The Common Technical Document (CTD)

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Glossary

- A **biosimilar product** is a biological product that is approved based on a showing that it is highly similar to an FDA-approved biological product, known as a reference product, and has no clinically meaningful differences in terms of safety and effectiveness from the reference product.
- **Pharmacovigilance** (PV or PhV), also known as drug safety, is the pharmacological science relating to the collection, detection, assessment, monitoring, and prevention of adverse effects with pharmaceutical products.

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Glossary

- **Certification of Suitability (CEP)**
- It is the certificate which is issued by Certification of Substances Division of European Directorate for the Quality of Medicines (EDQM), when the manufacturer of a substance provides proof that the quality of the substance is suitably controlled by the relevant monographs of the European Pharmacopoeia.

- **TSE compliance certificates**
- are a type of CEP (Certificate of Suitability to the European Pharmacopoeia). They are used to maximize safety when working with materials that could potentially be contaminated with TSE (**Transmissible spongiform encephalopathy)**.

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Glossary

- The **plasma master file** (**PMF**)
- It a compilation of all the required scientific data on the quality and safety of human **plasma** relevant to the medicines, medical devices and investigational products that use human **plasma** in their manufacture.
- The **Certificate of Pharmaceutical Product** (**CPP**)
- It is a **certificate** issued in the format recommended by the World Health Organization (WHO), which establishes the status of the **pharmaceutical product** and of the applicant for this **certificate** in the exporting country.

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Glossary

- The **Summary of Product Characteristics** (**SPC** or **SmPC**) is a specific document required within the European Commission before any medicinal product or biocidal product is authorized for marketing.
- A **novel excipient** is an **excipient** which is being used for the first. time in a drug product, or by a new route of administration.

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Common Technical Document (CTD)

- **CTD** is a set of specification for application file 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.
- In July 2003, the CTD became the mandatory format for new drug applications in the EU and Japan, and the strongly recommended format of choice for NDAs submitted to the FDA.

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Advantages of CTD

- It has facilitated the regulatory review processes
- It has eliminated the need to reformat the information for submission to the different ICH regulatory authorities
- It facilitated simultaneous submission in three regions.
- It led to harmonised electronic submission that, in turn, enabled implementation of good review practices.
- Faster availability of new medicines

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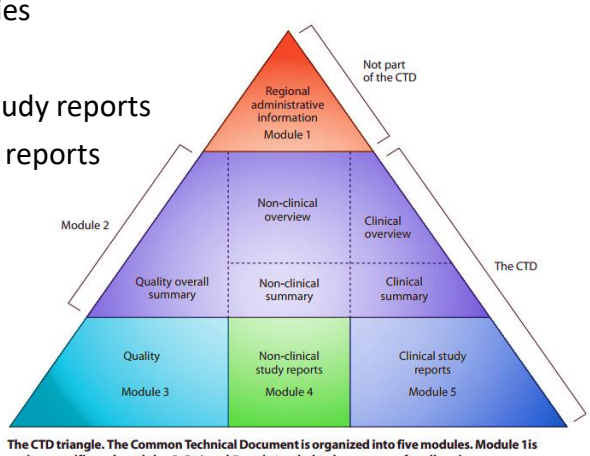
Organization of CTD

- Module 1: Administrative Information
- Module 2: CTD summaries
- Module 3: Quality
- Module 4: Nonclinical study reports
- Module 5: Clinical study reports



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.

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Organization of CTD

Module 1: JFDA Requirements (www.jfda.jo *F1/RDP-3/2011*)

1.0	**Cover Letter.**
1.1	**Comprehensive Table of Contents (Module 2-5).**
1.2	**Application Forms (JFDA forms):**
1.2.1	Check List ***(F1/RDP-3/2011)***
1.2.2	Drug Registration form ***(LF 4-RDP-7\2008)***
1.2.3	Technical Committee Form ***(F2/RDP-7\2008)***(5 copies)
1.2.4	Computer application Form ***(F3/RDP-7\2008*)**
1.2.5	JFDA Stability Report Form ***(F5/RDP-7\2008)***
1.3	**Product Information:**
1.3.1	SPC (Summary of product characteristics), Labeling, Package leaflet.
1.3.2	Mock-up.
1.3.3	Specimen (One Registration sample).

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Organization of CTD

Module 1: JFDA Requirements (www.jfda.jo)

1.4	**Specific Requirements for Different Types of Applications:**
1.4.1	Information for application type (Generic, Bio-similar ……..).
1.4.2	Information for submission type (Technology Transfer, under license …..)
1.5	**Information related to Pharmacovigilance:**
1.5.1	Pharmacovigilance System.
1.5.2	Risk-management System.
1.6	**Other information:**
1.6.1	List of Similar Product Available in Local Market.
1.6.2	Detailed Comparison between Generic Leaflet & Originator (for generic drugs).
1.6.3	Declaration from the manufacturer about the ingredient/s from human or animal origin included in the composition of the product and their source and the related certificates (*TSE CEP*).
1.6.4	List from manufacturer to declare the worldwide registration status: (registered\Marketed (date), under registration, rejected (with reason)).
1.6.5	Technical Contract (Open part) in case of contract manufacturing.
1.6.6	Health authority approval of the latest Plasma master file (if the product contain plasma derivatives).

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Organization of CTD

Module 1: JFDA Requirements (www.jfda.jo)

1.6.7	**Certificates:**
1.6.7.1	Certificate of Pharmaceutical product (CPP) according to WHO format Certified and Legalized.
1.6.7.2	SmPC certified and legalized from country of origin (excluding generics).
1.6.7.3	Price certificates:(for Exported products)(priced drug): - Public Price Certificate showing Price Structure: Ex.f, WSP, PP,(Certified and Legalized):if vat included specify . - Price structure from median countries (UK, Spain, France, Greece, Italy, Belgium, and Holland). - Export Price letter for Jordan & Export price to Saudi Arabia (if marketed).
1.6.7.4	Prices certificate: (for local products) Suggested Public price\ pharmacist price or hospital price (for priced drug).
1.6.7.5	JFDA approval certificate for the Manufacturing site/s (for the same production line)(or copy of the request letter for approval (date and number))
1.6.7.6	A copy of JFDA committee approval of the B.E or the Comparative Dissolution Profile should be provided (for generic drugs).

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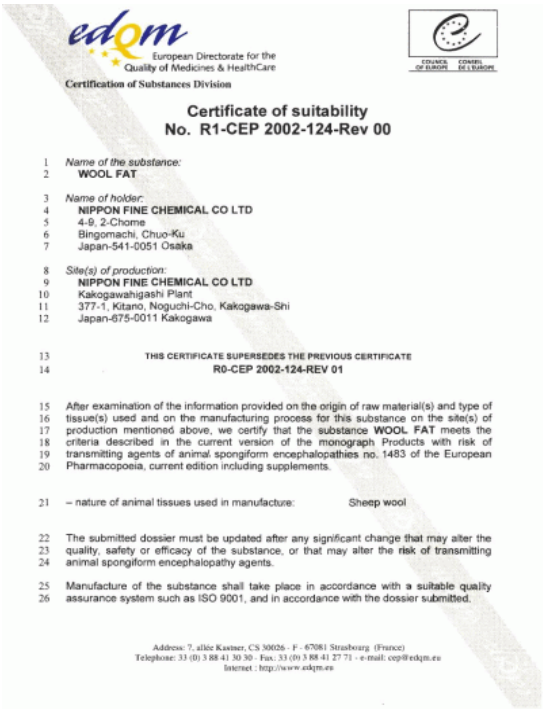

edqm
European Directorate for the Quality of Medicines & HealthCare
Certification of Substances Division

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

Certificate of suitability
No. R1-CEP 2002-124-Rev 00

Name of the substance:
WOOL FAT

Name of holder:
NIPPON FINE CHEMICAL CO LTD
4-9, 2-Chome
Bingomachi, Chuo-Ku
Japan-541-0051 Osaka

Site(s) of production:
NIPPON FINE CHEMICAL CO LTD
Kakogawahigashi Plant
377-1, Kitano, Noguchi-Cho, Kakogawa-Shi
Japan-675-0011 Kakogawa

THIS CERTIFICATE SUPERSEDES THE PREVIOUS CERTIFICATE
R0-CEP 2002-124-REV 01

After examination of the information provided on the origin of raw material(s) and type of tissue(s) used and on the manufacturing process for this substance on the site(s) of production mentioned above, we certify that the substance **WOOL FAT** meets the criteria described in the current version of the monograph Products with risk of transmitting agents of animal spongiform encephalopathies no. 1483 of the European Pharmacopoeia, current edition including supplements.

– nature of animal tissues used in manufacture: Sheep wool

The submitted dossier must be updated after any significant change that may alter the quality, safety or efficacy of the substance, or that may alter the risk of transmitting animal spongiform encephalopathy agents.

Manufacture of the substance shall take place in accordance with a suitable quality assurance system such as ISO 9001, and in accordance with the dossier submitted.

Address: 7, allée Kastner, CS 30026 - F - 67081 Strasbourg (France)
Telephone: 33 (0) 3 88 41 30 30 - Fax: 33 (0) 3 88 41 27 71 - e-mail: cep@edqm.eu
Internet : http://www.edqm.eu

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Organization of CTD

Module 1: Administrative Information and Prescribing Information

- This module should contain documents specific to each region;
- e.g.
  - application forms
  - the proposed label for use in the region.
- The content and format of this module can be specified by the relevant regulatory authorities.

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Organization of CTD

Module 2. Common Technical Document Summaries

- Module 2 should begin with a general introduction to the pharmaceutical, including its pharmacologic class, mode of action, and proposed clinical use. In general, the Introduction should not exceed one page.
- Module 2 should contain 7 sections in the following order :
  - ➢CTD Table of Contents
  - ➢CTD Introduction
  - ➢Quality Overall Summary
  - ➢Nonclinical Overview
  - ➢Clinical Overview
  - ➢Nonclinical Written and Tabulated Summaries
  - ➢Clinical Summary

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Organization of CTD

Module 3. Quality

- Information on Quality should be presented in the structured format described in Guideline M4Q.

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Organization of CTD

Module 3 : Quality

3.2.S DRUG SUBSTANCE (NAME, MANUFACTURER).
3.2.S.1 General Information
3.2.S.1.1 Nomenclature
3.2.S.1.2 Structure
3.2.S.1.3 General Properties
3.2.S.2 Manufacture
3.2.S.2.1 Manufacturer(s)
3.2.S.2.2 Description of Manufacturing Process and Process Controls
3.2.S.2.3 Control of Materials
3.2.S.2.4 Controls of Critical Steps and Intermediates
3.2.S.2.5 Process Validation and/or Evaluation
3.2.S.2.6 Manufacturing Process Development
3.2.S.3 Characterisation
3.2.S.3.1 Elucidation of Structure and other Characteristics
3.2.S.3.2 Impurities

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Organization of CTD
Module 3 : Quality

3.2.S DRUG SUBSTANCE (NAME, MANUFACTURER).
3.2.S.4 Control of Drug Substance
3.2.S.4`.1 Specification
3.2.S.4.2 Analytical Procedures
3.2.S.4.3 Validation of Analytical Procedures
3.2.S.4.4 Batch Analyses
3.2.S.4.5 Justification of Specification
3.2.S.5 Reference Standards or Materials
3.2.S.6 Container Closure System
3.2.S.7 Stability
3.2.S.7.1 Stability Summary and Conclusions
3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment
3.2.S.7.3 Stability Data

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Organization of CTD
Module 3 : Quality

3.2.P DRUG PRODUCT (NAME, DOSAGE FORM)
3.2.P.1 Description and Composition of the Drug Product
3.2.P.2 Pharmaceutical Development
3.2.P.2.1 Components of the Drug Product
3.2.P.2.1.1 Drug Substance
3.2.P.2.1.2 Excipients
3.2.P.2.2 Drug Product
3.2.P.2.2.1 Formulation Development
3.2.P.2.2.2 Overages
3.2.P.2.2.3 Physicochemical and Biological Properties
3.2.P.2.3 Manufacturing Process Development
3.2.P.2.4 Container Closure System
3.2.P.2.5 Microbiological Attributes
3.2.P.2.6 Compatibility

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Organization of CTD

Module 3 : Quality

3.2.P DRUG PRODUCT (NAME, DOSAGE FORM)
3.2.P.3 Manufacture
3.2.P.3.1 Manufacturer(s)
3.2.P.3.2 Batch Formula
3.2.P.3.3 Description of Manufacturing Process and Process Controls
3.2.P.3.4 Controls of Critical Steps and Intermediates
3.2.P.3.5 Process Validation and/or Evaluation
3.2.P.4 Control of Excipients
3.2.P.4.1 Specifications
3.2.P.4.2 Analytical Procedures
3.2.P.4.3 Validation of Analytical Procedures
3.2.P.4.4 Justification of Specifications
3.2.P.4.5 Excipients of Human or Animal Origin
3.2.P.4.6 Novel Excipients

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Organization of CTD

Module 3 : Quality

3.2.P DRUG PRODUCT (NAME, DOSAGE FORM)
3.2.P.5 Control of Drug Product
3.2.P.5.1 Specification(s)
3.2.P.5.2 Analytical Procedures
3.2.P.5.3 Validation of Analytical Procedures
3.2.P.5.4 Batch Analyses
3.2.P.5.5 Characterisation of Impurities
3.2.P.5.6 Justification of Specification(s)
3.2.P.6 Reference Standards or Materials
3.2.P.7 Container Closure System
3.2.P.8 Stability
3.2.P.8.1 Stability Summary and Conclusion
3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment
3.2.P.8.3 Stability Data

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Organization of CTD

Module 3 : Quality

3.2.P DRUG PRODUCT (NAME, DOSAGE FORM)
3.2.P.5 Control of Drug Product
3.2.P.5.1 Specification(s)
3.2.P.5.2 Analytical Procedures
3.2.P.5.3 Validation of Analytical Procedures
3.2.P.5.4 Batch Analyses
3.2.P.5.5 Characterisation of Impurities
3.2.P.5.6 Justification of Specification(s)
3.2.P.6 Reference Standards or Materials
3.2.P.7 Container Closure System
3.2.P.8 Stability
3.2.P.8.1 Stability Summary and Conclusion
3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment
3.2.P.8.3 Stability Data

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Organization of CTD

Module 4 : Non-clinical study reports

- Module 4 describes the format and organisation of the nonclinical (pharmaco-toxicological) data relevant to the application.

❑4.2 STUDY REPORTS

❑4.2.1 Pharmacology

❑4.2.2 Pharmacokinetics

❑4.2.3 Toxicology

❑4.3 literature references

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Organization of CTD

Module 5 : Clinical study reports

- Module 5 describes the format and organisation of the **clinical data relevant to the application**.
  - ❑5.3.1 Reports of Biopharmaceutical 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

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eCTD

- Electronic submission of CTD
- Files formats are PDF and xml in order to
  1. manage the large data for the entire submission and for each document within the submission.
  2. allow the eCTD submission to be viewed via a web browser and can be loaded on a Web server.
- other formats can be used for graphs and images.
  - *JPEG*
  - *PNG*
  - *GIF*

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