

Reference Standard Qualification

Qualify a primary or secondary (working) reference standard: identity, purity, the assigned content and the requalification date.

WRITES

Report

3.2.S.5

3.2.P.6

PRODUCT TYPE

Small molecule and
biologics

GUIDANCE IT FOLLOWS

ICH Q7 (11.17–11.19);
ICH Q6A, Q6B; USP
<11> Reference
Standards; FDA
Analytical
Procedures and
Methods Validation
for Drugs and
Biologics (2015),
section VII; Ph. Eur.
5.12 Reference
standards; WHO
TRS 943 Annex 3

TIME TO LEARN

About 20 minutes
with the example

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

1. What this module does

You enter the test results with their criteria. For a primary standard the tool assigns the content by mass balance (100 minus organic impurities, corrected for water, solvents and residue on ignition) and compares it with qNMR. For a secondary standard it assigns the mean assay against the primary standard.

It checks identity by at least two orthogonal techniques, every result against its criterion, the storage and the requalification date.

What you get

- A Word or PDF report: Reference standard qualification report.

2. Before you start

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

- The candidate lot and, for a secondary standard, the primary standard.
- Identity, purity, water, solvents, residue on ignition and qNMR or assay results.
- Storage conditions and requalification interval.

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/reference-standard.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 standard

Choose primary or secondary, and enter the lot and, for a secondary standard, the primary standard it is traced to.

CMCfy Reference Standard Qualification Projects All modules Training Security

Runs entirely on this device Training guide Protocol builder

PROJECTS Keep this work in a project, with version history and your company logo on every report. Choose projects folder Keep in this browser

- 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.

Report 3.2.S.5 3.2.P.6 Save project Open project Start blank Load example

Write the qualification report for a primary or secondary (working) reference standard. Each test result is checked against its criterion, the content is assigned by mass balance (primary) or by assay against the primary standard (secondary), and the requalification date is set.

Guidance: ICH Q7 (11.17–11.19); ICH Q6A, Q6B; USP <11> Reference Standards; FDA Analytical Procedures and Methods Validation for Drugs and Biologics (2015), section VII; Ph. Eur. 5.12 Reference standards; WHO TRS 943 Annex 3

1 STANDARD

Substance
CMX-101 (drug substance)

Regulations
Both US and EU

Type of standard
Primary (in-house) refer

Candidate lot
RS-CMX-101-002 (from API)

Report number
RS-R-002

Protocol number
RS-P-002

RESULT

RS-CMX-101-002 qualified · assigned 99.6%

Mass balance 99.55%; qNMR 99.4% (difference -0.15%). Requalify by 2028-09-30.

TYPE	ASSIGNED CONTENT	IDENTITY TESTS
Primary	99.6%	3

REQUALIFY BY
2028-09-30

RESULTS

TEST	PROCEDURE	RESULT	CRITERION	OUTCOME
------	-----------	--------	-----------	---------

2

Enter the results

One row per test with the result and criterion. A criterion can be a range, a limit or a statement. For a secondary standard, enter the assay results against the primary standard.

3

Read the result

The headline gives the lot and the assigned content: "RS-CMX-101-002 qualified · assigned 99.6%". The note gives the mass balance and qNMR values and the requalification date.

RESULTS				
TEST	PROCEDURE	RESULT	CRITERION	OUTCOME
Identity by IR	AM-0102	Concordant with structure	Concordant with structure	pass
Identity by ¹ H-NMR	AM-0110	Consistent with structure	Consistent with structure	pass
Identity by mass spectrometry	AM-0111	Consistent ([M+H] ⁺ 412.2)	Consistent with structure	pass
Chromatographic purity (total impurities)	AM-0143	0.18 %	≤ 0.50	pass
Largest single impurity	AM-0143	0.06 %	≤ 0.10	pass
Water (KF)	AM-0105	0.21 %	≤ 0.5	pass
Residual solvents (total)	AM-0107	0.04 %	≤ 0.5	pass
Residue on ignition	AM-0108	0.02 %	≤ 0.1	pass
Quantitative NMR	AM-0112	99.4 %	98.5–101.5	pass

Results and assigned content.

4

Resolve alerts and download

A failing result is critical. Too few identity tests, missing mass balance inputs, a qNMR difference above the limit and missing storage or requalification 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 review 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

Reference standard qualification report
 CMX-101 (drug substance) - RS-R-002 - US (FDA) and EU (EMA)

Substance	CMX-101 (drug substance)
Type	Primary reference standard
Lot	RS-CMX-101-002 (from API lot DS-2402, recrystallised)
Report number	RS-R-002
Protocol	RS-P-002
Regulations	US (FDA) and EU (EMA)

1. Objective
 To qualify lot RS-CMX-101-002 (from API lot DS-2402, recrystallised) as a primary reference standard for CMX-101 (drug substance) and to assign its content for quantitative use.

2. Results

Test	Procedure	Result	Acceptance criterion	Outcome
Identity by IR	AM-0102	Concordant with structure	Concordant with structure	Pass
Identity by 1H-NMR	AM-0110	Consistent with structure	Consistent with structure	Pass
Identity by mass spectrometry	AM-0111	Consistent ([M+H] ⁺ 412.2)	Consistent with structure	Pass
Chromatographic purity (total impurities)	AM-0143	0.18 %	≤ 0.50	Pass
Largest single impurity	AM-0143	0.06 %	≤ 0.10	Pass
Water (KF)	AM-0105	0.21 %	≤ 0.5	Pass
Residual solvents (total)	AM-0107	0.04 %	≤ 0.5	Pass

Download Word (.docx) Download PDF

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 • Standard

FIELD	WHAT TO ENTER
Substance	Type it in.
Regulations	Choose one: US: USP <11> and FDA guidance; EU: Ph. Eur. 5.12; Both US and EU.
Type of standard	Choose one: Primary (in-house) reference standard; Secondary (working) standard.
Candidate lot	Type it in.
Primary or compendial standard it is traced to	Type it in.
when it applies	

FIELD	WHAT TO ENTER
Report number	Type it in.
Protocol number	Type it in.

2 · Tests

One row per test. The criterion can be a range (99.0–101.0), a limit (≤ 0.5 , NLT 99.5) or a statement (concordant with the structure).

FIELD	WHAT TO ENTER
Results	Name tests clearly (Identity by IR, Water (KF), Residue on ignition): the tool uses the name to place each result in the mass balance. A table. Columns: Test Procedure Result Acceptance criterion Unit. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).
Assay against the primary standard (results, ";", separated) when it applies	Type it in.
Maximum %RSD of the assays when it applies	Type a number.
Assay acceptance range (%) when it applies	Type it in.
Maximum difference between qNMR and mass balance (%) when it applies	Type a number.

3 · Storage and requalification

FIELD	WHAT TO ENTER
Date qualified	Type it in.
Requalification interval (months)	Type a number.
Storage and packaging	Type it in.

FIELD	WHAT TO ENTER
Previous lot and requalification history	Type or paste text.

5. Checks and alerts

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

- Each result against its criterion.
- Two or more identity tests.
- Primary: organic impurities, water, solvents and residue for the mass balance; qNMR agreement. Secondary: traceability, number of preparations, %RSD and assay range.
- Storage and requalification date.

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
Report	Reference standard qualification report

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 USP <11> and section VII of the FDA analytical procedures guidance. EU follows Ph. Eur. 5.12. Both follow ICH Q7 11.17–11.19.

8. Working with other modules

- The standard is listed in 3.2.S.5 and 3.2.P.6; assemble them in the QOS Composer & Dossier Assembler.

9. Common pitfalls

- Assigning 100% to a primary standard without a mass balance.
- Using a secondary standard that is not traceable to a primary.

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. **Enter a high water result**

Change the water result from 0.21 to 0.8.

EXPECTED RESULT

The headline shows one test outside criteria.

2. **Qualify a working standard**

Set the type to secondary and enter the assays 99.2;99.4;99.1;99.6;99.3;99.5.

EXPECTED RESULT

The headline shows the lot qualified with an assigned content of 99.4%.

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.