mltox

PUBLIC DEMO REPORT

Small-Molecule Safety Triage Report

Synthetic small-molecule safety assessment showing endpoint risk, read-across evidence, dose and exposure context, uncertainty, and study-planning handoff before GLP animal studies.

Generated on 2026-07-23 | Example data only | MLTox Small Molecule Safety

This report is a synthetic public-facing demo. It is not a study report, not medical advice, and not a regulatory submission.

Executive Triage Snapshot

Decision framing for a synthetic discovery-stage small molecule before animal study commitment.

ACTION

Recommended decision

Do not enter a GLP repeat-dose animal study yet. Advance to focused in vitro confirmation and exposure clarification because hERG, DILI, and mitochondrial signals are plausible but not decisive.

OVERALL CALL

Gate

human review

CONFIDENCE

Med

domain gaps

RISK FLAGS

3

of 12 endpoints

NEXT TESTS

5

focused assays

Endpoint risk heatmap

Ames Moderate	**Clastogenicity** Low	**hERG** Elevated	**DILI** Moderate
Mito stress Moderate	**BSEP** Low	**CYP DDI** Moderate	**Phospholipidosis** Low
Acute oral Low	**Repeat-dose liver** Moderate	**CNS off-target** Low	**Skin sensitization** Low

Risk colors are synthetic. A real report must preserve model version, source provenance, applicability domain, and reviewer rationale per endpoint.

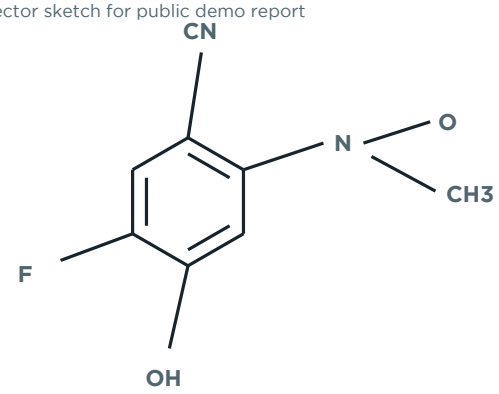
Report element	What this demo includes	Why a tox lead expects it
Identity	Compound ID, structure sketch, route, assumed exposure	Prevents endpoint calls from floating away from the actual decision context.
Evidence	QSAR, read-across, public data families, uncertainty	Supports weight-of-evidence review instead of a single opaque score.
Endpoint dashboard	Ames, hERG, DILI, organ systems, acute/repeat-dose signals	Mirrors the safety questions asked before GLP study design.
Handoff	In vitro package, animal-study readiness gates, residual questions	Turns prediction into an auditable next action.

Compound Identity and Scope

A report-grade tox artifact starts with controlled identity, study context, and explicit public-demo boundaries.

Synthetic small-molecule exemplar

Vector sketch for public demo report



Field	Synthetic value
Candidate ID	MLX-1024
Program context	Oral small-molecule lead optimization
SMILES status	Synthetic exemplar, not sponsor confidential
Route under consideration	Oral
Decision question	What evidence is needed before animal dose-range finding?
Report status	Public demo, not a regulatory submission

Pre-animal evidence workflow

Property	Value	Interpretation
MW	386.4 Da	Within typical oral small-molecule range.
cLogP	3.7	Lipophilicity may contribute to hERG and mitochondrial liability.
TPSA	74 A2	Moderate polarity; not an obvious permeability outlier.
pKa	8.4 basic center	Basic/lipophilic motif deserves cardiac and phospholipidosis review.
Solubility	42 uM at pH 7.4	Adequate for screening, may constrain high-dose formulation.
Pred free Cmax	0.23 uM	Synthetic exposure anchor for margin calculations only.
Main caveat	No wet-lab confirmation	All endpoint calls remain hypotheses until assay data arrive.

Endpoint Dashboard

Dense, reviewable triage across the major questions normally escalated before nonclinical study design.

Endpoint	Call	Risk	Confidence	Evidence snapshot	Next action
Ames/genotoxicity	Ambiguous	Moderate	Medium	Weak electrophile alert; mixed nearest analogs; statistical QSAR p=0.41.	Run GLP-compatible Ames or qualified screen.
Chromosomal damage	No strong signal	Low	Low-med	No high-confidence clastogenic alert; limited analog coverage.	Consider in vitro micronucleus if Ames positive.
hERG blockade	Plausible liability	Elevated	Medium	Basic/lipophilic motif plus modeled IC50 7.8 uM; free margin approx. 34x.	Confirm with manual or automated patch clamp.
DILI	Mechanistic concern	Moderate	Medium	Mito stress and PXR/CYP pattern; no direct DILI analog consensus.	Run hepatocyte stress/BSEP/CYP panel.
Mitochondrial stress	Possible	Moderate	Medium	Predicted AC50 9.4 uM; lipophilicity-associated analog pattern.	Add respirometry or high-content mito assay.
BSEP inhibition	Not prioritized	Low	Low	Modeled IC50 28 uM; sparse direct evidence.	Screen if exposure increases.
CYP DDI	CYP3A4/2D6 watch	Moderate	Medium	Inhibition flags near low micromolar range.	Microsome and recombinant CYP panel.
Acute oral toxicity	No early red flag	Low	Low-med	Synthetic LD50 class not severe; no strong reactive motif.	Use only for dose-range planning.
Repeat-dose liver	Watch item	Moderate	Low-med	Analog liver enzyme changes at high exposure; no target-organ proof.	Dose-range finding with clinical chemistry focus.
CNS off-target	No major signal	Low	Low	Limited off-target panel coverage.	Panel if CNS exposure intended.
Skin sensitization	No strong signal	Low	Low-med	No strong protein-reactive alert beyond weak motif.	Defer unless route/formulation changes.

Genotoxicity Weight Of Evidence

ICH M7-style reporting expects complementary QSAR methods, analog evidence, expert rationale, and explicit uncertainty.

ICH M7-style genotoxicity logic

Public demo output: no clean negative conclusion until wet-lab Ames and impurity context are reviewed.

Assessment item	Demo output	Interpretation
Knowledge/rule model	Weak structural alert near aryl amide motif	Not enough for a positive call, enough to prevent a clean negative.
Statistical model	Ames probability 0.41; model version Ames-Ensemble-2026.07	Near decision boundary; prediction set should be labeled ambiguous.
Applicability domain	In-domain for scaffold; thin analog set for nitrile substitution	Confidence reduced until additional analog or assay evidence.
Read-across	3 Ames-negative analogs, 1 Ames-positive analog, 1 missing	Conflicting local evidence requires expert review.
Expert conclusion	No final mutagenicity conclusion from in silico alone	Run Ames before GLP animal commitment or impurity-control decisions.

Analog	Tanimoto	Ames	Why it matters
A1	0.86	Negative	Closest scaffold match; lacks basic side-chain.
A2	0.81	Equivocal	Shares aryl amide motif; assay strain coverage incomplete.
A3	0.77	Positive	Electrophile-containing analog; may not share same reactivity context.
A4	0.73	Negative	Same nitrile substitution; lower lipophilicity.
A5	0.69	No data	Useful chemical neighbor but not outcome-bearing.

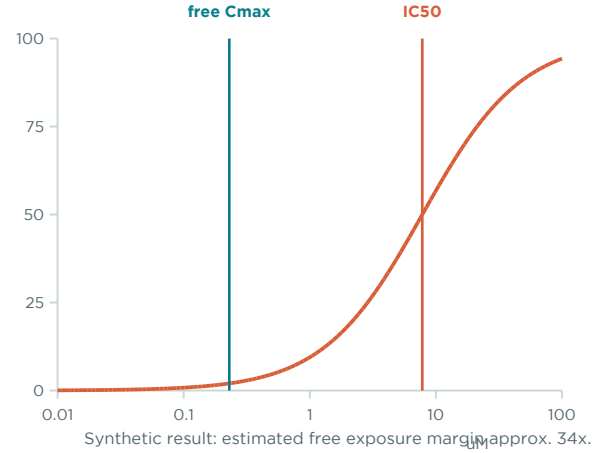
Reviewer note

A real report should avoid saying 'non-mutagenic' unless the two complementary methods, applicability domain, analogs, and any assay evidence support that conclusion for the stated context of use.

Cardiac, DILI, and Systems Toxicology

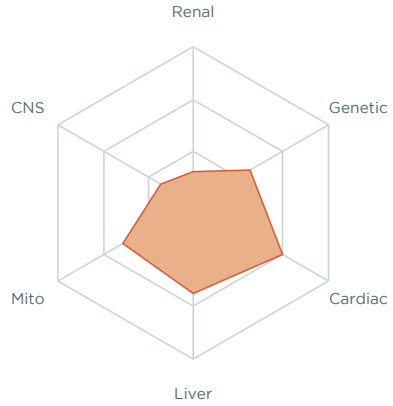
A useful early nonclinical triage report separates predicted hazard, exposure context, mechanism, and confirmatory tests.

hERG concentration-response context



Synthetic result: estimated free exposure margin approx. 34x.

Organ-system liability profile

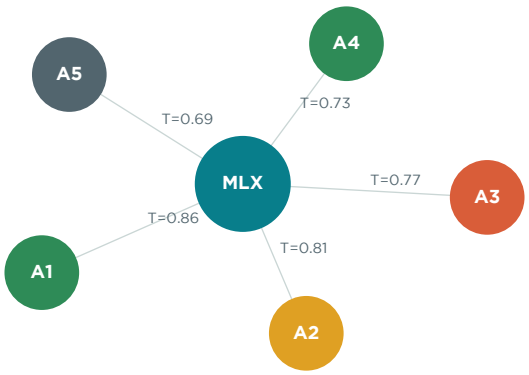


Signal family	Synthetic result	Decision weight	Confirmatory assay
hERG / repolarization	Modeled IC50 7.8 uM; free exposure margin approx. 34x	Medium. Follow-up before dose escalation.	Patch clamp plus solubility/protein binding.
DILI / liver stress	Mito stress and PXR/CYP pattern; no strong BSEP signal	Medium-low. Mechanistic screen first.	Hepatocyte stress, BSEP, bile acid transporter panel.
Mitochondrial toxicity	Predicted stress AC50 9.4 uM	Medium. Lipophilicity-linked signal.	Seahorse or high-content mitochondrial readout.
Tox21 pathway activity	NRF2 weak, ER stress negative, PXR moderate	Hypothesis-generating only.	Targeted pathway assays if program needs.

Read-Across Evidence and Applicability

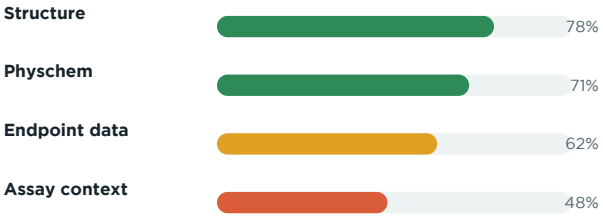
The report should show positive, negative, and missing analog evidence rather than only the most convenient neighbors.

Read-across neighborhood



Analog color: green negative, amber mixed, coral positive.
Gray indicates missing or insufficient endpoint data.

Applicability domain



Evidence class	What is available in this demo	How it affects the call
Nearest analogs	Five neighbors above Tanimoto 0.69, mixed Ames outcomes	Supports ambiguity rather than a single confident call.
Physchem match	Comparable MW/logP/TPSA, but basic center differs across analogs	In-domain for broad QSAR; lower confidence for hERG details.
Endpoint label quality	Ames labels stronger than DILI or repeat-dose labels	High priority endpoints get stronger language; organ tox remains hypothesis.
Negative evidence	Several close analogs negative for Ames and BSEP	Must be reported; prevents cherry-picking positive analogs.
Missing evidence	No direct chronic tox, reproductive tox, or formulation-specific data	Report should abstain, not invent certainty.

Dose, Exposure, and Nonclinical Study Handoff

Before formal nonclinical studies, a useful tox artifact should make dose logic, study endpoints, and readiness gates inspectable.

Dose and exposure context

Gate before animals	Pass condition	Owner
Identity and purity	Salt/form, stereochemistry, impurity profile, and analytical method locked	CMC / chemistry
Genotox triage	Ames result reviewed against two QSAR methods and analog evidence	Toxicology
Cardiac safety	hERG assay reviewed with free exposure and solubility context	Safety pharmacology
Liver mechanism	Hepatocyte/BSEP/CYP panel interpreted with DILI analogs	Translational safety
Formulation feasibility	Dose vehicle supports intended route and exposure range	DMPK / pharmaceutics

If gates pass: draft animal study plan element	What the report records
Dose-range finding	Rodent 7-day oral DRF with low/mid/high doses selected from exposure, tolerability, and formulation limits.
Repeat-dose tox endpoints	Clinical observations, body weight, food consumption, clinical pathology, organ weights, necropsy, histopathology, and toxicokinetics.
Safety pharmacology add-on	Cardiovascular and CNS/respiratory follow-up triggered by hERG/off-target profile.
Stopping rule	Escalate to expert panel if genotoxicity is positive or cardiac margin collapses after assay confirmation.

Method Governance and Limitations

Regulatory-style confidence comes from documented scope, model versions, data provenance, and restrained claims.

OECD QSAR governance checklist

Defined endpoint	yes
Unambiguous algorithm	versioned
Applicability domain	partial
Fit, robustness, predictivity	documented
Mechanistic interpretation	where possible
QMRF/QPRF-ready fields	complete

BOUNDARY

Public-demo limitations

The values in this report are synthetic and designed to show report shape. They should not be used to infer the safety of a real molecule. A real customer report would require authorized structure data, qualified models, source-linked evidence, and accountable scientific review.

Governance field	Demo entry
Product version	MLTox Small Molecule Safety v0.1-demo
Model package	Endpoint ensemble synthetic build 2026.07
Data families represented	Public toxicology databases, literature-derived analogs, model cards, and synthetic study context
Audit state	Report generated with fixed inputs; all example calls can be reproduced from the embedded demo data
Human review	Toxicologist review required before any experimental or regulatory action
Prohibited claims	Does not prove safety, does not replace GLP studies, does not establish clinical dose, does not submit to FDA/EMA

Recommended public-facing wording

MLTox produces toxicologist-readable evidence packets for earlier preclinical decisions. Reports combine model outputs, read-across evidence, applicability checks, dose/exposure context, and explicit limitations so teams can decide what to test next before committing to expensive animal studies.

Sources and Evidence Trail

Key standards, public resources, and paper-forward sources used to shape the demo report.

Source	Why it matters for this demo
ICH M7(R2) mutagenic impurities guideline and FDA implementation page	Frames complementary QSAR, impurity risk, acceptable intake logic, and expert review boundaries.
ICH S2(R1) genotoxicity testing and data interpretation	Defines the genetic toxicology battery and follow-up interpretation logic.
ICH M3(R2) nonclinical safety studies	Frames the timing and scope of nonclinical studies before human trials.
ICH M4S(R2) Common Technical Document safety format	Shows how nonclinical summaries and study reports are organized in regulated dossiers.
OECD QSAR validation principles and OECD QAF 2023	Supply model validity, applicability, and prediction reporting expectations.
FDA New Approach Methodologies pages and 2026 draft guidance announcement	Supports careful use of in silico and non-animal methods while keeping validation explicit.
EPA ToxCast and Tox21 public descriptions	Ground pathway-screening visuals and caveats for high-throughput assays.
ProTox 3.0 and ADMETlab 3.0 papers	Inform the kind of endpoint dashboards and ADMET panels users expect from predictive toxicology tools.
FDA DILIrank 2.0 dataset page	Shows how DILI evidence is label/literature-derived and must be interpreted with caution.
MLTox CX/R-paper run 2026-07-23	Local research packet used to cross-check report structure, caveats, and source coverage.

Demo-status statement

All compound names, model outputs, analog labels, assay values, and study-plan recommendations in this report are synthetic. The artifact is intended for website demonstration of report format and scientific posture only.