EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Interchangeability of biosimilars - Joint statement from EMA-HMA

Prof Steffen Thirstrup, MD, PhD
CMO

Stakeholder Event on Biosimilar Medicinal Products, Bruxelles 13 Dec 2022

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

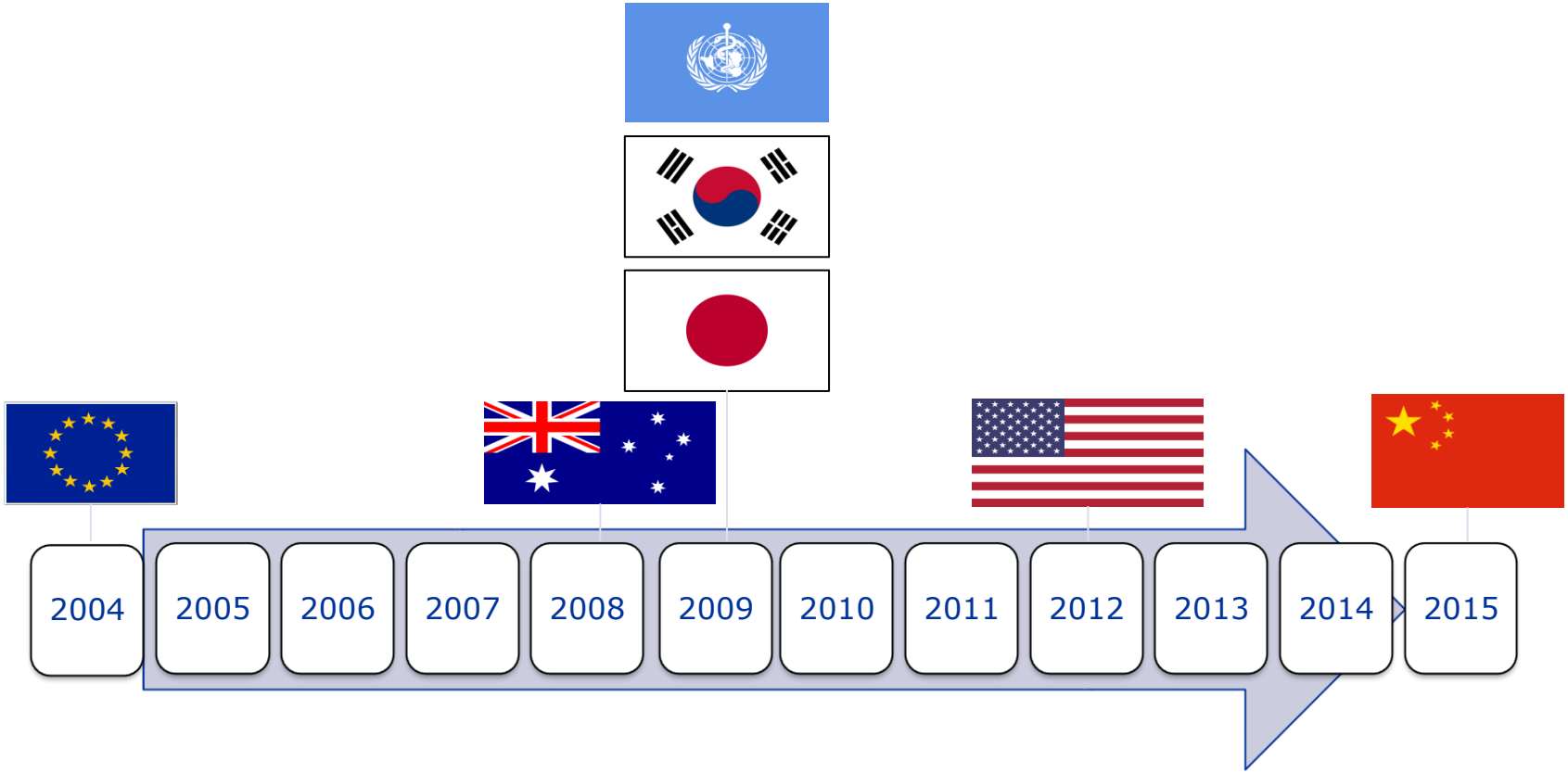
HMA
Heads of Medicines Agencies

19 September 2022
EMA/627319/2022

Statement on the scientific rationale supporting interchangeability of biosimilar medicines in the EU

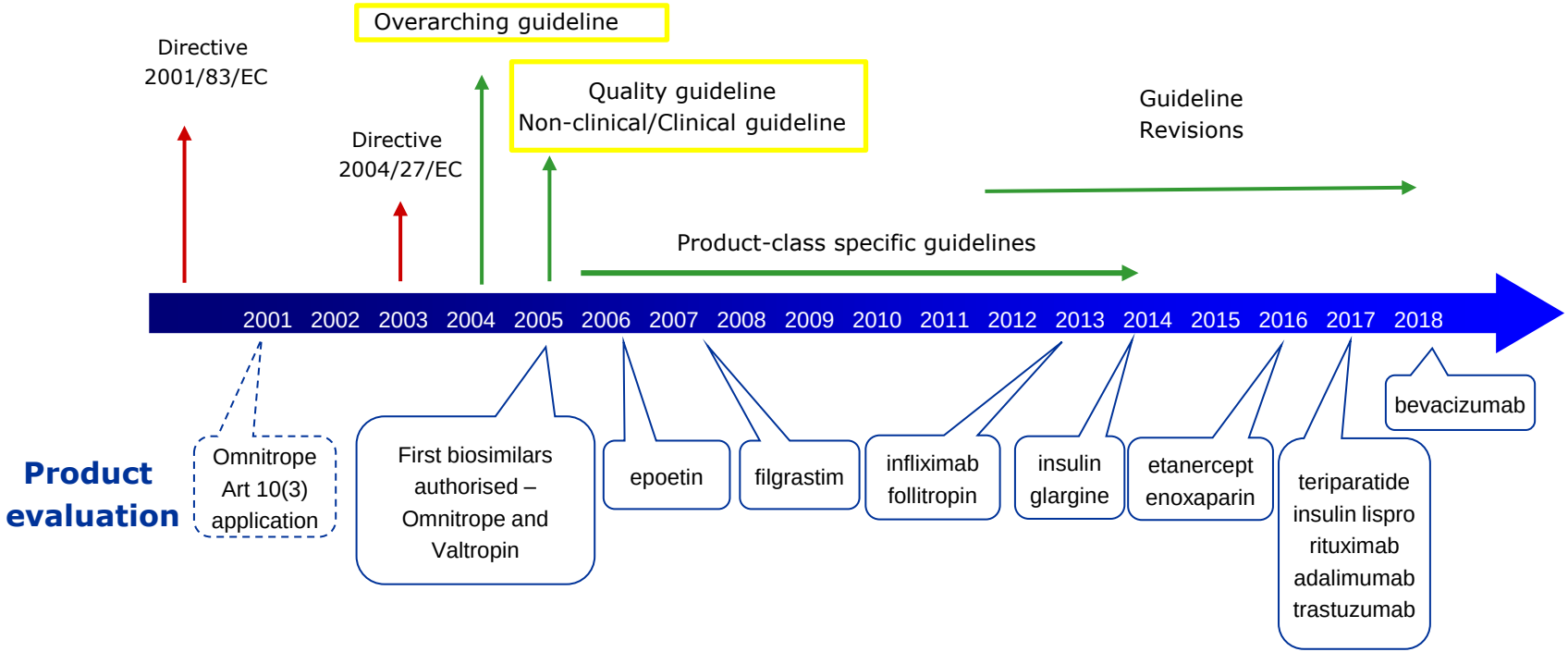
References:

1. Interchangeability of Biosimilars: A European Perspective. Pekka Kurki, Leon van Aerts, Elena Wolff-Holz, Thijs Giezen, Venke Skibeli, Martina Weise. BioDrugs 2017 Apr;31(2):83-91
2. Regulatory Information and Guidance on Biosimilars and Their Use Across Europe: A Call for Strengthened One Voice messaging. Liese Barbier, Allary Mbuaki, Steven Simoens, Paul Declerck, Arnold G. Vulto, and Isabelle Huys. Frontiers in Medicine 2022, Vol 9, 820755
3. Safety, Immunogenicity and Interchangeability of Biosimilar Monoclonal Antibodies and Fusion Proteins: A Regulatory Perspective. Pekka Kurki, Sean Barry, Ingrid Bourges, Panagiota Tsantili, Elena Wolff-Holz. Drugs 2021 Nov;81(16):1881-1896
4. The safety of switching between therapeutic proteins. Ebbers H, Muenzberg M, Schellekens H. Expert Opinion Biol Ther. 2012;12:1473-85
5. Biosimilars in the EU - Information guide for healthcare professionals (europa.eu)



Legislation

Guidance



Biosimilars in Europe (as of Sep 2022)*

EUROPEAN MEDICINES AGENCY

* Information on the EMA website

126 **MAAs submitted incl.duplicates**

114 **MAAs reviewed**

12 **MAAs under review**

Aflibercept (1)
Bevacizumab (1)
Eculizumab (2)
Filgrastim (1)
Natalizumab (1)
Pegfilgrastim (2)
Teriparatide (1)
Tocilizumab (1)
Trastuzumab (2)

EMA scientific committees and working parties

2 Negative

Interferon alfa (1)
Insulin (1)

23 Withdrawn (*pre-approval*)

Insulin (6)
Bevacizumab (1)
Epoetin (1)
Eptacog alfa (1)
Rituximab (2)
Pegfilgrastim (6)
Trastuzumab (2)
Adalimumab (1)
Infliximab (1)
Teriparatide (2)

89 Positive opinions

73 **MAs**

Somatropin (1)
Epoetin (5)
Filgrastim (7)
Infliximab (4)
Follitropin alfa (2)
Etanercept (3)
Bevacizumab (8)
Insulin aspart (3)
Insulin human (1)
Insulin glargine (2)
Insulin lispro (1)
Enoxaparin (1)
Teriparatide (4)
Rituximab (5)
Adalimumab (10)
Trastuzumab (6)
Pegfilgrastim (8)
Ranibizumab (2)

1 Awaiting EC decision
Ranibizumab (1)

15 Withdrawn (*post-approval*)

Filgrastim (2)
Somatropin (1)
Insulin glargine (1)
Adalimumab (4)
Rituximab (2)
Enoxaparin (1)
Pegfilgrastim (1)
Teriparatide (1)
Bevacizumab (2)

Let's get terms and responsibilities right!

Interchangeability is exchanging one medicine for another medicine that is expected to have the same clinical effect.

Reference product ← → Biosimilar

Biosimilar ← → Biosimilar (w/same ref prod)

EMA

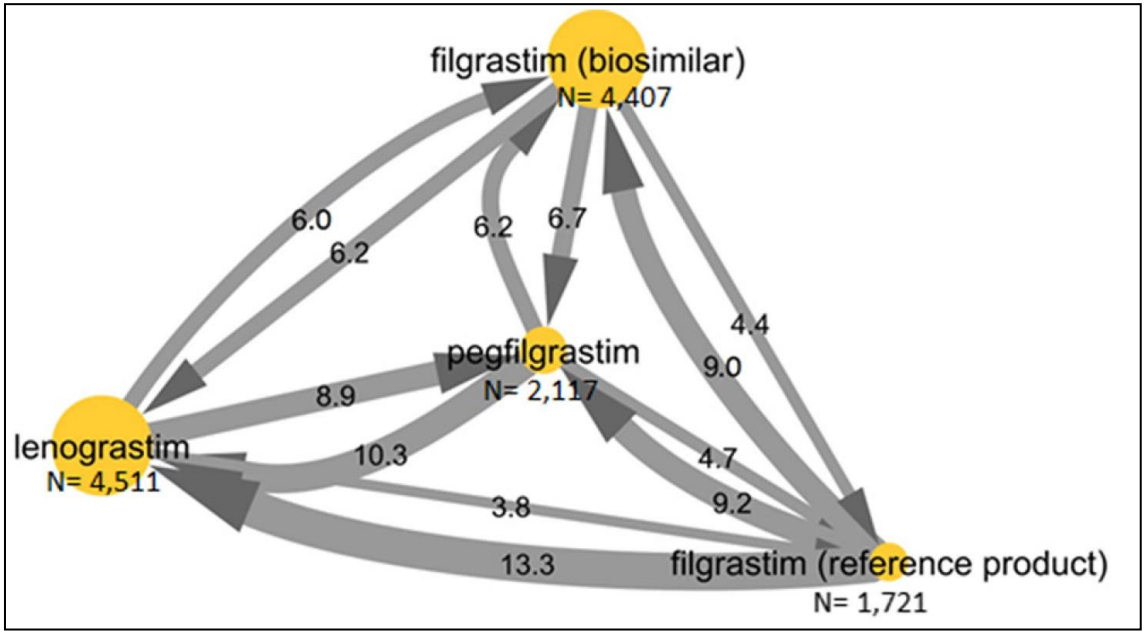
Replacement can be done by:

- **Switching**, which is when the prescriber decides to exchange one medicine for another medicine with the same therapeutic intent.
- **Substitution (automatic)**, which is the practice of dispensing one medicine instead of another equivalent and interchangeable medicine at pharmacy level without consulting the prescriber.

Member state

EMA information guide to prescribers

Switching is a common clinical practice!



BioDrugs (2016) 30:295–306

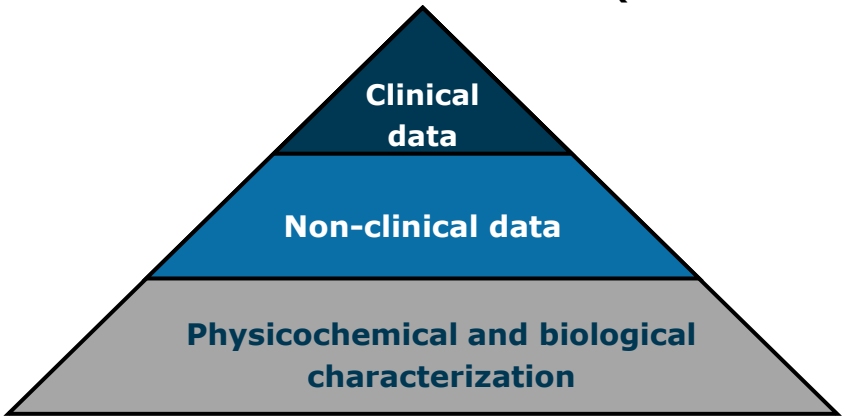
EU approval of biosimilars is based on rigorous scientific principles

The comparability exercise

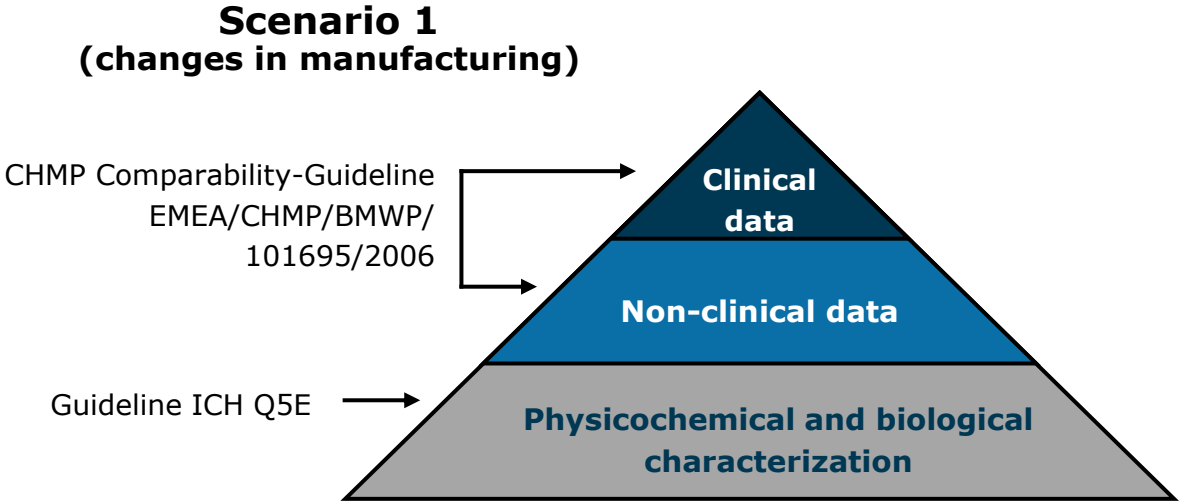
Comparability Exercise

Scenario 1
(changes in manufacturing)

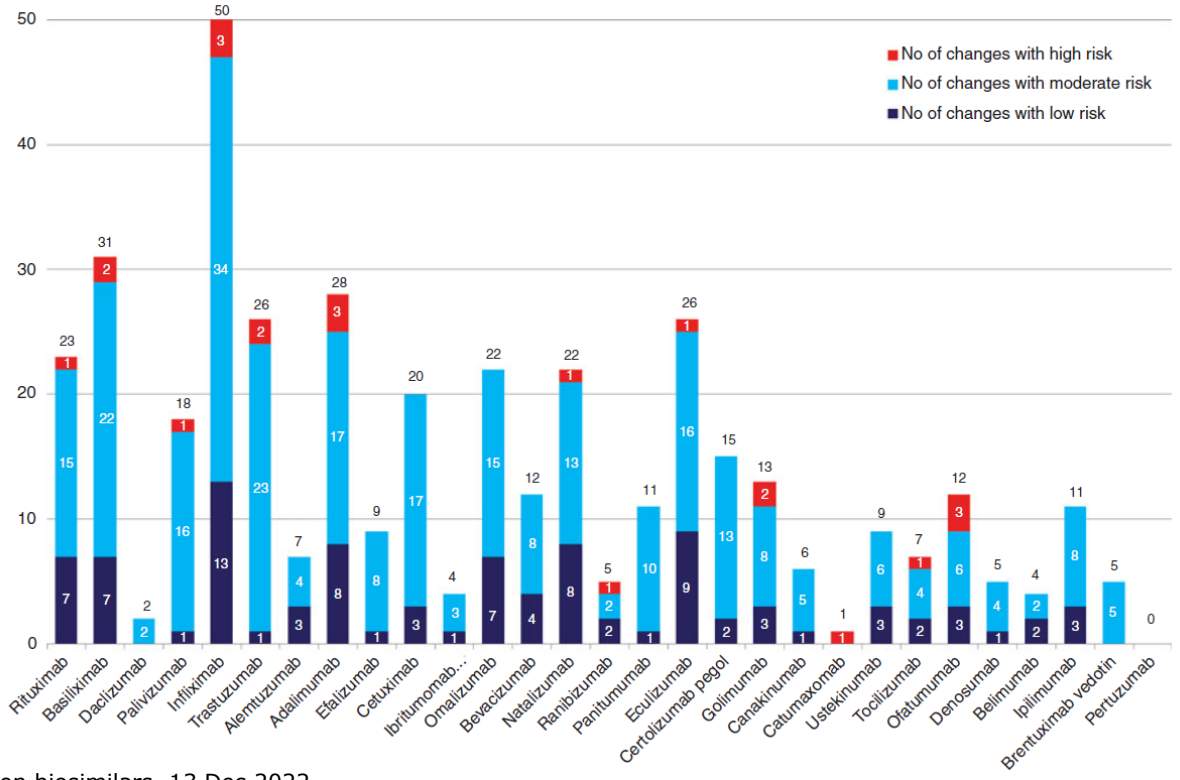
Scenario 2
(biosimilar development)



Comparability Exercise



Post-approval changes to originator biologics

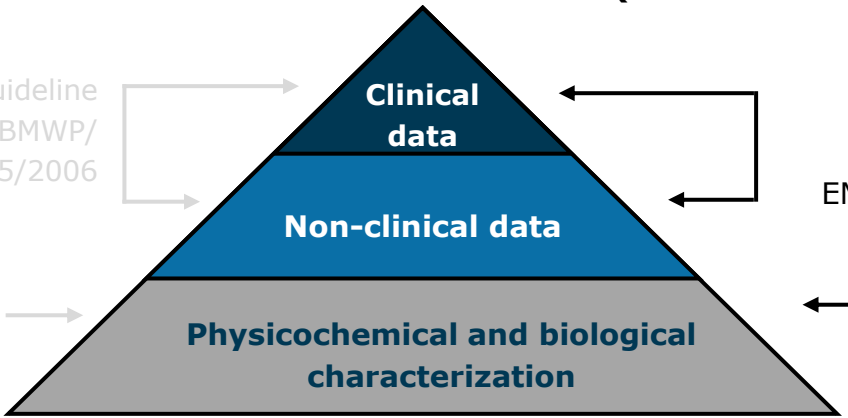


Vezér B. et al. *Curr Med Res Opin*. 2016;32:829-834

Comparability Exercise

Scenario 1
(changes in manufacturing)

Scenario 2
(biosimilar development)



CHMP Comparability-Guideline
EMEA/CHMP/BMWP/
101695/2006

Guideline ICH Q5E

CHMP/BMWP Non-clinical/
clinical guideline
EMEA/CHMP/42832/2005 Rev1

CHMP/BMWP/BWP
Quality guideline
EMA/CHMP/BWP/
247713/2012

Evidence in support of interchangeability

Switching between non-biosimilar biologicals are seldomly associated with adverse reaction, incl. in patients with pre-existing anti-bodies

EU approved biosimilars are highly similar to their reference product

No signs of change in efficacy nor safety in head-to-head clinical trials

- This is also supported by dedicated 'multiple switch studies'

Extensive clinical exposure (>1.3 mio PTY) with no sign of difference in adverse reaction pattern biosimilar><reference product

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

HMA
Heads of Medicines Agencies

19 September 2022
EMA/627319/2022

Statement on the scientific rationale supporting interchangeability of biosimilar medicines in the EU

References:

1. Interchangeability of Biosimilars: A European Perspective. Pekka Kurki, Leon van Aerts, Elena Wolff-Holz, Thijs Giezen, Venke Skibeli, Martina Weise. BioDrugs 2017 Apr;31(2):83-91
2. Regulatory Information and Guidance on Biosimilars and Their Use Across Europe: A Call for Strengthened One Voice messaging. Liese Barbier, Allary Mbuaki, Steven Simoens, Paul Declerck, Arnold G. Vulto, and Isabelle Huys. Frontiers in Medicine 2022, Vol 9, 820755
3. Safety, Immunogenicity and Interchangeability of Biosimilar Monoclonal Antibodies and Fusion Proteins: A Regulatory Perspective. Pekka Kurki, Sean Barry, Ingrid Bourges, Panagiota Tsantili, Elena Wolff-Holz. Drugs 2021 Nov;81(16):1881-1896
4. The safety of switching between therapeutic proteins. Ebbers H, Muenzberg M, Schellekens H. Expert Opinion Biol Ther. 2012;12:1473-85
5. Biosimilars in the EU - Information guide for healthcare professionals (europa.eu)

Thank you!

Further information

steffen.thirstrup@ema.europa.eu

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Telephone +31 (0)88 781 6000
Send us a question Go to www.ema.europa.eu/contact

Follow us on **@EMA_News**