacology/ toxicology)
Module 5: Clinical study reports (clinical trials).

Module 1: Regional administrative information

It contains region-specific documents like application forms and proposed labels, its content and format vary by Regulatory Authority.

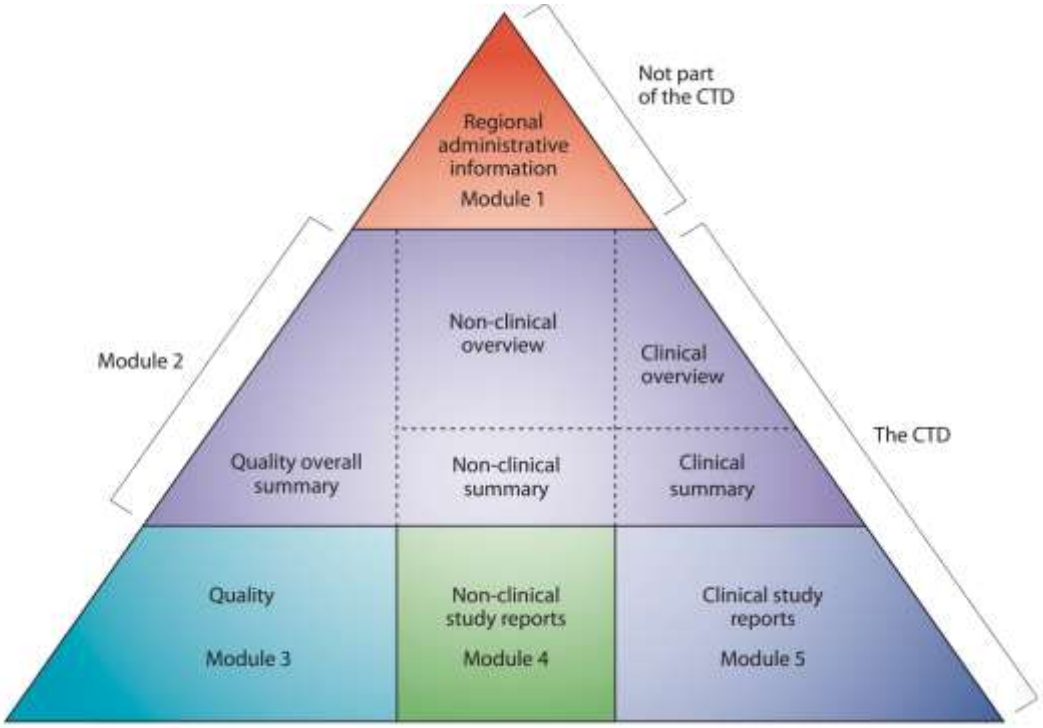

Figure: The CTD triangle.

Module 2: CTD overviews and summaries

Module 2 of the Common Technical Document (CTD) contains overviews and summaries of the data presented in Modules 3-5. It is intended to provide a high-level overview of the drug and its development to the regulatory authority. Module 2 contains 7 sections that should be maintained in the following order:

2.1 Table of contents
2.2 Introduction
2.3 Quality Overall Summary
2.4 Non-clinical Overview
2.5 Clinical Overview
2.6 Non-clinical Written and Tabulated Summaries
2.7 Clinical Summary.

Module 3: Quality

Module 3 compiles reports on the product's chemistry, manufacturing processes, and quality control. The ICH M4Q guideline provides detailed instructions for the contents of Module 3. This module is divided into sections for both the drug substance and the drug product, each with fixed headings that should not be altered.:

3.1. TABLE OF CONTENTS OF MODULE 3
3.2. BODY OF DATA
3.2.S DRUG SUBSTANCE
3.2.S.1 General Information
Nomenclature, Structure, General Properties
3.2.S.2 Manufacture
Manufacturer(s) , Description of Manufacturing Process and Process Controls, Control of Materials , Controls of Critical Steps and Intermediates , Process Validation and/or Evaluation , Manufacturing Process Development.
3.2.S.3 Characterisation
Elucidation of Structure and other Characteristics, Impurities
3.2.S.4 Control of Drug Substance
Specification, 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 System
3.2.S.7 Stability
Stability Summary and Conclusions, Post-approval Stability Protocol and Stability 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, Drug Product, Manufacturing Process Development, Container Closure System, Microbiological Attributes, Compatibility.
3.2.P.3 Manufacture
Manufacturer(s), 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, Justification of Specifications, Excipients of Human or Animal Origin, Novel Excipients.

3.2.P.5 Control of Drug Product

Specification(s), Analytical Procedures, Validation of Analytical Procedures, Batch Analyses, Characterisation of Impurities, Justification of Specification(s)

3.2.P.6 Reference Standards or Materials

3.2.P.7 Container Closure System

3.2.P.8 Stability

Stability Summary and Conclusion, Post-approval Stability Protocol and Stability Commitment , Stability Data.

3.2.A APPENDICES

3.2.A.1 Facilities and Equipment

3.2.A.2 Adventitious Agents Safety Evaluation

3.2.A.3 Excipients

3.2.R REGIONAL INFORMATION

3.3 LITERATURE REFERENCES

Module 4: Non-clinical study reports

The structure and content of Module 4 is specified in the ICH M4S guidelines. The main headings in this section should be maintained in the following order:

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.

Module 4 is not applicable to generic drugs

Module 5: Clinical study reports

The structure and content of Module 5 is specified in the ICH M4E guidelines. The main headings in this section should be maintained in the following order:

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 biopharmaceutic studies
  5.3.2 Reports of studies pertinent to pharmacokinetics using human biomaterials
  5.3.3 Reports of human pharmacokinetic (PK) studies
  5.3.4 Reports of human pharmacodynamic (PD) studies
  5.3.5 Reports of efficacy and safety studies
  5.3.6 Reports of post-marketing experience
  5.3.7 Case report forms and individual patient listings
5.4 Literature references.

Module 5 is replaced by bioequivalence study for the generic drugs

4. **The registration process for pharmaceutical products in Algeria**

According to the Algerian executive order 20-325, dated November 22, 2020, which sets out the conditions for registering pharmaceutical products, the registration in Algeria is as follows:

Pre-submission Request

i. Submit a pre-submission request to the National Agency of Pharmaceutical Products (ANPP) with 25% fee payment receipt.
ii. Receive a deposit receipt.
iii. The Director General of ANPP reviews the request and may:
    - Invite the establishment to submit a full registration dossier if the pre-submission is acceptable.
    - Seek the clinical experts committee's opinion and refer it to the registration commission.
    - Directly present the request to the registration commission.
iv. The commission provides its opinion within 30 days.

Submission Request

After the pre-submission request is accepted

i. Submit registration request along with samples within 1 year.
ii. File presented in CTD format.
iii. Pay additional registration fees 75%.
iv. Verify admissibility of the file within 8 days.
v. Conduct a technical evaluation.
vi. Address any observations.
vii. Declare no conflict of interest for experts.
viii. Consider site visits if necessary.
ix. Expedite evaluation for some medicines.
x. Involve energy sector for radiopharmaceutical drugs.
xi. Review by the commission within 30 days.
xii. Submit commission's opinion within 8 days.
xiii. Certify no modifications within 15 days.
xiv. Make a final decision within 150 days (extendable for up to 90 days in exceptional cases).
xv. Refuse if criteria not met, with justification.

The registration commission is composed of 10 experts or more as follows:

i. one representative of the minister responsible for the pharmaceutical industry, with skills and qualifications in the pharmaceutical field, president;
ii. one representative of the minister responsible for health, with skills and qualifications in the pharmaceutical field;
iii. one representative of the national health security agency, with skills and qualifications in the pharmaceutical field;
iv. one expert in pharmaceutical chemistry;
v. one expert in galenic pharmacy;
vi. one expert in pharmacology;
vii. one expert in toxicology;

viii. one expert in pharmacovigilance;
ix. one expert in biology;
x. one representative of the committee of clinical experts per therapeutic class concerned by the work of the commission, listed on the agenda.

The commission can call on any person who, because of their skills and qualifications, can help in its work.

1. Conclusion

The CTD has been largely successful in meeting its objectives of providing a common format for the information included in a submission dossier. However, it is of debate whether this has resulted in the suggested reductions in time and resources needed to compile applications.

References

- ICH M4 (R4) Guideline
- ICH M4E (R2) Guideline
- ICH M4Q (R1) Guideline
- ICH M4S (R2) Guideline
- Executive Decree No. 20-325 of 6 Rabie Ethani 1442 corresponding to November 22, 2020 relating to the terms of registration of pharmaceutical products. Official Journal Of The Algerian Republic N° 69.