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

medicines for europe
better access. better health.

Where are we with a global regulatory approach towards off-patent medicines in 2021?

Global development and global filing is still a bumpy road

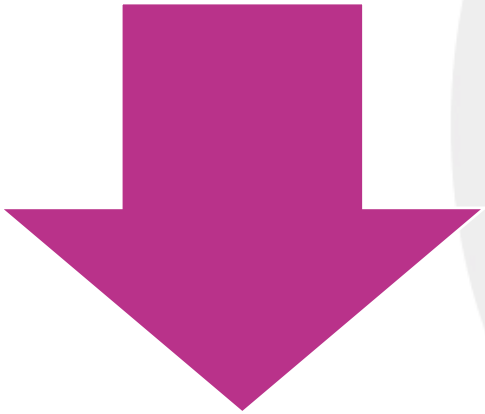
Picture in 2021

Progress:

ICH harmonisation

ICH Generics Discussion Group

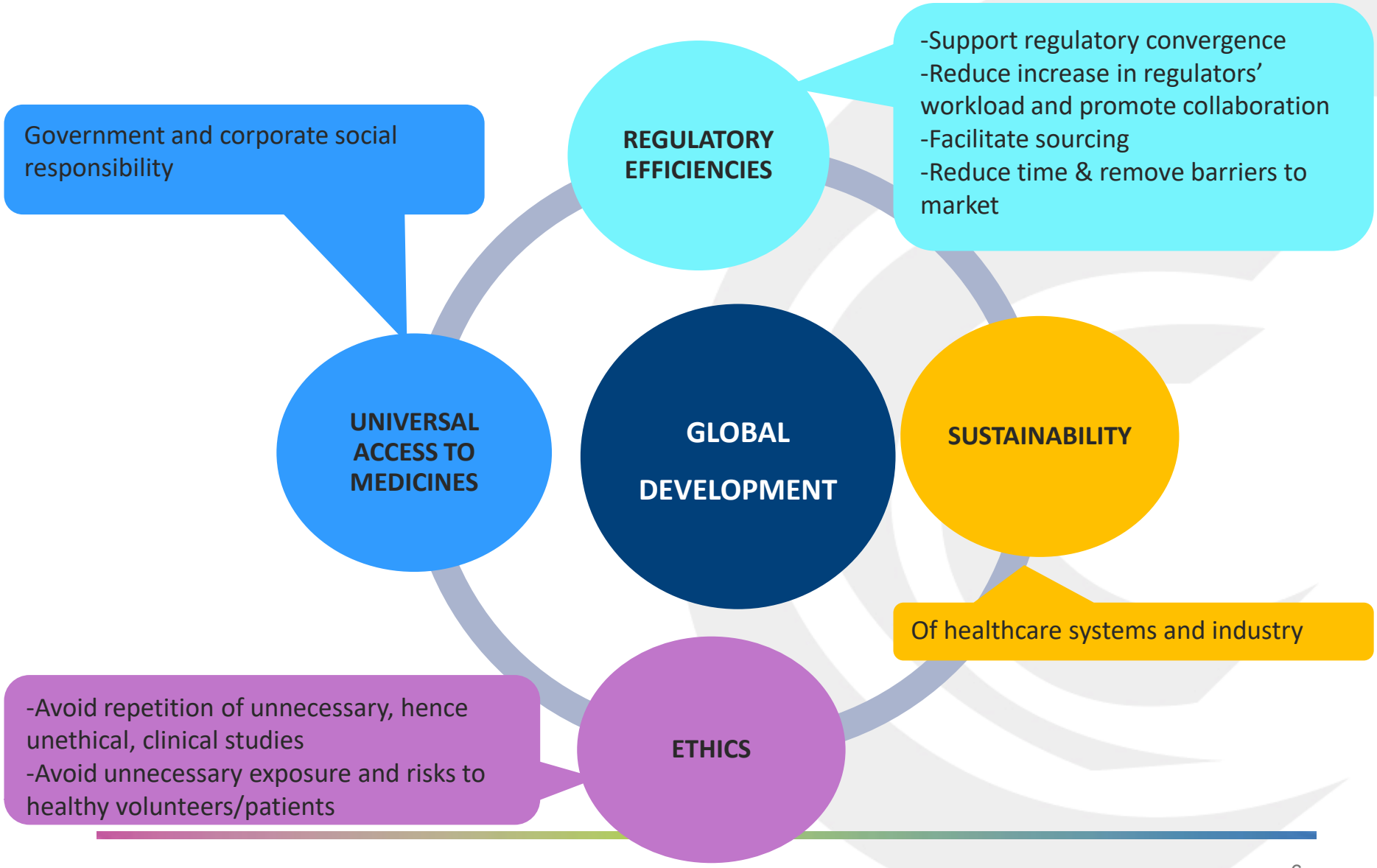
WHO – more reliance



Insufficient progress in global comparator for bioequivalence/ clinical studies

Still too much duplication/ inefficiency / fragmentation

Global Development, a MUST



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

The AAPS Journal (© 2017)
DOI: 10.1208/s12248-017-0068-6

Commentary

Global Harmonization of Comparator Products for Bioequivalence Studies

Luther Gwaza,[1,2] John Gordon,[3] Hubert Leufkens,[1] Matthias Stahl,[4] and Alfredo García-Arieta[5,6]

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.

regulated markets should be the global comparator. This harmonization is feasible as the concept already applies in the WHO prequalification program. It is ineffectual to harmonize 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)

World Health Organization. Annex 6 Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, In: WHO Expert Committee on Specifications for Pharmaceutical Preparations, Fifty-first report. WHO Technical Report Series, No. 1003, 2017, pg 184 - 236 [first published in 1996]

World Health Organization. Annex 8 Guidance on the selection of comparator pharmaceutical products for equivalence assessment of interchangeable multisource (generic) products, In: WHO Expert Committee on Specifications for Pharmaceutical Preparations, Forty-ninth report WHO Technical Report Series 992, 2015, pg 185 – 189. [first published in 2002]

World Health Organization. Annex 5 General background notes on the list of international comparator pharmaceutical products, In: WHO Expert Committee on Specifications for Pharmaceutical Preparations, Fifty-first report WHO Technical Report Series, No. 1003, 2017, pg 179-180 [first published in 2002]

Acceptance of foreign comparators

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

General aspects	Australia	Brazil	Canada	Colombia	European Union	Japan	Mexico	New Zealand	Singapore	South Africa	South Korea	Switzerland	Taiwan	US	WHO
Accept BE studies using foreign comparator products (under certain conditions)	Y	N	Y	N	N	N	N	Y	Y	Y	N	Y	Y	N	Y

Origin of foreign comparator products	Australia	Canada	New Zealand	Singapore	South Africa	Switzerland	Taiwan	WHO
Restricted to countries/regions with a comparable regulatory system	Y	Y	Y	N	Y	Y	N	(NA)
Has a positive list of countries/regions	N	N	N	N	Y	Y	N	(NA)
From same corporate entity as local comparator product	Y	Y	Y	Y	Y	Y	Y	(NA)

[a] 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.

Garcia Arieta A, Simon C, Lima Santos GM, Calderón Lojero IO, Rodríguez Martínez Z, Rodrigues C, Park SA, Kim JM, Kuribayashi R, Okada Y, Nolting A, Pfäffli C, Hung WY, Crane C, Braddy AC, Van Oudtshoorn J, Gutierrez Triana D, Clarke M. A Survey of the Regulatory Requirements for the Acceptance of Foreign Comparator Products by Participating Regulators and Organizations of the International Generic Drug Regulators Programme. J Pharm Pharm Sci. 2019;22(1):28-36.

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

ICH
harmonisation for better health

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

medicines for europe
better access. better health.

Let’s work together to make it happen one day!
Thank you