

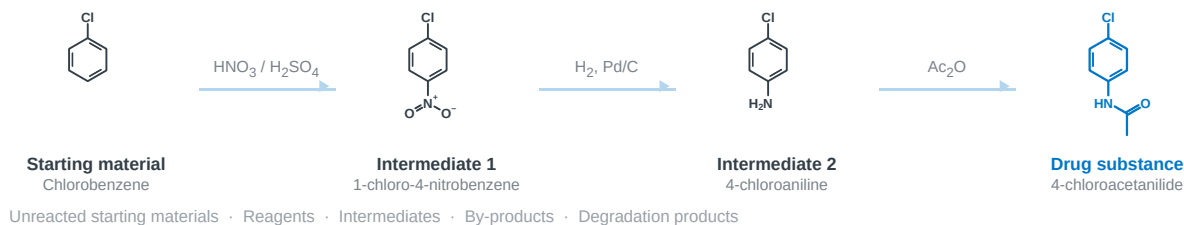
What does a defensible ICH M7 assessment look like?

You know what *in silico* tools do. This is how to apply them so the assessment holds.

1

Identify what needs assessing

Trace every impurity back to the route of synthesis: the ones that are there, and the ones that could be.



2

Establish what you already know

Use the evidence in front of you before you predict anything.

Mutagenicity data
Bacterial reverse mutation

Carcinogenicity data
Long-term rodent studies

Literature
Published and internal

Structural information
Known alerts and chemistry

3

Apply two complementary predictions

Two systems housed in the same platform: one expert rule-based, one statistical-based.



Expert rule-based

Structural alerts and mechanistic reasoning you can interrogate.

AGREE Greater confidence in the outcome

Expert review applies to every prediction. Agreement changes how much work it does, not whether you do it.



Statistical-based

Patterns from training data, with similar examples and a probability.

CONFLICT Focused expert review

4

Understand why the predictions differ

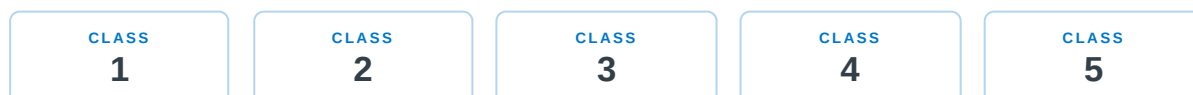
Do not just compare the calls. Understand the evidence behind them.



5

Reach one conclusion

Existing data, both predictions and expert review, weighed together into one classification.



6

Decide what the risk means for control

The assessment ends at what you do about it, not at whether it is mutagenic.

OPTION 1

Drug substance specification

OPTION 2

Upstream or in-process control

OPTION 3

Upstream control plus demonstrated purge

OPTION 4

Process understanding, no analytical testing

The better the fate and purge evidence, the less analytical testing you need to justify.

A decision you can defend.

Evidence-led. Scientifically justified. Ready for regulatory review.



shared knowledge • shared progress

Reflects ICH M7(R2). For guidance only. Consult the guideline for the full requirements.