

Nonclinical Overview & Summaries

Write the nonclinical overview (CTD 2.4), the toxicology tabulated summary (2.6.7) and the nonclinical section of the Investigator's Brochure from your study list, checked against ICH M3(R2) for the clinical stage you are supporting.

WRITES

2.4

2.6

IB 5

PRODUCT TYPE

Small molecule and
biologics

**GUIDANCE IT
FOLLOWS**

ICH M3(R2); ICH
S7A, S7B, S2(R1),
S5(R3),
S1A/S1B(R1), S10,
S11, S6(R1); ICH
M4S(R2); FDA
Estimating the
Maximum Safe
Starting Dose
(2005) / EMA first-
in-human
guideline; 21 CFR
Part 58 / OECD
GLP

TIME TO LEARN

About 20 minutes
with the example

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

1. What this module does

You choose the modality and the clinical stage, give the longest planned dosing, the clinical dose and human exposure, and list the studies with their species, duration, NOAEL, exposure and GLP status.

The tool checks the repeat-dose duration in a rodent and a non-rodent, the safety pharmacology core battery and hERG, the genotoxicity battery, the timing of reproductive studies (which differs between the US and the EU), carcinogenicity, photosafety and juvenile studies. It works out the human equivalent dose, the maximum recommended starting dose and the exposure margins.

What you get

- A Word or PDF document for each: 2.4 Nonclinical overview, 2.6.7 Toxicology tabulated summary, and IB section 5.

2. Before you start

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

- The study list with species, duration, NOAEL and GLP status.
- AUC at the NOAEL for the pivotal repeat-dose studies.
- The planned clinical dose, duration and population.

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/nonclinical-overview.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 programme

Choose the modality and the stage the package supports, and tick whether women of childbearing potential or children are included.

CMCfy Nonclinical Overview & Summaries Projects All modules Training Security Runs entirely on this device Training guide

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.

2.4 2.6 IB 5

Save project Open project Start blank Load example

Write the nonclinical overview (2.4), the toxicology tabulated summary (2.6.7) and the nonclinical section of the Investigator's Brochure from your study list. The tool checks the package against ICH M3(R2) for the planned clinical stage and duration, works out human equivalent doses, the maximum recommended starting dose and exposure margins, and flags non-GLP pivotal studies.

Guidance: ICH M3(R2); ICH S7A, S7B, S2(R1), S5(R3), S1A/S1B(R1), S10, S11, S6(R1); ICH M4S(R2); FDA Estimating the Maximum Safe Starting Dose (2005) / EMA first-in-human guideline; 21 CFR Part 58 / OECD GLP

1 · PROGRAMME

Product

CMX-101 (small-molecule kinase inhibitor)

Submission region

US: FDA (NDA, ANDA, BL)

Modality

Small molecule

Supports

Phase 2

Longest planned clinical dosing (weeks)

12

Document number

NC-101-24

Indication and population

RESULT

Nonclinical package supports phase 2

12 studies. Repeat-dose: rodent 13 weeks, non-rodent 13 weeks (needed 12 and 12 weeks for 12 weeks of dosing). Lowest HED 4.84 mg/kg; MRSD 29.0 mg.

STUDIES	RODENT	NON-RODENT
12	13 wk	13 wk

MRSD
29.0 mg

REPEAT-DOSE STUDIES AND SAFETY MARGINS

STUDY	SPECIES	WEEKS	NOAEL (MG/KG/DAY)	HED (MG/KG)	AUC MARGIN	GLP
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2 Enter the studies

One row per study. Name the endpoint in the title (Ames, micronucleus, hERG, CNS, embryo-fetal development) so the coverage check finds it.

3 Read the result

The headline gives the outcome: "Nonclinical package supports phase 2".

REPEAT-DOSE STUDIES AND SAFETY MARGINS						
STUDY	SPECIES	WEEKS	NOAEL (MG/KG/DAY)	HED (MG/KG)	AUC MARGIN	GLP
TX-001	rat	13	30	4.84	9.0×	yes
TX-002	dog	13	10	5.56	5.0×	yes

Safety margins and ICH M3(R2) coverage.

4 Resolve alerts and download

A repeat-dose study shorter than the clinical dosing, a missing core battery or Ames test, and a starting dose above the MRSD are critical. Non-GLP pivotal studies and exposure margins

below 1 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 preview 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

2.4 Nonclinical overview
 CMX-101 (small-molecule kinase inhibitor) · NC-101-24 · US (FDA)

Product	CMX-101 (small-molecule kinase inhibitor)
Indication	Moderate to severe plaque psoriasis in adults
Supports	Phase 2
Document	NC-101-24

2.4.1 Overview of the nonclinical testing strategy
 The programme follows ICH M3(R2). Pivotal studies were done under GLP (21 CFR Part 58).

2.4.2 Pharmacology

Study	Title	Species	Weeks	NOAEL (mg/kg/day)	GLP	Key findings
TX-003	CNS (Irwin) in rat	rat	–	100	Yes	No effects up to 100 mg/kg
TX-004	Cardiovascular telemetry in dog	dog	–	30	Yes	No effect on ECG intervals or blood pressure
TX-005	Respiratory (plethysmography) in rat	rat	–	100	Yes	No effects
TX-006	hERG assay	in vitro	–	–	Yes	IC50 32 µM (over 100-fold the free Cmax)

2.4.3 Pharmacokinetics

Study	Title	Species	Weeks	NOAEL (mg/kg/day)	GLP	Key findings
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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 · Programme

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.
Modality	Choose one: Small molecule; Biotechnology product (ICH S6).
Supports	Choose one: First-in-human (phase 1); Phase 2; Phase 3; Marketing application.
Longest planned clinical dosing (weeks)	Type a number.

FIELD	WHAT TO ENTER
Document number	Type it in.
Indication and population	Type it in.
Women of childbearing potential included	Tick the box if it applies.
Paediatric patients included	Tick the box if it applies.
Expected clinical use is chronic (6 months or more)	Tick the box if it applies.
Absorbs light at 290–700 nm (MEC above 1000 L/mol/cm)	Tick the box if it applies.

2 · Clinical dose

FIELD	WHAT TO ENTER
Highest planned clinical dose (mg/day)	Type a number.
Proposed starting dose (mg/day, first-in-human) when it applies	Type a number.
Human AUC at the highest dose (ng·h/mL, steady state)	Type a number.

3 · Studies

One row per study. Type: repeat-dose, safety pharmacology, genotoxicity, reproductive, carcinogenicity, phototoxicity, juvenile, pharmacokinetics or local tolerance. Name the endpoint in the title (Ames, micronucleus, hERG, CNS, EFD, fertility). Use ";" inside the findings.

FIELD	WHAT TO ENTER
Studies	Use ";" inside the findings column. Write "in vitro" as the species for in vitro assays. A table. Columns: Study ID Type Title Species Duration (weeks) NOAEL (mg/kg/day) AUC at NOAEL (ng·h/mL) GLP (yes/no) Key findings. 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:

- Repeat-dose duration against ICH M3(R2) Tables 1 and 2.
- Safety pharmacology, genotoxicity and reproductive timing.
- HED, MRSD, exposure margins and GLP status.

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: Overview and conclusions. 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
2.4	Nonclinical overview
2.6.7	Toxicology tabulated summary
IB 5	Investigator's Brochure nonclinical section

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: embryo-fetal development can follow early trials with contraception, before phase 3; 9-month non-rodent study for long trials; starting dose by the FDA 2005 guidance. EU: EFD before women of childbearing potential are dosed; 6-month non-rodent accepted; EMA first-in-human guideline.

8. Working with other modules

- Each pivotal toxicology study report is written in the GLP Toxicology Study Report.

9. Common pitfalls

- A rodent study shorter than the planned clinical dosing.
- Calling a dose range-finding study pivotal without GLP.

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. **Plan a longer trial**

Change the longest planned clinical dosing from 12 to 26 weeks.

EXPECTED RESULT

The headline shows two critical gaps: both repeat-dose studies are too short.

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.