

Biosimilar Analytical Similarity

Write the comparative analytical assessment of a proposed biosimilar against its reference product: quality ranges from the reference lots, the share of biosimilar lots inside them, profile comparisons, and the residual uncertainty.

WRITES

3.2.R

3.2.S.3.1

Report

PRODUCT TYPE

Biologics

GUIDANCE IT FOLLOWS

FDA Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations (2019 draft); FDA Scientific Considerations in Demonstrating Biosimilarity (2015); EMA Guideline on similar biological medicinal products containing biotechnology-derived proteins: quality issues (EMA/CHMP/BWP/2477); EMA Reflection paper on statistical methodology for the comparative assessment of quality attributes (EMA/CHMP/138502/2013); ICH Q6B; ICH Q5E

TIME TO LEARN

About 20 minutes
with the example

Open the tool at <https://app.cmcfy.com/app/biosimilar-similarity.html>. This guide is also online at <https://cmcfy.com/guides/biosimilar-similarity.html>

1. What this module does

You enter each attribute with its method, criticality, and the results of the reference and biosimilar lots (or the outcome of a profile comparison). The tool builds the quality range (reference mean $\pm$ k SD), counts the biosimilar lots inside it, shows the mean shift and the reference min–max, and groups attributes by category.

It checks the number of lots, that primary structure is identical, that higher-order structure and biological activity are covered, and that US and EU reference lots are bridged when both regions are chosen.

What you get

- A Word or PDF report: Comparative analytical assessment, with a chart of the attribute you choose.

2. Before you start

Have these ready. You can still start with the example data and replace it piece by piece.

- Results of at least 10 reference product lots and 6 to 10 biosimilar lots.
- Profile comparisons for structure.
- Structure–function data for any difference and the comparative stability results.

Your data stays on your computer. The bar under the title counts every network request the page makes; it stays at 0 because your data never leaves your computer. [Download offline](#) [copy](#) saves a single file that opens from your own computer with all network access blocked, for air-gapped PCs.

3. Step by step with the example

Open the tool at app.cmcfy.com/app/biosimilar-similarity.html. The example is loaded when the page opens, so every panel already has realistic data. Follow the steps to see how it works, then replace the example with your own data.

1 Describe the products

Enter the proposed biosimilar and the reference product, the k multiplier (3 by default) and the share of lots required in range (90% by default).

The screenshot shows the CMCfy Biosimilar Analytical Similarity tool interface. The top navigation bar includes the CMCfy logo, the title 'Biosimilar Analytical Similarity', and links for 'Projects', 'All modules', 'Training', and 'Security'. A status bar indicates 'Runs entirely on this device' and provides a 'Training guide' link.

The main content area is titled 'PROJECTS' and includes instructions: 'Keep this work in a project, with version history and your company logo on every report.' It offers two options: 'Choose projects folder' and 'Keep in this browser'.

Below the projects section, there are three status indicators:

- Network requests since load: 0**: Counted live by your browser. Your data never leaves this device.
- Works offline**: Everything the tool needs is inside this page.
- Locked offline copy**: Save a single file that opens from your own computer with all network access blocked.

The '3.2.R' section is active, showing a 'Report' button. Below this, there is a description of the tool's purpose: 'Write the comparative analytical assessment of a proposed biosimilar against its reference product. For each quantitative attribute the tool builds the quality range from the reference lots (mean $\pm$ k SD), counts the biosimilar lots inside it and compares means; qualitative attributes are compared as profiles. Attributes are ranked by criticality, and the number of lots and the reference product sourcing are checked.'

Guidance text is provided: 'FDA Development of Therapeutic Protein Biosimilars: Comparative Analytical Assessment and Other Quality-Related Considerations (2019 draft); FDA Scientific Considerations in Demonstrating Biosimilarity (2015); EMA Guideline on similar biological medicinal products containing biotechnology-derived proteins: quality issues (EMA/CHMP/BWP/247713/2012); EMA Reflection paper on statistical methodology for the comparative assessment of quality attributes (EMA/CHMP/138502/2017); ICH Q6B; ICH Q5E'.

The '1. PRODUCTS' section contains input fields for:

- Proposed biosimilar**: CMX-bs01 (proposed biosimilar to adalimumab)
- Regulations**: Both US and EU (dropdown menu)
- Report number**: BSA-R-001
- Reference product**: Humira (adalimumab), US-licensed and EU-authorized lots
- ☒ US-licensed and EU-authorized reference lots compared (three-way bridge)

The 'RESULT' section displays the outcome: 'Analytically similar on all 10 attributes'. It states: '12 reference and 8 biosimilar lots. Every attribute meets the quality range target.'

ATTRIBUTES	REFERENCE LOTS	BIOSIMILAR LOTS
10	12	8

Below the table, the 'QUALITY RANGE' is specified as 'mean $\pm$ 3 SD, $\geq$ 90% of lots'.

At the bottom, there is a section for 'AFUCOSYLATION (%)'.

2 Enter the attributes

One row per attribute. Results per lot separated by ";". For profiles, write identical or comparable.

3 Read the result

The headline gives the outcome: "Analytically similar on all 10 attributes". The table shows the quality range, the lots in range and the mean shift.



Comparative analytical assessment.

4 Resolve alerts and download

An attribute below the target share is flagged (critical for high criticality). Few lots, missing structure or function categories, a mean shift above 2 SD and missing bridging are flagged. Then preview and download.

Preview and review before download Close

Review

Checked on this device: gaps in the data, gaps in the report against ICH and regional expectations, and differences from the protocol.

No open gaps

No open gaps: the data, the report and the protocol (if given) match every rule checked, or you accepted the rest. Read the preview before you sign.

Compare with the protocol

Load or paste the approved protocol. Every requirement and acceptance criterion in it is looked for in the report.

Paste the protocol text here, or load the file.

Load protocol file Compare

AI review against guidance

AI reads the report, the protocol and the data against the ICH, FDA or EMA requirements for these sections, and lists gaps with the guideline it applies, protocol and data mismatches, and how to fix them. You see exactly what is sent before anything leaves this device. Results and pass/fail are not changed.

Run AI review

3.2.R Comparative analytical assessment

CMX-bs01 (proposed biosimilar to adalimumab) - BSA-R-001 - US (FDA) and EU (EMA)

Proposed biosimilar	CMX-bs01 (proposed biosimilar to adalimumab)
Reference product	Humira (adalimumab), US-licensed and EU-authorized lots
Reference lots	12
Biosimilar lots	8
Quality range	mean $\pm$ 3 SD; $\geq$ 90% of lots
Regulations	US (FDA) and EU (EMA)

1. Approach

Attributes were ranked by their potential impact on clinical performance. Quantitative attributes were compared with the quality range of the reference product; qualitative attributes were compared as profiles with orthogonal methods.

2. Results

Attribute	Category	Criticality	Quality range or reference	Biosimilar	Outcome
Amino acid sequence	Primary structure	high	identical	identical	Similar
Intact mass	Primary structure	high	comparable	comparable	Similar
Higher-order structure	Higher-order structure	high	comparable	comparable	Similar
TNF- α neutralisation potency (%)	Biological activity	high	91.82 - 108.85	mean 100.00; 8/8 in range	Similar
TNF- α binding (%)	Binding	high	94.42 - 105.58	mean 100.00; 8/8 in range	Similar
FcRn binding (%)	Binding	moderate	91.15 - 108.18	mean 100.00; 8/8 in range	Similar

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4. Field reference

Every input in the tool, panel by panel. Tables accept rows pasted straight from Excel, comma-separated text, or a loaded file; check the columns after loading a file. Fields marked “when it applies”

appear only for the choices that need them.

1 - Products

FIELD	WHAT TO ENTER
Proposed biosimilar	Type it in.
Regulations	Choose one: US: 351(k) BLA; EU: biosimilar MAA; Both US and EU.
Report number	Type it in.
Reference product	Type it in.
US-licensed and EU- authorised reference lots compared (three-way bridge) when it applies	Tick the box if it applies.
Quality range multiplier k	k = 3 is common; a smaller k is stricter. Type a number.
Biosimilar lots required within the quality range (%)	Type a number.

2 - Attributes

One row per attribute. Tier or criticality: high, moderate or low. Results per lot separated by ";". For profiles (peptide map, CD) write the comparison outcome instead.

FIELD	WHAT TO ENTER
Attributes	Criticality: high, moderate or low. A table. Columns: Attribute Method Criticality Reference lots Biosimilar lots. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).
Attribute to chart	Type it in.

3 - Residual uncertainty

FIELD	WHAT TO ENTER
Assessment of differences (structure–function)	Type or paste text.

FIELD	WHAT TO ENTER
Comparative stability and forced degradation	Type or paste text.

5. Checks and alerts

Calculations and pass/fail outcomes always come from fixed rules, never from AI. The tool checks:

- Share of biosimilar lots inside the quality range against the target.
- Mean shift in SD units.
- Lots: at least 10 reference and 6 biosimilar.
- Identical amino acid sequence; higher-order structure and biological activity compared; three-way bridge for US and EU.

How to resolve alerts

- **Critical** alerts block the download and must be fixed in the data. A failing result can instead be linked to an investigation: type the investigation reference and outcome and press **Record**.
- **Major** alerts block the download until you fix them or type a justification and press **Accept justification**.
- **Minor** alerts do not block anything. They are listed in the documents so the reviewer sees them.
- Some alerts have an **Apply fix** button that makes the change for you. **Reopen** undoes a justification.

Narratives

This module writes: Discussion and conclusion. Each narrative is written by fixed rules from your data. You can edit it in the box. **Rewrite with AI** (where your plan includes AI) rewrites it in regulatory style; every number in the text is checked against your data, and a number that does not match is flagged under the box and blocks the download until you correct it. **Reset to rule-based text** brings back the original.

6. Preview, gap review and download

1. Press **Preview** next to a section, or **Preview and download all**. The document opens in a preview window, exactly as the Word file will read.
2. The left side lists the review, run on your device: **gaps in the data** (missing values, open alerts), **gaps in the report** (missing content the guidance expects, placeholders such as [site] or TBD left in the text) and, if you load the approved protocol under **Compare with the protocol**,

differences from the protocol (requirements, criteria, batches or time points it plans that the report does not show).

3. Click a finding to jump to the place in the preview. Fix it in the tool, then preview again.
4. Optional **AI review**: a second read for contradictions, claims without data and vague wording. The report text is sent to Claude only when you press it, and only where your plan includes AI. Check every AI finding; AI can be wrong.
5. Press **Download Word (.docx)** or **Download PDF**. With several documents open, **All as Word (.zip)** and **All as PDF (.zip)** download the set. The download buttons stay disabled while a blocking alert is open; the preview still works.

Documents this module produces

SECTION	DOCUMENT
3.2.R	Comparative analytical assessment

Use **Save project** to keep your work as a file on your computer, and **Open project** to continue later. **Start blank** clears every field; **Load example** brings the example back. Nothing is stored on CMCfy servers.

7. US and EU submissions

US follows the FDA comparative analytical assessment guidance (2019 draft) and Scientific Considerations (2015). EU follows EMA/CHMP/BWP/247713/2012 and the reflection paper on statistical methodology (EMA/CHMP/138502/2017).

8. Working with other modules

- Characterisation methods are in the Biologics Characterisation & Specification module.

9. Common pitfalls

- Too few reference lots, which gives a narrow, unreliable quality range.
- Ignoring a mean shift because every lot is inside the range.

10. Practice exercises

Each exercise starts from the example (press **Load example** to reset). We run these on every update of this guide, so the result you see should match.

1. **Raise afucosylation**

Change the biosimilar afucosylation results to 10.8;11.4;10.9;11.2;10.6;11.0;11.3;10.7.

EXPECTED RESULT

The headline shows one attribute outside the quality range.

Guide updated 28 October 2026 for the current version of the tool. CMCfy drafts are for review by a qualified person before use in a submission.