Non-standard biotests – Intelligent testing to combine different needs and requirements for experimental and modelling approaches

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Aim: Development of a testing strategy to reduce experimental testing effort by combining tests for both experimental and modelling approaches

Requirements	Standard experimental acute test	Tests for use in TKTD modelling (GUTS) (EFSA 2018) [1]
Observation endpoint	Mortality/ immobility	Mortality/ immobility
Evaluation endpoint	LC_x/ EC_x	Threshold for effects (z), killing rate (kk), dominant rate constant (kd) LC_x/ EC_x from model predictions for variable exposure scenarios
Test duration	48 to 96 hrs (depending on test species)	Not specified, but should capture full toxicity (time needed for onset of effects, occurrence of delayed effects, accumulated toxicity, etc.)
No. of observation times after application	at least 2	at least 4 (for calibration) and 6 (for validation)
No. of test concentrations	at least 5 (in a geometric series)	Not specified
Exposure	constant	not specified for the calibration data set (concentrations have to be measured), but pulsed exposure design for model validation
Strength of effects	0-100% at the end of the test (sufficient data for EC_x calculation)	one concentration showing no or weak effects, at least one with strong effects (ideally up to 100%)

Test species and methods

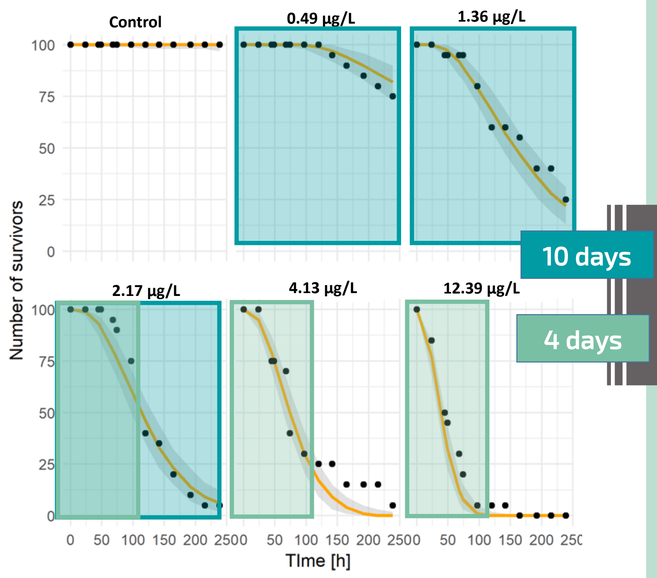
How to combine testing?

- Use more observation times and longer test periods than in standard testing.
- Include lower test concentrations.
- Include suitable feeding of test organisms (if test duration is longer than starvation resistance period).
- Conduct an additional experiment with pulsed exposure for model validation.

Exemplary results

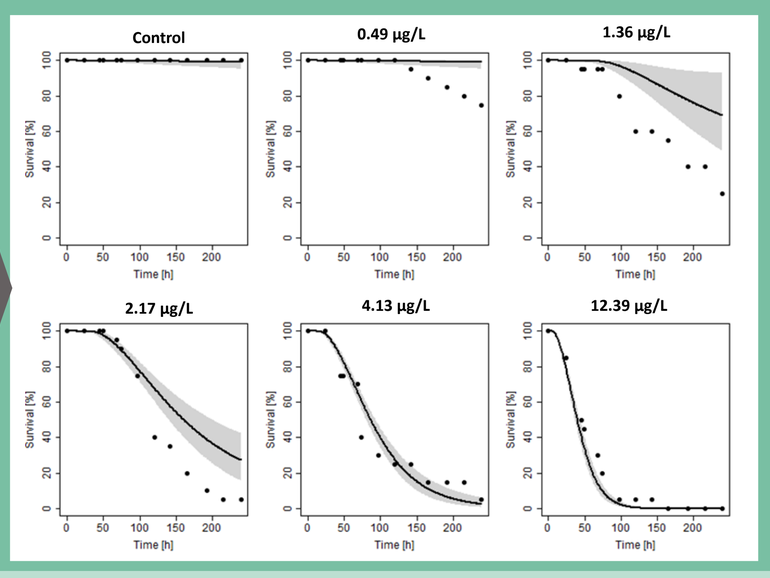
Chaoborus mortality experiment

- L4 larvae in M4 medium, 10°C, 10 days
- Toxicant: chlorpyrifos, pulsed exposure, 5 test concentrations (DT_{50}: 12 days)
- TKTD model: morse-package (V 3.2.2)
- GUTS-SD parametrisation based on:
  1) data for 4 days, 3 highest concentrations
  2) data for 10 days, 3 lowest concentrations

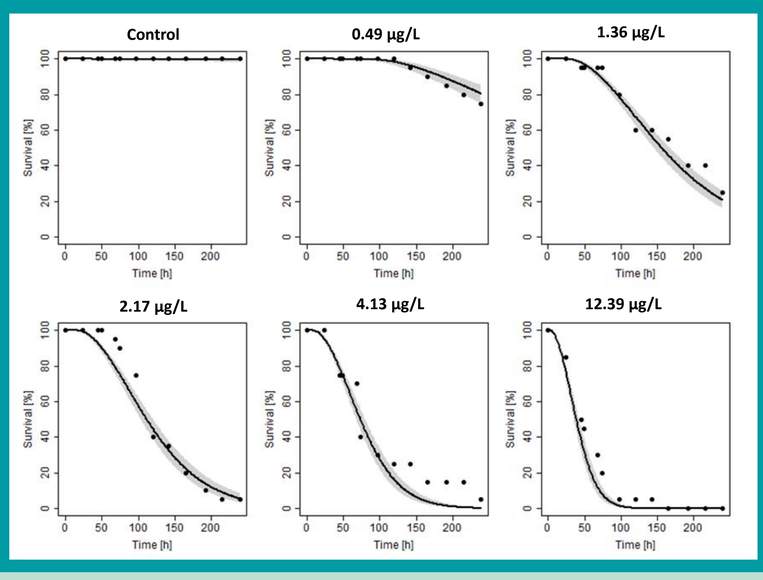


Parameter [µg/L]	Experimental data	GUTS model predictions based on short-term/ high concentration parametrisation	GUTS-SD model predictions based on longer-term/ low concentration parametrisation
4 days-LC_{50}	3.12	5.23	3.13
10 days-LC_{50}	0.85	1.68	0.83

Predictions based on short-term/ high concentration data for parametrisation



Predictions based on longer-term/ lower concentration data for parametrisation



Conclusions

- Standard experiments can be combined with experiments for GUTS parametrisation, but more observation times are needed.
- Both data sets used for model parametrisation fulfil the EFSA requirements and both show good model fits (model efficiency EF 0.89 /0.93).
- The test duration and the tested concentration range influences the accuracy of model predictions (see LC_{50} values). Predictions based on short-term/high concentration data did not capture effects at low concentrations especially after longer exposure.
- A prolongation of test duration and reduction of test concentrations increase the sensitivity of the test system and the accuracy of model predictions for longer-term effects at environmentally relevant low concentrations.

1: EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2018. Scientific Opinion on the state of the art of Toxicokinetic/Toxicodynamic (TKTD) effect models for regulatory risk assessment of pesticides for aquatic organisms. EFSA Journal 2018; 16(8): 5377, 188 pp. https://doi.org/10.2903/j.efsa.2018.5377

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