Streamlined development: From Past to Future

Dr Elena Wolff-Holz

Enabling Affordable Access to Lifesaving Biosimilars, Worldwide

Biocon Biologics has acquired the global biosimilars business of Viatris to become a unique, fully integrated, leading global biosimilars player.

Global Biosimilar Regulatory Updates 2015 – 2021

EMA (2015)

- Revised its overarching biosimilar guidelines, allowing the use of a foreign-sourced RP in clinical studies and enabling the waiver of comparative efficacy studies under specific circumstances

EMA Scientific Advice Pilot on Biosimilars ”Tailored path” (2017–2020)

- Focused on reducing clinical trial requirements through detailed review of quality and in vitro non-clinical data.
  - Key challenge: immaturity of quality data submitted by developers.
  - Developers frequently conducted efficacy studies in parallel to speed up timelines.
- Pilot had greater impact on improving quality data generation than reducing clinical study requirements

UK MHRA (Post-Brexit, 2021)

- Removed the requirement for in vivo animal studies.
- Stated that comparative efficacy studies are not necessary in most cases, only when
  - Biological function of the RP is not well understood.
  - CQAs are not sufficiently characterized.
  - Serious adverse drug reactions (e.g., pure red cell aplasia) are associated with the RP, requiring additional clinical safety data

CQA, critical quality attribute; EMA, European Medicines Agency; MHRA, Medicines & Healthcare Products Regulatory Agency; RP, reference product.

Global Biosimilar Regulatory Updates 2021 - 2027

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US FDA Q&A on Biosimilar Development and the BPCI Act Guidance for Industry (Sep 2021)

- Emphasized analytical studies as the cornerstone of biosimilar development.
- Stated that biosimilar product may differ in formulation or delivery device from its reference product, as long as it does not affect safety, purity, or potency.

WHO Guideline Update (April 2022)

- Encouraged reduction in the use of in vivo animal studies.
- Allowed use of non-locally sourced RPs.
- Indicated that comparative efficacy trials may not be necessary if biosimilarity is well supported by other data.

US FDA Modernization Act 2.0 (December 2022)

- Removed the requirement for animal studies in biosimilar or interchangeable biologic licensing

FDA Draft Guidance: Considerations in Demonstrating Interchangeability With a Reference Product: Update (June 2024)

- Biosimilar applicants can apply for the designation without need of additional clinical switching studies.

US FDA Biosimilar Regulatory Research Pilot Program: BsUFA III and BsUFA IV (2023-2027)

- Aims to improve efficiency in biosimilar and interchangeable biologic development.

2025 UK II: Updated MHRA Biosimilar Guidance

Category	2021 Guidance	2025 Guidance
Document structure	Single document covering biosimilars, ATMPs, and VMFs	**Biosimilars guidance separated** from ATMPs and VMFs for clarity
Scientific approach	Stepwise development encouraged; clinical studies *not necessary in most cases*	Stronger emphasis on non-clinical comparability; **clinical efficacy studies generally not required**
Justification for comparability beyond MOA/efficacy	**Risk-based immunogenicity assessment is part of framework**	Framework based **on clinical experience with Refernce drug and quality attributes,** not on whether risks are low or high. Clarifies that **injection-related reactions and ADA-mediated effects are common ADRs**
Animal studies	May be considered in some cases	**Explicitly discouraged; not requested**
Interchangeability	Focused on biosimilar vs reference product	In addition, clarifies **biosimilars are interchangeable with each other** if they reference the same RP
Reference product origin	EU-sourced RP generally acceptable	**Clarifies acceptability of non-UK sourced RP post-Brexit**
Patient-centric considerations	Limited mention	Includes **feedback from patient groups** (e.g., injection pain, allergens)
Regulatory context	EU-aligned framework	Reflects UK-specific regulation under the Windsor Framework (UK not GB)

ATMP, advanced therapy medicinal product; MHRA, Medicines & Healthcare Products Regulatory Agency; MOA, mechanism of action; RP, reference product; VMF, veterinary master files.

2023 and 2024: FDA Streamlined Biosimilars Development

80 biosimilar applications received by FDA

16 have received notices their application cannot be approved in the present form

Editorial › JAMA. 2024 Oct 15;332(15):1235-1236. doi: 10.1001/jama.2024.15225.

The Science of Biosimilars–Updating Interchangeability

Patrizia Cavazzoni [1], Sarah Yim [2]

plete response letter, for various reasons. Six of those included a concern, based on the CAA, that the biosimilar may not be "highly similar" to the reference product. In contrast, the results of clinical studies (including pharmacokinetic, safety, pharmacodynamic or efficacy, and immunogenicity data) did not identify any issues in 5 of those 6 applications. In only 1 of these 6 applications did the results of a clinical efficacy study also indicate a potential concern (ie, a trend against the biosimilar on a secondary clinical end point that could have been related to the analytical difference observed). Importantly, to date, we have had no applications in which clinical studies detected a potential issue that was not also detected by the CAA. This reflects the CAA's fundamental role in serving as a more sensitive evaluation for potential differences between biosimilars and their reference products.

Meta-Analysis › PLoS One. 2023 Oct 3;18(10):e0292231. doi: 10.1371/journal.pone.0292231. eCollection 2023.

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]

product. As familiarity with and understanding of the rigor of the analytical comparisons used to support biosimilar approvals increases, the amount and types of clinical data routinely performed as part of biosimilar development may be reduced, which in turn would reduce the time and cost of development.

CAA, Comparative Analytical Analysis; FDA, Food and Drug Administration.

2024: IRPR Streamlined Biosimilars Development

IPRP
International Pharmaceutical Regulators Programme

6 May 2024

Workshop Summary Report: Increasing the Efficiency of Biosimilar Development Programs — Reevaluating the Need for Comparative Clinical Efficacy Studies

IPRP Biosimilars Working Group (BWG)

comparable target and receptor binding activity using suitable in vitro bioassays. Multiple stakeholders expressed that successful functional characterization using in vitro bioassays may preclude the need for a CES, in part due to the high specificity and sensitivity of these functional characterization assays for detecting clinically meaningful differences. If a CES is to be used, it should be designed purposefully to answer a specific question that cannot be addressed from the comparative functional characterization.

CES, comparative efficacy study.

2025: EMA Streamlined Biosimilars Development

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 March 2025
EMA/CHMP/BMWP/60916/2025
Committee for Medicinal Products for Human Use (CHMP)

Reflection paper on a tailored clinical approach in biosimilar development

Draft

Draft for internal consultation agreed by Biosimilar Medicines Working Party	21 October 2024
Consultation with MWP, BWP and SAWP	17 January 2025
Draft agreed by Biosimilar Medicinal Products Working Party	12 February 2025
Adopted by CHMP for release for consultation	17 March 2025
Start of public consultation	1 April 2025
End of consultation (deadline for comments)	30 September 2025

Subject: Medicines for Europe proposal for key agenda points - EMA BMWP Workshop on Tailored Clinical Approaches in Biosimilar Development (22 September 2025)

Date: 16 June 2025

1. Framework for determining the utility of CESs

- **a) The obsolete stepwise approach**
  - i) Necessary level of information to enable Scientific Advice on tailored development
  - ii) Absence of CES becoming the default scenario: Reversal from requiring justification for not doing a CES towards a justification in doing a CES
- **b) Mechanism of Action (MoA)**
  - i) Definition of MoA as the initial biological events triggered by the primary binding events between the protein and its receptors and targets
- **c) Value of analytical and Pk data in demonstrating comparable immunogenicity – case study**
- **d) When is a CES needed**
  - i) CES should only be required if it is able to answer specific open question which cannot be addressed by analytical and PK data
  - ii) Justification for doing/not doing the CES

2. Limitations of usefulness of PD endpoints

- **a) As primary endpoint in CES studies (e.g., mAbs)**
- **b) As secondary endpoint in PK studies (e.g., insulins)**

3. Analytical Similarity

- **a) Use of terms for specifying "difference"**
  - i) Consistent use of terminology – industry recommendation
- **b) Similarity assessment protocol – clarification of role**
  - i) Level of pre-specification of similarity criteria
  - ii) Gaining product and process knowledge throughout development
- **c) Ensure consistency with the established regulation of manufacturing changes**
- **d) Statistical approaches**
  - i) Industry experience and recommendations

CES, comparative efficacy study; EMA, European Medicines Agency; mAbs, monoclonal antibodies; MoA, mechanism of action; PD, pharmacodynamics; PK, pharmacokinetics.

2025: HC Streamlined Biosimilars Development

565 *Comparative clinical efficacy and safety trial(s)*

566 In most cases, a comparative clinical efficacy and safety trial(s) is not required. Safety and
567 comparative immunogenicity data are still required and should be collected within the comparative
568 clinical pharmacology studies but could be supplemented with data collected using other trial
569 designs (e.g., studies designed to specifically focus on safety and/or immunogenicity). If a
570 comparative clinical efficacy and safety trial(s) is deemed necessary, sponsors should provide a
571 rationale to explain the purpose of the trial(s) in the context of a biosimilar submission.

189 efficacy and safety studies cannot address major differences in quality attributes between a
190 biosimilar candidate and its CRBD.

238 • The CRBD should have accumulated adequate safety and efficacy data in the pre- and post-
239 market setting such that the demonstration of a high degree of similarity between the
240 biosimilar candidate and the CRBD will bring into relevance for the biosimilar a substantial
241 body of reliable data derived from the CRBD.

CRBD, Canadian reference biologic drug; HC, Health Canada.

Health Canada. Guidance document: Information and submission requirements for biosimilar biologic drugs (2025 - Revised draft). Revised 10 June 2025. Link.

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Transforming Healthcare. Transforming Lives.

THANK YOU

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WHO

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EMA

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- European Medicines Agency. Concept paper for the development of a Reflection Paper on a tailored clinical approach in Biosimilar Development. EMA/CHMP/BMWP/35061/2024. Revised 24 November 2023. Link.
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Health Canada

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International Pharmaceuticals Regulators Programme

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