Essential technical standards for successful regulatory harmonization

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Core regulatory functions

Ideally medicines regulatory authority should be able to administer the full spectrum of regulatory activities, including at least the following functions:

- Marketing authorization for new products and variation of existing authorizations;
- GMP, GCP, GLP inspections;
- Licensing and post-license control of manufacturers, wholesalers and other distribution channels;
- Quality control laboratory testing;
- Adverse drug reaction monitoring;
- Provision of drug information and promotion of rational drug use;
- Enforcement operations;
- Monitoring of Drug Utilization, etc.
Current situation

1. 30% of NMRAs globally have limited capacity to perform all core regulatory functions

2. 90% of African NMRAs lack capacity to guarantee quality, safety, and efficacy

3. Sponsors / manufacturers face a landscape of disparate regulations, frequent delays, and limited transparency

As a result, needed medicines lack availability, affordability in low-income countries

- Fewer medicines are available in low-income countries than in the US, EU, etc.
- Cost of inefficient regulatory systems drives up medicines prices
Expectations from harmonization of technical requirements for registration of medicines

- To improve public health, by increasing timely access to safe and effective medicines of good quality for the treatment of priority diseases.

- This could be done by reducing the time it takes for essential medicines to be registered in-country, without compromising quality and, potentially, the time taken for essential therapies to reach patients in need.

- Will require capacity building to ensure transparent, efficient and competent regulatory activities, including assessments and inspections, to assure the quality, safety and efficacy of registered medicines.
Can registration harmonization increase regulatory efficiency?

<table>
<thead>
<tr>
<th>Current state</th>
<th>Possible objectives</th>
<th>Indicators of success</th>
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<tbody>
<tr>
<td>Different technical requirements</td>
<td>Common Technical Document format and a set of harmonized technical requirements</td>
<td>Shorter lead-times to dossier submission</td>
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<td>Disparate processes</td>
<td>Process streamlining &amp; strengthening</td>
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<tr>
<td>Capacity constraints</td>
<td>Capacity building (administrative and technical)</td>
<td>Faster registration</td>
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<tr>
<td>Lack of transparency</td>
<td>Increased transparency of requirements and processes</td>
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<tr>
<td>Lack of communication</td>
<td>Information sharing and recognition</td>
<td>Less duplication of effort</td>
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<td>Lack of collaboration</td>
<td>Joint evaluations/ inspections</td>
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Focus of CTD is on a common international format and structure for marketing authorization applications – not on content.

CTD format is rigorous and allows for adaptation to most / all submission types.
CTD Numbering System

Blue indicates those sections not needed for generics

Module 1
1.0 Admin Info & Prescribing Info (country specific)

Module 2
2.0 CTD Summaries
2.1 Table of Contents of the CTD (Mod 2-5)
2.2 Introduction
2.3 Quality Overall Summary
2.4 Nonclinical Overview
2.5 Clinical Overview
2.6 Nonclinical Summary
2.7 Clinical Summary

Module 3
Quality

Module 4
Nonclinical Study Reports

Module 5
Clinical Study Reports
Adaptation of the CTD format to "generics"

1.1 Table of Contents (Modules 1-5)
1.2 Application information
1.3 Product Labelling
1.4 ...
1.5 ...
1.6 ...

2.1 Table of Contents of the CTD (Modules 2-5)
2.2 Introduction
2.3 Quality Overall Summary

5.1 Table of Contents (Module 5)
5.2 Tabular Listing of all Clinical Studies
5.3 Clinical Study Reports
  5.3.1.2 Comparative BA & BE Study Reports
  5.3.1.4 Reports of Bioanalytical & Analytical Methods for Human Studies
  5.3.7 Case report forms and Individual Patient Listings
5.4 Literature References
Adapting the CTD to Local/Regional Regulatory Documentation Package

Regional Regulatory Documentation Package *could* contain built-in flexibilities (*similar to the ICH-CTD*) so that it can be appropriately tailored to local circumstances and preferences.

1) Adaptable Section

<table>
<thead>
<tr>
<th>Country-specific product labelling and other administrative requirements</th>
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<tbody>
<tr>
<td>Section A</td>
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<td>Section B</td>
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<td>Section C</td>
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<tr>
<td>Section X</td>
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<tr>
<td>Section Y</td>
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<tr>
<td>Section Z</td>
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</tbody>
</table>

**Country-specific Administrative Section**

2) Matrix Format

**Common Technical Section**

**Potentially including any country-specific technical requirements that are difficult to harmonise in the short-term, due to prevailing legislation for example**
Benefits of the CTD

**Industry**
- Logical order of presentation that follows the development scheme
- Reduction in resources required to compile applications
- Easier exchange of information
  - Industry to regulator
- Electronic submissions are easier to prepare

**Regulator**
- Logical order of presentation that follows the development scheme
- Facilitates the regulatory assessment process
- Easier exchange of information
  - Regulator to industry
- Easier exchange of information
  - Regulator to regulator

★ CTD is an important bridge to e-CTD
### WHO Guidelines on submission of documentation for a multisource (generic) finished product. General format: preparation of product dossiers in common technical document format

- Facilitates access to priority essential medicines that meet WHO-recommended norms and standards of acceptable quality;
- Assist applicants in the preparation of Product Dossiers for multisource products by providing clear general guidance on the format of these dossiers;
- Fully adopt the modular format of the CTD as developed by ICH; and
- Provide guidance on the location of regional information (Module 1) and other general data requirements.

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**Annex 15**

Guidelines on submission of documentation for a multisource (generic) finished product. General format: preparation of product dossiers in common technical document format

1. Introduction
   1.1 Background
   1.2 Objectives
   1.3 Scope
   1.4 General principles
2. Glossary
3. Organization of a product dossier for a multisource pharmaceutical product in common technical document format
4. Modules (including Module 1) of a product dossier for a multisource pharmaceutical product
   5. Module 3 — quality
   6. Module 5 of a product dossier for a multisource pharmaceutical product
   7. Guidance on format and presentation of a product dossier in common technical document format
      7.1 Guidance on format
      7.2 Guidance on presentation
7. Variations
8. References

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EAC MRH Project objectives

1. To implement an agreed common document (format and content) of technical requirements and procedures for registration of medicines in EAC Partner State NMRAs (this will take into account the existing WHO Regulatory Documentation Package, ICH and other relevant international standards and will include establishing an ongoing update process);

2. ....

3. ....
Conclusions

- The future is in regulatory harmonization, either first in more focused or in more broad meaning - eventually both;
- Due to sophistication of science, new amount of information and data to be assessed, there is no alternative for better and more efficient communication, collaboration and harmonization;
- A common application format is the cornerstone of a harmonized regulatory system;
- The CTD (or a CTD-type Regulatory Documentation Package) is the logical “standard” to adopt in the countries/regions moving towards harmonization.
Thank you!

www.who.int/medicines