Biosimilar Evidence Expectation Matrix 2026

What each regulator expects for a therapeutic protein biosimilar, by evidence category. India column reflects the CDSCO Draft Guidelines on Similar Biologics 2025 (the 2016 guideline remains in force until the draft is notified).

Evidence category	India (CDSCO)	European Union (EMA)	United Kingdom (MHRA)	United States (FDA)
Reference product	Innovator product licensed in India or an ICH country (USA, UK, Japan, Australia, Canada, EU); another similar biologic cannot be the reference; same product throughout; same dose and route	EU-authorized reference; bridging data where a non-EU comparator is used in clinical studies	UK reference, or EU reference shown to be representative of the UK product	US-licensed reference; bridging where a non-US comparator is used
Analytical and functional comparability	State-of-the-art orthogonal methods per ICH Q6B; all commercial-scale batches; min. 3 reference batches; predefined similarity ranges (x-sigma, min-max or tolerance interval); Fc receptor binding and ADCC/ADCP/CDC for mAbs	Foundation of the tailored approach; thorough characterization plus demonstrated physicochemical and functional similarity is the prerequisite for waiving the efficacy trial	Comparative analytical and functional data must support the justification for omitting the efficacy trial	Comparative analytical assessment (CAA) per the Sept 2025 final CAA guidance; CAA regarded as more sensitive than an efficacy study
Animal studies	Toxicity study waiver against 10 conditions; in vivo studies expected to be rare; 3Rs; no NHP repeat-dose studies; no safety pharmacology, repro-tox, geno-tox or carcinogenicity	Exceptional under the 2014 revised nonclinical and clinical guideline	Not requested	Addressed under separate guidance; generally minimal
Comparative PK study	Required where measurable; single-dose crossover preferred, parallel for long half-life mAbs; subcutaneous route preferred; 80 to 125% on the 90% CI; partial AUC for target-mediated clearance	Required; PK data plus analytical comparability can be sufficient under specific prerequisites	Required	Required; a PK similarity study must be feasible and clinically relevant for the streamlined approach
PD markers	Alongside PK where a marker exists; may replace the efficacy trial if predefined ranges, mechanism-reflecting, sensitive and validated (clamp for insulin, ANC/CD34+ for G-CSF, CTX-1/P1NP for denosumab)	Used where a relevant marker exists	Used where a relevant marker exists	Used where a relevant marker exists
Comparative efficacy trial	Not necessary if sufficient similarity shown elsewhere (2025 draft); confirmatory trial generally expected (2016); equivalence design preferred where a trial is run	No longer expected for products that can be thoroughly characterized (adopted 16 Mar 2026)	In most cases may not be necessary if sound scientific rationale supports this (May 2021)	May not be needed where CAA plus PK plus immunogenicity suffice and three conditions hold (Oct 2025 draft); intravitreal products excepted
Immunogenicity	Comparative unless justified; tiered ADA assays (screening, confirmatory, titer, neutralizing); population most likely to respond; real-time NAb testing for high-risk products; possible waiver for insulin, somatropin, filgrastim, teriparatide	Assessed within the PK study and the risk management plan	Assessed within the PK study; justification required for omission	Immunogenicity assessment is part of the streamlined package
Interchangeability	No designation; substitution follows formulary and tender practice	Interchangeable by EMA/HMA statement (19 Sep 2022, updated 21 Apr 2023); pharmacy substitution decided nationally	Interchangeable with reference and other biosimilars of the same reference (Nov 2022); prescribed by brand name	Separate 351(k)(4) designation permitting pharmacy substitution subject to state law; June 2024 draft: switching studies generally not needed
Post-marketing	Risk management plan, pharmacovigilance plan, ADR reporting and a post-marketing Phase IV study	RMP; PSURs	RMP; PSURs	Postmarketing commitments; REMS where applicable

Reading the matrix: a program intended for more than one market is built once to the most demanding cell in each row. The analytical row is decisive; every waiver in the efficacy row is conditional on it.

Sources: EMA/CHMP/BMWP/60916/2025 (16 Mar 2026); FDA draft guidance FDA-2011-D-0605 (Oct 2025); MHRA guidance (May 2021, updated Nov 2022); CDSCO Draft Guideline

General information only; not regulatory advice. Confirm the current position with the relevant authority.

Biosimilar Evidence-Gap Self-Assessment

Tick one box per line. Any line marked Gap or Not started before the first similarity batch is manufactured is a decision that will cost more to make later.

Item	Ready	Gap	Not started
1. Reference product			
Reference product is the innovator product, licensed in India or an ICH country (or in each target market)	☐	☐	☐
Sourcing plan covers at least three independent reference batches across campaigns and expiry dates	☐	☐	☐
Bridging plan exists for every target jurisdiction whose reference differs from the comparator used	☐	☐	☐
Reference batches used in clinical studies are included in the analytical comparison	☐	☐	☐
2. Analytical and functional comparability			
Critical quality attributes tiered by criticality with a documented rationale	☐	☐	☐
Statistical approach to similarity ranges (x-sigma, min-max, tolerance interval or equivalence testing) chosen and justified	☐	☐	☐
Overall similarity criterion (percent of batches within range) fixed before testing	☐	☐	☐
Assay battery covers every mechanism of action relevant to every indication claimed	☐	☐	☐
Glycan to Fc-function correlation established for monoclonal antibodies	☐	☐	☐
3. Nonclinical			
All ten CDSCO toxicity-waiver conditions checked against the program	☐	☐	☐
No waiver exclusion applies (novel excipient, new route, higher dose, unresolved safety difference)	☐	☐	☐
4. Clinical PK, PD and efficacy			
PK-only package accepted, or expected to be accepted, by every target market for this molecule	☐	☐	☐
Study design chosen (crossover or parallel) with population, route, dose and washout justified	☐	☐	☐
PD marker identified and built into the PK study where one exists	☐	☐	☐
If an efficacy trial is required, one design (margins, population, endpoint, timing) serves all markets	☐	☐	☐
Regulator agreement in principle obtained before trial initiation	☐	☐	☐
5. Immunogenicity and extrapolation			
Immunogenicity risk assessment written (product, formulation, patient factors)	☐	☐	☐
Tiered assay strategy validated; single-assay approach justified	☐	☐	☐
Population and sampling schedule satisfy the most demanding regulator	☐	☐	☐
Extrapolation argument documented per indication with supporting functional assays	☐	☐	☐
6. Post-approval and market access			
Interchangeability and substitution position stated for each market	☐	☐	☐
Post-marketing commitments listed and costed, including the Indian Phase IV study	☐	☐	☐
Budget impact model inputs identified; clinical studies collect the required variables	☐	☐	☐
Real-world evidence questions (switching, persistence, resource use) defined with data sources	☐	☐	☐
Medical affairs standard responses drafted from the same evidence base as the dossier	☐	☐	☐

Notes

Biosimilar regulatory consultant, medical writing and market access support
EvySaif Research Solutions, Pune. Reference product and bridging strategy, similarity statistics, PK/PD and efficacy trial design, immunogenicity summaries, CDSCO, EMA, MHRA and FDA submissions, budget impact models and value dossiers.

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Sources: EMA/CHMP/BMWP/60916/2025 (16 Mar 2026); FDA draft guidance FDA-2011-D-0605 (Oct 2025); MHRA guidance (May 2021, updated Nov 2022); CDSCO Draft Guideline