

Extractables & Leachables Study Report

Write the extractables and leachables report: the analytical evaluation threshold, the extractables that need identification and assessment, and the safety of each leachable.

WRITES

3.2.P.2.4

3.2.P.7 Report

PRODUCT TYPE

Small molecule and biologics

GUIDANCE IT FOLLOWS

USP <1663>
Assessment of extractables and <1664>
Assessment of drug product leachables; PQRI OINDP (2006) and PODP (2013) recommendations;
FDA Container Closure Systems guidance (1999);
EMA Guideline on plastic immediate packaging materials (2005);
ICH M7(R2); ICH Q3E (draft, 2025);
ISO 10993-18

TIME TO LEARN

About 20 minutes with the example

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

1. What this module does

You enter the route, the units per day and the uncertainty factor. The tool calculates the AET from the safety concern threshold (0.15 µg/day for inhalation, 1.5 µg/day otherwise, or your own).

It flags extractables at or above the AET that are not identified or assessed, and compares each leachable's daily exposure with its PDE, or with the TTC when it has a mutagenic alert.

What you get

- A Word or PDF report: Extractables and leachables study report.

2. Before you start

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

- The components, materials and extraction conditions.
- Extractables with levels, identification and PDEs.
- Leachables results on stability.

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/extractables-leachables.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 product

Choose the route and treatment duration, and enter the units per day and the uncertainty factor.

CMCfy Extractables & Leachables Study Report 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.P.2.4 3.2.P.7 Report Save project Open project Start blank Load example

Write the extractables and leachables study report. The tool calculates the analytical evaluation threshold from the safety concern threshold and the dosing, flags extractables that need identification and assessment, works out the daily exposure to each leachable, and checks it against its permitted daily exposure and against the extractables found.

Guidance: USP <1663> / USP <1663> (no Ph. Eur. chapter; CPMP/QWP/4359/03 applies) Assessment of extractables and <1664> Assessment of drug product leachables; PQRI OINDP (2006) and PODP (2013) recommendations; FDA Container Closure Systems guidance (1999); EMA Guideline on plastic immediate packaging materials (2005); ICH M7(R2); ICH Q3E (draft, 2025); ISO 10993-18

1 · PRODUCT AND DOSING

Product

CMX-mAb1 injection 100 mg/mL, 1 mL in a prefilled syringe

Regulations Route

Both US and EU Parenteral

Maximum units per day Safety concern threshold (µg/day; leave empty for the default for the route)

1

Analytical uncertainty factor Treatment duration

RESULT

3 leachables · all below the permitted exposure

AET 0.750 µg/unit (SCT 1.5 µg/day, 1 unit/day, uncertainty factor 2). 6 of 6 extractables at or above the AET.

AET	EXTRACTABLES	LEACHABLES
0.750 µg/unit	6	3
SCT		
1.5 µg/day		

EXTRACTABLES

2 Enter extractables and leachables

One row per extractable and component, and one row per leachable result. Put a name that contains a comma in quotes.

3 Read the result

The headline gives the outcome: "3 leachables · all below the permitted exposure".

EXTRACTABLES

AET 0.750 µg/unit. Compounds at or above the AET need identification and a safety assessment.

COMPOUND	COMPONENT	LEVEL (MG/UNIT)	≥ AET	IDENTIFICATION	MUTAGENIC /
2,4-Di-tert-butylphenol	Plunger stopper	3.20	yes	confirmed	no
Butylated hydroxytoluene (BHT)	Plunger stopper	1.10	yes	confirmed	no
Oligomeric siloxanes (D4-D8)	Syringe barrel	0.90	yes	confident	no
Bromobutyl oligomers (C13 brominated)	Plunger stopper	1.40	yes	confident	no
Stearic acid	Plunger stopper	6.50	yes	confirmed	no
Zinc	Plunger stopper	2.00	yes	confirmed	no

Extractables against the AET.

4

Resolve alerts and download

A leachable above its limit is critical. Extractables above the AET without identification or assessment, and leachables not seen as extractables, 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.

1 recommended

MISSING INFORMATION (1)

"Safety concern threshold (µg/day; leave empty for the default for the route)" is empty.

Enter it in the tool, or confirm it does not apply. Empty inputs show as placeholders or gaps in the report.

recommended · Product and dosing 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 shown.

Extractables and leachables study report

CMX-mAb1 injection 100 mg/mL, 1 mL in a prefilled syringe · EL-R-021 · US (FDA) and EU (EMA)

Product	CMX-mAb1 injection 100 mg/mL, 1 mL in a prefilled syringe
Report number	EL-R-021
Route	parenteral
AET	0.750 µg/unit
Regulations	US (FDA) and EU (EMA)

1. Container closure system

Component	Material	Contact
Syringe barrel	Type I borosilicate glass with baked-on silicone	Direct
Plunger stopper	Bromobutyl rubber with fluoropolymer coating	Direct
Needle shield	Polyisoprene rubber	Indirect

2. Extraction study

Controlled extraction of each direct-contact component: water, 10% ethanol and isopropanol, reflux for 4 h and 50 °C for 72 h; extract to surface area ratio scaled to the clinical configuration. Techniques: GC-MS (volatile and semi-volatile), headspace GC-MS, LC-UV/MS (non-volatile), ICP-MS (elements).

3. Analytical evaluation threshold

AET = 1.5 µg/day ÷ 1 unit/day ÷ 2 = 0.750 µg/unit.

4. Extractables

Compound	CAS	Component	Level (µg/unit)	Identification	Limit (µg/day)
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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 dosing

FIELD	WHAT TO ENTER
Product	Type it in.
Regulations	Choose one: US: USP <1663>/<1664>, FDA; EU: EMA plastic packaging guideline; Both US and EU.
Route	Choose one: Parenteral; Inhalation; Ophthalmic; Oral liquid; Topical.
Maximum units per day	Type a number.
Safety concern threshold (µg/day; leave empty for the default for the route)	Type a number.

FIELD	WHAT TO ENTER
Analytical uncertainty factor	Type a number.
Treatment duration	Choose one: Chronic (> 10 years); 1–10 years; 1–12 months; ≤ 1 month.
Report number	Type it in.

2 · Components and extraction study

FIELD	WHAT TO ENTER
Components	A table. Columns: Component Material Contact (direct/indirect). Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).
Extraction conditions	Type or paste text.
Techniques	Type it in.

3 · Extractables

One row per compound and component. Level in µg per unit (syringe).

FIELD	WHAT TO ENTER
Extractables	Leave the PDE empty when no assessment has been done. A table. Columns: Compound CAS Component Level (µg/unit) Identification (confirmed/confident/tentative) Mutagenic alert (yes/no) PDE (µg/day, if assessed). Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

4 · Leachables

Results from the drug product on stability (simulation or real-time). Level in µg per unit.

FIELD	WHAT TO ENTER
Leachables	A table. Columns: Compound Condition and time Batch Level (µg/unit). Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

FIELD	WHAT TO ENTER
Impact on product quality (interaction with the product)	Type or paste text.

5. Checks and alerts

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

- AET from the SCT, dosing and uncertainty factor.
- Identification and safety assessment above the AET.
- Leachable exposure against PDE or TTC; correlation with extractables.

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	Extractables and leachables study 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 <1663>/<1664> and the FDA container closure guidance (1999). EU follows the EMA guideline on plastic immediate packaging materials.

8. Working with other modules

- The container closure section (3.2.P.7) is written in the Container Closure & E&L.

9. Common pitfalls

- Tentative identities left unconfirmed above the AET.
- No leachables data at the end of shelf life.

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 a leachable**

Change the 6-month 25 °C result for 2,4-di-tert-butylphenol from 0.61 to 2000 µg/unit.

EXPECTED RESULT

The headline shows one leachable above the permitted exposure.

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.