

Viral Safety Studio

Write the adventitious agents safety evaluation (3.2.A.2): viral clearance totalled per model virus by ICH Q5A(R2) rules and the retrovirus safety margin calculated from particles, titre, yield and dose.

WRITES

3.2.A.2

PRODUCT TYPE

Biologics
(biotechnology
products)

**GUIDANCE IT
FOLLOWS**

ICH Q5A(R2)
(2023), ICH Q5D,
ICH Q6B; FDA
Points to Consider
in the
Characterization of
Cell Lines (1993)
and
Characterization
and Qualification of
Cell Substrates
(2010); EMA/410/01
rev.3

TIME TO LEARN

About 20 minutes
with the example

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

1. What this module does

The module writes 3.2.A.2 from three things: testing of cell banks, end-of-production cells and unprocessed bulk; viral clearance studies by step and model virus; and the controls on raw materials of biological origin.

It totals the log reduction values per virus, counting only one step per mechanism as ICH Q5A(R2) expects, then calculates how many retrovirus-like particles enter per dose and the safety margin after clearance.

What you get

- A Word or PDF file for 3.2.A.2 Adventitious agents safety evaluation.

- A summary file for the QOS Composer & Dossier Assembler.

2. Before you start

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

- Production cell line, maximum single dose, production titre and downstream yield.
- Retrovirus-like particles in unprocessed bulk (TEM), for rodent cell lines.
- Clearance results (log reduction value) per step for each model virus, the mechanism and the worst-case conditions tested.
- Adventitious agent test results for the MCB, WCB, end-of-production cells and unprocessed bulk.
- Raw materials of animal or human origin with source, country and controls.

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/viral-safety.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 Enter the product and cell substrate

Choose the production cell line and enter dose, titre, yield and particles per mL. The example (CHO, 1500 mg dose, 3.5 g/L, 70% yield) needs 612 mL of harvest per dose.

CMCfy Viral Safety Studio 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.

3.2.A.2

Write the adventitious agents safety evaluation for a biotechnology product. Viral clearance is totalled per model virus by ICH Q5A(R2) rules, and the retrovirus safety margin is calculated from the particles in unprocessed bulk, the titre, the yield and the dose.

Guidance: ICH Q5A(R2) (2023), ICH Q5D, ICH Q6B; FDA Points to Consider in the Characterization of Cell Lines (1993) and Characterization and Qualification of Cell Substrates (2010); EMA/410/01 rev.3

Save project Open project Start blank Load example

1. PRODUCT AND CELL SUBSTRATE

Product
CMB-201 (humanised IgG1 monoclonal antibody), drug subs

Submission region
US: FDA (NDA, ANDA, BL)

Production cell line
CHO (Chinese hamster ovary)

Maximum single dose (mg)
1500

Production titre (g/L harvest)
3.5

Downstream yield, harvest to drug substance (%)
70

Retrovirus-like particles in unprocessed bulk (particles/mL, by TEM)
2.1e8

RESULT

Retrovirus safety margin 9.3 log10

About 1.3e+11 retrovirus-like particles enter per dose before purification; the process clears at least 20.4 log10 of X-MuLV, leaving an estimated 1 particle per 2.0e+9 doses.

CELL SUBSTRATE	HARVEST PER DOSE	TOTAL LRV X-MULV
CHO (Chinese hamster ovary)	612 mL	≥ 20.4
TOTAL LRV MVM	TOTAL LRV PRV	TOTAL LRV REO-3
10.8	≥ 19.2	≥ 8.1

VIRAL CLEARANCE (LOG10 REDUCTION)

Grey values are not counted: 1 log or less, or a second step with the same mechanism.

2 Enter clearance studies

One row per step with its mechanism and the LRV for X-MuLV, MVM, PRV and Reo-3. Write "≥ 5.2" when no virus was detected, and leave blank or "n.t." when not tested.

3 Read the clearance totals and margin

The headline gives the retrovirus safety margin: 9.3 log10. About 1.3e+11 particles enter per dose before purification; the process clears at least 20.4 log10 of X-MuLV, leaving about 1 particle per 2.0e+9 doses.

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CHO (Chinese hamster ovary)	612 mL	≥ 20.4
TOTAL LRV MVM	TOTAL LRV PRV	TOTAL LRV REO-3
10.8	≥ 19.2	≥ 8.1

4 Check the testing table

Tests are grouped by material. Any positive result is critical.

VIRAL CLEARANCE (LOG10 REDUCTION)					
Grey values are not counted: 1 log or less, or a second step with the same mechanism.					
STEP	MECHANISM	X - MULV	MVM	PRV	REO - 3
Protein A affinity chromatography	Affinity capture	3.1	1.2	2.8	–
Low pH viral inactivation	Low pH inactivation	≥ 5.4	–	≥ 5.0	–
Anion exchange chromatography (flow-through)	Anion exchange	≥ 4.6	4.9	≥ 4.4	3.3
Virus filtration (Planova 20N)	Virus filtration	≥ 5.3	4.7	≥ 5.1	≥ 4.8
Cation exchange chromatography	Cation exchange	2.0	(0.8)	1.9	–
Total counted		≥ 20.4	10.8	≥ 19.2	≥ 8.1

Viral clearance by step and model virus.

5 Resolve alerts

The example has a minor alert: ion exchange clearance was shown only with new resin. Add end-of-lifetime data or justify.

ALERTS TO RESOLVE	
All blocking alerts are fixed, justified or accepted. Minor alerts are listed in the Word files.	
MINOR Cation exchange chromatography: clearance shown only with new resin.	
Viral clearance - ICH Q5A(R2) 6.3	
Show clearance with resin at the end of its lifetime, or justify from cleaning and reuse data.	
Justification	Accept justification

6 Preview and download

Preview 3.2.A.2, read the review 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.

1 to fix 1 recommended

DATA AND INPUTS (1)

Cation exchange chromatography: clearance shown only with new resin.

Show clearance with resin at the end of its lifetime, or justify from cleaning and reuse data.

recommended · Viral clearance · ICH Q5A(R2) 6.3 Ignore

REPORT CONTENT (1)

Placeholder left in the report: [State the overall conclusion on viral safety, citing the testing and clearance data ab...]

Replace the placeholder with the real information, or delete the sentence if it does not apply.

major 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.

3.2.A.2 Adventitious agents safety evaluation

CMB-201 (humanised IgG1 monoclonal antibody), drug substance · US (FDA)

Materials of biological origin

Material	Source	Country	Controls	Used at
Fetal bovine serum	bovine	New Zealand	EDQM CEP R1-CEP 2000-001; gamma irradiated (≥ 25 kGy); tested to 9 CFR 113.47	Cell bank (MCB) only
Recombinant insulin	recombinant	—	Animal-component-free	Production medium

Testing of cell banks and unprocessed bulk

Material	Test	Result
MCB	Sterility (bacteria and fungi)	Negative
MCB	Mycoplasma (culture and indicator cell)	Negative
MCB	In vitro adventitious viruses (MRC-5; Vero; CHO-K1)	Negative
MCB	In vivo adventitious viruses (suckling and adult mice; embryonated eggs)	Negative
MCB	Retroviruses: TEM	Type A and C retrovirus-like particles seen (expected for CHO)
MCB	Retroviruses: reverse transcriptase (PERT)	Positive (expected for CHO)
MCB	Retroviruses: infectivity (Mus dunni co-culture)	Negative
MCB	Hamster antibody production (HAP) test	Negative
MCB	Identity (isoenzyme and STR)	Chinese hamster
WCB	Sterility; mycoplasma; in vitro adventitious viruses	Negative
EOPC	In vitro adventitious viruses; retroviruses (TEM; infectivity)	Negative for adventitious viruses; RVLP as for MCB

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 · Product and cell substrate

FIELD	WHAT TO ENTER
Product	Type it in.
Submission region	Choose one: US: FDA (NDA, ANDA, BLA, IND); EU: EMA and national agencies (MAA); Both US and EU.
Production cell line	Choose one: CHO (Chinese hamster ovary); NSO (murine myeloma); Sp2/O (murine hybridoma); Other murine hybridoma; HEK293 (human); PER.C6 or other human line; Insect (Sf9, High Five); E. coli; Yeast (Pichia, Saccharomyces).
Maximum single dose (mg)	Type a number.
Production titre (g/L harvest)	Type a number.

FIELD	WHAT TO ENTER
Downstream yield, harvest to drug substance (%)	Type a number.
Retrovirus-like particles in unprocessed bulk (particles/mL, by TEM) when it applies	Shown for rodent cell lines; from transmission electron microscopy of unprocessed bulk. Type a number.

2 · Viral clearance studies [shown when it applies](#)

Log10 reduction values (LRV) per step and model virus. Write "≥ 5.2" when no virus was detected, and leave blank or "n.t." when not tested.

FIELD	WHAT TO ENTER
Clearance results	Use "≥" for no virus detected; blank or "n.t." when not tested. A table. Columns: Step Mechanism (inactivation / removal) X-MuLV MVM PRV Reo-3 Conditions tested (worst case, resin age). Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

3 · Adventitious agent testing

Tests on the cell banks, end-of-production cells and each lot of unprocessed bulk.

FIELD	WHAT TO ENTER
Tests and results	A table. Columns: Material (MCB / WCB / EOPC / unprocessed bulk) Test Result. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).
Next-generation sequencing used in place of in vivo tests	Tick the box if it applies.

4 · Materials of biological origin

FIELD	WHAT TO ENTER
Raw materials of animal or human origin	A table. Columns: Material Source (bovine / porcine / human / recombinant / plant) Country of origin Controls (CEP, irradiation, testing) Used at (cell bank / culture / purification). Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

5. Checks and alerts

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

- MCB tested for sterility, mycoplasma, in vitro and in vivo adventitious viruses, retroviruses and identity; species-specific tests for rodent lines; end-of-production cells and WCB tested.
- Unprocessed bulk tested for mycoplasma and adventitious viruses; any positive result is critical.
- Clearance studies include X-MuLV and a small non-enveloped virus (MVM), a panel of more than two viruses, an effective inactivation step and an effective removal step, ideally a virus filter; worst-case conditions and resin age stated.
- Steps with the same mechanism are not added twice to the total.
- Retrovirus safety margin: particles, dose, titre and yield given; X-MuLV clearance above the particle load (critical if not), and at least a 6 log10 margin.
- Raw materials of animal or human origin have TSE and viral safety controls.

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: Viral safety evaluation 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.A.2	Adventitious agents safety evaluation

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

ICH Q5A(R2) applies in both regions. US mode cites FDA guidance and 9 CFR 113.47 for bovine materials; EU mode cites the EMA note for guidance on virus validation studies, Ph. Eur. 5.2.8 (TSE) and EU requirements for bovine serum. Next-generation sequencing in place of in vivo tests is accepted under Q5A(R2) when justified.

8. Working with other modules

- Cell banks and raw materials are also listed in the Biologics Process Writer; keep them the same.

- Segregation before and after viral clearance belongs in the Facilities & Equipment Writer module.

9. Common pitfalls

- Adding two chromatography steps with the same mechanism to the total.
- Using a clearance value from new resin only, when the resin is reused for many cycles.
- Forgetting the yield, which changes the particles per dose.
- Writing "0" instead of "n.t." for a virus that was not tested.

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 the particle load

Change `Retrovirus-like particles in unprocessed bulk` to 2.1e12.

EXPECTED RESULT

A major alert says the safety margin is below the 6 log10 target.

2. Remove the clearance studies

Clear the `Clearance results` table.

EXPECTED RESULT

A major alert says no viral clearance studies are entered.

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.