

Impurity & Risk Studio

Assess organic, mutagenic (ICH M7), nitrosamine and elemental (ICH Q3D) impurities, with limits computed from your dose, duration and route, and write each as its CTD section and a standalone report.

WRITES

3.2.S.3.2

3.2.P.5.5

PRODUCT TYPE

Small molecule

**GUIDANCE IT
FOLLOWS**

ICH Q3A(R2),
Q3B(R2), M7(R2),
Q3D(R2); FDA
Control of
Nitrosamine
Impurities in
Human Drugs (Rev.
2, 2024) and
Recommended AI
Limits for NDSRIs
(2023)

TIME TO LEARN

About 20 minutes
with the example

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

1. What this module does

The module writes 3.2.S.3.2 or 3.2.P.5.5 and three standalone reports: the ICH M7 mutagenic impurity assessment, the nitrosamine risk assessment and the ICH Q3D elemental impurities risk assessment.

Limits are calculated from the maximum daily dose, the treatment duration and the route: the M7 acceptable intake for class 1 to 3 impurities, nitrosamine limits from the published intake or the CPCA category, and Q3D concentrations from the PDE and the daily intake of drug product.

What you get

- Word or PDF files for the impurities section and the three risk assessment reports.
- 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.

- Maximum daily dose of drug substance, daily intake of drug product (g/day), route and treatment duration.
- Organic impurities with origin, maximum found and where each is controlled.
- For M7: each potentially mutagenic impurity with its class, (Q)SAR results from two complementary methods, levels found, control option and, for Option 4, the level at introduction and predicted purge factor.
- The nitrosamine risk factors, and any nitrosamines tested with their CPCA category or published name.
- Elements found (or calculated from components) and their sources.

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/impurity-risk-studio.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 dose, route and duration

Choose the section and enter the doses, route and [Treatment duration \(ICH M7\)](#). The headline gives the M7 limit for a class 1–3 impurity: 15.0 ppm (1.5 µg/day at 100 mg/day for lifetime use).

CMCfy Impurity & Risk 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.S.3.2 3.2.P.5.5 Save project Open project Start blank Load example

Assess organic, mutagenic, nitrosamine and elemental impurities. Limits are computed from your dose, duration and route, and each assessment is written as its CTD section and as a standalone report.

Guidance: ICH Q3A(R2), Q3B(R2), M7(R2), Q3D(R2); FDA Control of Nitrosamine Impurities in Human Drugs (Rev. 2, 2024) and Recommended AI Limits for NDSRIs (2023)

1 - PRODUCT, DOSE AND ROUTE

Section Submission region
 Drug product (3.2.P.5.5) US: FDA (NDA, ANDA, BL)

Product or substance name
 CMX-101 Tablets, 50 mg

Maximum daily dose of drug substance (mg/day) Daily intake of drug product (g/day)
 100 0.4

Route Treatment duration (ICH M7)
 Oral > 10 years to lifetime (1.5)

RESULT

No impurity above its acceptable limit

M7 limit for a class 1-3 impurity: 15.0 ppm (1.5 µg/day at 100 mg/day). Nitrosamine fractions of AI add up to 0.04.

SECTION	MUTAGENIC (CLASS 1-3)	NITROSAMINE RISK FACTORS
3.2.P.5.5	2	2
ELEMENTS ASSESSED	8	

MUTAGENIC IMPURITIES (ICH M7)

IMPURITY	CLASS	LIMIT (PPM)	MAX FOUND	OPTION	PURGE RATIO	CHECK
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2 Enter organic and mutagenic impurities

For each mutagenic impurity choose the M7 class and the control option. For Option 4, give the level where it enters the process and the predicted purge factor; the tool calculates the predicted level and the purge ratio.

3 Tick the nitrosamine risk factors

Tick each factor that applies. In the example the drug substance has a secondary amine (NDSRI risk) and the blister lidding has nitrocellulose. Enter each nitrosamine assessed with its CPCA category; the tool adds up the fractions of the acceptable intake (0.04 here).

MUTAGENIC IMPURITIES (ICH M7)

IMPURITY	CLASS	LIMIT (PPM)	MAX FOUND	OPTION	PURGE RATIO	CHECK
Compound 4 (bromo intermediate)	3	15.0	< 5	1	–	Controlled
Hydrazine	1	15.0	–	4	7500	Controlled
Compound 2	5	–	–	–	–	Non-mutagenic
Desmethyl CMX-101	5	–	–	–	–	Non-mutagenic

Mutagenic impurities against the M7 limit.

4 Enter elemental impurities

Enter each element with its level in the drug product. Each is compared with its permitted concentration for the route and with the 30% control threshold.

5 Resolve alerts

The example has a major alert because two complementary (Q)SAR methods are not documented for one impurity, and a minor alert for a known mutagen without batch data.

ALERTS TO RESOLVE

1 alert to fix, justify, or proceed without before export. It is your call: "Proceed without it" lets you continue when the information is not available.

MAJOR Compound 2: two complementary (Q)SAR methods are not documented.

Mutagenic impurities · ICH M7(R2) 6

Give expert rule-based and statistical (Q)SAR results, or an Ames result.

MINOR Hydrazine is a known mutagen but no batch data are given.

Mutagenic impurities · ICH M7(R2) 8

Confirmatory data on several batches strengthen the control strategy.

6

Preview and download

Preview the CTD section and each report, check the review and download.

quaternary amine; packaging contains nitrocellulose.

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 to fix 1 recommended

MISSING INFORMATION (1)

Hydrazine is a known mutagen but no batch data are given.
Confirmatory data on several batches strengthen the control strategy.
recommended · Mutagenic impurities · ICH M7(R2) 8

Ignore

DATA AND INPUTS (1)

Compound 2: two complementary (Q)SAR methods are not documented.
Give expert rule-based and statistical (Q)SAR results, or an Ames result.
major · Mutagenic impurities · ICH M7(R2) 6

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.P.5.5 Characterisation of impurities

CMX-101 Tablets, 50 mg · US (FDA)

Organic impurities

Impurity	Origin	Max found (%)	Fate or control
CMX-101 N-oxide	degradation	0.21	Controlled in drug product specification
Desmethyl CMX-101	process and degradation	0.12	Controlled in drug substance and drug product specifications
Compound 4 (bromo intermediate)	process	< 0.05	Purged in steps 5 and 6; tested in drug substance
Unknown at RRT 1.32	degradation	0.08	Controlled as specified unidentified

The potential and actual impurities of CMX-101 Tablets, 50 mg were identified from the route of synthesis, forced degradation and stability studies. For a maximum daily dose of 100 mg, the identification threshold is 0.2% and the qualification threshold 0.2% (ICH Q3B(R2) for an MDD of 100 mg).

CMX-101 N-oxide (degradation): highest level in batches 0.21%. Controlled in drug product specification

Desmethyl CMX-101 (process and degradation): highest level in batches 0.12%. Controlled in drug substance and drug product specifications

Compound 4 (bromo intermediate) (process): highest level in batches < 0.05%. Purged in steps 5 and 6; tested in drug substance

Unknown at RRT 1.32 (degradation): highest level in batches 0.08%. Controlled as specified unidentified

Mutagenic impurities

Impurity	Class	(Q)SAR	Limit (ppm)	Max found (ppm)	Control
Compound 4 (bromo intermediate)	3	Expert rule-based positive (alkyl bromide); statistical positive	15.0	< 5	Option 1

Fix or justify the 1 blocking alert before downloading. Or choose "Download anyway".

Download anyway 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, dose and route

FIELD	WHAT TO ENTER
Section	Choose one: Drug product (3.2.P.5.5); Drug substance (3.2.S.3.2).
Submission region	Choose one: US: FDA (NDA, ANDA, BLA, IND); EU: EMA and national agencies (MAA); Both US and EU.
Product or substance name	Type it in.
Maximum daily dose of drug substance (mg/day)	Type a number.

FIELD	WHAT TO ENTER
Daily intake of drug product (g/day)	Needed for the Q3D concentration limits. Type a number.
Route	Choose one: Oral; Parenteral; Inhalation.
Treatment duration (ICH M7)	Sets the M7 acceptable intake: 120, 20, 10 or 1.5 µg/day. Choose one: ≤ 1 month (120 µg/day); > 1–12 months (20 µg/day); > 1–10 years (10 µg/day); > 10 years to lifetime (1.5 µg/day).

2 · Organic impurities

FIELD	WHAT TO ENTER
Impurities	A table. Columns: Impurity Origin (process / degradation / starting material / reagent) Max found in batches (%) Fate or where it is controlled. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

3 · Mutagenic impurities (ICH M7)

Class 1–3 need control to the acceptable intake. For Option 4, give the level where the impurity enters and the predicted purge factor.

FIELD	WHAT TO ENTER
Assessment	A table. Columns: Impurity M7 class (1–5) (Q)SAR result Max found (ppm) Control option (1–4) Level at introduction (ppm) Predicted purge factor. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

4 · Nitrosamines

FIELD	WHAT TO ENTER
The drug substance, or one of its impurities, contains a secondary, tertiary or quaternary amine (NDSRI risk)	Tick the box if it applies.

FIELD	WHAT TO ENTER
Excipients or process materials contain amines	Tick the box if it applies.
Nitrite may be present (excipients, water, process reagents)	Tick the box if it applies.
Nitrosating agents are used in the process (sodium nitrite, nitrous acid, NO _x)	Tick the box if it applies.
Recovered or recycled solvents, reagents or catalysts are used	Tick the box if it applies.
Starting materials or reagents come from processes with a known nitrosamine risk	Tick the box if it applies.
Packaging contains nitrocellulose (for example blister lidding)	Tick the box if it applies.
Nitrosamines assessed or tested	A table. Columns: Nitrosamine Published name (e.g. NDMA) or CPCA category (1–5) Max found (ppm) Batches tested. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

5 - Elemental impurities (ICH Q3D)

Give the highest level found in the drug product, or the level calculated from component data (Option 2a, 2b or 3).

FIELD	WHAT TO ENTER
Elements	A table. Columns: Element Intentionally added (yes/no) Max level in drug product (µg/g) Main source. 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:

- Every organic impurity has an origin and a fate or control.
- Process-related impurities have an M7 assessment and class; class 3 impurities have two complementary (Q)SAR methods; class 1–3 impurities have a control option and levels within the limit; Option 4 has purge data and the predicted level is below the limit.
- When risk factors are ticked, nitrosamines are assessed; an amine in the drug substance needs an NDSRI assessment; each nitrosamine has an intake basis and a result; levels against the limit (critical above, major above 10% of it); the sum of fractions of the acceptable intake.
- Q3D: daily intake given; elements recognised; intentionally added elements have a level; levels against the permitted concentration (critical above) and the 30% control threshold.

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: Organic impurities: origin and fate; Mutagenic impurities (ICH M7); Nitrosamine risk assessment; Elemental impurities risk assessment. 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 / 3.2.S.3.2	Characterisation of impurities / Impurities
Report	Mutagenic impurity assessment (ICH M7)
Report	Nitrosamine risk assessment
Report	Elemental impurities risk assessment (ICH Q3D)

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 mode cites the FDA guidance on nitrosamine impurities and the FDA acceptable intake limits for NDSRIs. EU mode cites the EMA Article 5(3) nitrosamine outcomes and the EMA question-and-answer document. Both use the CPCA approach for nitrosamines without a published limit. ICH M7 and Q3D apply in both.

8. Working with other modules

- Impurity limits in the specification are written by the Specification Builder.
- Elemental contributions from excipients connect with the statements in the Excipients Writer module.
- Packaging nitrocellulose and leachables are covered in the Container Closure & E&L.

9. Common pitfalls

- Choosing the wrong duration: most marketed products are lifetime (1.5 µg/day).
- Claiming Option 4 without a purge factor or the level at introduction.
- Ticking a risk factor but entering no nitrosamine assessment.
- Entering element levels in ppm of drug substance instead of µg/g of drug product.

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. Change the treatment duration

Set [Treatment duration \(ICH M7\)](#) to "≤ 1 month (120 µg/day)".

EXPECTED RESULT

The headline note gives the M7 limit as 1200.0 ppm (120 µg/day at 100 mg/day).

2. Remove the nitrosamine assessment

Clear the [Nitrosamines assessed or tested](#) table.

EXPECTED RESULT

A major alert says risk factors are present but no nitrosamine is assessed or tested.

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.