



*Making Medicines Affordable*

# Breaking Barriers to Biologics Access

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# Need to Break Barriers to Biologics Access



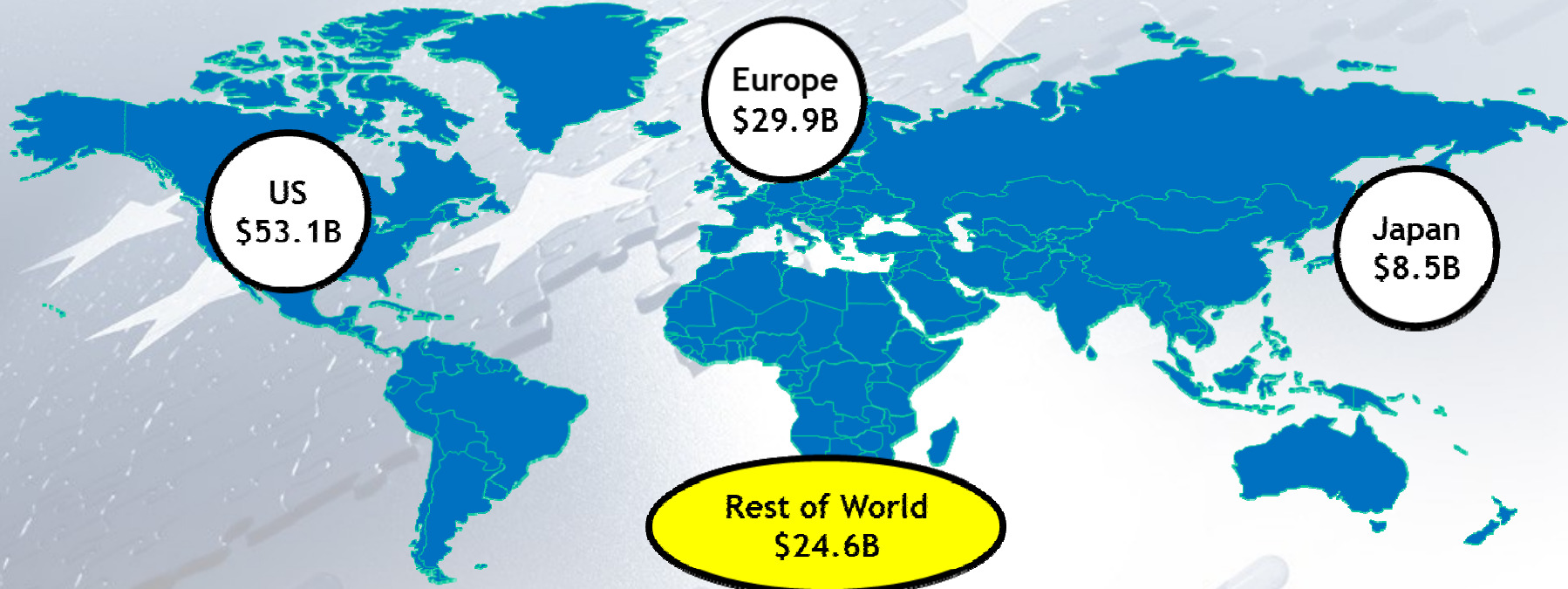
- Ageing population, worldwide challenge
  - in 2000, global population of people aged 60 and over was 600 million
  - by 2025 there will be 1.2 billion
  - by 2050, almost 2 billion
- 70% of all older people now live in low or middle-income countries
- Population ageing can be seen as a success story for public health policies and for socioeconomic development, but it also challenges society to adapt
  - Increasing challenge: availability and accessibility of effective health care including availability and accessibility of high quality medicines
  - Ageing: risk of developing certain chronic and debilitating diseases significantly higher

source: WHO website



# Increasing Challenge for Health Care Systems Worldwide

**Global Biologics Total \$116B; Growing at 6.3% Per Year**



With courtesy of Hospira

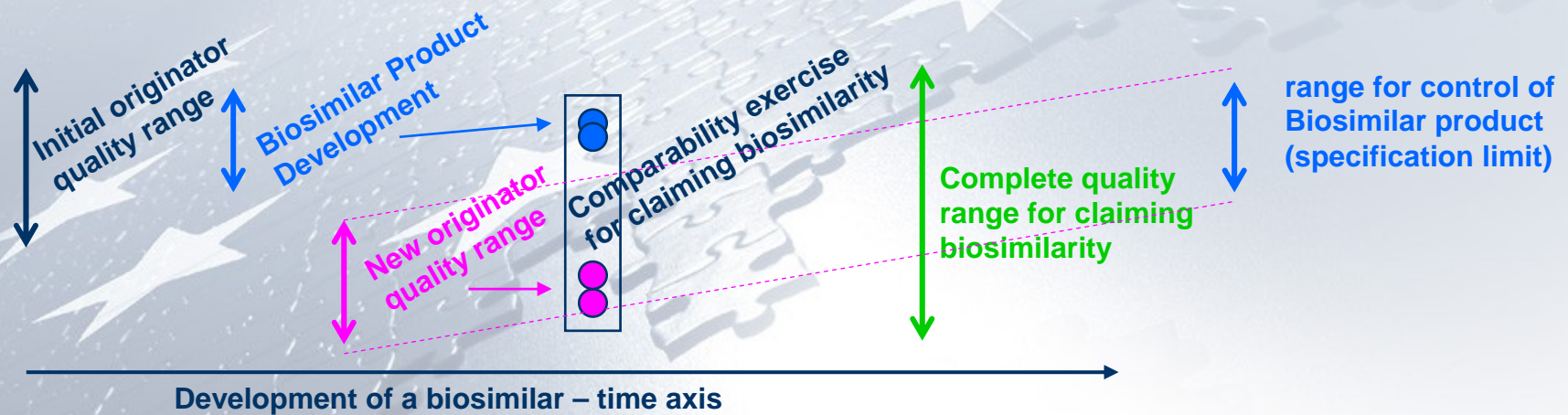


# Opportunities Represented by High Quality Biosimilars

i.e. Follow-on biologic of an already licensed ICH standard reference product with demonstrated **similarity** in physico-chemical characteristics, efficacy and safety, **based on a comprehensive comparability exercise**

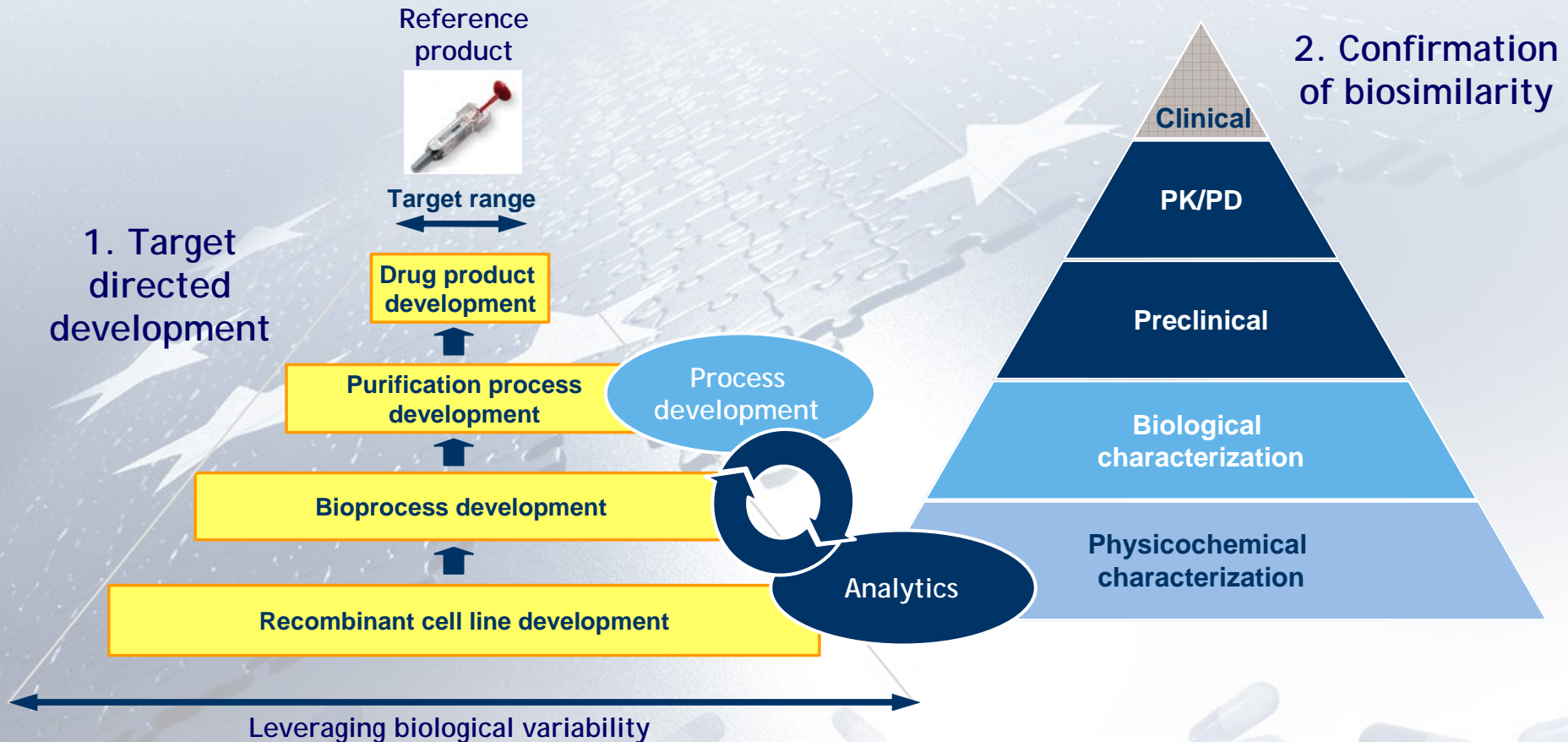


# Variability in Reference Products is Significant and Sets the Goal Posts



## Target Directed Biosimilar Development

# Target Directed Development and Confirmation of Biosimilarity



**Biosimilar development is fundamentally comparative**



# Approvable Biosimilars are Systematically Engineered to Match the Reference Product

Define target

Development of Manufacturing process  
Target directed approach

Confirmation:  
Final comparability exercise

- Characterize multiple lots of the Reference Product
- Variability in the reference product over time provides 'goal posts'
- Iterative optimization of all process steps using
- sophisticated analytical tools

## Our experience:

- Risk based approach
- Rank quality attributes for their criticality

*"Quality cannot be tested into a product, it has to be built in by design"; International Guideline ICH Q8*



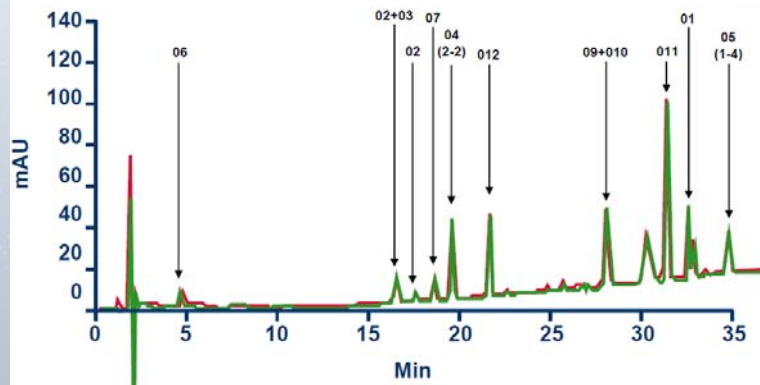
# Comparability Exercise: Cornerstone of Biosimilar Development

## ■ Concept of 'Comparability' is fundamental for all biologics

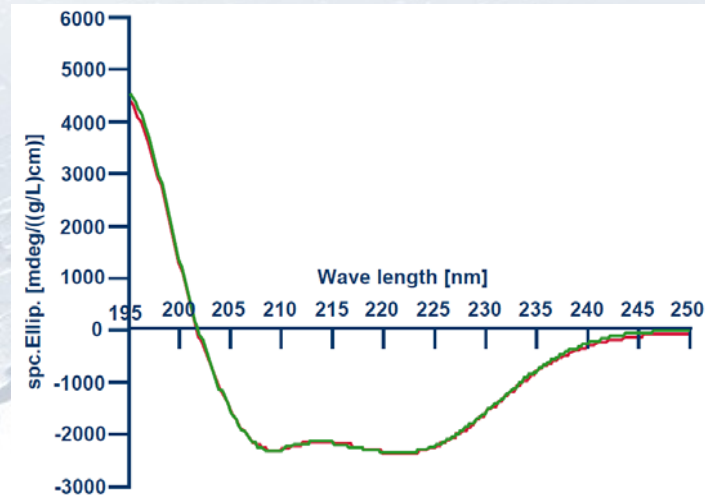
- *'The scientific principles underlying the comparability exercise required for changes in the manufacturing process of a given biological product and for development of a biosimilar product are the SAME'*

# Example of a Biosimilar Filgrastim: Highly Similar to Reference Product

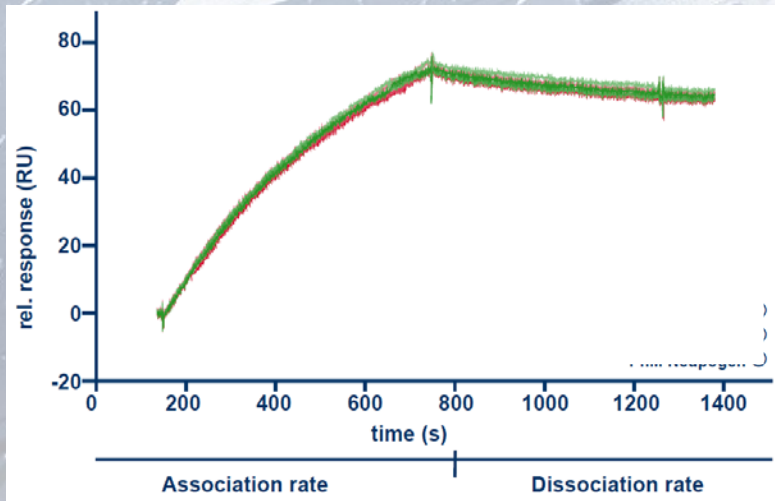
Primary structure – peptide mapping



Higher order structure – UV CD spectroscopy



Bioactivity – Surface plasmon resonance spectroscopy



Comparability performed for EU Biosimilar application showed highly similar results with state of the art methods

With courtesy of Sandoz

# Implications for Clinical Practice

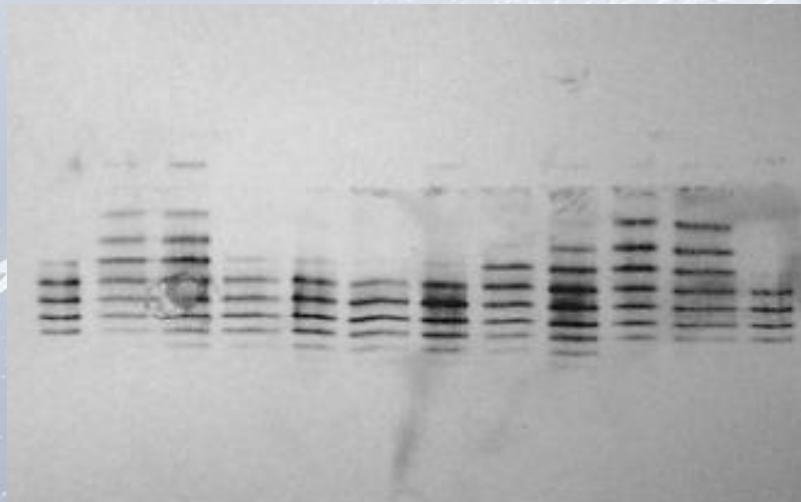


- Only very small differences between biosimilar and reference which are clinically irrelevant
  - Extrapolation of clinical indications is possible (including for future biosimilar mAbs) as well as interchangeability with reference product
  - More than 5 years safe and efficacious use of biosimilars demonstrated in the EU
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# “Non-Comparable Copy Biologics” are NOT Biosimilars

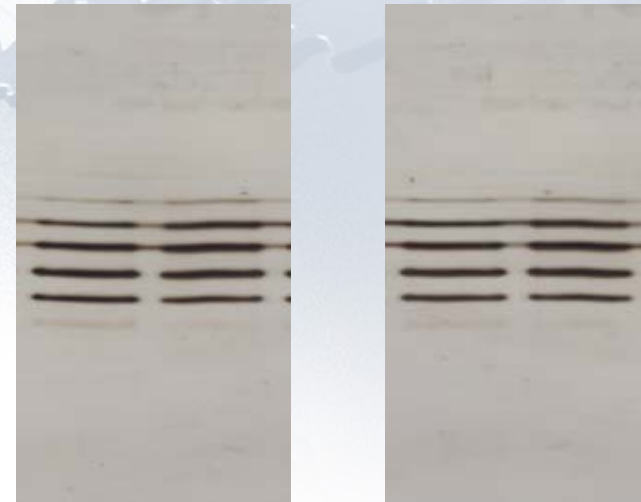
Isoelectric focusing gels

Non comparable copy biologics  $\neq$  biosimilars  
NOT similar to Reference E



Sample E IA IB IIA IIB IIIA IIIB IV V VII VIII E

Approved biosimilar in EU  
NO difference to originator



Sample 1 2 3 4

Schellekens H *et al.* *Eur J Hosp Pharm Pract* 2004;3:43-7

Brockmeyer C, Seidl A *et al.* *Eur J Hosp Pharm Pract* 2009;15:34-40

These copy biologics cannot be called ‘Biosimilars’



# First Pillar for Access to High Quality Biosimilars: Global Regulatory Harmonisation

- Global consensus on regulatory data requirements needed
  - Regulatory dialogue and international cooperation
  - Capacity building
- Further rolling out of the WHO guidelines which contain the same key concepts as already laid down in a number of existing regional guidelines (e.g. EU, JP, Canada)
  - Building technical expertise in National Regulatory Agencies worldwide
  - Workshops on comparability exercise
  - Development of training curricula





## 2<sup>nd</sup> Pillar for Access: Regulatory Framework Allowing Global Development

- Except Canada and WHO guidance, EU guideline and other jurisdictions currently require the use of a reference product authorized and sourced from their jurisdiction **despite the fact that the reference products are often the same** or highly similar in different countries
  - This would mandate the performance of **separate, full development programs** for each ICH country or jurisdiction utilising the reference product **sourced** from each jurisdiction
  - This is **unnecessary, unethical** (duplication of preclinical and clinical studies) and **uneconomical**
  - This approach constitutes a **majour barrier to access to high quality biosimilars**
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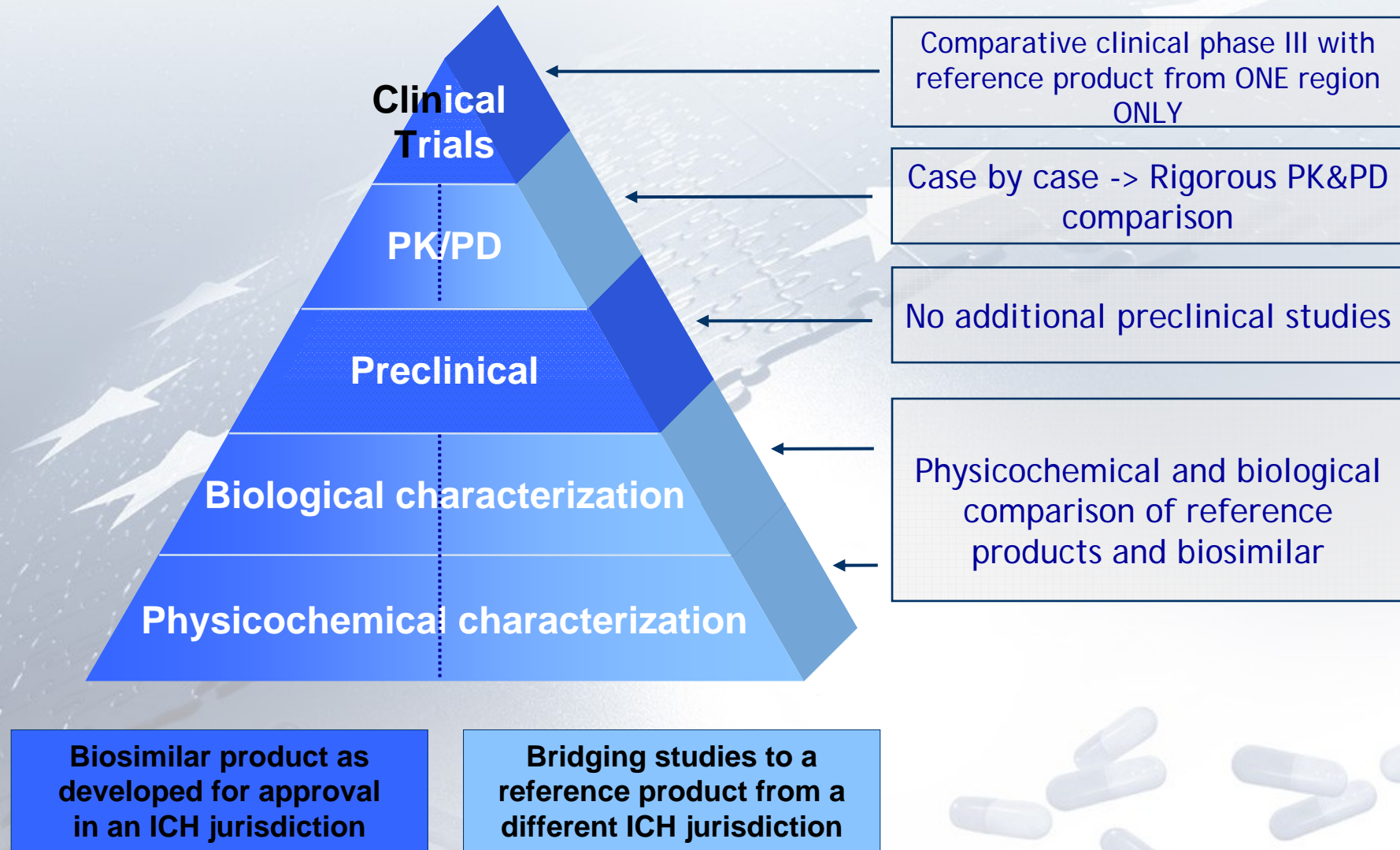

# Additional Challenges in Establishing a Single Global Biosimilar Development Programme

- Level of expertise (and confidence) within the EU not yet replicated in many other agencies globally
- The approved formulation and/or presentations of the reference product may vary globally
- Extrapolation across indications in different therapeutic areas not readily accepted by all agencies
- Different agencies have still differing views on how to measure “similarity” through endpoints & equivalence margins

# Common Reference Approach for the Comparability Exercise

- When the same reference product (made by a single facility for worldwide use) is licensed in several jurisdictions, the same comprehensive comparability data package should be sufficient for the submission and approval of a biosimilar/similar biotherapeutic product (SBP) worldwide
- Reference product used throughout the comparability exercise should be sourced from a jurisdiction with the highest possible standards
- Agreements between regulatory authorities can recognize suitable reference products
- New identification of medicinal products (IDPM) international standards will facilitate exchange of regulated pharmaceutical product information

# The Global Biosimilar Development: The Proposal





# Global Development: New Regulatory Paradigm

- Biosimilar 'cluster' between FDA and EMA created (regular exchanges take place)
- There is a strong move to reduce animal experiments (3 R principles: replacement, reduction, refinement)
- 3 R principles should also be implemented for studies on humans
- All jurisdictions should establish 'global' biosimilar pathway (using single global reference product)
  - No change of legislation needed in the EU, only adaptation of the overarching biosimilar guideline

# Conclusion



- Biosimilars can have a major impact on the affordability and availability of important biological medicines worldwide
- Global biosimilar development is the key to worldwide access to high quality biologicals
- No single country worldwide can afford ignoring the need for global development

THANK YOU

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