Toxicology Study Design Guide

Designing studies that actually support your IND

Nonclinical tox study design is one of the most consequential decisions in a drug development program. Get it right and you generate data that moves your program forward. Get it wrong and you generate data that raises questions — right when you're trying to file your IND.

This guide gives you the framework to design nonclinical studies that actually do their job.

Study Design Is a Strategic Decision

It's common to treat nonclinical tox study design as a methods question — which assay, which timepoints, how many animals, which endpoints. That's not wrong, but it's incomplete.

Study design is a strategic decision. Every choice has downstream consequences for your nonclinical program, your IND package, and your regulatory interaction. The question isn't just what does this study measure — it's what does this study need to prove, and does this design actually prove it?

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4 Questions to Answer Before Designing Any Nonclinical Study

Before writing a single endpoint, picking a species, or sending anything to a CRO — answer these four questions. They determine everything else.

01

What does this study need to support?

Not what it measures — what decision does it enable? Is it a NOAEL for IND? A dose range for a GLP repeat-dose study? A safety margin for the proposed clinical dose? If it can't be answered in one sentence, redesign.

02

What is the minimum dataset that answers that question?

More data is not better data. Every extra endpoint, timepoint, and group adds cost, complexity, and findings that will need to be explained. Design for adequacy — not comprehensiveness.

03

Is the dose selection defensible?

The high dose needs justification grounded in prior PK/TK data. 'Maximum feasible dose' is not a rationale. 'Based on AUC at X dose in the pilot study, the high dose achieves Y-fold exposure over the proposed clinical dose' is a rationale.

04

Will this design withstand regulatory scrutiny?

Read the relevant ICH guideline. Then ask: if FDA reviewed this protocol, what would they question? Ask that question before they do. If there isn't a solid answer, fix the design.

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The 5 Most Common Nonclinical Tox Study Design Mistakes

These are the patterns that appear most often in nonclinical programs. All fixable — but only before the study locks.

Running GLP before the dose range is established

A GLP repeat-dose study built on a poorly characterised dose range is one of the most expensive mistakes in nonclinical development. Run a non-GLP dose range finding study first. Establish TK. Then design the GLP study on solid ground.

Selecting species by default, not by science

The right species is the one that is pharmacologically relevant for the target and molecule. If the compound does not engage the target in the chosen species, that data may not adequately support human risk assessment. Species selection needs an explicit scientific rationale.

Designing for the guideline minimum, not scientific adequacy

The guideline tells you the minimum. FDA assesses scientific adequacy. Those are not the same thing. A study that is conspicuously absent for a given molecule type — with no documented rationale — becomes a regulatory question at IND review.

Omitting recovery groups when findings are anticipated

If the molecule's pharmacology could produce findings at high dose, include recovery animals. The ability to characterise a finding as reversible is one of the most powerful tools for contextualising safety signals and supporting IND progression.

Treating endpoints as a checklist rather than a scientific argument

Every endpoint should be there for a reason that can be articulated. 'It's standard' is not sufficient. 'It detects early hepatocellular injury consistent with the known class effects of this target' is a rationale. Reviewers notice the difference.

Study design mistakes are expensive in every direction — time, money, and credibility with FDA. Most of them aren't caught until the data is locked and the damage is already done. The fix isn't more data. It's earlier, more intentional thinking about what the data needs to show and why.

Dessi McEntee, MS, DABT | Toxistrategy LLC | toxistrategy.com

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Pre-Protocol Review Checklist

Run every nonclinical tox study protocol through this checklist before it locks. If any answer is no — the protocol isn't ready.

1. ☐ Can the purpose of this study be stated in one sentence?
2. ☐ Is dose selection documented and grounded in prior PK/TK data?
3. ☐ Are species selection and route of administration scientifically justified?
4. ☐ Does study duration match the proposed clinical exposure?
5. ☐ Have the relevant ICH guidelines been reviewed and all applicable requirements addressed?
6. ☐ Are recovery groups included if findings at high dose are anticipated?
7. ☐ Is the NOAEL expected to support an adequate safety margin for the intended clinical dose?
8. ☐ Are all endpoints included for a scientific reason, not just because they are standard?
9. ☐ Has the study been reviewed by a toxicologist before it was sent to the CRO?
10. ☐ If a finding occurs, does the study give you enough data to characterize and contextualize it?

Want the full framework?

My book, *Data Is Not Strategy*, breaks down how board-certified toxicologists actually think — the interpretation, the judgment calls, and the nonclinical decisions that move a program forward.

Get the book on Amazon: https://a.co/d/03vUZEIM

Dessi McEntee, MS, DABT | Toxistrategy LLC | toxistrategy.com