10/11/202

The Common Technical Document (CTD)

Prof. Nizar Al-Zoubi

What is CTD?

What is CTD?

- The **Common Technical Document (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.
- currently there are Four ICH guidlines on the CTD (M4, M4Q, M4S and M4E)

١] لما يكون هنا شكل محدد فهو للتسهيل علينا انه نعبيه Magnufacturers (applicant) اعبيه و ال regulatory reviewers

انه يشوفوه ويراجعوه، فيسهل عليه ال revision من ال Regulatory Autharoties

10/11/202

٢] كونه معتمد بأكثر من منطقة دا هنا متبعين ال ICH guidlines الموجودين معناته مافي داعي اني اكتب ال Format

فمثلا اذا امريكا بتطلبه شكل وكانت ال Europe بتطلبه شكل ثاني (بسبب هما بينهم اتفاقية) فما في داعي اعمل reformating [reintrpretation]

الهدف :- المعلومات [المعلومات نفسها بين كل واحد لما الهم شكل]

Advantages of CTD

هي ذي البروتوكول . فبكتبه حسب ال format المتفق عليه ويصير ابعثه على هاي المناطق بنفس الوقت .

1] • It has facilitated the regulatory review processes

2] • It has eliminated the need to reformat the information for submission to the different ICH regulatory authorities

3] • It facilitated simultaneous submission in three regions.

4] • It led to harmonised [electronic submission] that, in turn, enabled implementation of good review practices.

5] • Faster availability of new medicines

انه مش انت تروح تقدم ال paper work

تبعتك ، فهاد سهل انه يصير Application لل Good revision practice

تبعك وبالتالي بسرعة ح ياخذوا القرار ، واذا كان القرار لصالحك

انه الدوا بيروح للسوق فهاد نتيجتها [5] Faster availability of New Medicine

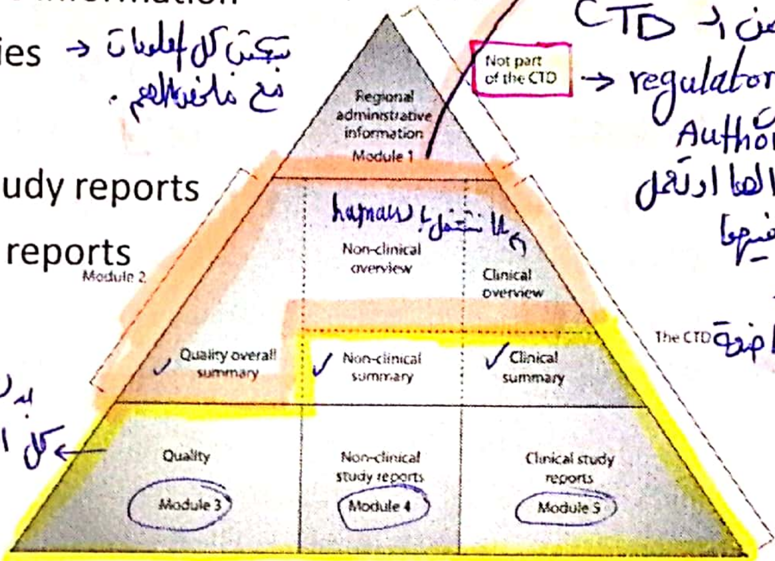
هدول تبعك DATA وبتقدر تناقش وتكتب ال story تبعتك

وشو ال opinion تبعك [can interpret your DATA]

Organization of CTD

5 Modules:-

- Module 1: Administrative Information → general information تبعتي
- Module 2: CTD summaries → بتحكي كل المعلومات مع ملخصاتهم.
- 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 1 is region specific and modules 2, 3, 4 and 5 are intended to be common for all regions.

عادة لا يعتبر جزء من ال CTD

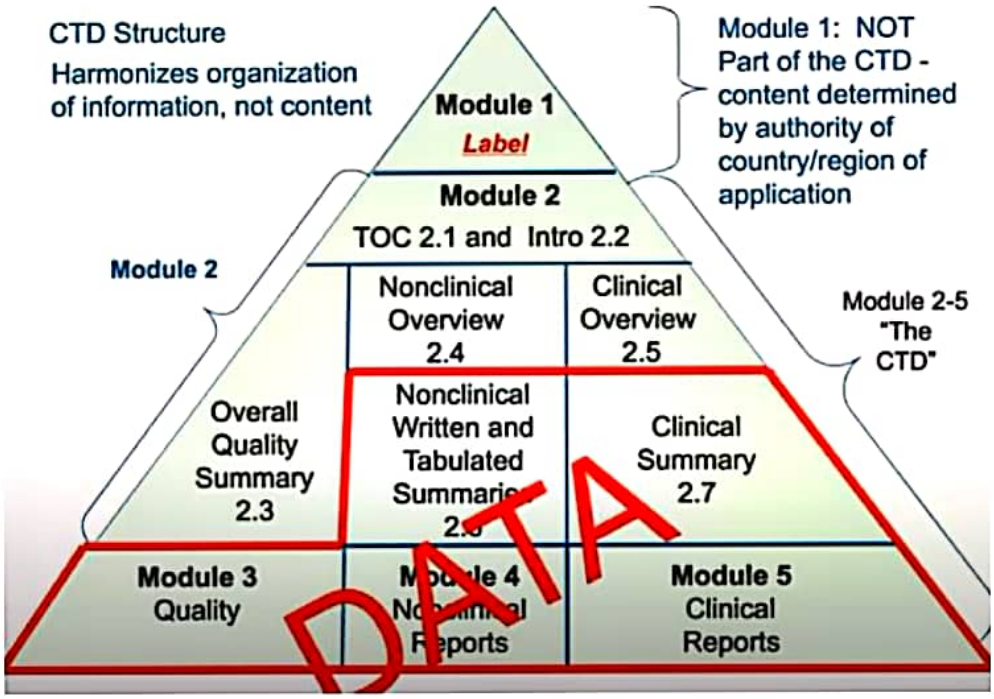
Not part of the CTD → بكون تابع ال regulatory Authorities للمنطقة اللي بدك تبعث الها ادويتك للدولة تبعك فيها registration مثلاً اذا بالاردن هاي ال Administrative infor. لازم تكون خاصة ... شو بتعطينا ال FDA الاردنية وشو بتطلب لازم اعطه وهكذا.

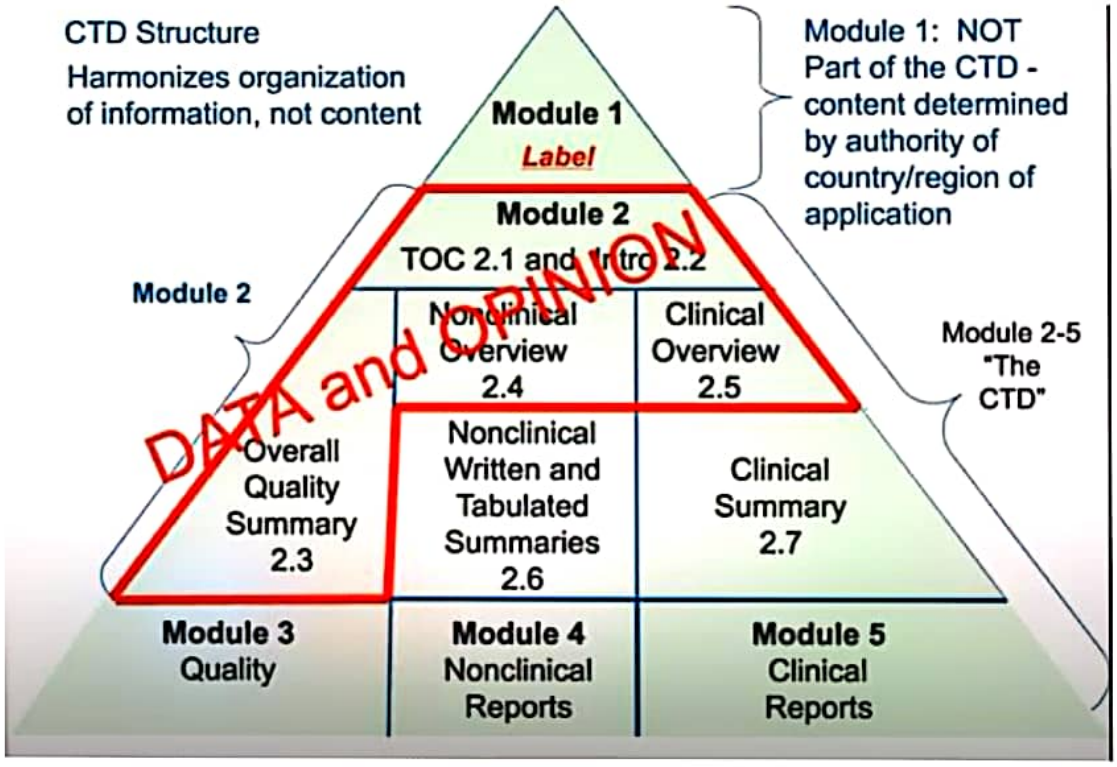
لا تشتغل بال humans

بدك تكتب كل ال Quality test كل التفاصيل والنتائج تبعتهم

* ال Module1 عادة Not part of CTD وبتعتمد زي ال Authorities بطلبة زي ال lable واحكينا [بالاردن مش زي بلدان ثانية]

هدول pure DATA اللي طلع معنا النتيجة
علماً Test معين طلع معنا نتيجة معينة فبنا نكتبهم
مش مسموحلنا نعطي رأينا بال Result زي ما طلع
من الجهاز نكتب زي ما هي بدون اي تغيير هنا
مثلاً conc. معين بالدم نكتب زي ما هو.





Organization of CTD

prescribing information

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.

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).

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).

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).

edqm

European Directorate for the Quality of Medicines & HealthCare

Certification of Substances Division

هيك شكل الـ certificate الي لازم
تكون مرفقة مع النماذج الي انت تبعتهم .

مثال

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

للـ EMA

Name of the substance:
WOOL FAT

Name of holder:
NIPPON FINE CHEMICAL CO LTD
4-8, 2-Chome
Bingomachi, Chuo-Ku
Japan-541-0051 Osaka

الشركة ومكانها

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

قرأت هون →

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.

→ انه هاد الـ product
Meets the criteria

– 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.

هاي الشهادة لازم نعرفها خلال عملية Registration

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

Organization of CTD

Module 3. Quality

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

بنتكلم عن Quality

↓

suitable for intended use or predetermined specification.

✓ كل اشي بين اقوسين بنا نكتب عنه

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

Organization of CTD
Module 3 : Quality

Drug Substance ال** عنها 7 parts

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

should be Justified

container, مواصفات

FDA مرات ب تطلب list طويلة من specification عشان يعرف انها تعمل واحد فيهم او تعمل جزء منه و تتوافق

stability مرات ما يجي خلال فترة Registration انه يسمح Registration قبل ما يكمل الـ stability فلازم اعمل commitment

Long term الـ stability

Organization of CTD
Module 3 : Quality

Stability

Organization of CTD

Module 3 : Quality

6 parts

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 → pharmaceutical Active ingredient
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

characteristics

other excipient

formulation

Lactose Filler

cellulos → Disintegrat

Mg stearate → lubricant

Tablet

bunch

Active pharmaceutical ingredient

compatible

degredation

complexation

release

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 ✓ → درسنا عنهم بال Drug substance ونفسهم موجودين بال Drug Product
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 كلها
3.2.P.4.2 Analytical Procedures
3.2.P.4.3 Validation of Analytical Procedures
3.2.P.4.4 Justification of Specifications → عنها skip ذي ما حكينا الشي مرات بدنا نحكي
3.2.P.4.5 Excipients of Human or Animal Origin → لازم تكون فيها كود في فهم وحفظنا شرحها
3.2.P.4.6 Novel Excipients

→ هي ال excipients التي تستخدم لأول مرة

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

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

مثلاً :- Toxicology على animal
مثلاً: لنعطي الفئران
بالحقن propanalol وشفنا
هل قلل الضغط او لا.
✓ فهنا نحكي عن Pharmacological effect للدوا
✓ كيف صار الـ absorption و Elimination
والباقي الي هاد Pharmacokinetics للدوا

* هدول كلهم لازم يكونوا في Module 4 سواء كنت
بشتغل على Animal او على tissue culture
← NON clinical كله

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

Electronic version

eCTD

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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eCTD

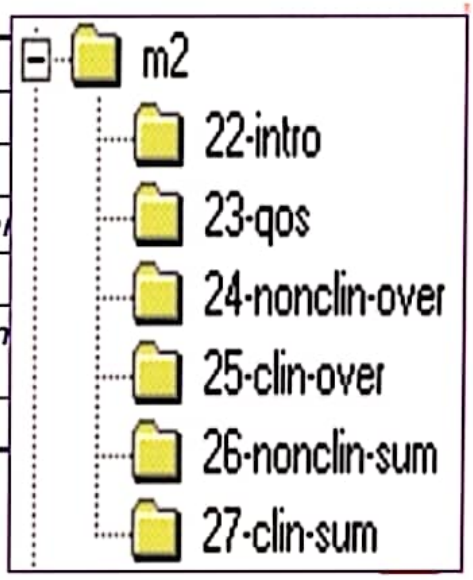
- Electronic submission of CTD
- eCTD being mandatory for the centralised procedure in the EU since 2010.
- It is a software (e.g. Paraxel, Extedo, Lorenz, Global submit, and eCTDExpress)
- Files formats are PDF and xml in order to
  1. manage the large data for the entire submission and for each document 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*

Benefits of eCTD

- Improved reviewer efficiency
- Reduced time to approval
- Submission via Electronic Submissions Gateway (ESG) (US) and Common European Submission Platform (CESP) (Europe) enable immediate receipt by the regulatory body
- Improved handling and archiving of submissions (both sponsor and regulatory body)
- Search functionality and increased tracking ability
- Accessibility of documentations across modules
- Ability to re-purpose documents for submission in other regions
- Simplified lifecycle management

Example: Module 2

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*



سلايد ناقص .

١+٢ ← سهلت الخلافات

10/11/2022

٣ ← حصول على الـسريع مجرد ماتعمل click عالـسريع بتحدد regulatory body فتزيد

الـ submission ويزيد القبول [انه تقبل الدولة] ok

يزيد (٥) الـ Accessibility of documentation سهولة بتنتقل من Module لـ Module ويزيد (٤) للانتقال

زي ما مشينا

٦- انه كسبت صرف احنا لـ US وهناك للـ Europe

Glossary

سلايدات # فهم Defination لكل اشي حكتة الدكتورة

- 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. to detect and evaluate S/E

Glossary

- *What is a 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).**

Glossary

- The **plasma master file** (**PMF**) is 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** (abbreviated: CPP) 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.

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.