The Common Technical Document- Quality (CTD-Q)

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with thanks to
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CTD : what is it?

- **IT IS :**

  A common harmonised FORMAT for applications for preparing marketing authorisations in the three ICH regions.

  a TEMPLATE for presenting data in the dossier.

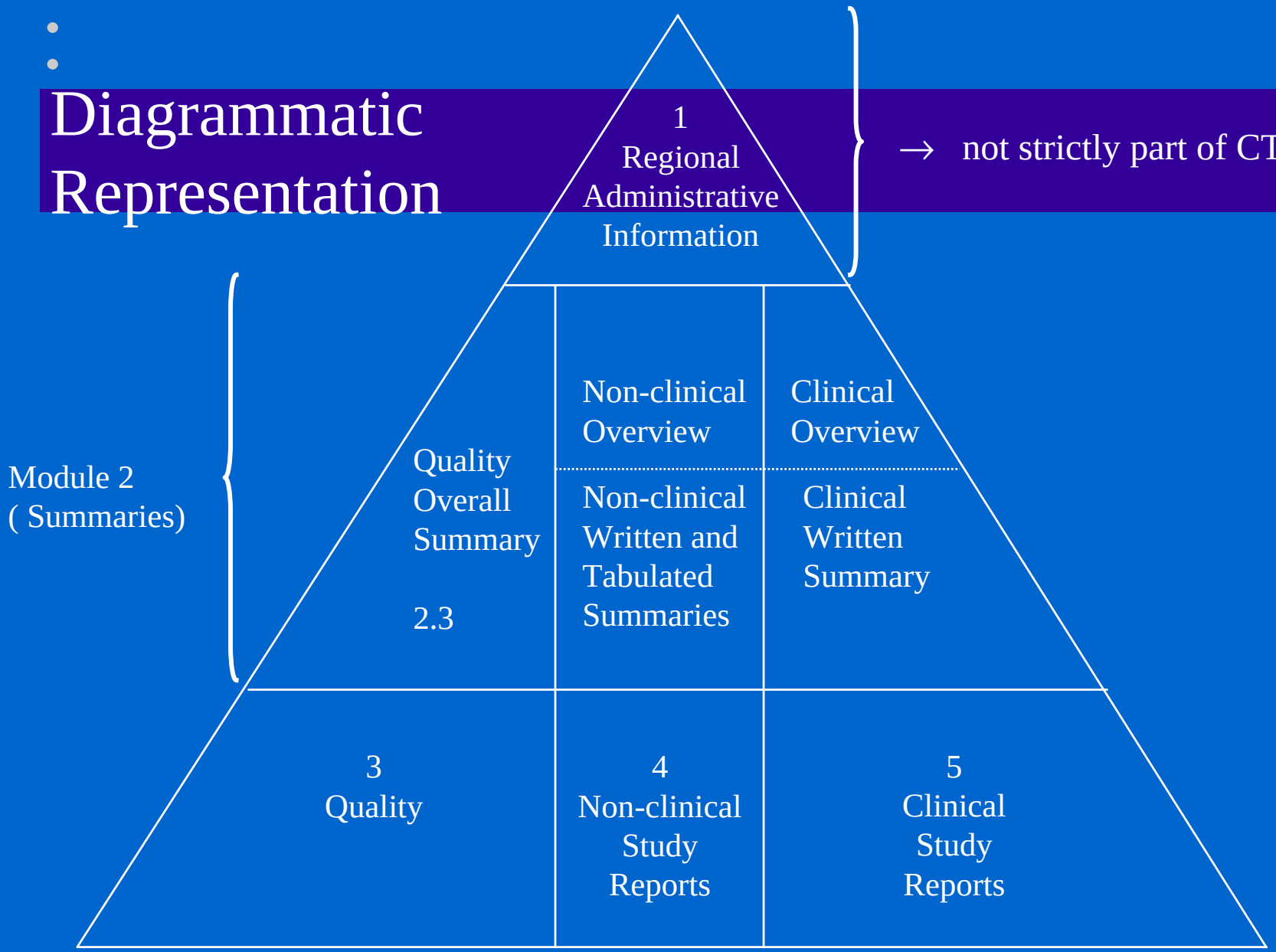
- **IT IS NOT:**

  A statement of data requirements for applications

CTD : regulatory sources

- Notice to Applicants , Eudralex Vol. 2B : “NTA Guidance” June 2006 : Structure is defined here.
  http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-2/b/ctd_06-2006.pdf
- Q&A Document
  http://www.ich.org/LOB/media/MEDIA620.pdf
- ‘Location issues’ (Quality) - see CPMP/ICH/4680/02
- ICH Updates
  http://www.ich.org

Diagrammatic Representation



CTD-Q basic structure

- **MODULE 1**

Admin and Regional Specific Information

Don't forget molecular structure aspects re: Similarity (1.7)

- although these are outside the main quality/safety/efficacy benefit-risk evaluation for an authorisation.

- **MODULE 2**

CTD Summaries

- Quality Overall Summary (2C) - QOS

- **MODULE 3**

Main body of Quality Data

i.e. The Q dossier will be basically modules 2.3 & 3

Module 1:
Administrative Regional Information

- 1.1 Table of Contents
- 1.2 Application forms
- 1.3 Product Information, SPC/Labelling/ Package Leaflet
- 1.4.1 Expert declarations & signatures for the QOS
- 1.5 ‘Specific Requirements’ for types of application bibliographic, generic, biosimilar, informed consent etc.
- 1.6 Environmental Risk Assessment (GMO?)
- 1.7 Orphan issues, structural similarity
- 1.8, 1.9 Pharmacovigilance and Clinical Trials

Module 2: Quality Overall Summary

- This is probably what EU assessors will read first
- **Quality Overall Summary**
  - Written text summary following the outline and scope of the ‘Body of Data’, Module 3 .
  - Not required to be critical
  - No formal tabulated summary structure
  - Key parameters of the active substance & product which may have an impact on efficacy or safety should be emphasised
  - Relevant tables/figures could be incorporated
  - External Drug Master File (ASMF Open part) will be summarised here. Closed/Restricted part should be in the ASMF itself.

Module 3: CTD-Q (guideline)

Note : Same structure for ‘ NCE ’ & ‘ Biotech ’ products

Scope of the guidance , i.e. format

- 3.1 Table of Contents – helpful to assessors
- 3.2 **Body of Data** ’
  - **3.2.S Drug Substance**

    External Drug Master File (ASMF) should also follow this structure for both the Open and Closed/Restricted parts.
  - **3.2.P Drug Product**
    - 3.2.A Appendices
      - A.1 Facilities and equipment (biotech)
      - A.2 Adventitious Agents contamination
      - A.3 Excipients (novel)

Scope

- Addresses the format/structure of applications for MAs of active substances and their corresponding drug products.
- NTA Guidance : The text following the section titles is intended to be explanatory and illustrative only i.e. It merely indicates the location where information has to be provided.
- The actual content of these sections in the dossier should include relevant information described in existing CHMP- and CHMP-ICH guidelines
- The section Regional Information addresses information unique to this region

Example of a ‘network’: Polymorphism

- Cross reference between section P2 (Pharm. Development) and relevant sections in S (Drug Substance) and in P (Drug Product)
  - S 1.3 Properties of the active substance
  - S.2 Manufacture
  - S 3.1 Studies on Polymorphism (experimental data)
  - S 4.1 Specifications relating to control of physical forms
  - S.4.3 Analytical methods used
  - S 4.5 Justification of Specifications
  - P 2: Influence of the polymorphic forms on product characteristics – dissolution, stability , etc.
  - P 5.1 Product Specifications, need to control polymorphs?
  - P 5.6 Justification of Specifications

Body of Data – 3.2.A: Appendices

- A 1 Facilities and Equipment:
  applies for Biotech. products

- A 2 Adventitious Agents Safety Evaluation:
  applies for NCEs and Biotech;
  including TSE requirements
  viral inactivation studies, etc.

Body of Data 3.2.R : Regional

- Process Validation scheme, manufacture of product
- Medical Devices, if included in the presentation of the product, CE-mark info. etc.
- Certificates of Suitability , where relevant (e.g. generics ?)
- Materials of animal and/or human origin

issues

- Implementation not equal in all regions?
- Nothing to do with e-CTD (although the e-CTD is of course based on the agreed CTD structure)
- In EMEA, for publication purposes (EPARS) we still prefer to avoid ‘drug’

  Drug substance becomes Active Substance

  Drug Product becomes Medicinal Product

Conclusions

- Benefit for industry
  - Format: yes, better utilisation of global resources
  - Content: identical within the 3 regions but can it lead to an expectation of more data ?
- Benefit for regulators
  - Format: yes, easy to evaluate in general
  - Content: same as before really, no change.
- Benefit for the patient
  - Expedited evaluation is a benefit, especially with a positive conclusion and early marketing.