

Modelling effects of time variable exposure to mixtures of sulfonyl urea herbicides on *Lemna*

Alan J. Jones¹, Tessa Scown¹, Alan Samel¹, Judith Klein², Udo Hommen²

¹FMC Agricultural Solutions, 1090 Elkton Road, Newark, DE 19711, USA

²Fraunhofer Institute for Molecular Biology and Applied Ecology, Auf dem Aberg 1, 57392 Schmallenberg, Germany

E-mail contact: Alan.Jones@fmc.com

1. Introduction

The Tier 1 risk assessment of plant protection products for aquatic macrophytes is usually based on the growth rate inhibition (ErC₅₀) of the duckweed *Lemna sp.* under 7-day constant exposure [1]. In the next Tier, additional species can be tested to reduce species sensitivity uncertainty and/or testing can be conducted under modified exposure regimes to account for more realistic exposures (often predicted to be shorter than 7 days). Toxicokinetics-Toxicodynamics (TK-TD) models can help to extrapolate from the tested exposure regime to the diversity of exposure regimes predicted by the FOCUS surface water models [2]. Such models can be used to simulate laboratory tests with time variable exposures, but they can also be coupled with a population model to estimate effects of the full FOCUS exposure profile on a population in the field over a year.

In the project presented here, we used an extensive laboratory *Lemna sp.* data sets with different sulfonyl urea (SU) herbicides to calibrate and validate a TK-TD model of the growth inhibition. In the next step, validated models for single active substances were combined to predict the effects of plant protection products including two active substances. Laboratory studies with end use products were used to validate the model for the product mixtures.

2. Results and discussion

2.1. Available data

Several laboratory tests with *Lemna sp.* were available for each of four SU active substances: one or more standard tests, some of them extended by a recovery period, four full tests with short-term exposure events (0.5 – 4 days) followed by a recovery period until Day 7, and a test with exposure under low temperature followed by recovery under standard temperature.

2.2. The model

The *Lemna* model used was based on Schmitt et al. [3]. The description of modifications, implementation and testing is available at [4]. The TK-TD is modelled by the use of four parameters, permeability of the cuticula for the given substance, partition coefficient between water and plant tissue, and ErC₅₀ and slope for the logistic concentration response function related to the internal unbound concentration of the active substance. The mixture effect was modelled by introducing a single additional parameter which allows to consider additive, synergistic or antagonistic effects [5].

2.3. Calibration and validation of model of single active substances

The pulse exposure tests were used for calibration because these recent tests are considered high quality and most relevant for the exposure profiles to be assessed. An example for metsulfuron-methyl is given in Figure 1. Other reliable tests were used for validation of the calibrated model (Figure 2) by comparing predicted and observed growth.

2.4. Modelling binary blends

Under the assumption of concentration addition [1], the models for metsulfuron-methyl and tribenuron-methyl were able to predict conservatively the outcome of a test with a 1:1 mixture of both active substances (Figure 3, left). However, for a test with exposure over 14 days to a 1:2 mixture followed by recovery, effects during exposure were overestimated while recovery at the higher concentration was underestimated. The latter is not considered relevant for risk assessment since under the Ecological Threshold Option, the model can not refine situations when the exposure duration is longer than standard 7-day test duration.

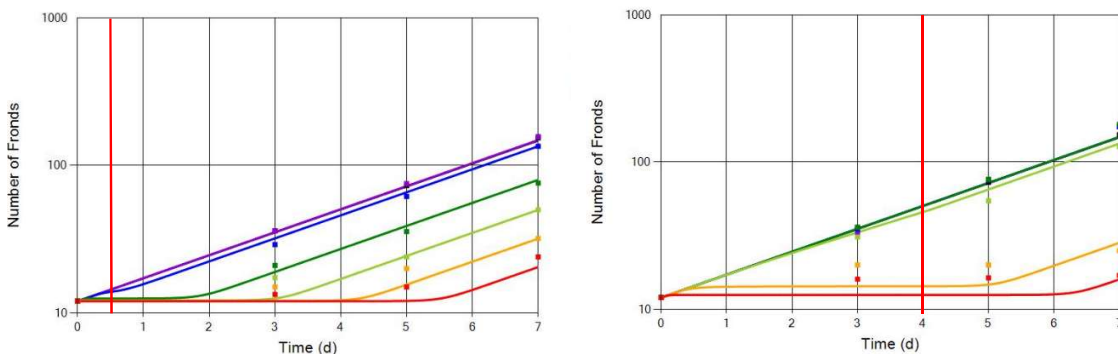


Figure 1: Calibration using *Lemna gibba* tests with 0.5 and 4 days of exposure to MSM (indicated by the red vertical line) as examples. Symbols = observations, lines = simulations

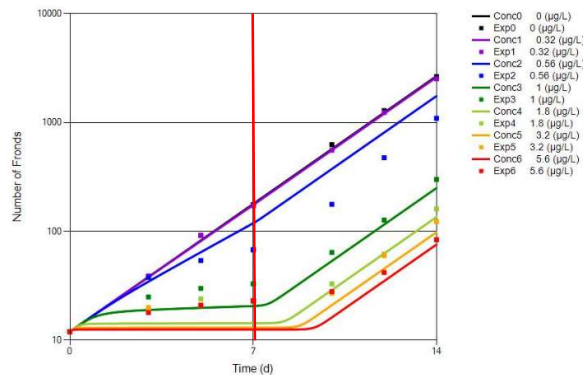


Figure 2: Validation example: *Lemna gibba* exposed over 7 days to MSM followed by a recovery period over 7 days. Symbols = observations, lines = predictions

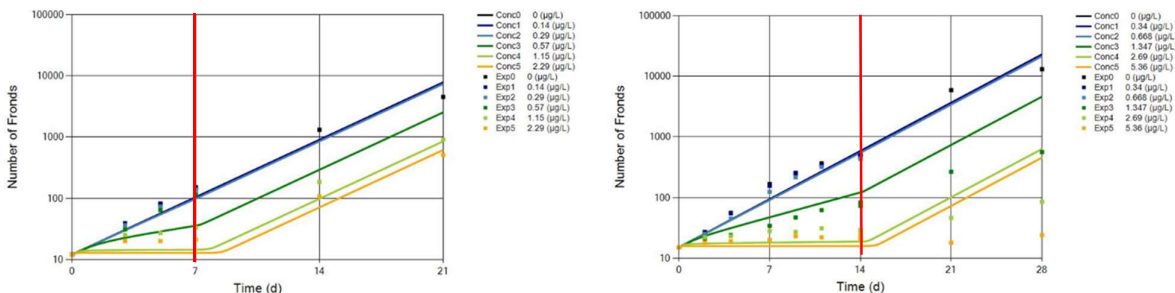


Figure 3: Prediction of the effects of a 1:1 (left) and 1:2 mixture (right) of MSM and TBN on growth of *Lemna gibba* assuming concentration addition

3. Conclusions

The *Lemna* TK-TD model could be parameterized to simulate the herbicidal effects of four sulfonyl urea active substances. First analysis indicates that effects of binary mixtures can be modelled under the assumption of concentration addition, which is expected for substances with the same mode of action.

4. References

- [1] EFSA PPR Panel. 2013. Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. *EFSA Journal* 2013;11(7):3290, 268 pp.
- [2] EFSA PPR Panel. 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.
- [3] Schmitt et al. 2013. Mechanistic TK/TD model simulating the effect of growth inhibitors on *Lemna* populations". In: *Ecological Modelling* 255, pp. 1–10
- [4] Klein J. Hommen U. 2018. https://www.ime.fraunhofer.de/en/Research_Divisions/business_fields_AE_BR/Businessareas_AE/Software_E/MoLePo.html. Assessed 27.11.2018
- [5] Plummer, John L. and Tim G. Short. 1990. Statistical modeling of the effects of drug combinations. In: *Journal of Pharmacological Methods* 23.4, pp. 297–309.