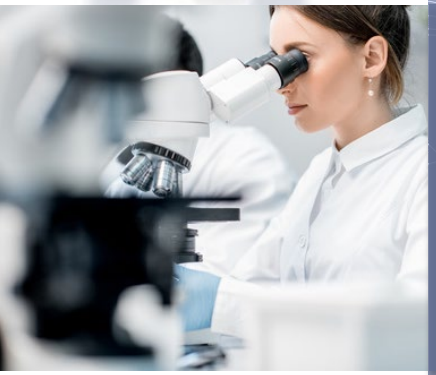


The Case For Single Global Development

Nicholas Cappuccino, PhD

IGBA Annual Conference 2023
February 16, 2023
Orlando, Florida, USA

IGBA

INTERNATIONAL GENERIC AND
BIOSIMILAR MEDICINES ASSOCIATION

About International Generic and Biosimilar Medicines Association (IGBA)

- Founded in March 1997 as the International Generic Pharmaceutical Alliance
- Renamed International Generic and Biosimilar Medicines Association in September 2015
- Legally incorporated in Geneva, Switzerland
- Admitted as ICH Assembly Member in 2016 and ICH Management Committee since 2017
- Accredited WIPO Observer since September 2019
- Admitted as non-State actor in official relations with WHO in January 2022
- Maintains constant dialogue with the WHO, WTO, WIPO and other national, regional, and international bodies

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

IGBA Mission Statement

- The International Generic and Biosimilar medicines Association (IGBA) strengthens cooperation between associations representing manufacturers of generic and biosimilar medicines from around the world. Adopting a patient centric approach, IGBA is at the forefront of globally improving patients' access to quality-assured, safe and cost-effective medicines by preserving competition as well as enabling innovation in the pharmaceutical sector and sustainable economic contributions for all stakeholders.

- For more details, regarding IGBA and its member associations, see the IGBA website at: www.igbamedicines.org.

- Full IGBA profile

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Generic Development: An Evolving Landscape

- More complex products
- Increasingly complex clinical development
- Niche therapeutics and orphan products
- Personalized medicine

Risk of fewer follow-on products

Less competition, less access

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Generic Development: Solutions

- **Goal:**
  - Offer access globally and tailor development, based on scientific discussion

- **How:**
  - Acceptance of single development for multiple jurisdictions, to avoid the repetition of unnecessary studies

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

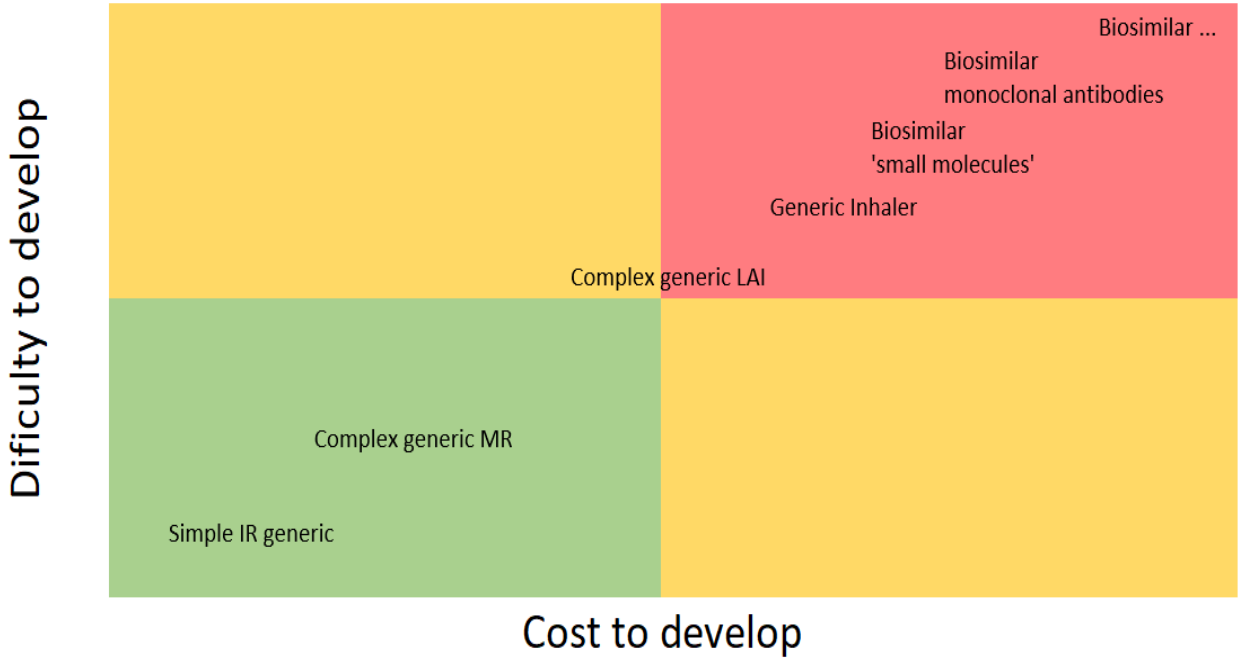
Single Global Development

- Supports consistent high quality worldwide - synergistic with GMP, Compendia, ICH compliance, etc.
- Standard approach for originator development
- Now commonly acceptable for biosimilar development – though regulatory discretion is significant
- Foreign comparators already accepted for generic development by several highly regulated regions

(*We will come back to this point.*)

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Development of Off Patent Products



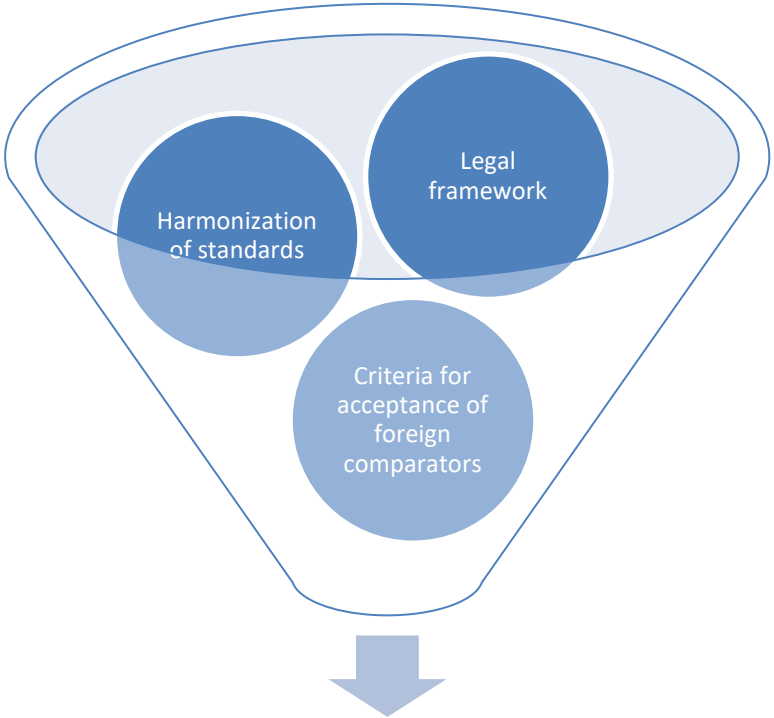
IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Development of Off Patent Products

- Not all small molecules follow on products are “easy to develop”
- Streamlining development for complex generics and biosimilars is key for **patient access**
- Failing to recognize the challenges for development of off patent products could compromise patient access to affordable medicines!

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Generic Single Global Development
3 pillars that must advance simultaneously



Single global development of generic medicines

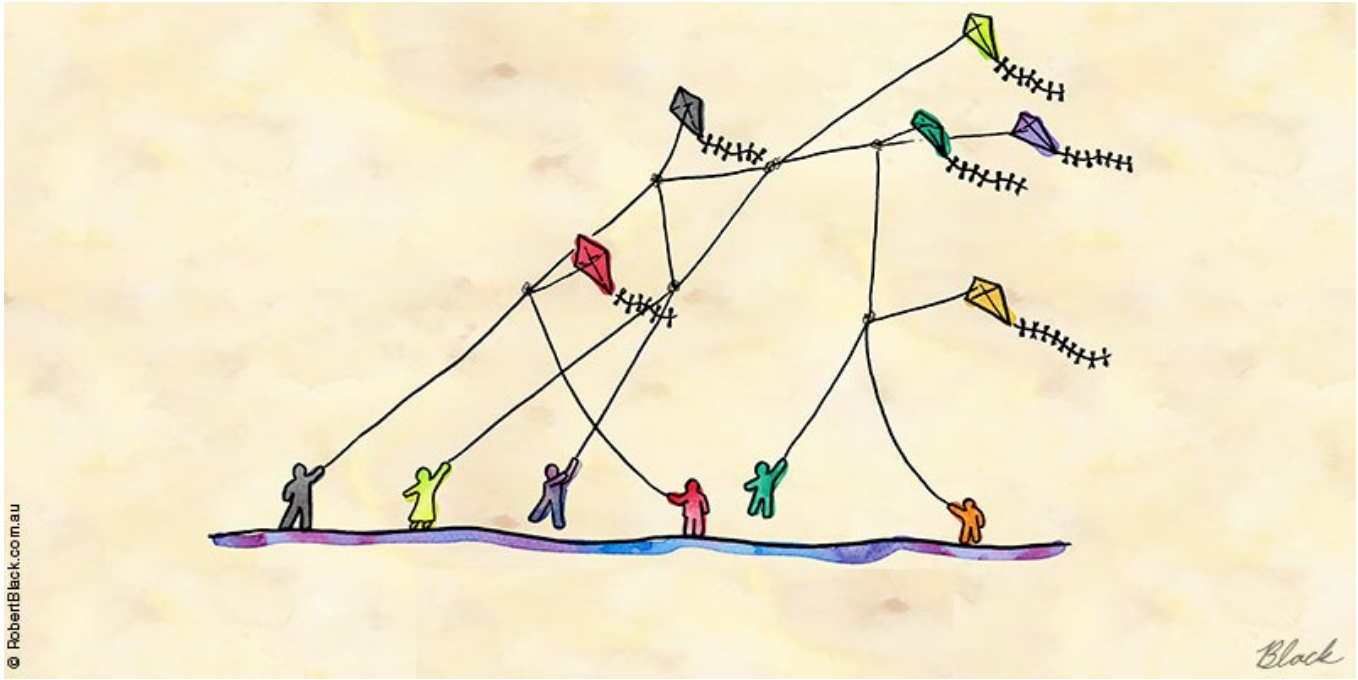
IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

1. Harmonization of Bioequivalence Standards

- Ongoing and advancing
- Draft of first ICH international guideline (Immediate Release Oral Dosage Forms) released for public comment as M13 in December 2022
- Public consultations are underway globally by ICH Regulators
- Additional ICH BE Guidelines for more complex dosage forms are planned

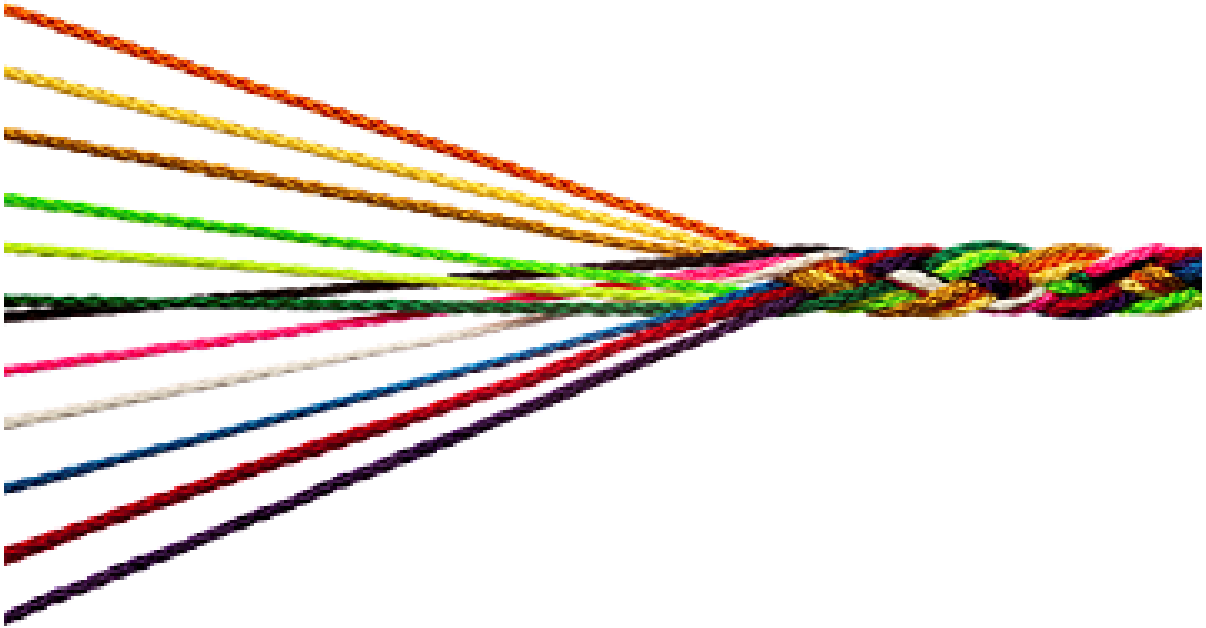
IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Before M13:
Multiple Standards (a tangled mess)



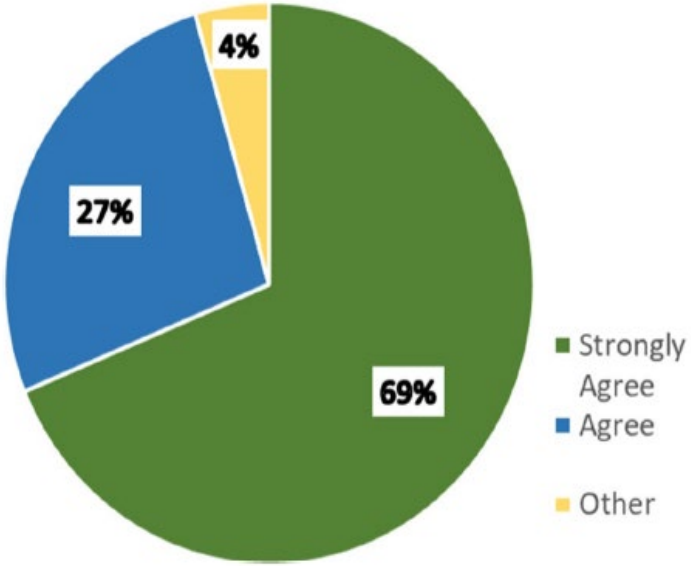
IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

After M13:
Harmonization and Convergence



IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Harmonization of BE: Does it Matter?



- It matters A LOT!
- Recent international survey on complex generics:
- 96% Agree or Strongly Agree on the importance of a harmonized international approach for complex generics

Stern S, Coghlan J, Krishnan V, Raney SG, Babiskin A, Jiang W, Lionberger R, Xu X, Schwendeman A, Polli JE. Research and Education Needs for Complex Generics. Pharm Res. 2021 Dec;38(12):1991-2001. doi: 10.1007/s11095-021-03149-y. Epub 2021 Dec 24. PMID: 34950975.

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

2. Legal Framework

- Several jurisdictions already accept the use of foreign comparator products in generic development

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Terminology is Important

Two important – yet distinct – terms:

- Reference product – usually originator registered in the local market
- Comparator product – which is the product to be used used in the BE studies

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

3. Which foreign comparators are acceptable?

- An international guideline is needed!
- Scientific criteria and the conditions of acceptability of foreign comparators for bioequivalence determination
- Who: Local competent authorities (jointly, or together with more regions)

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Use of Foreign Comparators is not a new concept!

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.

UK joined this list

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.

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Let’s use the knowledge that is already available

Source: https://dev.to/quantumsheep/why-you-should-reinvent-the-wheel-4ha2

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Size Matters!?

- Acceptance of foreign comparators appears to correlate reasonably well with the market size*

- For Orphan Medicines, Niche Therapeutics, Personalized Medicine, Complex Products:

Is any market large enough?

* 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.

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Sourcing of comparator product is a barrier to generic development in some jurisdictions!

Access to Product Samples: The CREATES Act

The law widely known as CREATES, which was enacted in December 2019 as part of the Further Consolidated Appropriations Act of 2020, makes available an important new pathway for developers of potential drug and biological products to obtain samples of brand products[1] that they need to support their applications. The full text of the new law is available here (/media/136039/download). CREATES establishes a private right of action that allows developers to sue brand companies that refuse to sell them product samples needed to support their applications. If the product developer prevails, the court will order the sale of samples, award attorneys' fees and litigation costs to the product developer, and may impose a monetary penalty on the brand company.

The product developer must take a number of specific steps (outlined in the law) before the brand company must sell them product samples under CREATES. One of these steps – if the brand product for which samples are sought is subject to a Risk Evaluation and Mitigation Strategy (REMS) with elements to assure safe use (ETASU) – is that the product developer must first obtain a Covered Product Authorization (CPA) from FDA. CREATES does not require this step for products that are not subject to REMS with ETASU.[2]

Q: How do I obtain a CPA from FDA?

Government of Canada / Gouvernement du Canada

Competition Bureau and Health Canada strengthen on key issues in the pharmaceutical industry

From: Competition Bureau Canada

News release

January 10, 2022 – GATINEAU, QC – Competition Bureau

- The Bureau and HPFB have collaborated on a variety of issues, such as mergers and ac misleading claims and claims of abuse of dominance. More recently, the ability for gene samples of reference products has been an area of ongoing collaboration.
- Given the guidance and warnings provided from the Bureau and HPFB on this issue, br should continue to anticipate that the Bureau will treat any explanation for a failure to s a timely manner, with an extremely high degree of skepticism.
- Should generic manufacturers face similar issues in the future, they are encouraged to Bureau's attention at an early stage.

03/02/2021 SEI/ANVISA - 1317510 - Voto

ANVISA
Agência Nacional de Vigilância Sanitária

VOTO Nº 08/2021/SEI/DIRE2/ANVISA

Processo nº 25351.941370/2020-00
Expediente nº 0244343/21-7

Analisa a solicitação de excepcionalidade para aquisição do produto Revlimid (lenalidomida) para realização de ensaios comparativos para registro de medicamento genérico/similar.

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Importance of Single Global Development

- ✓ Avoids redundant (hence unethical) clinical trials
- ✓ Helps increase patient access to generic medicines
  - Especially important in certain cases, i.e., **orphan drugs or complex generics**
- ✓ Contributes to competition, therefore increases access
- ✓ Leverages the benefits of harmonizing BE standards
- ✓ Helps to overcome challenges on sourcing of the comparator products, in some regions
- ✓ Enables regulatory reliance and mutual recognition agreements

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

The Way Forward

Internationally:

- Advance harmonization and dialogue

Locally or Jointly:

- Regions/countries to assess their legal frameworks:
  - Move forward if there are no legal barriers!
  - Address any potential legal barriers

- Define (ideally common) criteria for acceptance of foreign comparators in international guidelines

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

Take Home Messages

- Single global development is fundamental to support global access & global competitiveness of generic medicines
- In order to leverage the benefits of harmonization of bioequivalence, the use of foreign comparators is necessary – criteria should be defined
- The time to act is now

IGBA
INTERNATIONAL GENERIC AND BIOSIMILAR MEDICINES ASSOCIATION

THANK-YOU!

info@igbamedicines.org

www.igbamedicines.org

INTERNATIONAL GENERIC AND
BIOSIMILAR MEDICINES ASSOCIATION