The Importance of Global Regulatory Harmonization for Biosimilar Medicines

Suzette Kox, Secretary General, International Generic and Biosimilar Medicines Association

4 November 2019, Bethesda North Marriott Hotel & Conference Center

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Outline

- About IGBA
- Generic and biosimilars' contribution to the United Nation Sustainable Development Goals
- Next steps in the biosimilars regulatory framework: global biosimilar development
  - Regulatory cooperation and convergence of requirements
  - Use of global comparator product
  - Waiving of bridging studies
  - Tailoring of clinical development programs
  - RWE of biosimilar medicines
- WHO latest developments
- Conclusion and recommendations

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About the 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** in 2018
- Accredited **WIPO Observer** since September 2019
- **WHO signed a MoU with IGBA to promote access** in October 2019
- Maintains constant dialogue with the WHO, WTO, WIPO and other national, regional and international bodies
- Open to national and regional associations

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IGBA Goals

- Promote regulatory cooperation and convergence of requirements for approval of generic and biosimilar medicines through international regulatory fora and trade negotiations
- Promote the widest possible access of high quality, safe and effective medicines to patients globally
- Promote generic and biosimilar friendly intellectual property regimes globally which foster innovation while supporting competition and preventing risks of IP abuses
- Attract the widest assembly of members who are committed to subscribing to our standards and principles
- Represent our members and support and co-operate with relevant international bodies and initiatives including the WHO, WTO, WIPO, ICH, IGDRP, IPRF, etc.
- Support parties in international and regional agreement negotiations to remove barriers to and facilitate the registration and supply of generic and biosimilar medicines
- Foster the sustainability of medicine manufacturers in the interests of healthcare systems and patients

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IGBA Members

- Association for Accessible Medicines (AAM-United States**)**
- Canadian Generic Pharmaceutical Association (CGPA-Canada)
- Generic and Biosimilar Medicines Association of Southern Africa
- Indian Pharmaceutical Alliance (IPA-India)
- Jordanian Association of Pharmaceutical Manufacturers (JAPM-Jordan)
- Japan Generic Medicines Association (JGA-Japan)
- Medicines for Europe (Europe)
- Taiwan Generic Pharmaceutical Association (TGPA-Taiwan)

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

In addition, IGBA includes:

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

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UN shared vision: equity of access to medicines

United Nation Sustainable Development Goals (2015):

Goal 3**: Promote health and well-being**

Shared responsibility:

- IGBA Members: key role in worldwide access to high-quality, safe, and effective generic and biosimilar medicines
- Policy-makers at all levels: role to play in creating an environment for medicines to address inequities in health
- Regulatory authorities: central role to ensuring a sustainable environment for medicines development, approval and access

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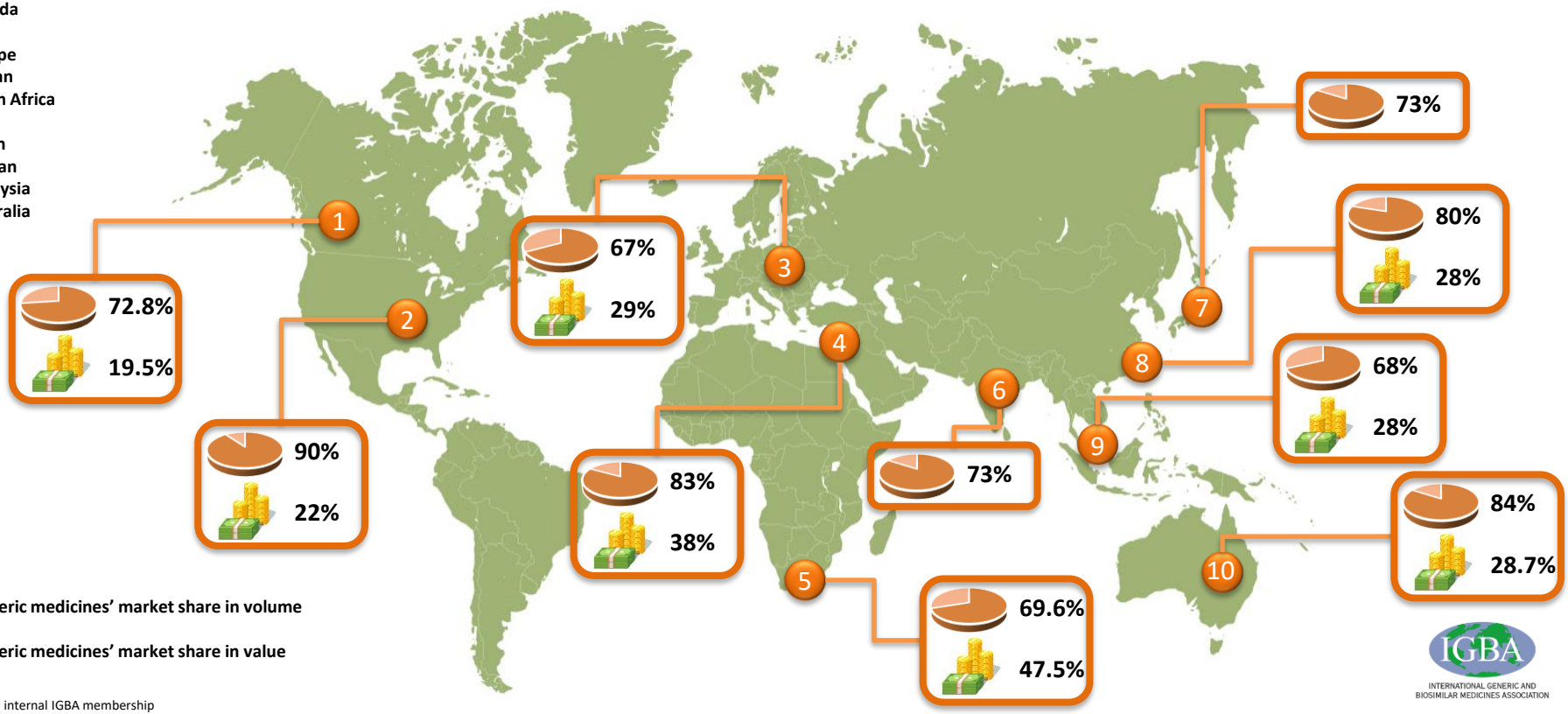
Market penetration of generic medicines

1. Canada
2. USA
3. Europe
4. Jordan
5. South Africa
6. India
7. Japan
8. Taiwan
9. Malaysia
10. Australia



Generic medicines' market share in volume

Generic medicines' market share in value

Source of data: internal IGBA membership

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Biological medicines have revolutionized the treatment of many disabling and life-threatening diseases

- **Biological medicines:**
  - include a wide range of products such as vaccines, blood and blood components, allergenics, somatic cells, gene therapies, tissues, and recombinant therapeutic proteins
  - are highly specific and targeted medicines
  - help to treat or prevent many rare and severe diseases, including:

Cancers | Arthritis | Psoriasis | Inflammatory digestive disorders | Growth disorders | Diabetes

Biological medicines are developed based on a deep understanding of the disease biology

References: FDA. Vaccines, Blood & Biologics. Available at: http://bit.ly/2qf3Ebs. Accessed July 2017.

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Health systems must adapt to meet the growing demand for the treatment of chronic conditions[1]

In the US, **chronic conditions** account for:

two thirds of all healthcare costs[2]

and **93% of Medicare*** spending[3]

With the global prevalence of age-related chronic diseases rising, **access to cost-effective medical treatment will become increasingly important** over the next decades

Access to cost-effective treatment is paramount for the short, medium, and long-term sustainability of healthcare systems[1]

Footnotes: *Medicare is a US federal health insurance program for elderly patients.

References: 1. United Nations. World Aging Report. Available at: http://bit.ly/1Y2LeF4. Accessed April 2017; 2. Centers for Disease Control and Prevention. The State of Aging and Health in America 2013. Available at: http://bit.ly/2q3y8w0. Accessed July 2017; 3. Chronic Conditions Among Medicare Beneficiaries, Chart Book 2012. Available at: http://go.cms.gov/2pGq5tk. Accessed July 2017.

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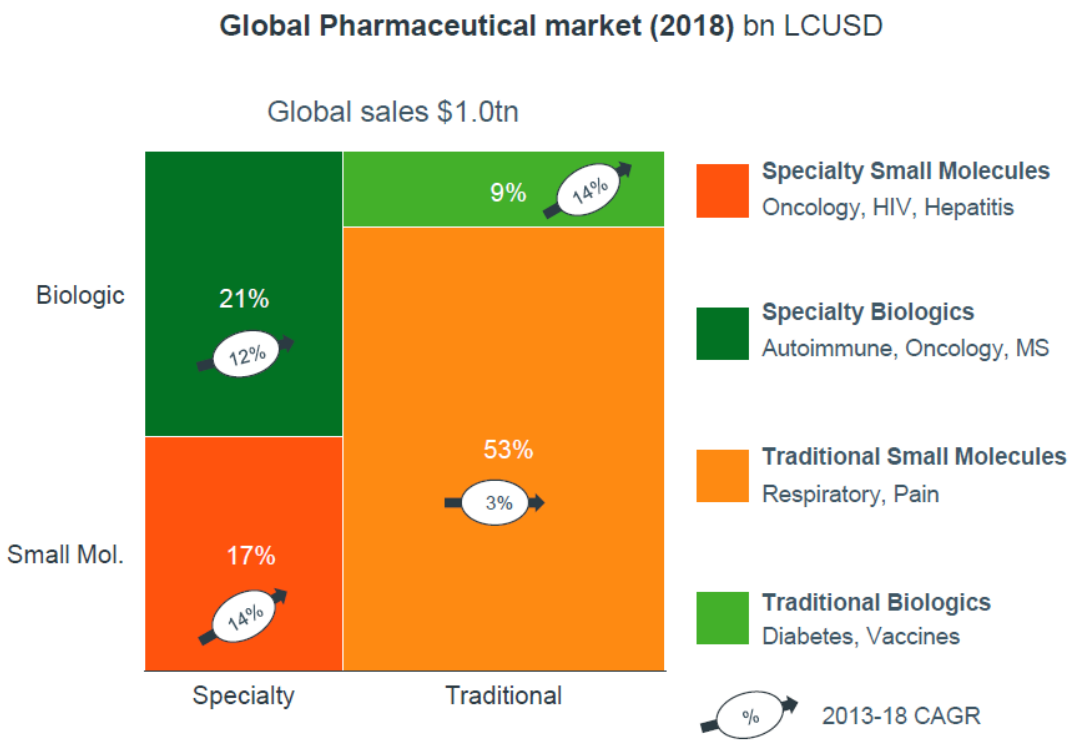
Specialty small molecules and biologics will continue to define high value medicines in the near future → sustainable?



Source: IQVIA European Thought Leadership Analysis; IQVIA MIDAS MAT Q4 2018; Rx only

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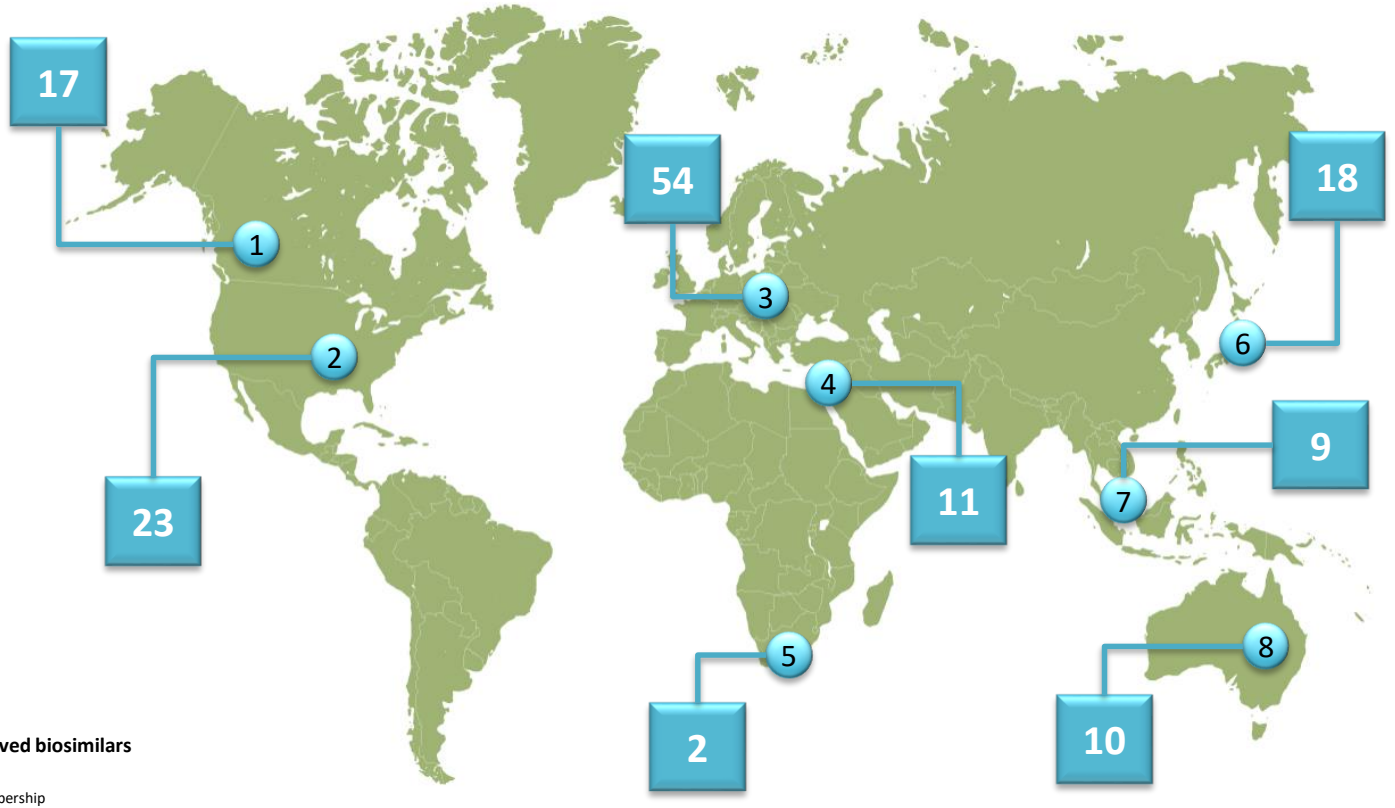
Biosimilar medicines: opportunity to generate competition in the biologics space

1. Canada
2. USA
3. Europe
4. Jordan
5. South Africa
6. Japan
7. Malaysia
8. Australia



17 Number of approved biosimilars

Source of data: internal IGBA membership

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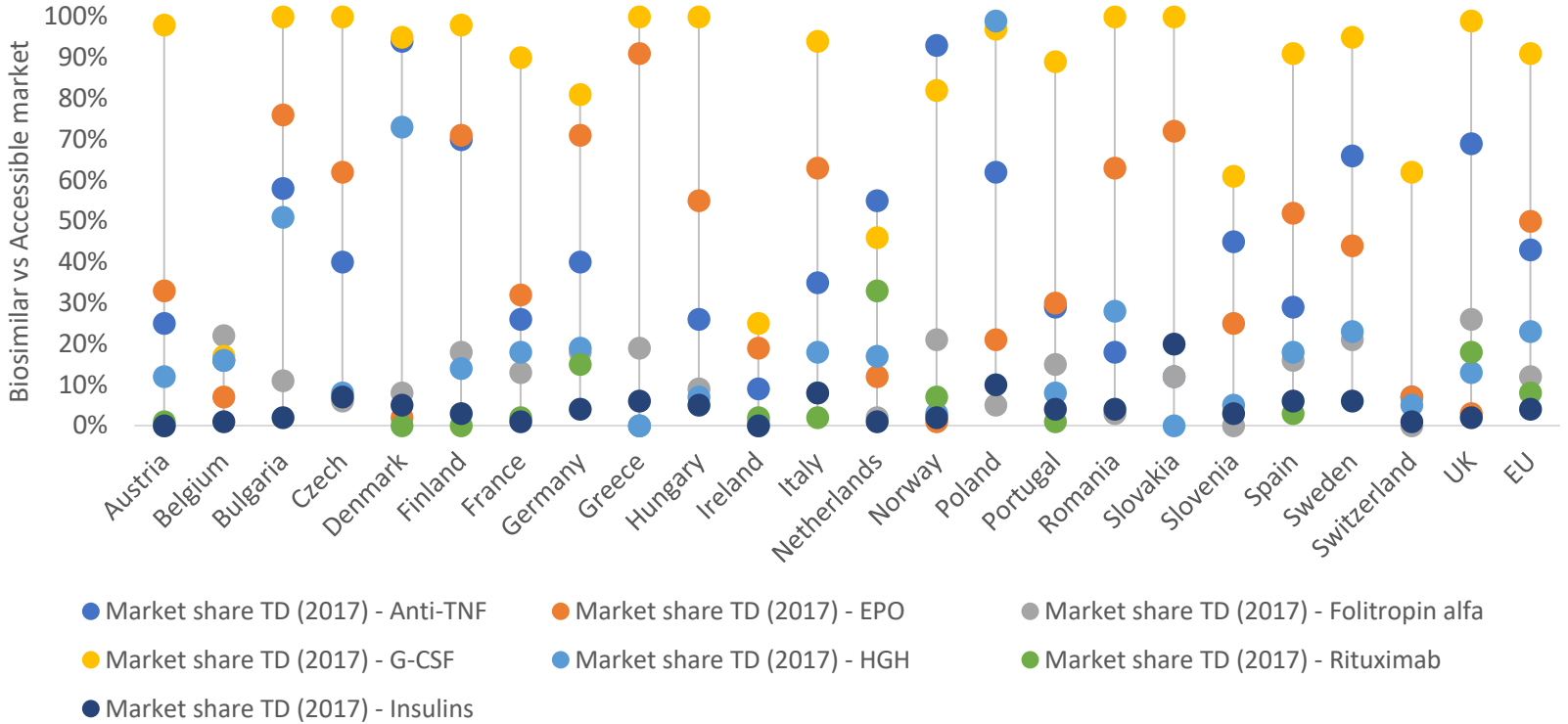
Use of biosimilar medicines in EU varies greatly by country and therapeutic area



IQVIA. *The Impact of Biosimilar Competition in Europe*. (2018).

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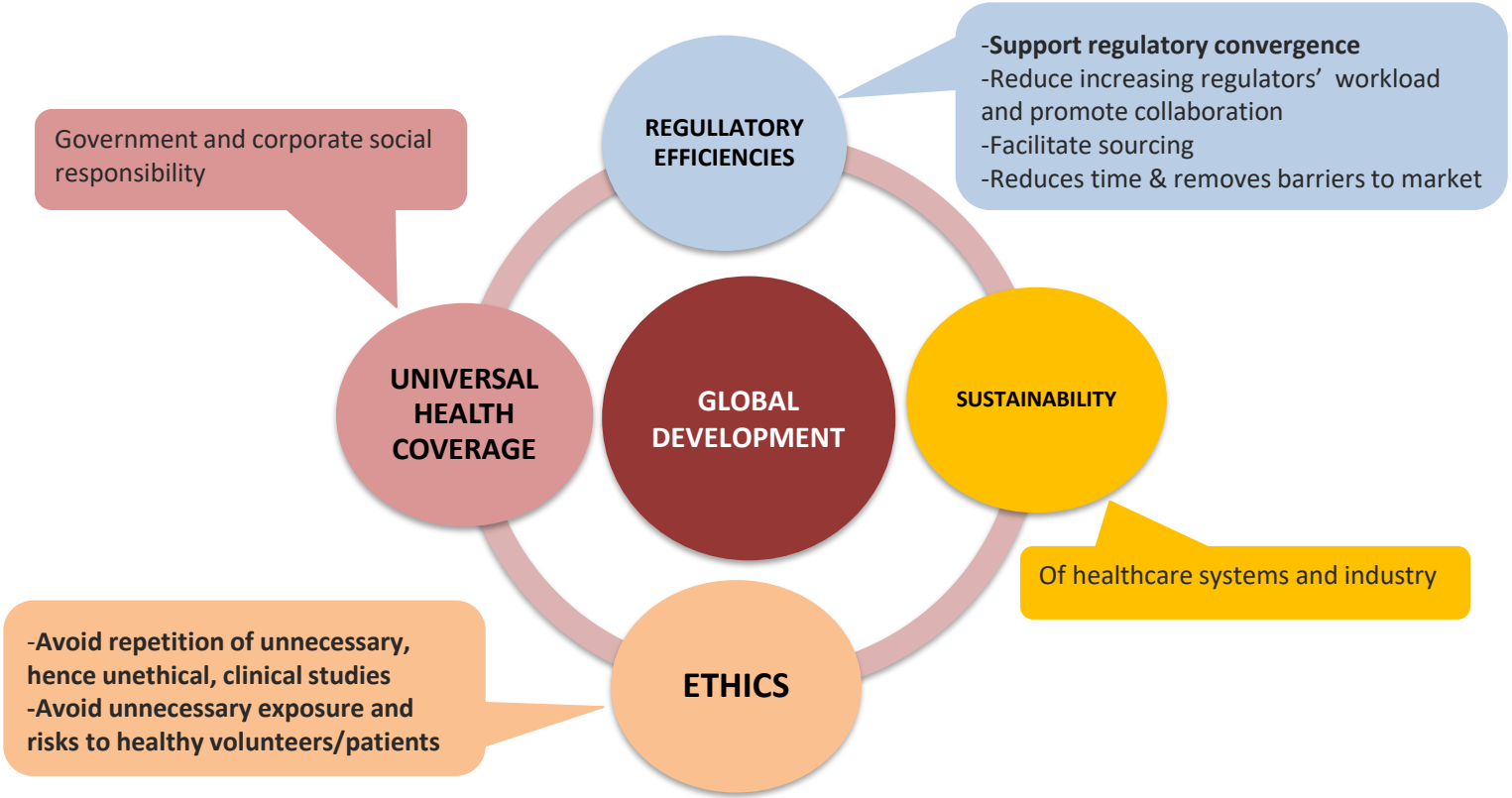
Next step in the biosimilars framework: global biosimilar development



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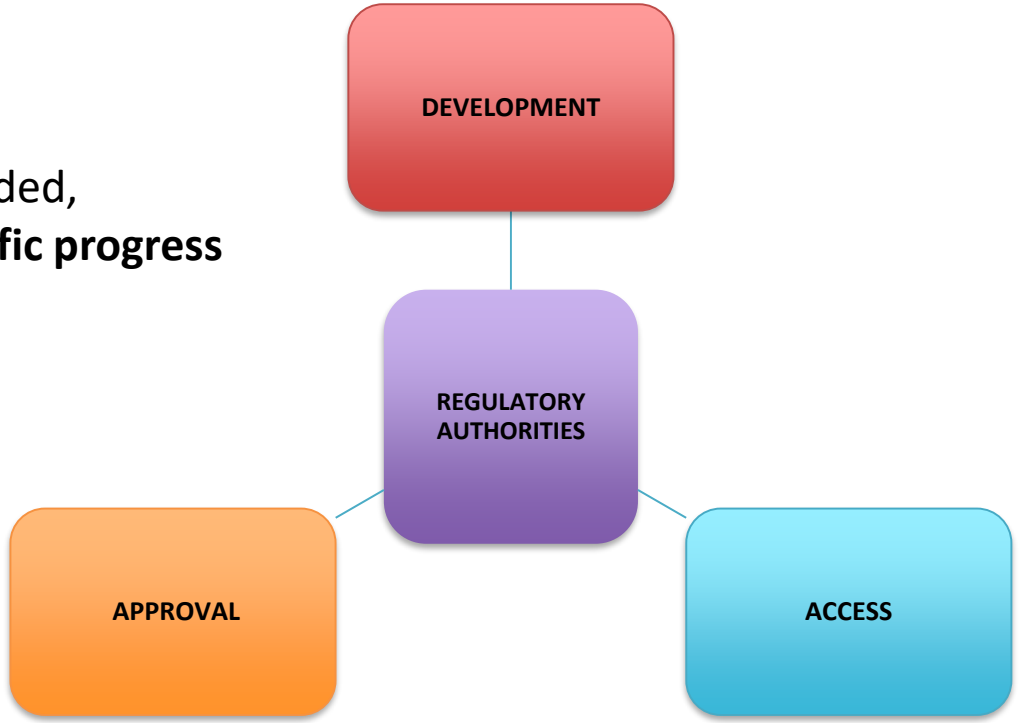
Regulatory authorities: central role to ensure a sustainable environment for biosimilar medicines development, approval and access

To deliver the promise of biosimilars, adjustment of the regulatory requirements is needed, based on **analytical** and **scientific progress** and **accumulated experience**



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Need for a true global biosimilar development framework: venues to be tackled in parallel

*https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/five-things-to-know-about-biosimilars-right-now, accessed 9 Sep 2019

Use of a global comparator product and waiving of bridging studies

Regulatory convergence and tailoring of clinical development programs

Current biosimilar development costs range from $100 – $300 million*

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Key venues for global biosimilar development

Regulatory convergence

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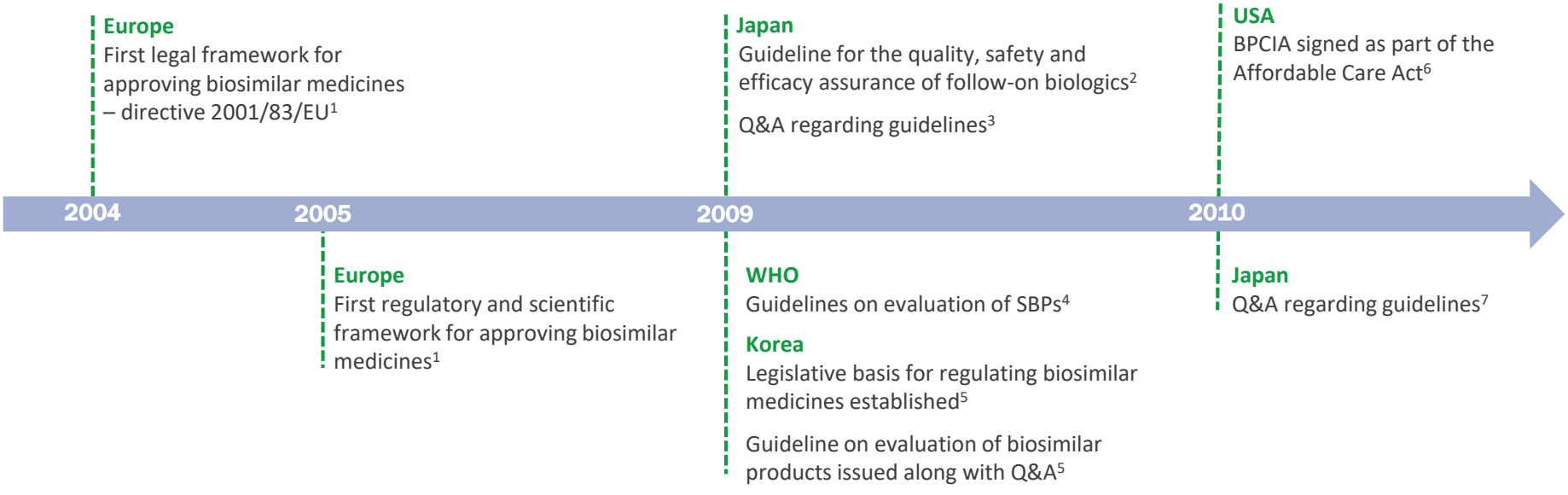
First scientific, regulatory, and legal frameworks established around the world



Abbreviations: BPICA, Biologics Price Competition and Innovation Act; EMA, European Medicines Agency; JGA, Japan Generic Medicines Association; MHLW, Ministry of Health, Labour and Welfare; SBP, similar biotherapeutic products; WHO, World Health Organisation.

References: 1. EMA. Biosimilar. Available at: http://bit.ly/2qfmPF0. Accessed July 2017; **2.** MHLW. Guideline for the Quality, Safety, and Efficacy Assurance of Follow-on Biologics. Available at: http://bit.ly/2pq8AKX. Accessed July 2017; **3**.JGA. Available at: http://bit.ly/2rnaVqm. Accessed July 2017; **4.** WHO. Guidelines on evaluation of similar biotherapeutic products (SBPs). Available at: http://bit.ly/2oU099B. Accessed July 2017; **5.** Park Y, et al. Presented at Biosimilars Medicines Group conference, London 2016; **6.** US government. Available at: http://bit.ly/2qo3Dl6. Accessed July 2017; **7.** JGA. Available at: http://bit.ly/2qooDee. Accessed July 2017.

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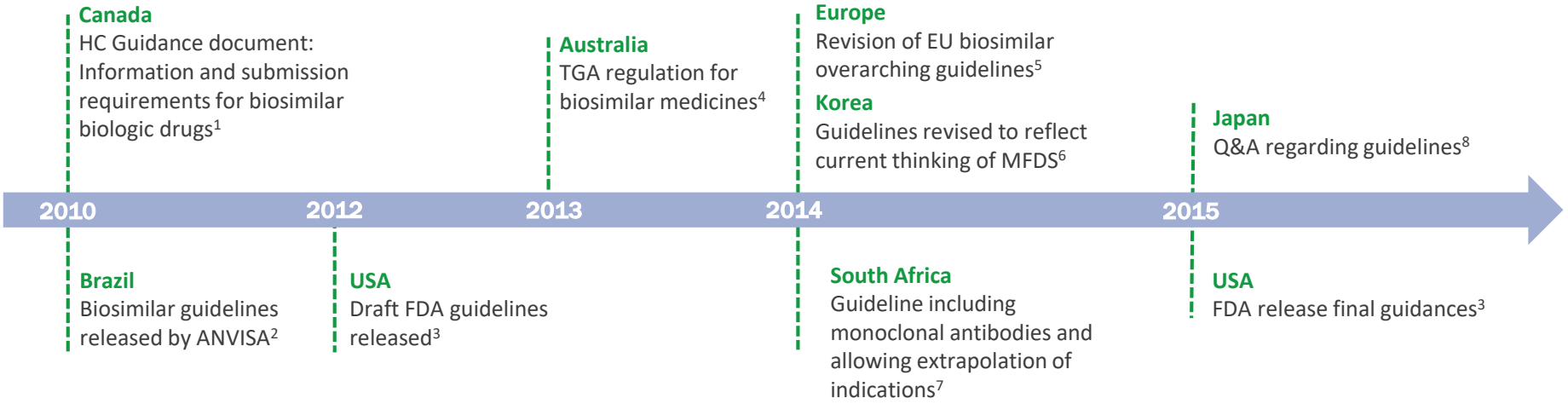
Further scientific, regulatory, and legal frameworks established around the world



Experience accumulated and science and technologies have evolved

Abbreviations: ANVISA, The Brazilian Health Regulatory Agency; EMA, European Medicines Agency; FDA, Food and Drug Administration; HC, Health Canada; JGA, Japan Generic Medicines Association MFDS, Ministry of Food and Drug Safety; MCCZA, Medicines Control Council of South Africa; TGA, Therapeutic Goods Administration.

References: 1. Health Canada. Information and Submission Requirements for Biosimilar Biologic Drugs. Available at: http://bit.ly/2tJYGZJ. Accessed July 2017; **2.** ANVISA. Resolution - RDC Nº 55. Available at: http://bit.ly/2uPanhJ. Accessed July 2017; **3.** FDA. Biosimilars. Available at: http://bit.ly/2oTOoA5. Accessed July 2017; **4.** TGA. Regulation of biosimilar medicines. Available at: http://bit.ly/2pquwpe. Accessed July 2017; **5.** EMA. Biosimilar. Available at: http://bit.ly/1trteeH. Accessed July 2017; **6.** Park Y, *et al.* Presented at Biosimilars Medicines Group conference, London 2016; **7.** MCCZA. Biosimilar medicines quality, non-clinical and clinical requirements. Available at: http://bit.ly/2uPivil. Accessed July 2017; 8. JGA. Available at: http://bit.ly/2rcqRyt. Accessed July 2017.

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FDA supports multinational development programs

- "*Creating efficient economies of scale for biosimilars requires a global market. This* ***means harmonizing requirements for their development, and sharing regulatory experience across national boundaries.*** *And so, we're especially focused on strengthening partnerships with regulatory authorities in Europe"*
  - Commissioner Dr. Gottlieb speech: "Capturing the Benefits of Competition for Patients" @ America's Health Insurance Plans' (AHIP) National Health Policy Conference; 7 March 2018

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Increase of regulatory networks supporting collaboration, convergence and ultimately reliance

- International Coalition of Medicines Regulatory Authorities (ICMRA)
  - provides strategic directions for enhanced cooperation on common scientific, regulatory or safety challenges, improved communication and information sharing between its members and effective global crisis response mechanisms
- ACSS - Australia, Canada, Singapore, Switzerland Consortium
  - Work focuses on concrete regulatory work sharing initiatives (covering recently also biosimilars)
- IPRP Biosimilars Working Group (International Pharmaceutical Regulators Programme)
  - supports international regulators develop safe and effective regulatory frameworks for biosimilars
- WHO Similar Biotherapeutic Products (SBP) Guidelines
  - Q&A to be updated to reflect experience, advances in science and technologies
  - Implementation workshops
- WHO Listed Authorities (WLA) ongoing initiative based on a Global Benchmarking Tool (GBT)
  - aiming at reliance
  - WHO survey (June 2019) on reliance and recognition https://bit.ly/34pAUjC

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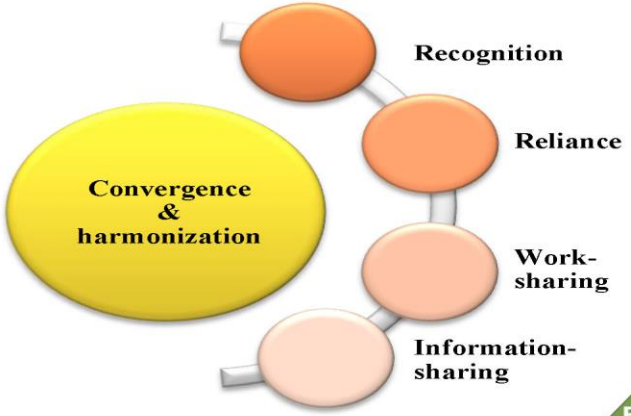
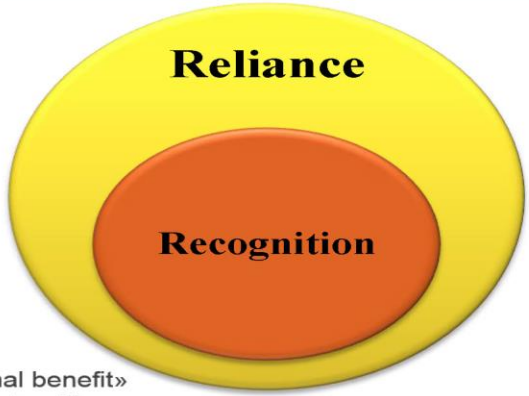
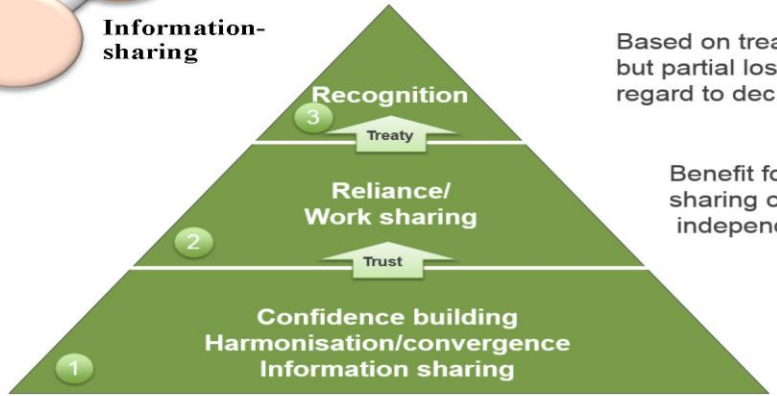
Views on Reliance and Recognition







Based on treaties; «maximal benefit» but partial loss of sovereignty with regard to decision-making

Benefit for regulators; sharing of workload, but independent decisions

«Foundation», Equivalence of requirements

World Health Organization

Key venues for biosimilar global development

Use of a global comparator product

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A ‘Global Reference’ Comparator for Biosimilar Development

BioDrugs
August 2017, Volume 31, Issue 4, pp 279–286 | Cite as

A ‘Global Reference’ Comparator for Biosimilar Development

Authors | Authors and affiliations

Christopher J. Webster, Gillian R. Woollett

Open Access | Current Opinion
First Online: 19 May 2017

Open Access at : https://link.springer.com/article/10.1007/s40259-017-0227-4

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Same pivotal clinical data supporting the approvals of biologics in multiple jurisdictions

Biologic	Trade Name	Sponsor	Countries in which First Approvals Were Based on the Same Studies*	Studies Submitted for First Approvals in More Than One Country	Indications Studied
Infliximab	Remicade	Janssen	US, EU, Canada, Australia	T16, T21	Crohn's disease
Etanercept	Enbrel	Amgen	US, EU, Canada, Australia	16.009, 16.014	Rheumatoid arthritis
Adalimumab	Humira	AbbVie	US, EU, Canada, Australia	DE009, DE011, DE019, DE031	Rheumatoid arthritis
Pegfilgrastim	Neulasta	Amgen	US, EU, Canada, Australia	980226, 990749	Febrile neutropenia in treatment of non-myeloid cancers
Bevacizumab	Avastin	Genentech/Roche	US, EU, Canada, Australia	AVF2107g, AVF0780g	Metastatic colon cancer
Ranibizumab	Lucentis	Genentech	US, EU, Canada, Australia	FVF2598g, FVF2587g, FVF3192g	Age-related macular degeneration

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A 'Global Reference' comparator for biosimilar development, Christopher J. Webster – Gillian R- Woollett

BioDrugs_published online 19 May 2017, Volume 31, Issue 4, pp 279–286 http://link.springer.com/article/10.1007%2Fs40259-017-0227-4

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There is effectively only a single comparator approved globally
Clinical properties and label remain unchanged after manufacturing changes

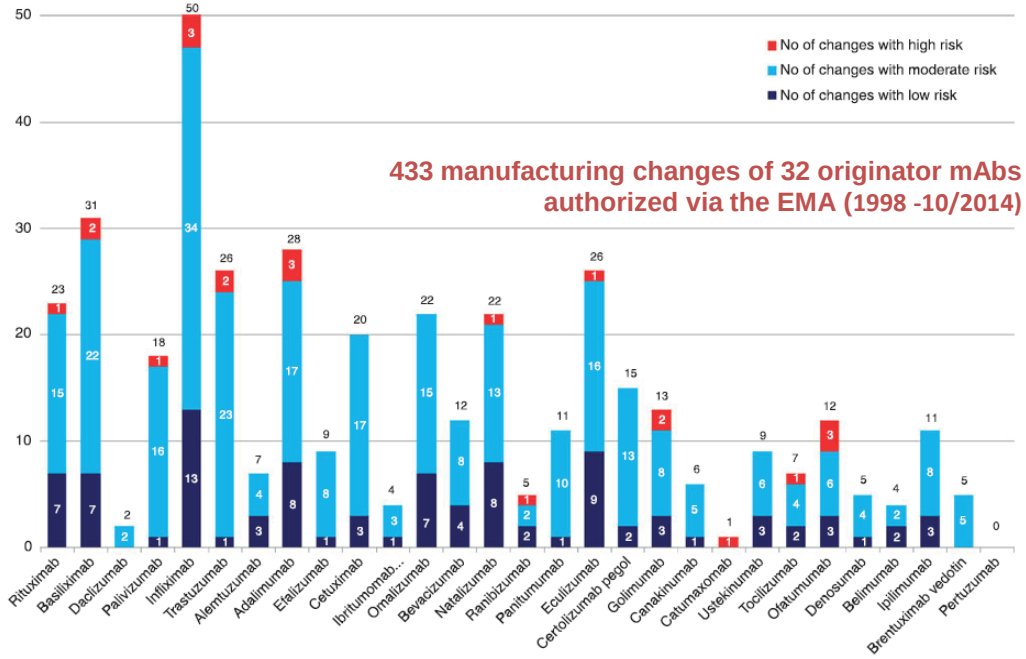

Figure 2. Number of manufacturing changes for monoclonal antibodies in their European Public Assessment Reports according to risk category (during the search period all non-proprietary names relate only to the trade named medicines listed in Table 1).

Vezér B, Buzás Zs, Sebeszta M, Zrubka Z.: Authorized manufacturing changes for therapeutic monoclonal antibodies (mAbs) in European Public Assessment Report (EPAR) documents. Curr Med Res Opin. 2016 May;32(5):829-34

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Are foreign-sourced reference products accepted as comparator products? (1)

- **From a purely scientific perspective, a comparability exercise against the EU- and/or the US-sourced reference product (or sourced from any other „Stringent Regulatory Authoritiy“) is sufficient to enable a global biosimilar development**

A detailed internal review* of existing biosimilar guidance from various countries reveals diverging regulatory environments, which can be categorized as follows:

Category 1: Countries **that explicitly accept reference products** sourced outside their jurisdiction as comparator, without asking any additional (analytical) bridging study

Category 2: Countries that **do not object reference products** sourced outside their jurisdiction as comparator, and do not ask for any additional (analytical) bridging study, according to experience gained with submitting biosimilar candidate products in these countries, which are silent on this topic in their individual biosimilar guideline (if available)

*Review performed by T. Kirchlechner/Sandoz for IGBA; results to be validated by IPRP Biosimilars Working Group

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Are foreign-sourced reference products accepted as comparator products? (2)

Category 3: Countries that **conditionally accept reference products** sourced outside their jurisdiction as comparator, e.g. if sameness of reference manufacturing site can be proven by public domain information (same site supplying foreign and local jurisdiction)

Category 4: Countries **that do not accept reference products** sourced outside their jurisdiction as comparator, without at least analytical bridging studies against locally-sourced reference product

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EU and US do not accept foreign-sourced reference product as comparator ….unless….

- EU and US (category 4) **do not accept** a biosimilar development that has been **entirely** based on a reference product sourced outside their jurisdiction, but require a **bridging study** at least at the analytical level, between their own / local, and the foreign reference product.
  - EMA guideline on similar biological medicinal products (2014):
    - As a scientific matter, the type of bridging data needed will **always include data from analytical studies (e.g., structural and functional data) that compare all three products (the proposed biosimilar, the EEA-authorized reference product and the non-EEA-authorized comparator), and may also include data from clinical PK and/or PD bridging studies for all three products.**
  - FDA Guidance for Industry: Scientific Considerations in Demonstrating Biosimilarity to a Reference Product (2015):
    - As a scientific matter, **analytical studies and at least one clinical PK study and, if appropriate, at least one PD study,** intended to support a demonstration of biosimilarity for purposes of section 351(k) of the Public Health Service Act must include an adequate comparison of the proposed biosimilar product directly with the US-licensed reference product unless it can be scientifically justified that such a study is not needed.

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Impact on single, global biosimilar development

- A single, global biosimilar development can be used for the majority bulk of countries in categories 1 and 2

- Countries in category 3 can often be covered by a single, global biosimilar development by paper-based evidence proving the sameness of reference products manufacturing sites. Failing that, an additional analytical comparability exercise needs to be done

- However, the countries assigned to category 4 cannot be covered by a single, global biosimilar development but require additional development efforts to generate analytical, and in some cases also PK data comparing the biosimilar product candidate and/or batches of the comparator product against batches of the locally-sourced reference product
  - **Costs are significant and multiplied – in addition, studies must be repeated by each company that develops a biosimilar to the same locally-sourced reference product**
  - **Uncessary additional clinical studies are unethical**

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Key venues for biosimilar global development

Waiving of bridging studies

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Bridging studies required for a submission as a biosimilar product in selected countries[1] in addition to a complete comparability exercise conducted against the EU RP

complete comparability exercise against EU-authorized reference product	+ US [3]	+ JP [3]	+ CH [3]	+ AU [3]	+ SK [3]
Clinical: 2-way efficacy & safety study, EU vs biosimilar	Clinical: add. obligations (transition study for chronic indications; switching for nterchangeability	Clinical package includes either 1) sub-group analysis with JP subjects			
PK/PD: 2-way study: EU vs. Biosimilar (potentially 3-way required if bridging to US-licensed product in efficacy and safety study is requested)	PK/PD: 3-way: EU vs.US vs. Biosimilar	2) PK studies with JP subjects vs. JP reference product 3) PK studies with JP subjects vs authorized foreign reference product			
In-vivo[2]: 2-way: EU vs. biosimilar Includes: PK/PD, Toxicity, Efficacy, local tolerance, tissue cross reactivity					
In vitro: 2-way: EU vs. biosimilar Includes: approximately 10 functional assays, i.e. binding (e.g. target binding, receptor binding), mode-of-action (e.g. ADCC, CDC, apoptosis)	3-way: EU vs. US vs. Biosimilar	customized package including additional comparability against the local JP reference product	EU package plus comparability against CH reference product	EU package plus comparability against AU reference product	EU package plus comparability against SK reference product
Physico-chemical: 2-way: EU vs. biosimilar Includes: 30-60 quality attributes like primary structure, higher order structure, size variants, charge heterogeneity (e.g. C- and N-terminal), post-translational modifications (e.g. glycosylation, glycation, oxidation, deamination), comparative stability, forced degradation studies	3-way: EU vs. US vs. Biosimilar	customized package including additional comparability studies against the local JP reference product	EU package plus comparability against CH reference product	EU package plus comparability against AU reference prod	EU package plus comparability against SK reference product

[1] = *Jurisdictions selected on the basis of their Agency's requirement of a comprehensive comparability exercise.*
[2] = *in vivo animal studies are becoming significantly less relevant for biosimilars and are expected to be considered unethical in the near future*
[3] = *sizes of the boxes represent the relative additional work needed to bridge to the requirements of thespecific region EU: European Union; US: United States; JP: Japan; CA: Canada; CH: Switzerland; AU, Australia; SK: South Korea;*

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Circumstances where bridging studies between local and foreign-sourced reference product can be waived

Foreign-sourced Reference Product:

- meets the criteria to qualify for comparator product ie. must have been approved by a Stringent Regulatory Authority
- contains a version of the same active pharmaceutical ingredient (API), and has the same pharmaceutical form and same route of administration as the locally-approved reference product (local reference)
- has the same composition of excipients as the local reference, or, if the qualitative compositions of excipients are different, the sponsor provides a justification showing the excipients have been assessed and are not expected o impact clinical efficacy and safety
- was approved in the respective jurisdiction based on essentially the same original data package as the local reference as demonstrated via evidence in the public domain
- subsequent manufacturing changes were regulated according to ICH Q5E principles to ensure that the clinical properties remain unchanged

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Key venues for global biosimilar development

Tailoring of
clinical development programs

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Clinical trial tailoring in biosimilar development makes sense scientifically

- 35 years of experience with biologic medicines and their manufacturing changes
- 15-plus years of regulatory and clinical experience with biosimilar medicines
- Progressive knowledge of structure-function relationships and disease-specific mechanisms of actions of therapeutic proteins
- Advances in technical, analytical and characterisation capabilities
- Learning is continuous – regulatory science advances
- **Regulators must actively engage in optimizing processes for biosimilars,** creating fit-for-purpose requirements and risk-based approaches considering the available body of evidence and experience with the reference biologic and the biosimilars

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Latest science-based papers that SHOULD change the regulatory environment for biosimilar medicines worldwide

- Interchangeability of Biosimilars: A European Perspective
  - Jan 2017
- A ‘Global Reference’ Comparator for Biosimilar Development
  - May 2017
- An Efficient Development Paradigm for Biosimilars
  - Aug 2019
- Evolution of the EU Biosimilar Framework: Past and Future
  - Sep 2019
- Delivering on the Promise of Biosimilars
  - Oct 2019

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Ongoing study by the IGBA working group on tailored clinical biosimilar development

- Review of EMA European Public Assessment Reports (EPARs) and FDA assessments published 2006 – May 2019
- Interim findings:
  - 33 (i.e., **94 %**) of 35 biosimilar programs, the comparative efficacy/safety trials just confirmed biosimilarity and would not have been necessary from a retrospective view
  - In only 2 (i.e., 6 %) of 35 biosimilar programs, the E/S study results triggered manufacturing process improvements to enable approval in EU and/or US
    - Issues in both cases caused by process impurities, while efficacy remained equivalent

1. https://www.accessdata.fda.gov/scripts/cder/daf/, accessed Aug 2019
2. https://www.ema.europa.eu/en/medicines/human, accessed Aug 2019

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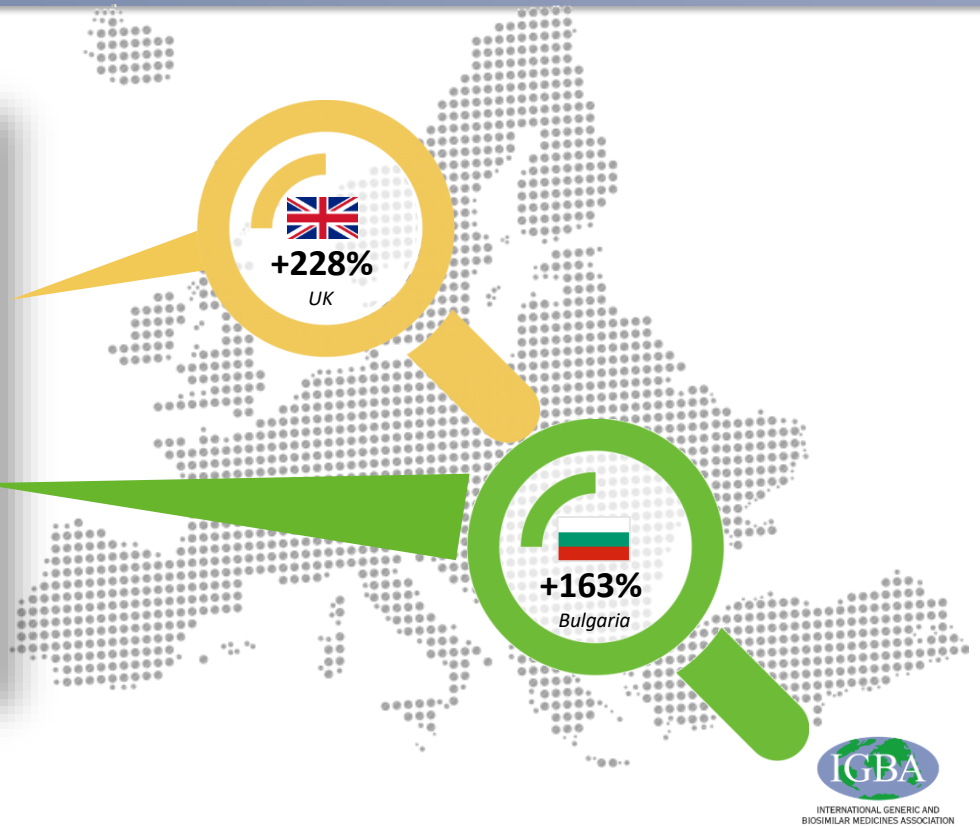
Real Word Evidence (RWE)

Biosimilar medicines increase patient access in Europe

Change in # of treatment days (2016 vs. year before biosimilar entrance)	
Epoetin	**+66%**
G-CSF (filgrastim)	**+122%**
Growth hormone (somatropin)	**+41%**
Anti-TNF (infliximab & etanercept)	**+19%**
Fertility (follitropin alfa)	**+16%**
Insulins	**+19%**



Source: QuintilesIMS (2017) The Impact of Biosimilar Competition in Europe

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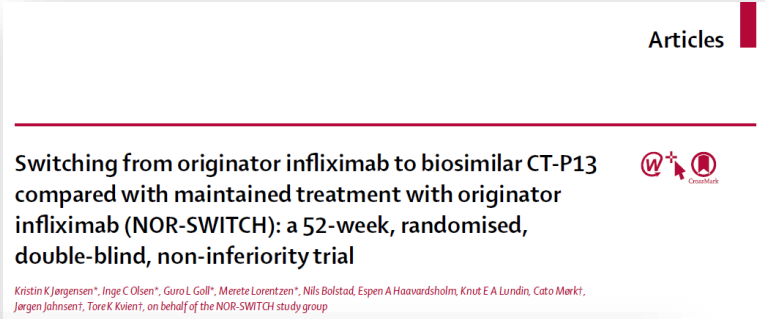
Large body of confirmatory evidence 13 + years of European biosimilar medicines clinical use

Real-world experience (2017)

>700 million

"Over the last 10 years, the EU monitoring system for safety concerns has not identified any difference in the nature, severity or frequency of adverse effects between biosimilars and their reference medicine" [2]

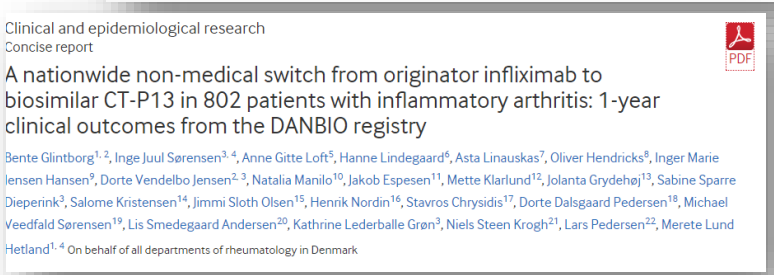
Controlled experience



Articles

Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial

Kristin K Jørgensen, Inge C Olsen*, Guro L Goll*, Merete Lorentzen*, Nils Bolstad, Espen A Haavardsholm, Knut E A Lundin, Cato Mørk†, Jørgen Jahnsen†, Tore K Kvien†, on behalf of the NOR-SWITCH study group*



Clinical and epidemiological research
Concise report

PDF

A nationwide non-medical switch from originator infliximab to biosimilar CT-P13 in 802 patients with inflammatory arthritis: 1-year clinical outcomes from the DANBIO registry

Bente Glintborg[1, 2], Inge Juul Sørensen[3, 4], Anne Gitte Loft[5], Hanne Lindegaard[6], Asta Linauskas[7], Oliver Hendricks[8], Inger Marie Jensen Hansen[9], Dorte Vendelbo Jensen[2, 3], Natalia Manilo[10], Jakob Espesen[11], Mette Klarlund[12], Jolanta Grydehøj[13], Sabine Sparre Dieperink[3], Salome Kristensen[14], Jimmi Sloth Olsen[15], Henrik Nordin[16], Stavros Chrysidis[17], Dorte Dalsgaard Pedersen[18], Michael Veedfald Sørensen[19], Lis Smedegaard Andersen[20], Kathrine Lederballe Grøn[3], Niels Steen Krogh[21], Lars Pedersen[22], Merete Lund Hetland[1, 4] On behalf of all departments of rheumatology in Denmark

[1] Medicines for Europe information based on EMA Post-authorisation Safety Update Reports (PSURs) 2017
[2] EMA – European Commission: Biosimilars in the EU – Information guide for healthcare professionals, 2017 (link)

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Switching studies confirm no differences in safety, efficacy or immunogenicity

Scientific literature (1993-2017) on switching					
Single or multiple switch	Reference → Biosimilar	90 studies	7 molecules	14 indications	14 225 individuals

Unchanged risk of immunogenicity-related safety concerns or diminished efficacy after switching	
Huge majority of single switch studies **did not report differences in safety, efficacy or immunogenicity** compared to patients not switched.	Small number (three) of multiple switch studies published, but likewise **no differences detected**.

Source: H. P. Cohen – Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes

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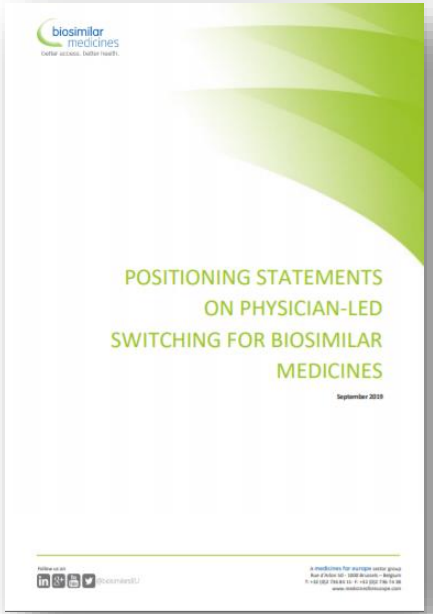
EU: Clinical use and experience inform medical societies' positions



2015

eular

BIOSIMILARS: WHAT DO PATIENTS NEED TO CONSIDER?

2017

Ann Rheum Dis. 2018 Feb;77(2):165-174. doi: 10.1136/annrheumdis-2017-211937. Epub 2017 Sep 2.

Consensus-based recommendations for the use of biosimilars to treat rheumatological diseases.

Kay J[1], Schoels MM[2], Dörner T[3], Emery P[4], Kvien TK[5], Smolen JS[2,6], Breedveld FC[7], Task Force on the Use of Biosimilars to Treat Rheumatological Diseases.

⊕ Collaborators (18)

⊕ Author information

Abstract

The study aimed to develop evidence-based recommendations regarding the evaluation and use of biosimilars to treat rheumatological diseases. The task force comprised an expert group of specialists in rheumatology, dermatology and gastroenterology, and pharmacologists, patients and a regulator from ten countries. Four key topics regarding biosimilars were identified through a process of discussion and consensus. Using a Delphi process, specific questions were then formulated to guide a systematic literature review. Relevant English-language publications through November 2016 were searched systematically for each topic using Medline; selected papers and pertinent reviews were examined for additional relevant references; and abstracts presented at the 2015 and 2016 American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) annual scientific meetings were searched for those about biosimilars. The experts used evidence obtained from these studies to develop a set of overarching principles and consensus recommendations. The level of evidence and grade of recommendation were determined for each. By the search strategy, 490 references were identified. Of these, 29 full-text papers were included in the systematic review. Additionally, 20 abstracts were retrieved from the ACR and EULAR conference abstract databases. Five overarching principles and eight consensus recommendations were generated, encompassing considerations regarding clinical trials, immunogenicity, extrapolation of indications, switching between bio-originators and biosimilars and among biosimilars, and cost. The level of evidence and grade of recommendation for each varied according to available published evidence. Five overarching principles and eight consensus recommendations regarding the evaluation and use of biosimilars to treat rheumatological diseases were developed using research-based evidence and expert opinion.

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[Overview of positions on EU physician-led switching for biosimilar medicines]

EULAR 2018 position: https://www.eular.org/myUploadData/files/biosimilars_paper_updated_2018_09_14_dw.pdf

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World Health Organization developments

WHO signs MoU with IGBA to promote access Oct. 2019

Streamlining development of biosimilar medicines while maintaining high quality and safety standards

https://bit.ly/2JybZSZ

WHO Prequalification Procedure (PQ) preparing the ground for global reference product

- Rituximab and trastuzumab added to the WHO Essential Medicines List (EML) and more biologics in 2019
- Pilot prequalification procedure (PQ) for rituximab and trastuzumab still ongoing
- PQ abridged assessment of biosimilars approved by “Stringent Regulatory Authorities”
- Once prequalified, biosimilars can participate at UN, regional and national tenders
- Reference product used as comparator product for PQ products will de facto become a **global comparator product**

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Conclusion and recommendations to increase patient access to biologics

- True global biosimilar development framework is needed to reduce complexity, duration, costs and increase patients access to biologics
- Multiplication of bridging studies by each sponsor is unnecessary, hence unethical
- Tailored biosimilar clinical development also enables biosimilar competition to reference medicines for which comparative efficacy trials would jeopardize business case
  - Biologics with smaller market size, and/or with
  - Shorter product lifecycles, and/or when
  - Comparative efficacy trials are simply not feasible
- **Convergence of requirememts very much needed, hence increased joint regulatory efforts to overcome scientific challenges**

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Time to Act!

Millions of patients are desperately waiting

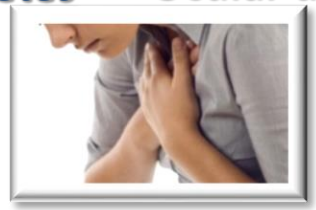
Cancer

Rheumatic disorders, Psoriasis

Growth & Hematopoietic disorders

Diabetes

Ocular diseases



Asthma

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THANK YOU!

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