

Contents and structure of different CTDs

*DCVMN Common Technical Document
(CTD) Workshop*

Brazil, 18 to 20 June 2018

Dr. Nora Dellepiane

Rationale for reliance and harmonization

Main objective

The public health objective is to facilitate access of medicinal products including vaccines of assured quality, safety and efficacy available to the populations of the world that need it most in timely manner and at affordable prices

Key words:

- ❖ ACCESS,
- ❖ ASSURED QUALITY SAFETY AND EFFICACY
- ❖ POPULATIONS IN NEED
- ❖ TIMELY
- ❖ AFFORDABLE

Regulatory Strategies

- Leverage on WHO prequalification system
- Harmonization of registration across countries
 - Harmonized application forms
 - Harmonized dossier in format and contents
 - Harmonized procedures

Leveraging on WHO-PQ

- ✓ The United Nations System for vaccine procurement is mostly served by UNICEF and the PAHO RF. It relies on the WHO prequalification system for eligibility/acceptability of vaccines for purchase as well as for the monitoring of field performance
- ✓ Such vaccines undergo three levels of authorization:
 - NRA in the producing country
 - WHO prequalification
 - MA in the user countries

Leveraging on WHO-PQ (2)

- ✓ Although these three levels of authorization are required, ideally, a vaccine that is well regulated in the producing country and is WHO prequalified, should be subject to an accelerated and facilitated review process in the receiving countries based on reliance on the two levels of evaluation performed.
- ✓ WHO promotes a collaborative procedure between the NRAs and WHO for the registration in user countries, which is based on reliance on the PQ work and information sharing of the PQ reports. However, the implementation of this approach remains low

Harmonization is critical

- There are vaccines that are not WHO prequalified. These products are targeted either at private markets or may be purchased directly by countries that do not require prequalification.
- Such vaccines are still subject to two levels of review for marketing authorization; in the producing and the importing countries
- This should be multiplied by the number of countries where the vaccine needs to be registered

What happens in practice

- ✓ In practice, manufacturers applying for registration of these products are required to go through a similar process three times and subject to different requirements in different countries.
- ✓ The concern from manufacturers regarding the divergence in requirements in different countries has been highlighted many times in different international fora with poor results
- ✓ In spite of numerous alignment efforts by regulatory agencies, economic blocks, regulatory networks and others; the problem remains unsolved

Main ICH objectives and activities

Main ICH objectives as stated in the Network mission.

- To make recommendations towards harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration and the maintenance of such registrations;
- To monitor and update harmonised technical requirements
- To avoid divergent future requirements through harmonisation of selected topics
- To encourage the implementation and integration of common standards

Main ICH objectives and activities (2)

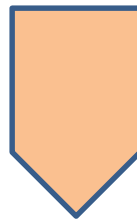
- Development of the Common Technical Document (CTD) as a harmonized and unifying dossier with common structure (format) and suggested contents
- Introduction of the CTD as the common technical document in all ICH member countries starting with EU, USA and Japan and later expanding to additional member countries

ICH membership

More and more countries are becoming members of ICH

Others have observers status before becoming official members

- Regulatory agencies from countries applying to ICH membership commit to implementation of certain key set of ICH guidelines
- Industry Members are required to support and encourage compliance with ICH guidelines.
- All Members shall also support the aims of the ICH Association and take part in ICH meetings and ICH working groups.



Hence, members, observers and yet other non-ICH countries are adopting the CTD as the required registration dossier format

CTD adoption

Increasing number of countries or regions adopting CTD format with adaptations



This trend expected to lead to convergence



However, because of the adaptations introduced, the degree of convergence does not seem to increase significantly

Vaccine manufacturers have engaged in assessing the degree of similarity/ differences between CTDs used in different countries around the world

CTD adoption (2)

WHO-PQ used the Product Summary File as their dossier format



WHO-PQ is adopting the CTD format for alignment purposes

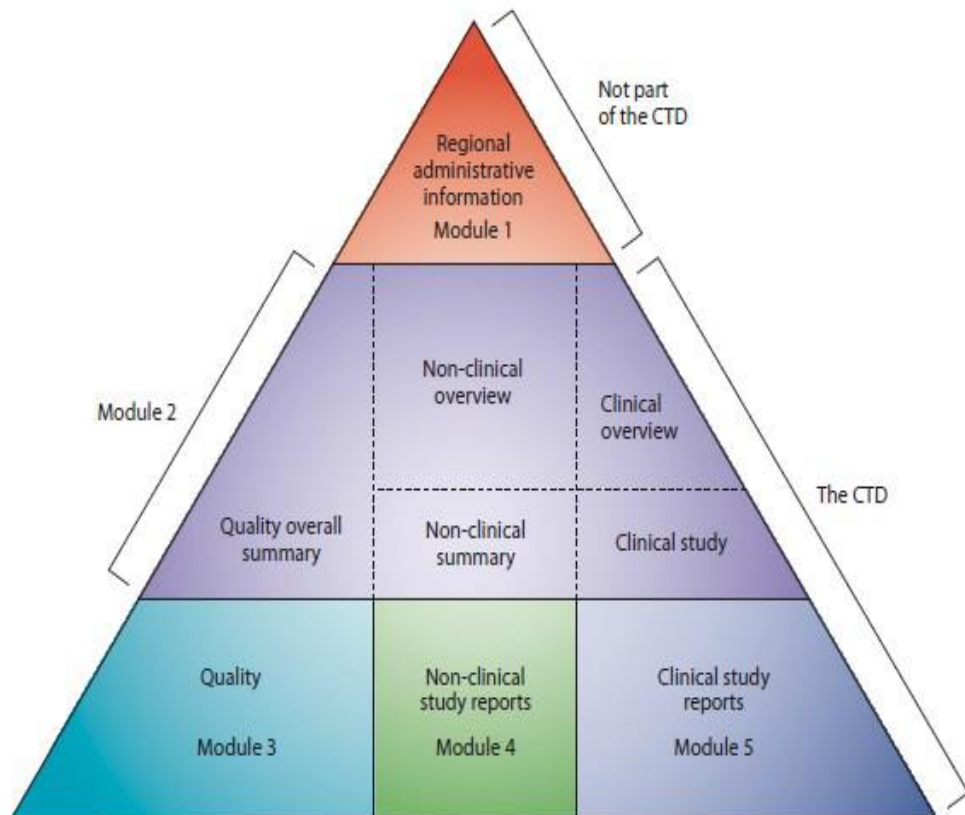


WHO-PQ is requesting the UN related information in a WHO specific module 1, the contents of which is currently in draft

Vaccine manufacturers have engaged in assessing the degree of similarity/ differences between WHO proposed module 1 and that required by countries/regions

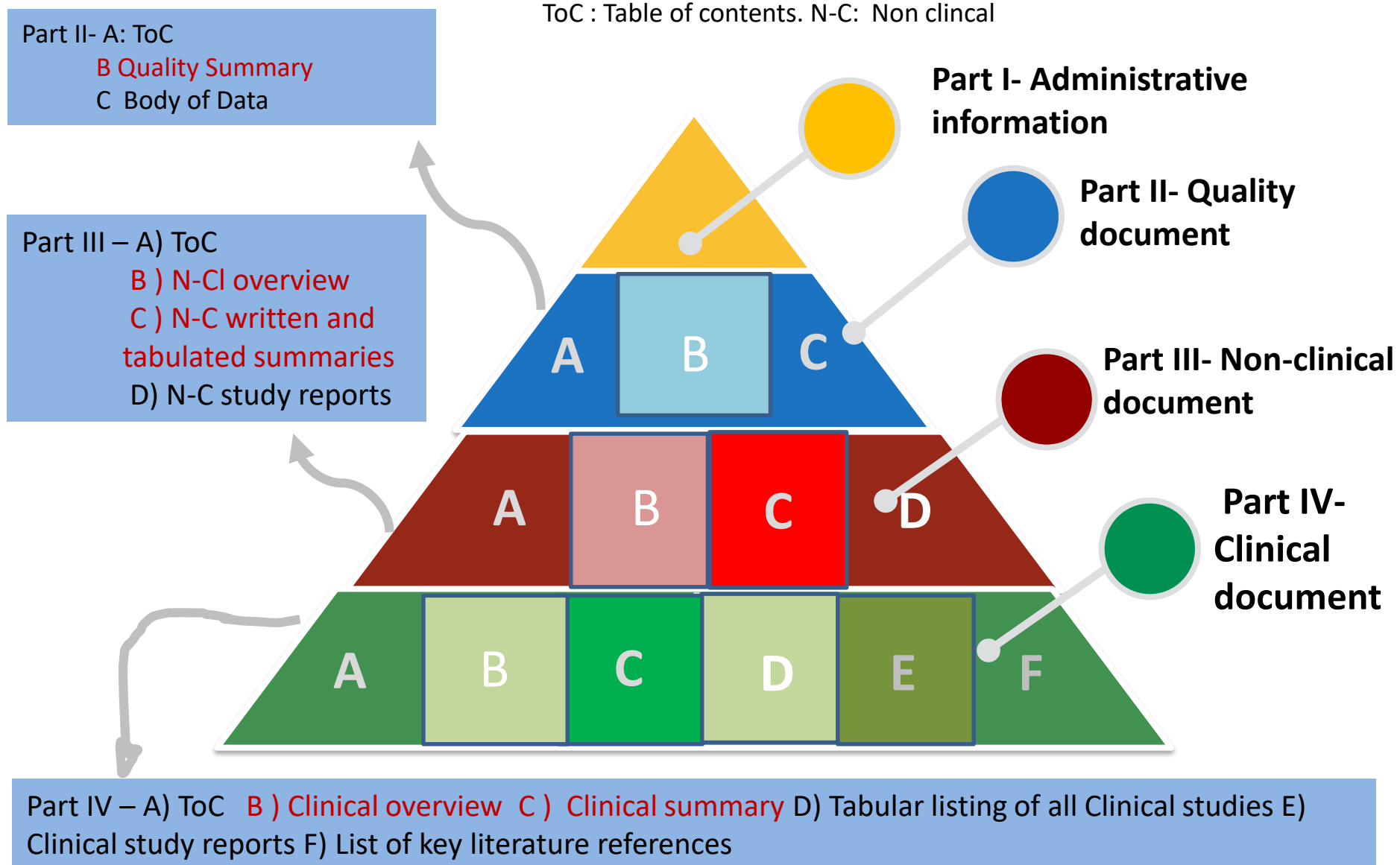
ICH CTD architecture

ICH developed the Common Technical Document as a harmonized dossier both in format and contents



- ✓ Module 1 is not aligned. Contains region specific information that is not common between the ICH parties
- ✓ Modules 2-5 are harmonized
- ✓ **Module 2: Common Technical Document Summaries**

ASEAN CTD architecture



Structure and contents of CTDs

- ASEAN CTD does not contain module 2. Information from this module is integrated into the specific technical sections II) III) and IV)
- This radical structural difference creates difficulties in dossier preparation and comparison of information
- ICH CTD is applicable to both medicines and biological products while the PAHO CTD is specific for vaccines and biological products only.

Worldwide distribution of MA dossier formats



- I ICH CTD
- II PAHO CTD
- III ASEAN CTD
- IV Diversity of formats

PAHO COUNTRIES ADOPTING CTD FORMAT ARE FEW, HOWEVER WORLDWIDE THE NUMBER IS INCREASING

Situation in Africa

- The African continent is divided in several economic blocks.
- Some of these blocks are engaged in regulatory harmonization efforts which are expected to lead to a convergence in dossier format and requirements
- AVAREF is a WHO Network of regulators and Ethics Committees from all African countries engaged in harmonization of requirements within and between blocks
- This continent offers opportunities towards a harmonized CTD adoption since the harmonization efforts are currently ongoing

Rationale for comparing CTDs

- Based on the experience from manufacturers in the complexities to build CTD for submission to different countries due to differences in requirements and,
- On a recommendation from the regulatory experts panel held at the 2016 DCVMN annual meeting,
 - It was decided to make a comparison of CTDs from different countries in order to quantify similarities and differences
 - CTDs were compared between each other for module 1 (non-harmonized) and against the ICH CTD for modules 2-5 (harmonized modules).

Rationale for assessing differences

Modules 2-5 comparison

CTDs from different countries were considered “different” from the ICH CTD if one of the following situations applied:

- Country X did not require a specific item required in the ICH CTD)
- Country X required data/information not required in the ICH CTD (other information)
- Country X contained in its requirements the same heading (or similar) as contained in the ICH CTD but the data/information expected to be provided under such heading was not specified, while being specified in the ICH CTD
- Country X contained in its requirements the same heading (or similar) as contained in the ICH CTD but the data/information expected to be provided under such heading was specified, while not being specified in the ICH CTD
- Country X requires different information from ICH under the same heading

Some examples of differences found

- [..\Basis for differences btwn CTDs\Examples of differences observed in CTDs.docx](#)

THANK YOU
OBRIGADO
GRACIAS