Available evidence on interchangeability of biosimilars

Multi-Stakeholder event on Biosimilar Medicines
Brussels, 13 December 2022

Liese Barbier, PharmD, PhD
Department of Pharmaceutical and Pharmacological Sciences

KU Leuven

Affiliations

KU Leuven, Dept. of Pharmaceutical and Pharmacological Sciences, Regulatory Sciences unit

MABEL Fund - Market Analysis of Biologics including Biosimilars following Loss of Exclusivity
https://pharm.kuleuven.be/clinpharmacotherapy/mabel

IBN the Netherlands https://www.biosimilars-nederland.nl/

ISPOR Biosimilar SIG
https://www.ispor.org/member-groups/special-interest-groups/biosimilars

Stanford **METRICS** group

Link to PhD thesis

> 15 years of regulatory and clinical experience with biosimilars, yet...

- The value biosimilars bring is clear; beyond cost savings, increasing access to biologicals for patients
- Over 15 years of experience: considerable exposure and excellent safety record
- Still doubts and hesitancy among healthcare providers and patients about their safe use, and especially on interchangeability of biosimilars

What's in a name?

Interchangeability

The **possibility** of exchanging one medicine for another medicine that is **expected to have the same clinical effect**. This could mean replacing a reference product with a biosimilar (or vice versa) or replacing one biosimilar with another

Replacement can be done by

Switching

The **practice** of the **prescriber** deciding to exchange one medicine for another medicine with the same therapeutic intent

Substitution

The **practice** of dispensing one medicine instead of another equivalent and interchangeable medicine **at pharmacy level** without consulting the prescriber

EMA (2017) Biosimilars in the EU. Information guide for healthcare professionals

Systematic review on switching

REVIEW

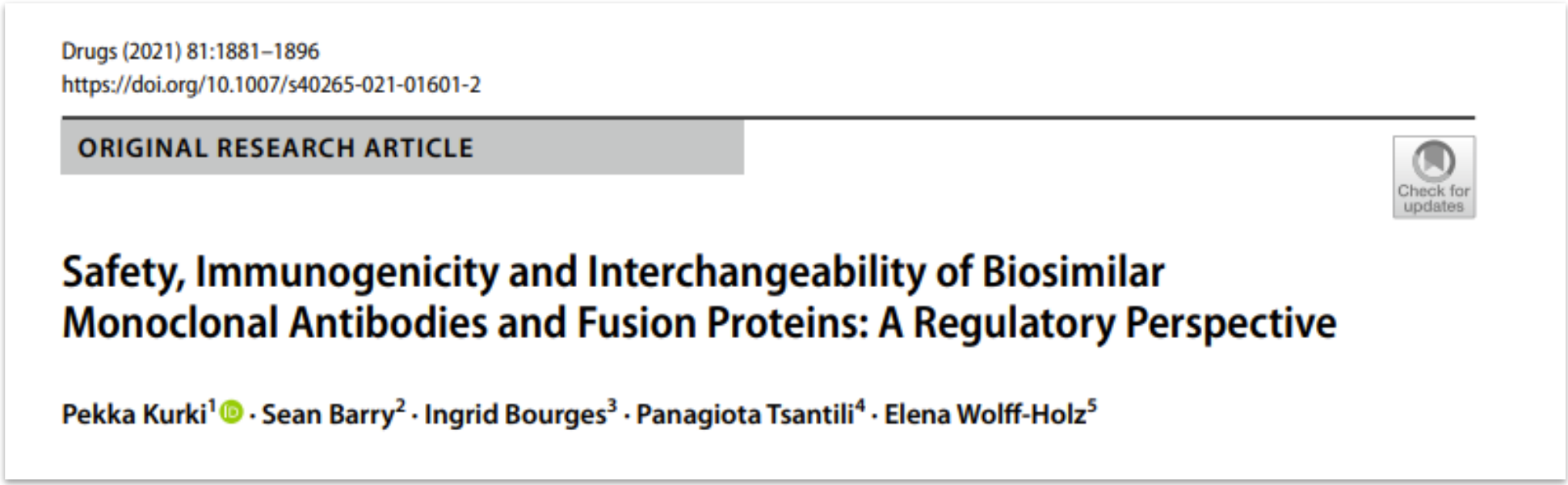
The Efficacy, Safety, and Immunogenicity of Switching Between Reference Biopharmaceuticals and Biosimilars: A Systematic Review

Liese Barbier[1,*], Hans C. Ebbers[2], Paul Declerck[1], Steven Simoens[1], Arnold G. Vulto[1,3,†] and Isabelle Huys[1,†]

- 178 studies, >20.000 switched patients
- Combination of RCTs, open-label extension studies, observational studies, registries
- No signs of efficacy, safety, or immunogenicity issues
- In open studies, we observed a potential nocebo effect

Barbier *et al.* (2020) CPT

Interchangeability data in regulatory documents (EMA)



Drugs (2021) 81:1881–1896
https://doi.org/10.1007/s40265-021-01601-2

ORIGINAL RESEARCH ARTICLE

Check for updates

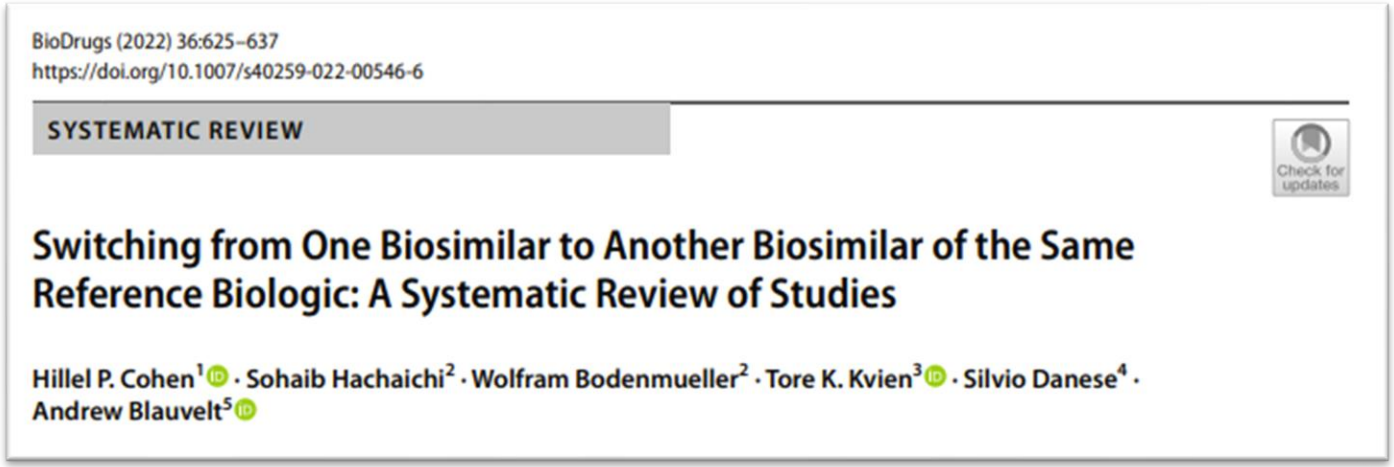
Safety, Immunogenicity and Interchangeability of Biosimilar Monoclonal Antibodies and Fusion Proteins: A Regulatory Perspective

Pekka Kurki[1] · Sean Barry[2] · Ingrid Bourges[3] · Panagiota Tsantili[4] · Elena Wolff-Holz[5]

- Comprehensive analysis of postmarketing surveillance data of mAbs biosimilars and etanercept
- > 1 million patient-treatment years of safety data with no safety concerns
- Biosimilars in the EU highly similar to and interchangeable with their reference products

Kurki. *et al.* (2021) Drugs

Reviews on biosimilar to biosimilar switching



BioDrugs (2022) 36:625–637
https://doi.org/10.1007/s40259-022-00546-6

SYSTEMATIC REVIEW

Check for updates

Switching from One Biosimilar to Another Biosimilar of the Same Reference Biologic: A Systematic Review of Studies

Hillel P. Cohen[1] · Sohaib Hachaichi[2] · Wolfram Bodenmueller[2] · Tore K. Kvien[3] · Silvio Danese[4] · Andrew Blauvelt[5]

No reduction in effectiveness or increase in adverse events in biosimilar-to-biosimilar switching studies conducted to date

Drugs (2021) 81:1859–1879
https://doi.org/10.1007/s40265-021-01610-1

REVIEW ARTICLE

Check for updates

Biosimilar-to-Biosimilar Switching: What is the Rationale and Current Experience?

Eduardo Mysler[1] · Valderilio Feijó Azevedo[2] · Silvio Danese[3] · Daniel Alvarez[4] · Noriko Iikuni[5] · Beverly Ingram[6] · Markus Mueller[7] · Laurent Peyrin-Biroulet[8]

No unexpected findings or concerns from emerging real-world evidence for switching between biosimilars

Cohen. et al. (2022) BioDrugs; Mysler. et. al. (2021) Drugs

What can we conclude

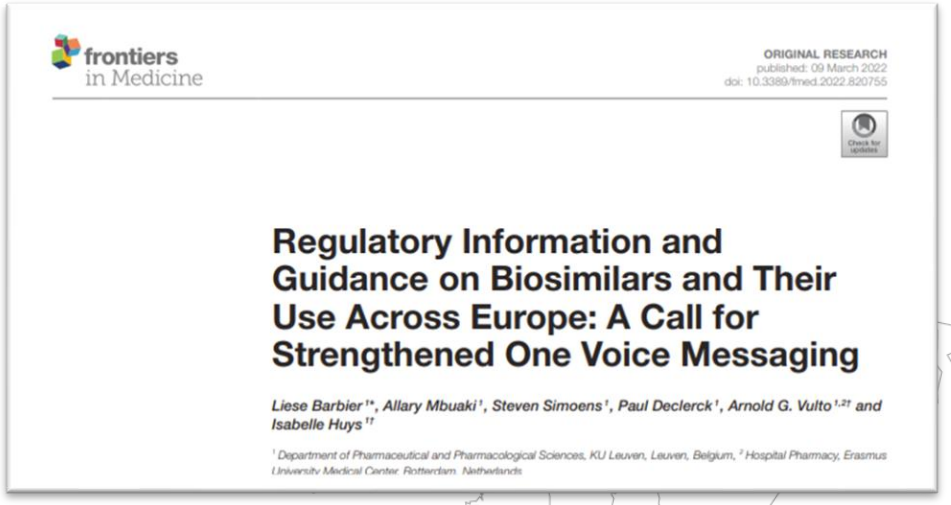
- The suggestion of switch-related adverse effects is not supported by current evidence
- All biosimilars in the EU are proven highly similar to and interchangeable with their reference products
- Clinical switch studies are not able to detect potential rare adverse effects; risk management should be based on pharmacovigilance
- Additional systematic switch studies are not needed to support the switching of patients

Kurki (2022) GaBI Journal; Kurki. *et al.* (2021) Drugs; Barbier & Vulto (2021) Drugs

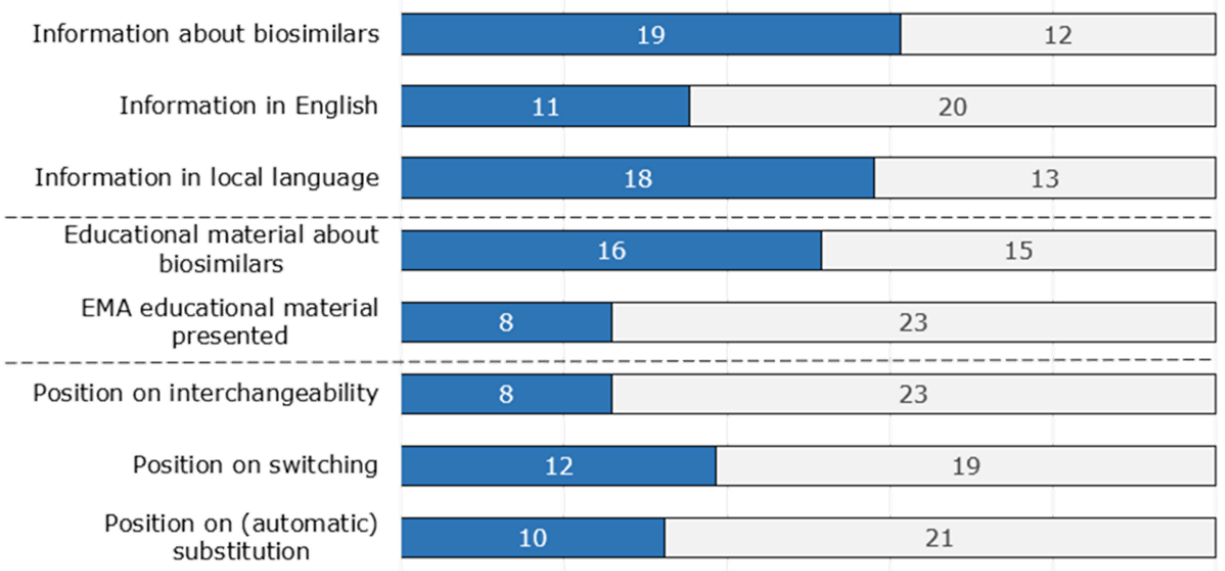
Solid evidence base yet...

- **Gap to bridge between scientific data and stakeholder awareness and trust**
  - Effective communication of scientific insights about biosimilars and their use towards patients, healthcare providers, policy makers is key
  - Regulators have in this an important role
  - Centralised regulatory evaluation *versus* decisions related to prescribing practices which are the responsibility of the individual Member States; translation has been lacking

Regulatory guidance on interchangeability, switching & substitution
A scattered European landscape

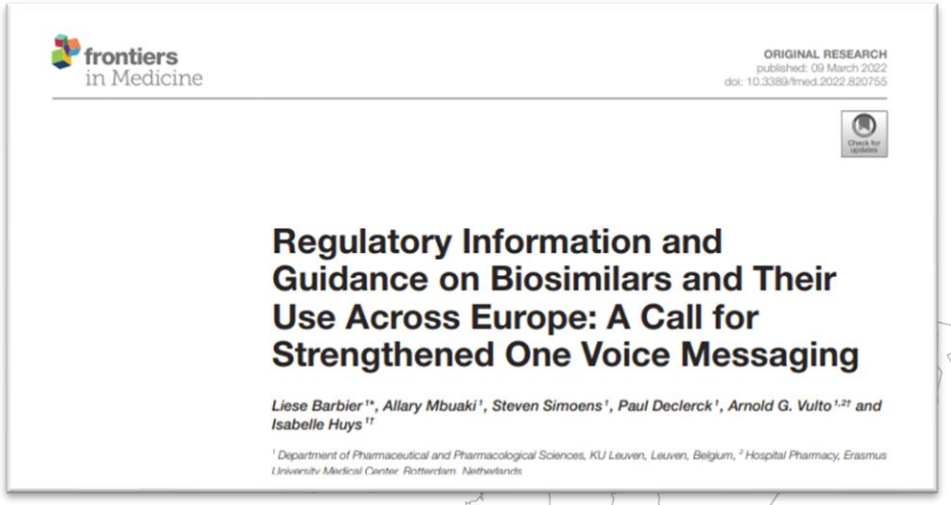


Biosimilar information & guidance from national medicines agencies* (N =31)

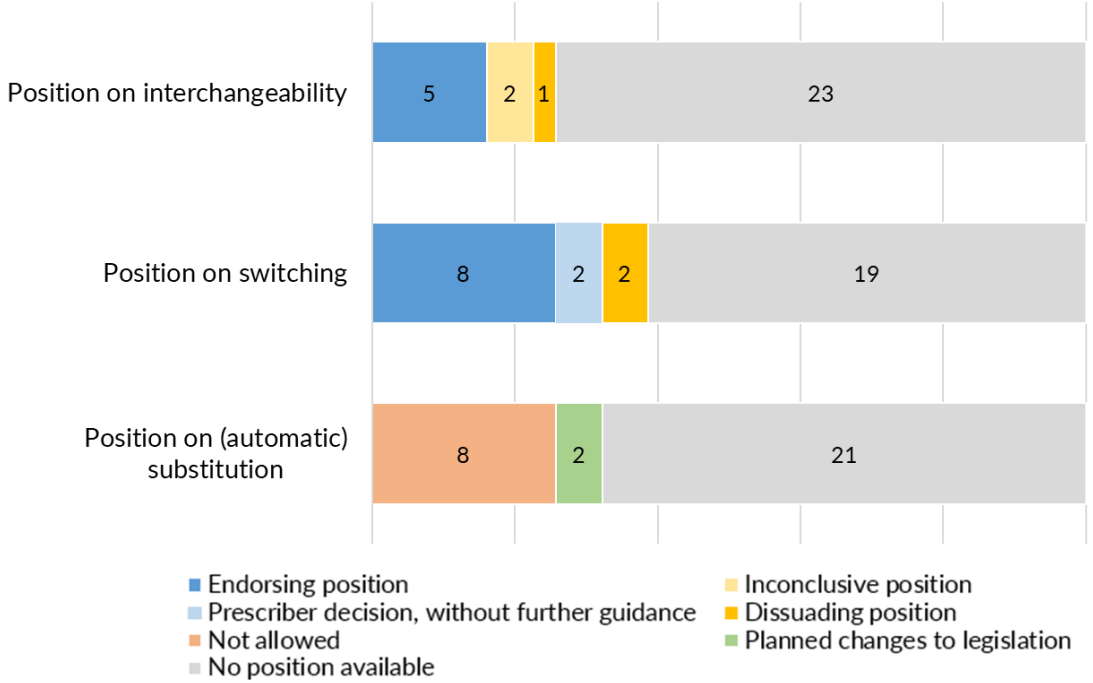


Barbier. et al. (2022) Frontiers in Medicine; * EU Member States + UK + EEA countries

Regulatory guidance on interchangeability, switching & substitution
A scattered European landscape

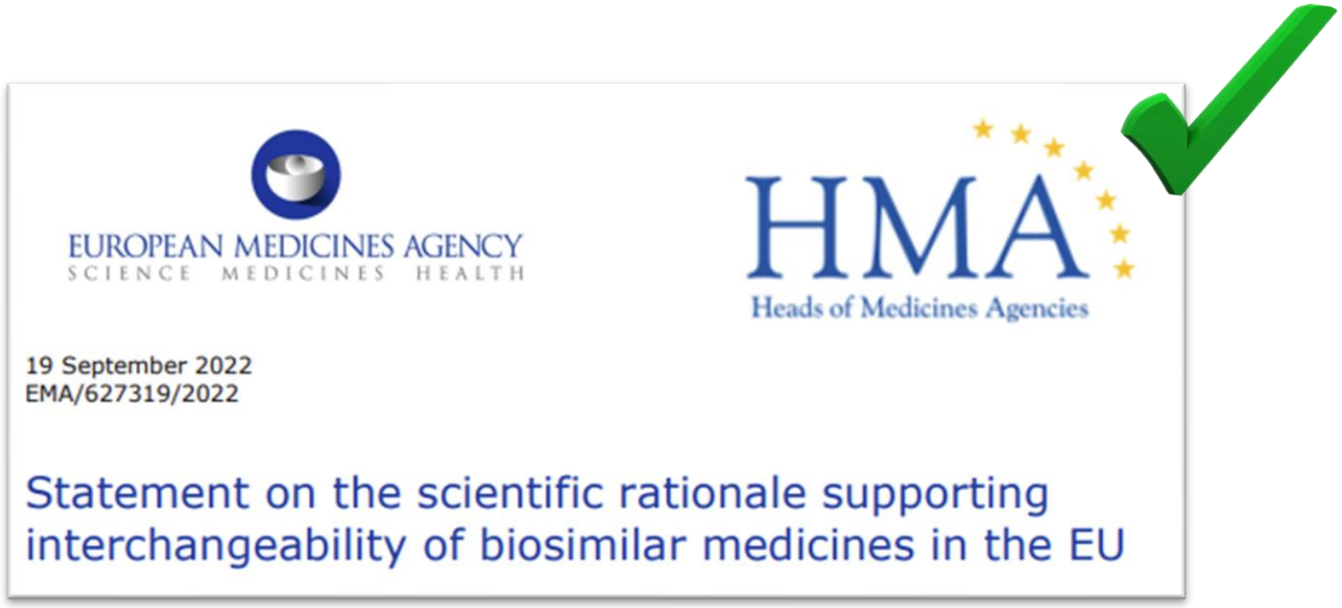


Biosimilar position statements from national medicines agencies* (N =31)



Barbier. et al. (2022) Frontiers in Medicine; * EU Member States + UK + EEA countries

EMA/HMA interchangeability statement, Sept 2022



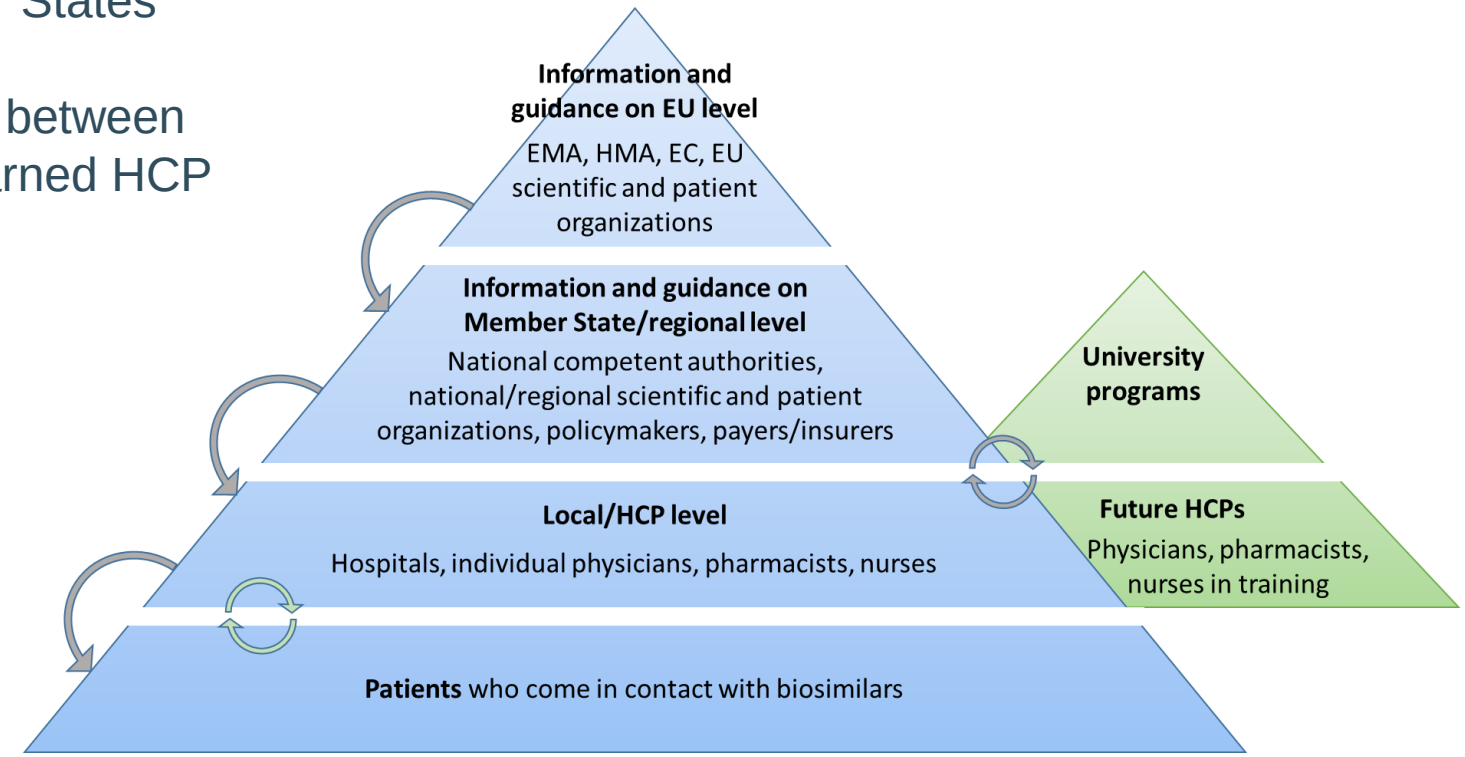
HMA and EMA consider that once a biosimilar is approved in the EU it is interchangeable, which means the biosimilar can be used instead of its reference product (or vice versa) or one biosimilar can be replaced with another biosimilar of the same reference product

Link to full statement

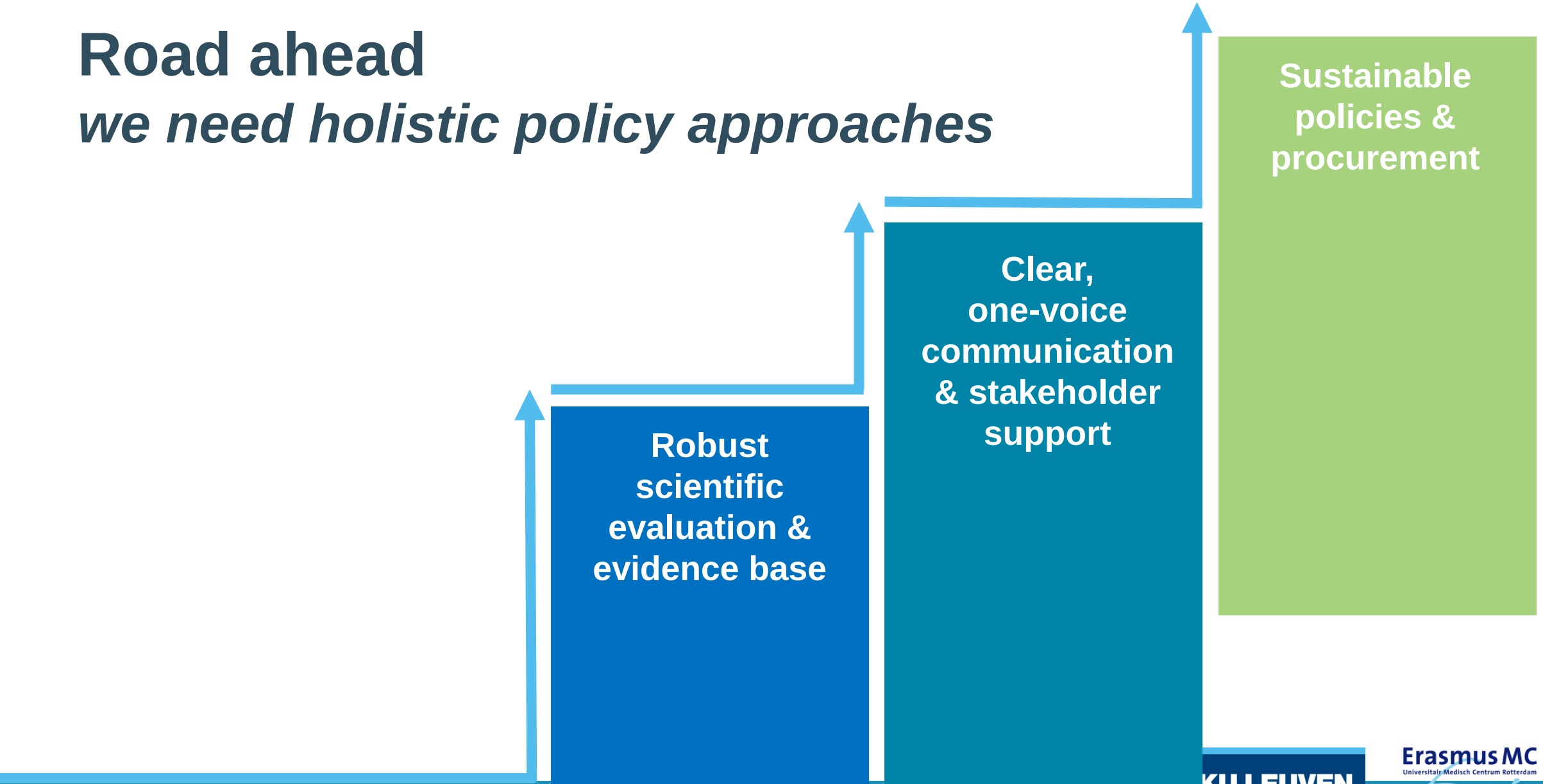
Road ahead

- Leveraging EU-developed one-voice information & guidance at the national level for homogenous (scientific) messaging across Member States

- Informing stakeholders = a joint effort between regulators (central & national) and learned HCP and patient societies



Road ahead
we need holistic policy approaches



Key take aways

- Interchangeability of EU-licensed biosimilars has been confirmed; robust EU biosimilar regulatory framework and solid evidence base
- One-voice scientific messaging about biosimilars and their use is essential
  - There are untapped opportunities at the national level
- To capture the benefits of biosimilar competition for patients and healthcare systems, now and in the future
  - Holistic approach needed to foster sustainable market
  - Concerted action on a European and national level; all hands on deck

Thank you!

Contact

liese.barbier@kuleuven.be

https://www.linkedin.com/company/mabel-fund/

https://gbiomed.kuleuven.be/english/research/50000715/52577001/mabel