Perspective on International Harmonisation

Regulatory Cooperation on Generic and Biosimilar Medicines: a policy and a legal perspective

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Two-fold Dimension:

- **Policy Dimension**
  - Why?
  - What benefits?
  - At what costs?

- **Legal Dimension**
  - What body of rules?
  - What is allowed?
  - Any change needed?

THE POLICY DIMENSION

Why:

- ✓ Globalised supply chains & growing complexity
- ✓ Global regulatory oversight
- ✓ Reduce regulatory public expenditures
- ✓ Growing number of inspections
- ✓ Align agendas of regulatory agencies

What:

- ✓ **ICH** - Harmonise requirements for registration of medicines
- ✓ **PIC/S** - Develop & promote harmonised GMP standards and guidance
- ✓ **IGDRP** - Promote collaboration & convergence in generic medicines programs
- ✓ **Bilateral initiatives** – e.g., MRAs, Single Development Programmes, etc.

…and beyond:

- ✓ Bilateral & plurilateral cooperation through trade agreements

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THE POLICY DIMENSION

Benefits:

- ✓ Increase patient access to high quality medicines
- ✓ Share scientific knowledge between regulators
- ✓ Promote high standards globally
- ✓ Lower development costs
- ✓ Optimise use of available resources
- ✓ Reduce unnecessary/unethical duplications
- ✓ Create potential for global cooperation

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EXAMPLES OF PLURI-/BI-LATERAL COOPERATION

a. Mutual Recognition of Good Manufacturing Practice (GMP) Inspections

b. Single Development for Biosimilar Medicines

c. Single Development for Generic Medicines

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a. MUTUAL RECOGNITION OF GMP INSPECTIONS

- **Recognition of each others inspections to avoid duplicative work**
  - Share scientific knowledge
  - Align on high standards for inspections
  - Reduce duplications for industry & regulators
  - More efficient use of regulatory resources
  - Devote more resources to inspect emerging markets

- **Results already achieved: EU-US MRA on GMP Inspections**
  - Differences in the legal frameworks & in practices
  - Between & within US & EU
  - MRA agreed in March 2017
  - Into force on 1 November 2017 covering 8 EU Member States
  - Progressive expansion of the scope until 2019
  - Possible expansion to 3rd countries

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b. SINGLE DEVELOPMENT FOR BIOSIMILAR MEDICINES

- **Alignment on approval processes & requirements for biosimilar medicines**
  - Reduction of development costs
  - Removal of unethical duplication of clinical trials
  - Faster & increased access to biopharmaceuticals
  - Sustainability of healthcare systems
  - Promote highest standards globally

- **Guideline/guidance amended:**
  - **EU:** EMA guideline CHMP/437/04 Rev 1 on "*Similar Biological Medicinal Products*"
  - **US:** FDA Guidance for Industry: "*Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product*"

- **Results already achieved between US & EU:**
  - allowed by EU guideline & US guidance since 2015
  - 75% of biosimilar applications in EU request this pathway
  - first biosimilars approved in US

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c. SINGLE DEVELOPMENT FOR GENERIC MEDICINES

- **Alignment on approval processes & requirements for generic medicines**
  - Reduction of clinical development costs
  - Opportunity to re-invest potential savings
  - Reduction of unethical repetition of studies
  - Increased patient access to quality, safe and effective generic medicines in many regions simultaneously
  - Sustainability of healthcare systems
  - Promote highest standards globally
  - Particularly relevant for complex generics

- **Examples:**
  - Transdermal Patches: Cost saving up to 4,5 Million Euro (4.9 Million US$) per product
  - Injectables: 0.45 Million Euro (0.49 Million US$) per product
  - Products with larger clinical studies: up to 35 Million Euro (38 Million US$) per product

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REGULATORY COOPERATION FOR MEDICINES: THE POLICY DIMENSION

Regulatory cooperation for generic and biosimilar medicines from a *policy perspective*: an opportunity for patients, industry, regulators and governments!

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THE LEGAL DIMENSION

- **What legal framework?**
- **What interpretation is given to the law?**
- **What is allowed?**
- **How does cooperation translate in practice?**
- **Any legislative change needed?**
- **Is soft-law enough?**

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CONCRETE EXAMPLE

- **Single Development of Complex Generic Medicines**

  – In line with the common US-EU approach on Biosimilars: *with a step-wise approach, allow an applicant to compare its product with a non-EU/US comparator that is authorised by a regulatory authority with similarly stringent scientific and regulatory standards*

  – In EU: same definition of the reference product in Art 10 point 2 (a) of the EU Directive 2001/83/EC applies to biosimilar, generic and hybrid applications (under Art. 10.1, Art 10.3 and Art 10.4)

  – In US: applications subject to “abbreviated applications”

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THE LEGAL QUESTION: THE EU SITUATION

- The same definition of the reference product in Art 10 point 2 (a) of the EU Directive 2001/83/EC applies to biosimilar, generic and hybrid applications (under Art. 10.1, Art 10.3 and Art 10.4)

- The relevant guidelines on studies supporting generic and hybrid applications (*i.e. in the Guideline on the investigation of bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1*) can be amended to explicitly allow the sourcing of the reference product from other regions with high regulatory standards

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THE LEGAL QUESTION: THE US SITUATION 1

- Statutory provisions governing FDA's generic drug review require reference to a US-approved brand product, but are silent on whether studies of non-US versions of such reference products can be considered by FDA in review of generic application.

- Same is true for biosimilars provisions passed by Congress in 2009 in BPCIA. BPCIA requires that a biosimilars applicant compare its test product to a reference product licensed under section 351(a) of the Public Health Service Act.

- In April 2015, FDA Industry Guidance stated expressly that a biosimilars applicant "*may seek to use data derived from animal or clinical studies comparing a proposed product* ***with a non-U.S. licensed comparator product*** *to address, in part, the [statutory] requirements*." A following FDA "Q&A" document confirmed.

- Nothing in the Hatch-Waxman Amendments prevents application of these same regulatory principles to determine the propriety of using non-US-approved small molecule drug products in studies accompanying US generic drug applications

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THE LEGAL QUESTION: THE US SITUATION 2

- Legally permissible regulatory framework
- It would be Applicant's responsibility to demonstrate that the comparator authorized outside the US is comparable to the US-approved reference product.
- The relative simplicity of small-molecule drug products supports even greater reliance on non-US reference products than in the biosimilars context
- There is nothing in US statutory law to prevent FDA from taking the same guidance-based approach in the context of small molecule generic drugs that it has taken in the biosimilars context

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US-EU SINGLE DEVELOPMENT

Legal Opinion

A Single US-EU Regulatory Framework for Development of Generic Medicines, by Zuckerman Spaeder LLP and Taylor Wessing LLP, September 2016

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THANK YOU

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BACK UP & TEMPLATE SLIDES

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International Generic and Biosimilar Medicines Association (IGBA)

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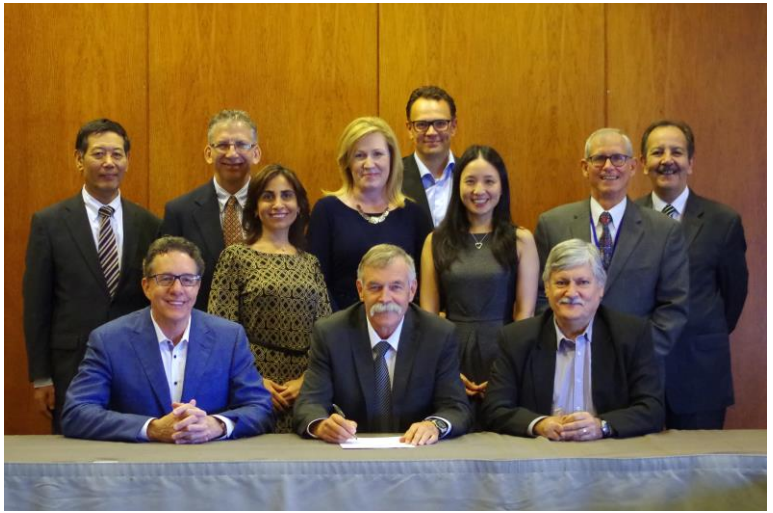
ABOUT IGBA

- Founded in March 1997 as the International Generic Pharmaceutical Alliance
- Renamed **International Generic and Biosimilar Medicines Association (IGBA)** in September 2015
- Legally incorporated in Geneva, Switzerland
- Admitted as Assembly Member of ICH in June 2016
- Maintains constant dialogue with the WHO, WTO, WIPO, ICH and other national, regional and international bodies



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MEMBERS

- IGBA is committed to promoting generic and biosimilar medicines worldwide, and consists of the following associations:

  - Canadian Generic Pharmaceutical Association (CGPA-Canada)
  - Association for Accessible Medications (AAM-United States)
  - Japan Generic Medicines Association (JGA-Japan)
  - Jordanian Association of Pharmaceutical Manufacturers (JAPM-Jordan)
  - Medicines for Europe (Europe)
  - Generic and Biosimilar Medicines of Southern Africa (GBM-South Africa)
  - Taiwan Generic Pharmaceutical Association (TGPA-Taiwan)

  The generic and biosimilar medicines associations of Australia, Brazil, Malaysia and Mexico are Associate Members.

- In addition, IGBA includes:

  – Biosimilars Canada
  – Biosimilars Council (AAM Division)
  – Biosimilar Medicines Group (Medicines for Europe Sector Group)

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IGBA Goals

- Promote regulatory cooperation and convergence for approval of generic and biosimilar medicines
- Promote the widest possible access of medicines globally with high quality, safety and efficacy
- Promote intellectual property regimes which foster innovation and allow timely launch of generic and biosimilar medicines, while supporting fair competition and preventing risks of IP abuses globally
- Support and co-operate with international bodies and initiatives including the WHO, WTO, WIPO, ICH, IGDRP, IPRF, etc.
- Support parties in international and regional agreement negotiations to remove barriers and facilitate the registration and supply of generic and biosimilar medicines
- Foster sustainability of medicine manufacturers in the interests of healthcare systems and patients
- Advance better access to generic and biosimilar medicines globally by organizing international conferences for the industry, stakeholders and regulators

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