

Elemental Impurities Risk Assessment

Write the ICH Q3D risk assessment: which elements to assess for the route, the daily intake of each from component data or product testing, and the comparison with the PDE and the 30% control threshold.

WRITES

3.2.P.5.5

3.2.P.5.6

Report

PRODUCT TYPE

Small molecule and
biologics

GUIDANCE IT FOLLOWS

ICH Q3D(R2)
Guideline for
elemental
impurities (2022);
USP <232> and
<233>; Ph. Eur.
5.20 and 2.4.20;
FDA Elemental
Impurities in Drug
Products (2018);
EMA
Implementation
strategy of ICH
Q3D
(EMA/CHMP/QWP/11549)

TIME TO LEARN

About 20 minutes
with the example

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

1. What this module does

You enter the route, the daily dose, the components and the element data you have. The tool lists the elements that must be assessed (class 1, 2A, intentionally added and route-specific class 3).

It sums the contribution of each component, compares the intake with the PDE, and gives the Option 1 and Option 2a concentration limits.

What you get

- A Word or PDF report: Elemental impurities risk assessment (3.2.P.5.5).

2. Before you start

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

- The maximum daily dose of the drug product and the amount of each component in it.
- Element data for each component (supplier, published or measured) or the finished product.
- Elements intentionally added (catalysts).

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/elemental-impurities.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 approach, enter the daily dose and any intentionally added elements.

The screenshot shows the CMCfy Elemental Impurities Risk Assessment tool interface. The top navigation bar includes the CMCfy logo, the title 'Elemental Impurities Risk Assessment', and links for 'Projects', 'All modules', 'Training', and 'Security'. Below the navigation bar, there are three tabs: 'Runs entirely on this device' (selected), 'Training guide', and 'Protocol builder'.

The main content area is divided into several sections:

- PROJECTS:** A section with a description and two buttons: 'Choose projects folder' and 'Keep in this browser'.
- Network requests since load: 0:** A section with a description and a button: 'Works offline'.
- Locked offline copy:** A section with a description and a button: 'Save a single file that opens from your own computer with all network access blocked'.
- 3.2.P.5.5 3.2.P.5.6 Report:** A section with three buttons: 'Save project', 'Open project', 'Start blank', and 'Load example'.
- Write the ICH Q3D risk assessment for a drug product:** A section with a description and a button: 'Load example'.
- 1 - PRODUCT:** A section with input fields for 'Product' (CMX-201 tablets 20 mg), 'Regulations' (Both US and EU), 'Route' (Oral), 'Maximum daily dose of drug product (g/day)' (0.5), and 'Approach' (Summation of component).
- RESULT:** A section with a green header 'All 8 elements below 30% of the PDE' and a table showing the results of the assessment.
- ELEMENTS:** A section with a table showing the elements assessed.

The table in the 'RESULT' section shows the following data:

ROUTE	ELEMENTS ASSESSED	ABOVE 30%
Oral	8	0

The table in the 'ELEMENTS' section shows the following data:

DAILY DOSE	0.5 g

2 Enter components and data

One row per component with its amount in the daily dose. One row per component and element with the level in µg/g.

3 Read the result

The headline gives the outcome: "All 8 elements below 30% of the PDE".

ELEMENTS						
Intake from the summation of component data (or the finished product). Control threshold 30% of the PDE.						
ELEMENT	CLASS	WHY ASSESSED	PDE (MG/DAY)	INTAKE (MG/DAY)	% OF PDE	OP
Cd (Cadmium)	1	required for the route	5	0.003	0.1%	0.
Pb (Lead)	1	required for the route	5	0.114	2.3%	0.
As (Arsenic)	1	required for the route	15	0.062	0.4%	1.
Hg (Mercury)	1	required for the route	30	0.005	0.0%	3.
Co (Cobalt)	2A	required for the route	50	0.009	0.0%	5.
V (Vanadium)	2A	required for the route	100	0.009	0.0%	10
Ni (Nickel)	2A	required for the route	200	0.176	0.1%	20
Pd (Palladium)	2B	intentionally added	100	0.183	0.2%	10

Elements and intake.

4 Resolve alerts and download

An element above the PDE is critical; above 30% without a control is major. Required elements without data 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)

"Controls for elements above the control threshold" is empty.

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

recommended · Other sources and control 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.

3.2.P.5.5 Elemental impurities risk assessment

CMX-201 tablets 20 mg · EI-RA-007 · US (FDA) and EU (EMA)

Product	CMX-201 tablets 20 mg
Report number	EI-RA-007
Route	Oral
Maximum daily dose	0.5 g/day
Regulations	US (FDA) and EU (EMA)

1. Approach

The assessment follows ICH Q3D(R2): identify potential sources, evaluate the levels against the PDEs and decide on controls. The control threshold is 30% of the PDE.

2. Elements and intake

Element	Class	PDE (µg/day)	Intake (µg/day)	% of PDE	Outcome
Cd (Cadmium)	1	5	0.003	0.1	Below 30%
Pb (Lead)	1	5	0.114	2.3	Below 30%
As (Arsenic)	1	15	0.062	0.4	Below 30%
Hg (Mercury)	1	30	0.005	0.0	Below 30%
Co (Cobalt)	2A	50	0.009	0.0	Below 30%
V (Vanadium)	2A	100	0.009	0.0	Below 30%
Ni (Nickel)	2A	200	0.176	0.1	Below 30%
Pd (Palladium)	2B	100	0.183	0.2	Below 30%

3. Component contributions

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

FIELD	WHAT TO ENTER
Product	Type it in.
Regulations	Choose one: US: USP <232>, FDA guidance; EU: Ph. Eur. 5.20, EMA; Both US and EU.
Route	Choose one: Oral; Parenteral; Inhalation.
Maximum daily dose of drug product (g/day)	Type a number.
Approach	Choose one: Summation of component data (Option 2b); Finished product testing (Option 3).
Report number	Type it in.

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FIELD	WHAT TO ENTER
Elements intentionally added (catalysts, reagents)	Write element symbols, for example "Pd, Pt". Type it in.

2 · Components

Amount of each component in the maximum daily dose. For Option 3, list the drug product only.

FIELD	WHAT TO ENTER
Components	A table. Columns: Component Amount in daily dose (mg). Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

3 · Element data

One row per component and element. Level in µg/g (ppm). "<0.5" counts at the LOQ.

FIELD	WHAT TO ENTER
Element data	A table. Columns: Component Element Level (µg/g) Source. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

4 · Other sources and control

FIELD	WHAT TO ENTER
Manufacturing equipment	Type or paste text.
Water	Type or paste text.
Container closure	Type or paste text.
Controls for elements above the control threshold	Type or paste text.

5. Checks and alerts

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

- Elements required for the route.
- Intake against the PDE and the control threshold.

- Sources: components, equipment, water and container closure.

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: Risk assessment 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.P.5.5	Elemental impurities risk 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

ICH Q3D(R2) applies in both regions. US: USP <232>/<233>. EU: Ph. Eur. 5.20 and 2.4.20.

8. Working with other modules

- Element results also appear in the Impurity & Risk Studio and the Specification Builder.

9. Common pitfalls

- Leaving out a class 2A element because it is not expected.
- Using the wrong PDE column for the route.

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 palladium

Change the palladium level in the drug substance from 4.2 to 800 µg/g.

EXPECTED RESULT

The headline shows one element above the control threshold.

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.