

Framing Global Convergence on Streamlined Biosimilar Development & the Promise of ICH M18

NOVEMBER 2-4, 2026
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Martin Schiestl
Global Head Regulatory Policy

AAM GRx+Biosims 2026
2-4 November, Rockville

Framing Global Convergence on Streamlined Biosimilar Development

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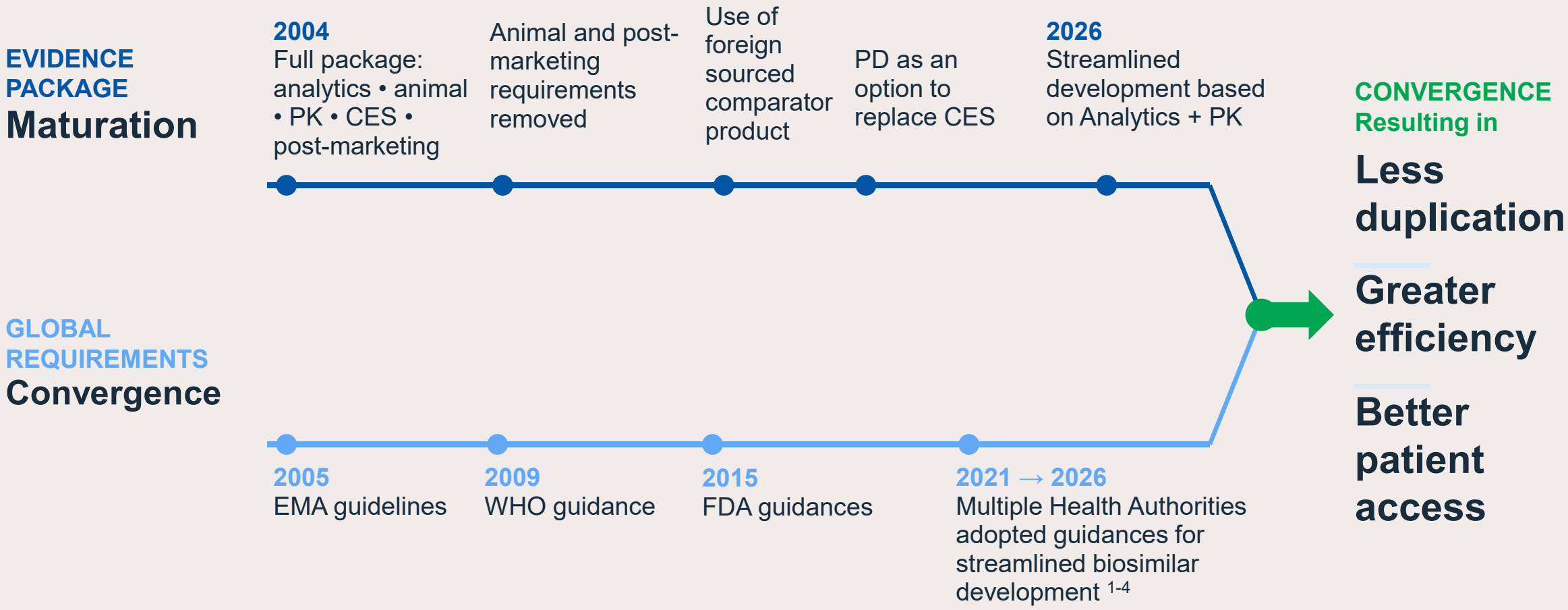
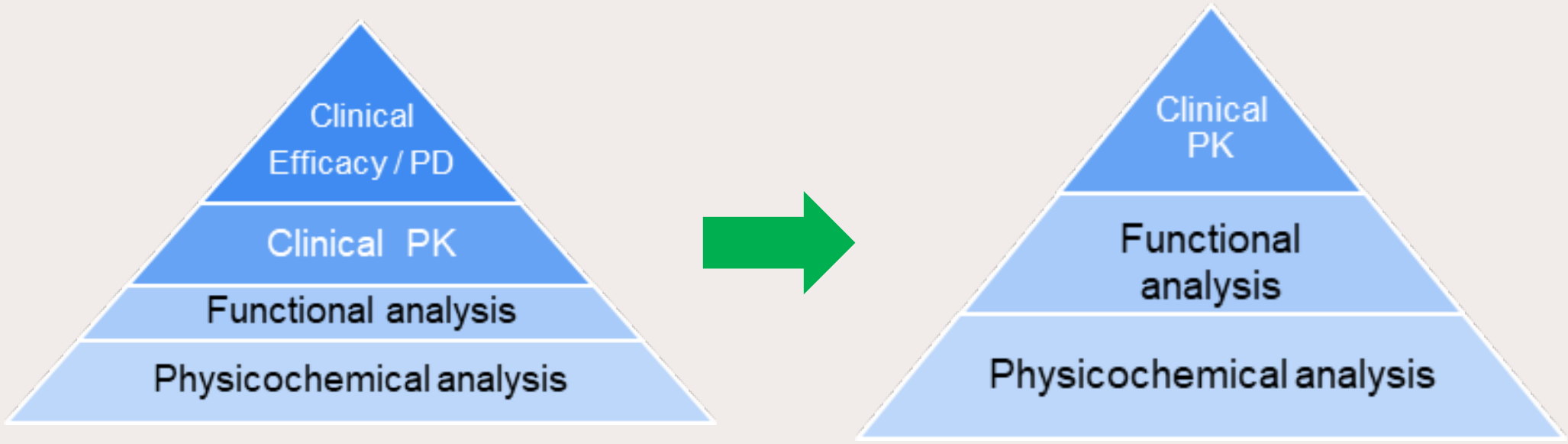
Maturation of the biosimilar pathway
Converging requirements



PK: clinical pharmacokinetic study, CES: Clinical Comparative Efficacy Study, PD: Clinical pharmacodynamic study

1. MHRA 2025, https://www.gov.uk/government/publications/guidance-on-the-licensing-of-biosimilar-products/guidance-on-the-licensing-of-biosimilar-products
2. FDA 2025, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/scientific-considerations-demonstrating-biosimilarity-reference-product-updated-recommendations
3. EMA 2026, https://www.ema.europa.eu/en/documents/other/reflection-paper-tailored-clinical-approach-biosimilar-development_en.pdf-0
4. Health Canada 2026, https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/information-submission-requirements-biosimilar-biologic-drugs.html

Harmonization of streamlined biosimilar development



Expectations until recently

Expectations for Streamlined development

PD: Pharmacodynamic (clinical study)
PK: Pharmacokinetic

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Streamlined biosimilar development is based on sound science:

- **EU regulators**
  - Guillen et al. Drugs 2025;85(5), 601-608. https://doi.org/10.1007/s40265-025-02168-y
  - Kirsch-Stefan et al. BioDrugs 2023;37, 855–871. https://doi.org/10.1007/s40259-023-00631-4
  - Guillen et al. Clin Pharmacol Ther, 2023;113, 108-123. https://doi.org/10.1002/cpt.2785
- **US regulators**
  - Herndon et al. Blood 2026; 148 (7): 807–817. doi: https://doi.org/10.1182/blood.2025031673
  - Ji et al., J. Clin. Pharmacol. 2025;65(4) 499–507. https://doi.org/10.1002/jcph.6165
  - Cavazzoni P, Yim S. JAMA. 2024;332(15):1235–1236. https://doi.org/10.1001/jama.2024.15225
- **Japan regulators**
  - Goto et al. PharmMed 19 Sep 2025; https://doi.org/10.1007/s40290-025-00583-w
  - Kuribayashi et al. PharmMed 2024;38:225–239. https://doi.org/10.1007/s40290-024-00525-y
- **UK regulators**
  - Bielsky et al. Drug Discov. 2020;25, 1910-1918. https://doi.org/10.1016/j.drudis.2020.09.006
- **Industry**
  - Schiestl et al, BioDrugs 2025;39;769-776. https://doi.org/10.1007/s40259-025-00733-1
  - Schiestl et al. BioDrugs 2020;34, 97–306. https://doi.org/10.1007/s40259-020-00422-1

- **IPRP** (International Pharmaceutical Regulators Programme)
  - IPRP, Workshop Summary Report: Increasing the Efficiency of Biosimilar Development Programs — Reevaluating the Need for Comparative Clinical Efficacy Studies, May 2024. https://admin.iprp.global/sites/default/files/2024-07/IPRP_BWG_Final%20IPRP%20Scientific%20Workshop%20Summary%20Report_2024_0506.pdf
  - IPRP Regulatory Perspectives on the Utility of Comparative Efficacy Studies in Biosimilar Development Programs 20 Feb 2026, https://admin.iprp.global/sites/default/files/files/2026-02/IPRP_BWG_Reg_Perspectives_CES_2026_0220.pdf

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Questions for harmonizing streamlined development

- Overcoming mental roadblocks in understanding regulatory science
  - Step-wise- approach
  - The concept of complexity
- Enabler
  - A study conducted must be designed to by able to address a specific scientific question required for regulatory decision making
  - Reverse the burden of proof from justifying why a CES is not needed to why a CES is needed for regulatory decision making
    - Resulting in the new default of streamlined development

Status at regulatory agencies – April 2026

Health Authority	Streamlining implemented in guideline	Streamlining Guideline status	Comment
MHRA	Yes	Final since 2021 Latest update 2025[1]	Pioneering guideline stating that a CES may not be necessary in most cases
FDA	Yes	Draft 2025 [2]	Strong encouragement to sponsors to consider streamlining
EMA	Yes	Final 2026 [3] (Reflection paper)	Reflection paper enables streamlining as the new default in EU in most cases
Health Canada	Yes	Final 2026 [4]	Most progressive guideline as it reverses the burden of proof from justifying why a CES is not needed to why a CES is needed for regulatory decision making. Health Canada guidance may serve as the role model for other Health Authorities.

1. MHRA 2025, https://www.gov.uk/government/publications/guidance-on-the-licensing-of-biosimilar-products/guidance-on-the-licensing-of-biosimilar-products
2. FDA 2025, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/scientific-considerations-demonstrating-biosimilarity-reference-product-updated-recommendations
3. EMA 2026, https://www.ema.europa.eu/en/documents/other/reflection-paper-tailored-clinical-approach-biosimilar-development_en.pdf-0
4. Health Canada 2026, https://www.canada.ca/en/health-canada/services/drugs-health-products/biologics-radiopharmaceuticals-genetic-therapies/applications-submissions/guidance-documents/information-submission-requirements-biosimilar-biologic-drugs.html

ICH M18 guideline facilitates will global harmonization enormously

- ICH M18 guideline on “Framework for Determining Utility of Comparative Efficacy Studies in Biosimilar Development Programs” [1]
- Issues to be Resolved:
  - Factors that are relevant to consider for the context of determining the utility of CES, or other clinical studies, in biosimilar development programs.
  - In a framework where there is no CES in a biosimilar development program, how efficacy, safety, and an acceptable immunogenicity profile are assured.

- ICH M18 will enable fast alignment on regulatory requirements for streamlining globally
  - M18 working group joined by regulators of 22 jurisdictions [2], covering 3.2 billion of the world population
- **Timeline**
  - November 2025: First Meeting of the M18 Expert Working Group
  - Finalization of M18 expected by 2028

1. ICH M18 concept paper, 2025, https://database.ich.org/sites/default/files/ICH_M18_Final_Concept_Paper_MCEndorsed_2025_1119.pdf
2. Working group list of M18 Expert Working Group at https://ich.org/page/multidisciplinary-guidelines

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Center for Drug Evaluation and Research

fda.gov/biosimilars

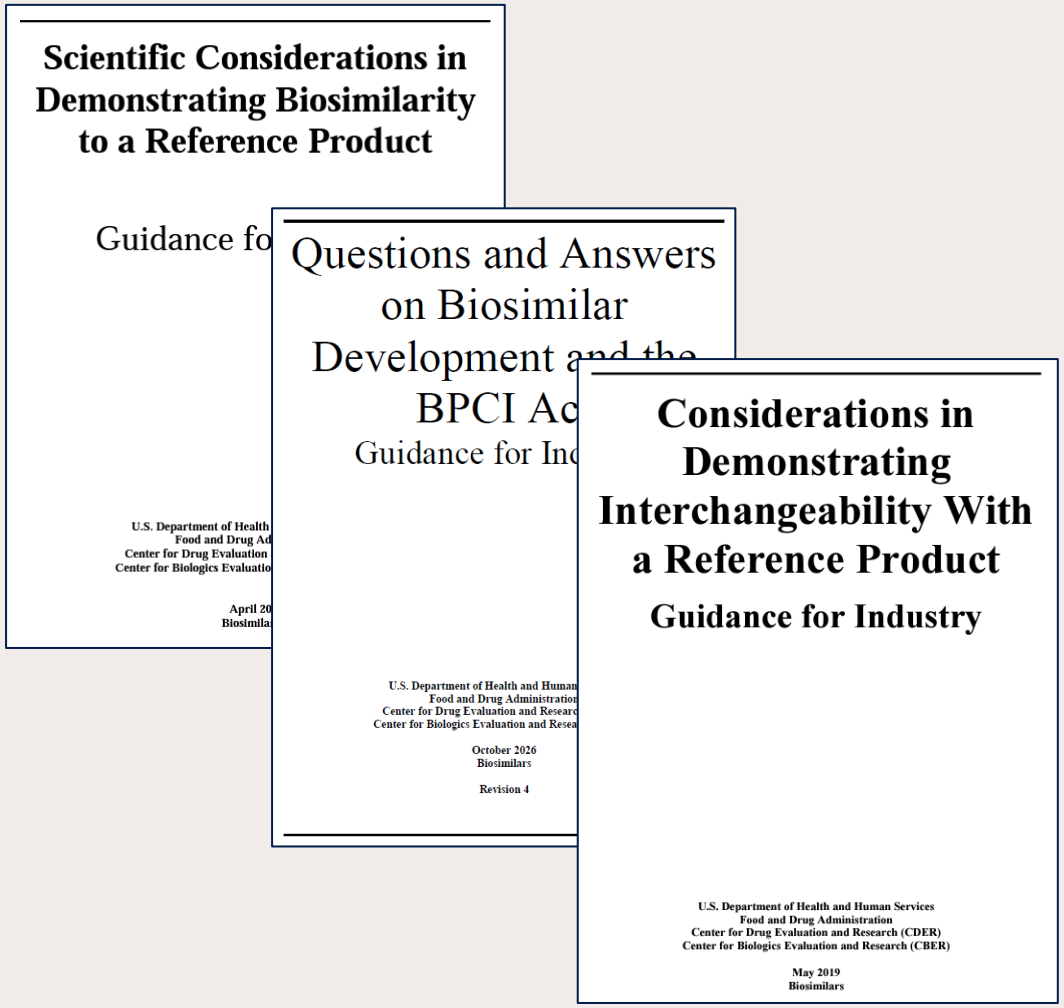
GRX+BIOSIMS 2026

FDA Convergence on a Streamlined Biosimilar Development Pathway

November 2, 2026

M. Stacey Ricci, M.Eng., Sc.D.
Director, Scientific Review Staff
Office of Therapeutic Biologics and Biosimilars
Office of New Drugs | CDER | FDA

Building the Pathway: Clinical Data Takes Center Stage



Direct PK comparison to the U.S. RP

plus

Comparative efficacy study or PK/PD

plus

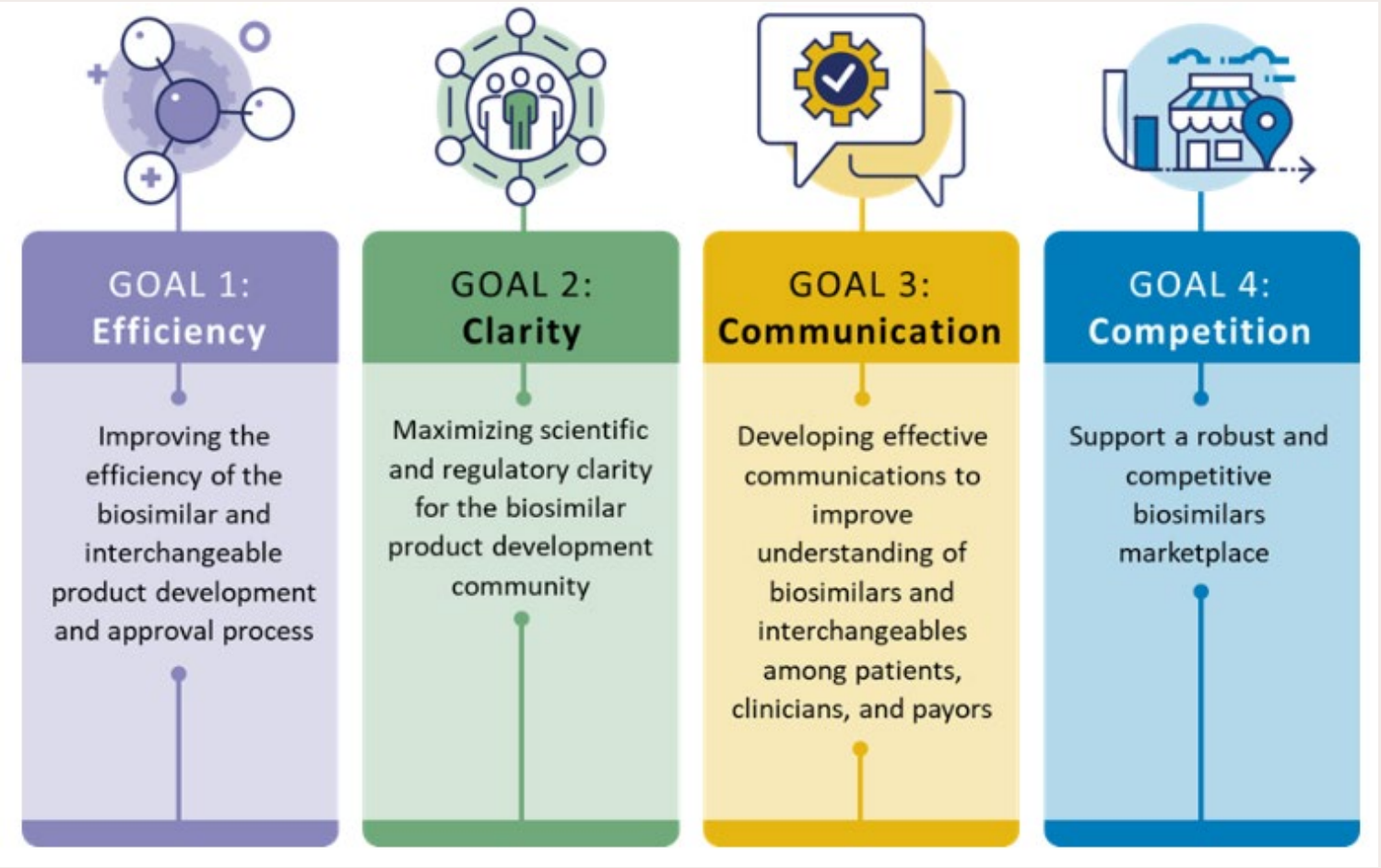
3-way PK expected if the CES used a non-US comparator

plus

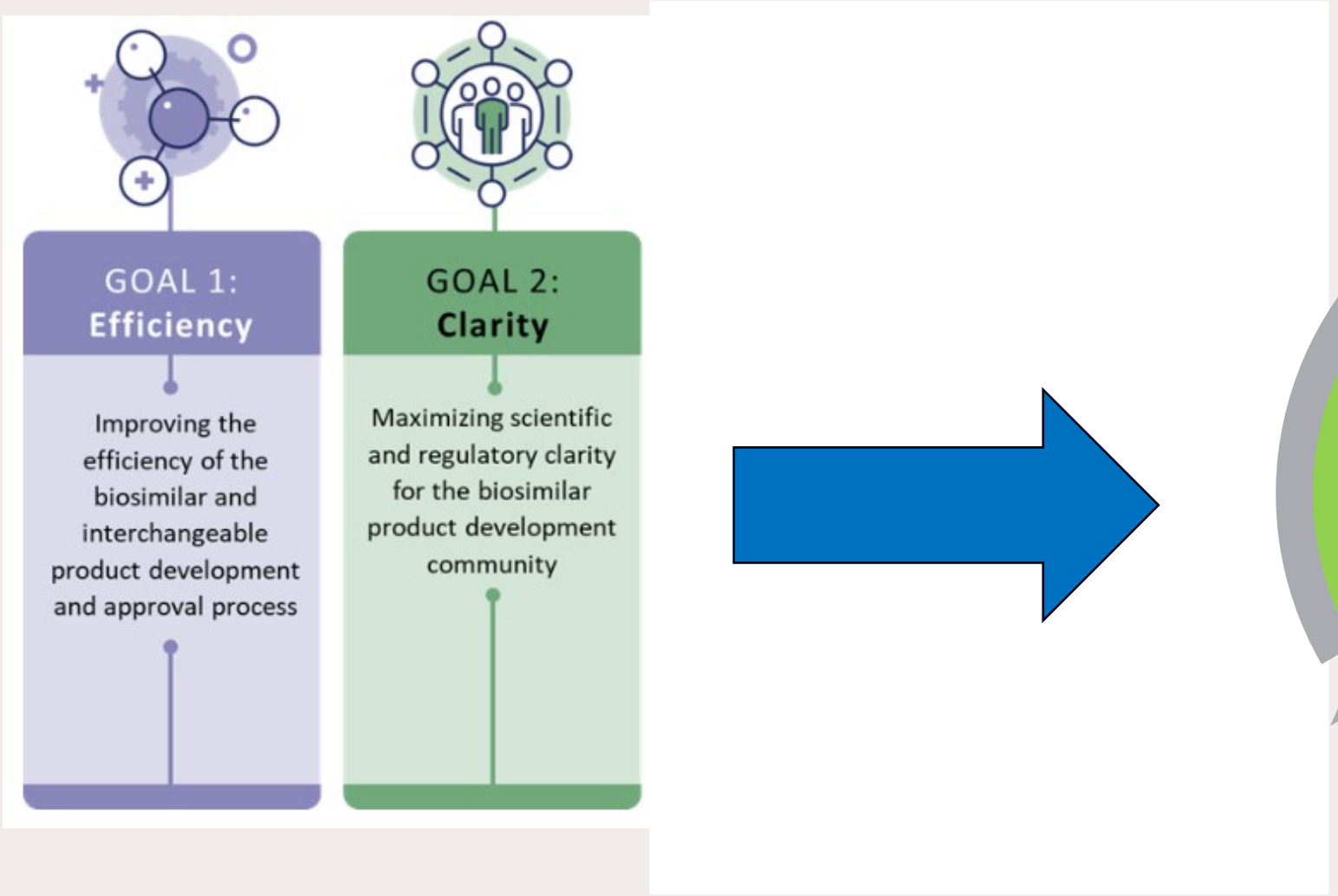
Switching studies for interchangeability

Fulfilling the Promise of the BPCI Act

The Biologics Price Competition and Innovation Act of 2009 created an **abbreviated approval** pathway to help provide patients with greater access to safe and effective biological products.

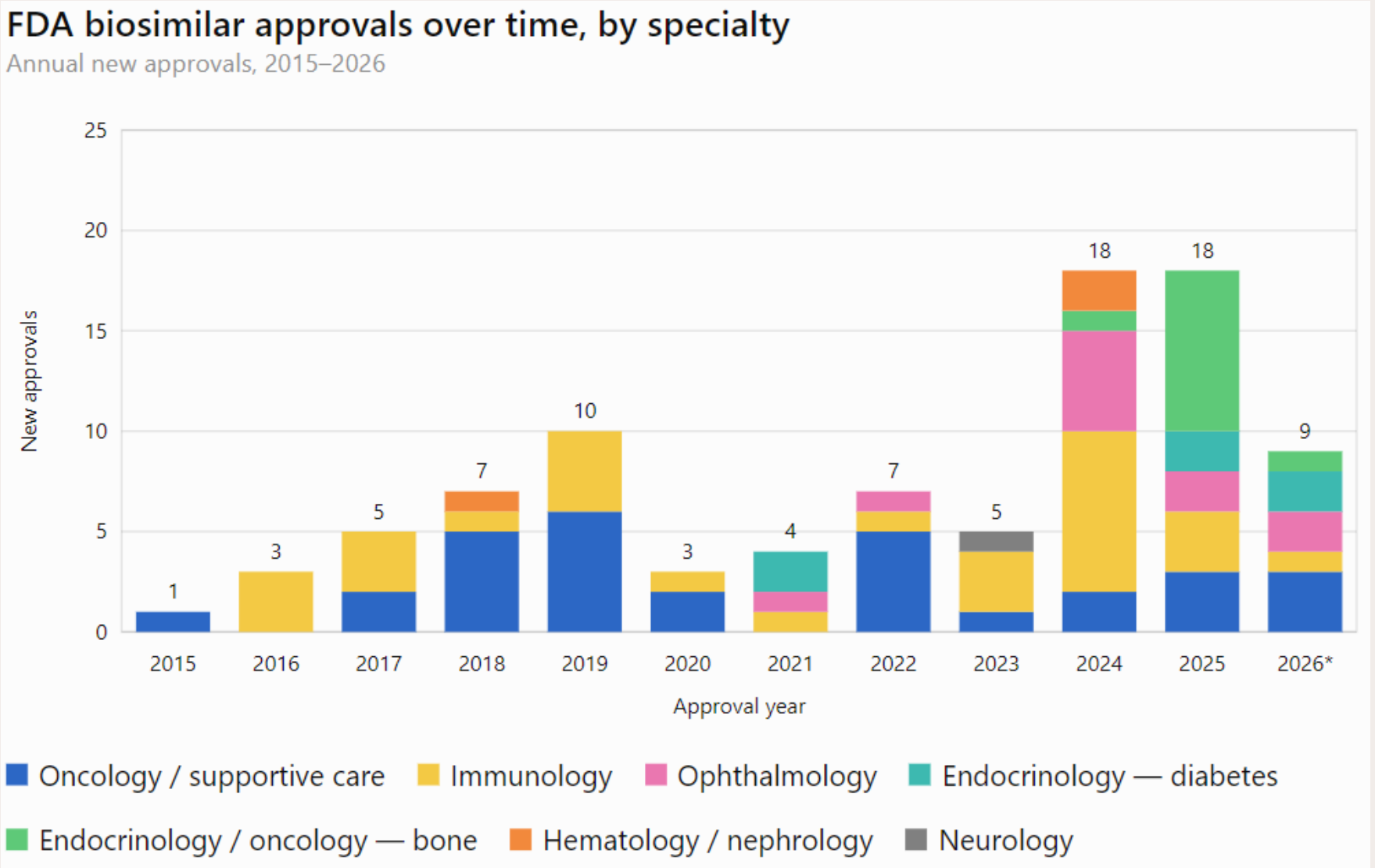


A Winning Playbook for Reaching Our Goals





FDA Reviewer Experience Plays an Essential Role...

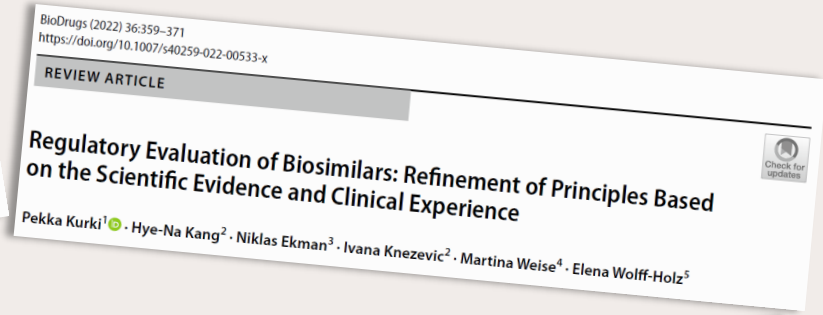


…as do Meta-Analyses and Other Scientific Research



Streamlined approval of biosimilars: moving on from the confirmatory efficacy trial

Marie-Christine Bielsky, marie.bielsky@mhra.gov.uk, Anne Cook, Andrea Wallington, Andrew Exley, Shahin Kauser, Justin L. Hay, Leonard Both and David Brown

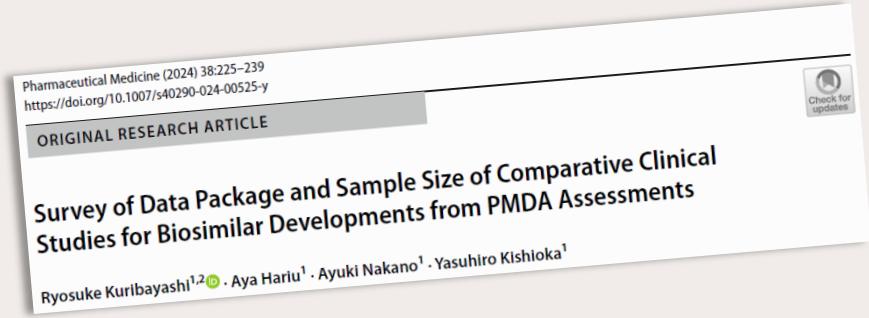


BioDrugs (2022) 36:359–371
https://doi.org/10.1007/s40259-022-00533-x

REVIEW ARTICLE

Regulatory Evaluation of Biosimilars: Refinement of Principles Based on the Scientific Evidence and Clinical Experience

Pekka Kurki[1] · Hye-Na Kang[2] · Niklas Ekman[3] · Ivana Knezevic[2] · Martina Weise[4] · Elena Wolff-Holz[5]



Pharmaceutical Medicine (2024) 38:225–239
https://doi.org/10.1007/s40290-024-00525-y

ORIGINAL RESEARCH ARTICLE

Survey of Data Package and Sample Size of Comparative Clinical Studies for Biosimilar Developments from PMDA Assessments

Ryosuke Kuribayashi[1,2] · Aya Hariu[1] · Ayuki Nakano[1] · Yasuhiro Kishioka[1]



Drugs (2018) 78:463–478
https://doi.org/10.1007/s40265-018-0881-y

SYSTEMATIC REVIEW

Switching Reference Medicines to Biosimilars: A Systematic Literature Review of Clinical Outcomes

Hillel P. Cohen[1] · Andrew Blauvelt[2] · Robert M. Rifkin[3] · Silvio Danese[4] · Sameer B. Gokhale[5] · Gillian Woollett[6]

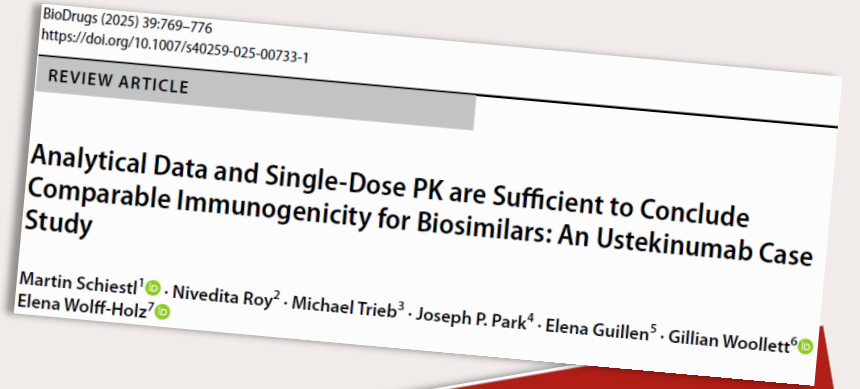


PLOS ONE

RESEARCH ARTICLE

Safety outcomes when switching between biosimilars and reference biologics: A systematic review and meta-analysis

Thomas M. Herndon[1]*, Cristina Ausin[1], Nina N. Brahme[1], Sarah J. Schrieber[1], Michelle Luo[1], Frances C. Andrada[1], Carol Kim[1], Wanjie Sun[2], Lingjie Zhou[2], Stella Grosser[2], Sarah Yim[1], M. Stacey Ricci[1]

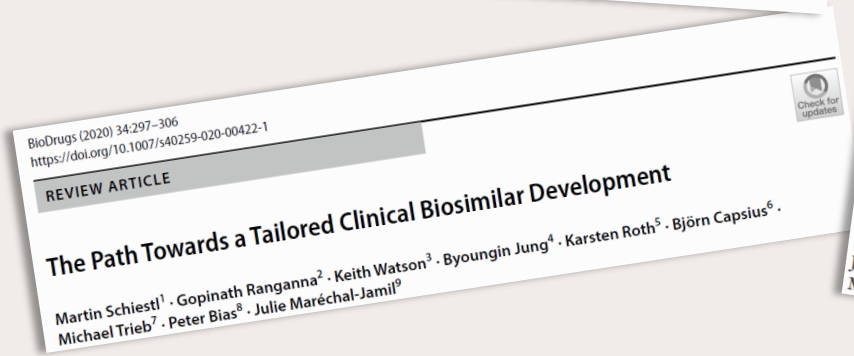


BioDrugs (2025) 39:769–776
https://doi.org/10.1007/s40259-025-00733-1

REVIEW ARTICLE

Analytical Data and Single-Dose PK are Sufficient to Conclude Comparable Immunogenicity for Biosimilars: An Ustekinumab Case Study

Martin Schiestl[1] · Nivedita Roy[2] · Michael Trieb[3] · Joseph P. Park[4] · Elena Guillen[5] · Gillian Woollett[6] · Elena Wolff-Holz[7]

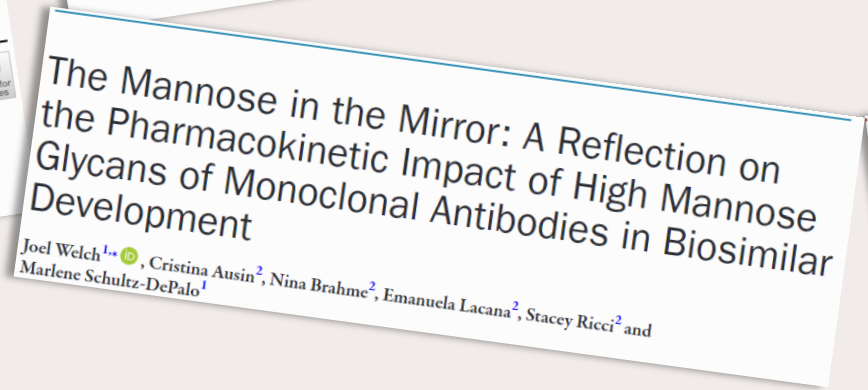


BioDrugs (2020) 34:297–306
https://doi.org/10.1007/s40259-020-00422-1

REVIEW ARTICLE

The Path Towards a Tailored Clinical Biosimilar Development

Martin Schiestl[1] · Gopinath Ranganna[2] · Keith Watson[3] · Byoungin Jung[4] · Karsten Roth[5] · Björn Capsius[6] · Michael Trieb[7] · Peter Bias[8] · Julie Maréchal-Jamil[9]



The Mannose in the Mirror: A Reflection on the Pharmacokinetic Impact of High Mannose Glycans of Monoclonal Antibodies in Biosimilar Development

Joel Welch[1]*, Cristina Ausin[2], Nina Brahme[2], Emanuela Lacana[2], Stacey Ricci[2] and Marlene Schultz-DePalo[1]



blood® Review Article

Biosimilars approved for hematology use: lessons from comparative efficacy studies and comparative analytical assessments

Thomas M. Herndon, Nina N. Brahme, and M. Stacey Ricci

Engaging Stakeholders and Global Regulators is Key

FDA Public Workshop, Sept. 19, 2022

- Increasing the Efficiency of Biosimilar Development Programs

BsUFA III Regulatory Science Pilot Program, 2023

- Improve the efficiency of biosimilar product development
- Advance the development of interchangeable products

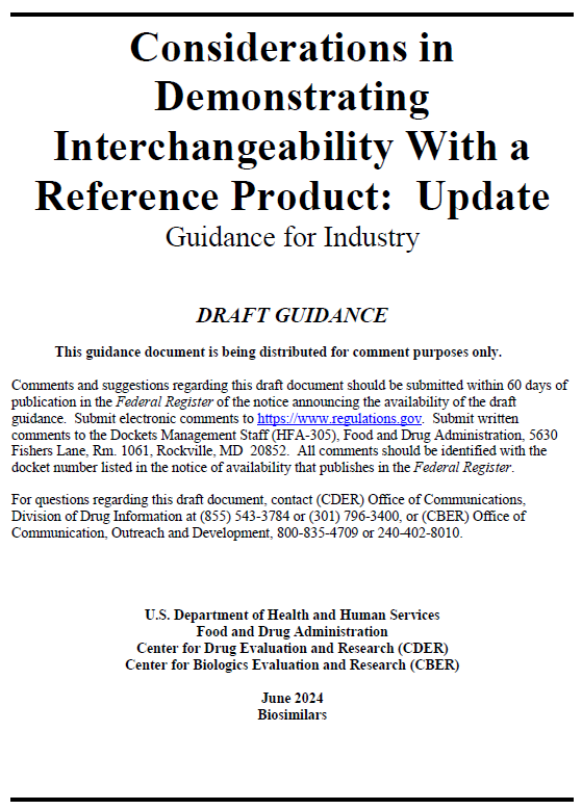
FDA hosts IPRP Biosimilar Working Group Workshop, September 2023,

- Increasing the Efficiency of Biosimilar Development Programs—Reevaluating the Need for Comparative Clinical Efficacy Studies

ICH M18 Guideline development begins May 2025

- Framework for Determining Utility of Comparative Efficacy Studies in Biosimilar Development Programs

Maturing the Pathway: Making Analytical Data the Star



Considerations in Demonstrating Interchangeability With a Reference Product: Update

Guidance for Industry

DRAFT GUIDANCE

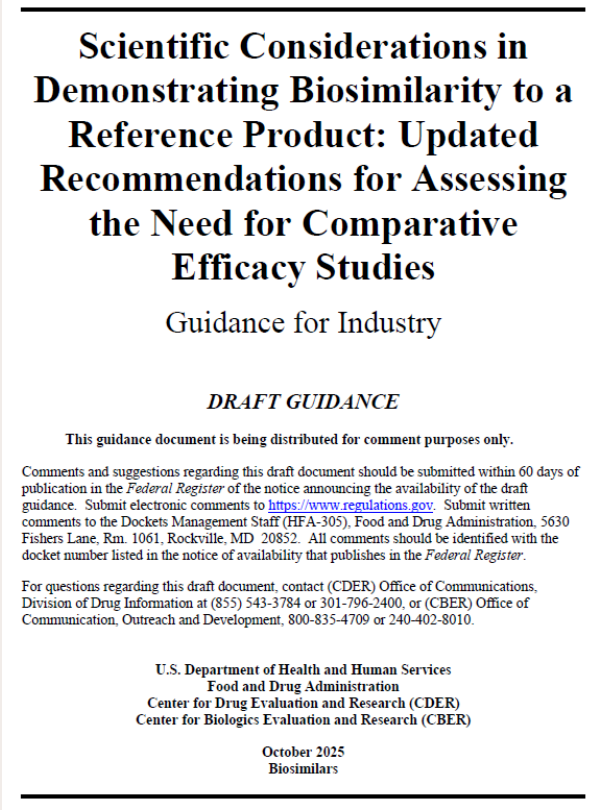
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Office of Communications, Division of Drug Information at (855) 543-3784 or (301) 796-3400, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

June 2024
Biosimilars



Scientific Considerations in Demonstrating Biosimilarity to a Reference Product: Updated Recommendations for Assessing the Need for Comparative Efficacy Studies

Guidance for Industry

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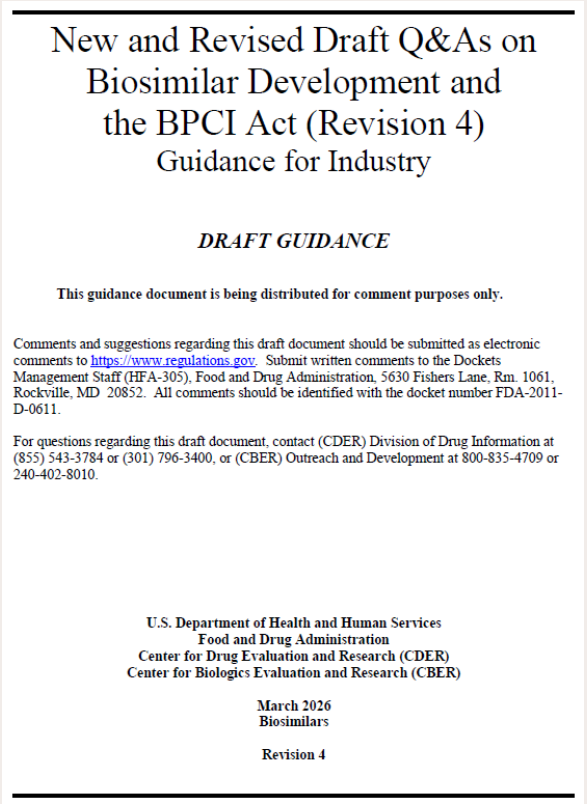
October 2025
Biosimilars



New and Revised Draft Q&As on Biosimilar Development and the BPCI Act (Revision 4)

Guidance for Industry

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U.S. Department of Health and Human Services
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Center for Biologics Evaluation and Research (CBER)

March 2026
Biosimilars

Revision 4

Streamlining Clinical Data Expectations: PK study alone is sufficient

also possible to use a non-US sourced product for that comparison

Reaching Our Goals—a Plotline That Works

- 90 Approved Biosimilars to 21 Reference Products, including: mAbs, fusion proteins, growth factors, insulins



- Conduct scientific and regulatory research projects
- Publish results and provide education

- Engage internal and external stakeholders
- Communicate new/revised recommendations

Thank you