

Biologics Comparability (ICH Q5E)

Write the ICH Q5E comparability report for a manufacturing change: each quality attribute of the post-change batches compared with a range from the pre-change batches, the stability comparison, and the impact of any difference.

WRITES

3.2.S.2.6

3.2.R Report

PRODUCT TYPE

Biologics

GUIDANCE IT FOLLOWS

ICH Q5E
Comparability of
Biotechnological/Biological
Products Subject to
Changes in Their
Manufacturing
Process (2004);
ICH Q5C; ICH Q6B;
ICH Q9(R1); FDA
Comparability
Protocols for
Postapproval
Changes to the
CMC Information
(2022); FDA
Demonstration of
Comparability of
Human Biological
Products (1996);
EMA Guideline on
comparability of
biotechnology-
derived medicinal
products after a
change in the
manufacturing
process
(EMA/CHMP/BMWP/10)

TIME TO LEARN

About 20 minutes
with the example

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

1. What this module does

You describe the change and the risk assessment, and enter each attribute with its method, criticality, criterion and the pre- and post-change results. The criterion can be a tolerance interval, mean $\pm$ 3 SD, the pre-change min–max, a fixed limit or a qualitative comparison.

The tool builds each range, finds the post-change results outside it, charts the attribute you choose and writes the report. A difference in a high-criticality attribute must be recorded with its impact assessment.

What you get

- A Word or PDF report: Comparability report (ICH Q5E), for 3.2.S.2.6 or 3.2.R.

2. Before you start

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

- The change description and risk assessment.
- Pre-change and post-change results for each attribute, with the criteria in the comparability protocol.
- The stability comparison and any structure–function data.

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/biologics-comparability.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 change

Enter the change, the risk assessment, the batches and the tolerance interval coverage and confidence (99% and 95% by default).

The screenshot shows the CMCfy Biologics Comparability interface. At the top, there's a navigation bar with 'CMCfy', 'Biologics Comparability', and links to 'Projects', 'All modules', 'Training', and 'Security'. Below this is a sub-header with 'Runs entirely on this device', 'Training guide', and 'Protocol builder'. 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.' There are buttons for 'Choose projects folder' and 'Keep in this browser'. Below this, 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.), and 'Locked offline copy' (Save a single file that opens from your own computer with all network access blocked.).

The main form area is titled '3.2.S.2.6 3.2.R Report'. It contains a text area for writing the ICH Q5E comparability report for a manufacturing change. Below this is a 'Guidance' section with references to ICH Q5C, ICH Q5B, ICH Q9(R1), FDA Comparability Protocols for Postapproval Changes to the CMC Information (2022), FDA Demonstration of Comparability of Human Biological Products (1996), and EMA Guideline on comparability of biotechnology-derived medicinal products after a change in the manufacturing process (EMA/CHMP/BMWP/101695/2006).

The form is divided into two main sections: '1 - CHANGE' and 'RESULT'. The '1 - CHANGE' section includes fields for 'Product' (CMX-mAb1 (IgG1 monoclonal antibody) drug substance), 'Regulations' (Both US and EU), 'Report number' (CMP-R-002), and 'Manufacturing change' (Transfer of drug substance manufacture from Site A (2000 L) to Site B (2000 L), same process, new chromatography skid and new cell bank vial thaw procedure.). The 'RESULT' section shows a headline: '1 attribute outside the pre-change range'. Below this, it states: 'Galactosylation G1F+G2F (%): 3 results outside 38.20–41.00. Impact assessment recorded.' A table shows the following data:

ATTRIBUTES	HIGH CRITICALITY	PRE-CHANGE BATCHES
8	4	10
POST-CHANGE BATCHES		
3		

At the bottom, there's a section for 'GALACTOSYLATION G1F+G2F (%)'.

2 Enter the attributes

One row per attribute. Criterion: TI, 3SD, minmax, a fixed limit (for example ≤ 100) or qual. Results separated by ";".

3 Read the result

The headline says whether the batches are comparable: "1 attribute outside the pre-change range". The chart shows the pre- and post-change results against the range.



Comparability by attribute.

4 Resolve alerts and download

A difference in a high-criticality attribute is critical. Missing post-change results, too few pre-change results, no potency comparison, and missing risk, stability or impact assessments are flagged. Then preview and download.

Preview and review before download

Review

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

1 recommended

DATA AND INPUTS (1)

Galactosylation G1F+G2F (%): 41.6, 42.1, 41.8 outside 38.20-41.00.

Confirm the impact assessment covers this attribute, with structure-function data.

recommended · Comparability · ICH Q5E 2.4, 2.5 Ignore

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 shared.

3.2.5.2.6 Comparability report (ICH Q5E)

CMX-mAb1 (IgG1 monoclonal antibody) drug substance · CMP-R-002 · US (FDA) and EU (EMA)

Product	CMX-mAb1 (IgG1 monoclonal antibody) drug substance
Report number	CMP-R-002
Pre-change batches	DS-101 to DS-110 (Site A)
Post-change batches	DS-201, DS-202, DS-203 (Site B)
Regulations	US (FDA) and EU (EMA)

1. Description of the change

Transfer of drug substance manufacture from Site A (2000 L) to Site B (2000 L), same process, new chromatography skid and new cell bank vial thaw procedure.

2. Risk assessment

Risk assessment RA-CMP-002 (ICH Q9(R1)) rated glycosylation, charge variants, HMW species and potency as most likely to be affected; all CQAs are included.

3. Comparability of quality attributes

Ranges are built from the pre-change results. Tolerance intervals cover 99% of the population with 95% confidence.

Attribute	Method	Criticality	Criterion	Range	Post-change	Outcome
Potency (% of reference)	Cell-based bioassay	high	Tolerance interval	87.04 - 113.96	101; 99; 103	Comparabl e
HMW species (%)	SEC-HPLC	high	Tolerance interval	0.35 - 1.39	0.9; 1; 0.9	Comparabl e
Main peak charge variants (%)	cIEF	medium	Mean ± 3 SD	60.73 - 64.35	61.9; 62.8; 62.4	Comparabl e

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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 - Change

FIELD	WHAT TO ENTER
Product	Type it in.
Regulations	Choose one: US: FDA; EU: EMA; Both US and EU.
Report number	Type it in.
Manufacturing change	Type or paste text.
Risk assessment and attributes selected	Type or paste text.
Pre-change batches	Type it in.
Post-change batches	Type it in.
Tolerance interval coverage (%)	Type a number.
Tolerance interval confidence (%)	Type a number.

2 - Attributes

One row per attribute. Criterion: TI (tolerance interval), 3SD, minmax, a fixed limit such as ≤ 2.0 , or qual. Criticality: high, medium or low. Results separated by ";".

FIELD	WHAT TO ENTER
Attributes	With fewer than six pre-change results a tolerance interval is very wide; min-max is often more sensitive. A table. Columns: Attribute Method Criticality Criterion Pre-change results Post-change results. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).
Attribute to chart	Type the attribute name exactly as in the table. Type it in.

3 · Stability and conclusion

FIELD	WHAT TO ENTER
Stability comparison	Type or paste text.
Impact assessment of any difference	Type or paste text.
Further nonclinical or clinical studies needed	Tick the box if it applies.

5. Checks and alerts

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

- Each post-change result against its range; high-criticality differences are critical.
- Number of pre- and post-change results; potency included.
- Risk assessment, stability comparison, impact assessment and further studies.

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.

- 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).
- Click a finding to jump to the place in the preview. Fix it in the tool, then preview again.
- 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.
- 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.S.2.6	Comparability report with results table and chart

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

Both regions follow ICH Q5E. The EU guideline on comparability after a manufacturing change (EMA/CHMP/BMWP/101695/2006) and the FDA guidance on comparability protocols (2022) apply.

8. Working with other modules

- Classify the change in Post-approval Change Classifier and assess it in Change Control.
- Characterisation methods are in the Biologics Characterisation & Specification module.

9. Common pitfalls

- Setting the range after seeing the post-change data.
- Using a tolerance interval from three batches, which is too wide to detect a difference.

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. **Introduce a potency shift**

Change the post-change potency results from 101;99;103 to 101;99;125.

EXPECTED RESULT

The headline shows two attributes outside the pre-change 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.