Global View on Regulatory Affairs

Beata Stepniewska
Deputy Director General, Head of Regulatory Affairs
25.02.2021
Vision:
Operating a regulatory framework supporting true global development

- There is an urgent need for an operating regulatory framework supporting global development for generic, complex generic and biosimilar medicines
Where are we with a global regulatory approach towards off-patent medicines in 2021?
Global development and global filing is still a bumpy road
Picture in 2021

Progress:
ICH harmonisation
ICH Generics Discussion Group
WHO – more reliance

Insufficient progress in global comparator for bioequivalence/clinical studies
Still too much duplication/inefficiency/fragmentation
Global Development, a MUST

- Support regulatory convergence
- Reduce increase in regulators’ workload and promote collaboration
- Facilitate sourcing
- Reduce time & remove barriers to market

Government and corporate social responsibility

UNIVERSAL ACCESS TO MEDICINES

REGULATORY EFFICIENCIES

GLOBAL DEVELOPMENT

SUSTAINABILITY

Of healthcare systems and industry

ETHICS

-Avoid repetition of unnecessary, hence unethical, clinical studies
-Avoid unnecessary exposure and risks to healthy volunteers/patients
Single development: 3 paths that must advance in parallel

- Legal framework
- Criteria for acceptance of global comparator
- Harmonisation of standards (Harmonisation of Bioequivalence)
Legal framework

• No tool for global harmonisation (outside of the ICH scope)
• Individual country’s decision on its legal framework and acceptance of foreign comparator
Global Harmonization of Comparator Products for Bioequivalence Studies

Luther Gwaza, John Gordon, Hubert Lenfkes, Matthias Stahl, and Alfredo Garcia-Arieta

Received 8 November 2016; accepted 24 February 2017

..the exclusive use of the local comparator to ensure switchability is ethically and scientifically questionable.

It is ineffectual to harmonise only the requirements for performing bioequivalence studies, if such a study has to be repeated for every single country simply because of the different comparator products.
One Global Reference product still a dream

- EMA: Reference product from an EU member state
- FDA: Reference product from the US (Reference Listed Drug)
- WHO: Global Reference product (WHO PQteam Comparator lists [https://extranet.who.int/prequal/content/bioequivalence-0])


Acceptance of foreign comparators

Table 1. Comparison of General Aspects of Foreign Comparator Product Acceptance (Y: Yes; N: No)

<table>
<thead>
<tr>
<th>General aspects</th>
<th>Australia</th>
<th>Brazil</th>
<th>Canada</th>
<th>Colombia</th>
<th>European Union</th>
<th>Japan</th>
<th>Mexico</th>
<th>New Zealand</th>
<th>Singapore</th>
<th>South Africa</th>
<th>South Korea</th>
<th>Switzerland</th>
<th>Taiwan</th>
<th>US</th>
<th>WHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accept BE studies using foreign comparator products (under certain conditions)</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

*Brazil, Colombia, the EU, Japan, Mexico, South Korea and US are not mentioned in this table as they do not currently accept foreign comparator products.


Alfredo Garcia Arieta- Medicines for Europe Regulatory Conference 2019
UK from 1 January 2021

Guidance on Comparator products in Bioequivalence/Therapeutic Equivalence studies

• Non-Great Britain comparator products

• Where a comparator product used in bioequivalence and therapeutic equivalence studies is not sourced from the Great Britain market, the applicant should provide evidence that it is representative of the reference medicinal product
Criteria for acceptance of a global comparator

- What are the scientific data and analytical tools that provide evidence that a reference product sourced in region “A” and a reference product sourced in region “B” are similar enough that BE comparisons will be the same?
- How can the comparators be different in each country if they were approved in all the countries based on the same clinical development?
- Regulatory authorities are not always able to use that information for reasons of confidentiality and/or legal restrictions
- A regulatory policy system in each region that will allow scientifically sound data to be used
Harmonisation of Standards

M 9 and M10
- Biopharmaceutics Classification System-based biowaivers (adopted in 2019)
- Bioanalytical Methods validation (Step 2b after public consultation)

M13
- Bioequivalence for Immediate Release Solid Oral Dosage Forms (on-going) - study design and data analytics
- Next steps: more advanced bioequivalence study design topics.

Generics Discussion Group
- Mapping of future needs for harmonisation:
  - Modified Released
  - Long Acting Injectables
  - Inhalation
- Transdermal forms
  - ...
What are the Opportunities?

- Movement towards common standards and global development for generics can improve access to generic products
  - Products with small markets/ small populations may not be economically viable unless markets can be aggregated across regions
  - Investment in development of complex generics can be supported by entrance into multiple markets
  - Bioequivalence studies world-wide can be conducted according to common expectations
    - Increases efficiency of generic drug development
    - Increases quality of generic drug development
  - It is the essential first step towards the global development of generic products
Conclusions

- Urgent need for an operating regulatory framework supporting global development for generic, complex generic and biosimilar medicines
- Tackle scientific, legal and regulatory aspects in parallel
- Concept of global Comparator product needs to be translated into regulatory science
- Consensus among regulators regarding information needed
  - Product, assessment report, decision report
  - Global reference product as a priority topic in international regulators fora (IPRP)
  - Work closer with WHO
- Move towards Information Sharing amongst Regulators
- Established or achievable prerequisites for sharing of information
  - Similar scientific and regulatory standards
  - Trust based on collaboration experience
  - Confidentiality/secrecy arrangements
  - New future tool: Implementation of ISO IDMP STANDARDS linked to business and regulators needs
    - ISO IDMP have been specifically developed over many years to allow consistent and reliable sharing of information on medicines between regulatory agencies
Let’s work together to make it happen one day! Thank you