Session: Effect Modelling for Regulatory Risk Assessment: Current Applications and Future Directions (I)
Platform presentation, Session Room 101 CD, ID 9
Monday May 27th, 2019, 9:05 AM

Application of TKTD models in aquatic ERA for pesticides

Theo Brock[1;2], Maria Arena[1;3], Nina Cedergreen[1;4], Sandrine Charles[1;5], Sabine Duquesne[1;6], Andreas Focks[1;2], Alessio Ippolito[1;3], Michael Klein[1;7], Melissa Reed[1;8], Ivana Teodorovic[1;9]

[1]EFSA PPR working group on TKTD models in aquatic ERA for pesticides; [2]Wageningen Environmental Research, The Netherlands;[3]European Food Safety Authority, Italy; [4]University of Copenhagen, Denmark;

[5]University of Lyon, France; [6]Umweltbundesamt, Germany; [7]Fraunhofer, Germany; [8]Health and Safety Executive, UK; [9]University of Novi Sad, Serbia; E-mail contact: theo.brock@wur.nl

1. Introduction

This presentation aims to illustrate the regulatory use of validated GUTS models (General Unified Threshold models of Survival), as proposed by EFSA (see *EFSA Journal 2018;16(8):5377*), in the aquatic Tier-2 environmental risk assessment for an hypothetical organophosphorus insecticide (based on real data for two related substances). The case study compares the outcome of the experimental effect assessment tiers (Tier 1 and 2) with results of GUTS modelling to put these results into perspective.

2. Aquatic risks on basis of FOCUS exposure scenarios and experimental data

Two FOCUS surface water exposure scenarios are selected, viz. Stream D5 characterised by the highest $PEC_{sw;max}$ (0.035 µg/L) and a single pulse exposure, and Stream R3 also characterised by a relatively high $PEC_{sw;max}$ (0.034 µg/L) but by repeated pulse exposures due to run-off (Figure 1).

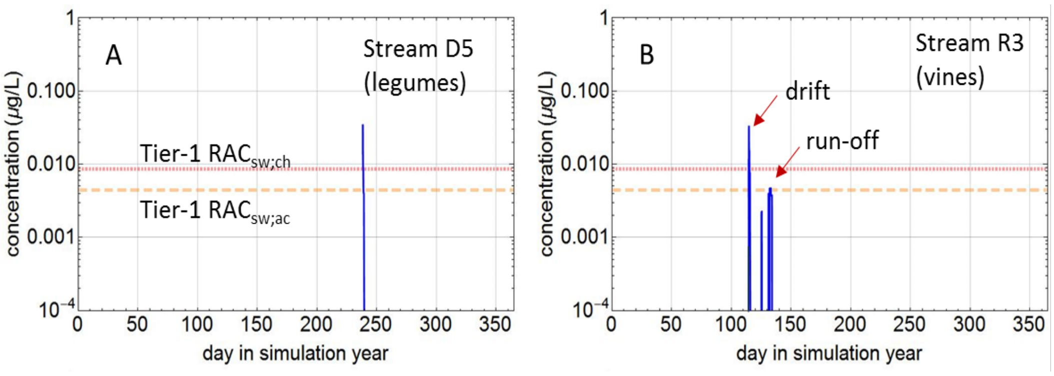

Figure 1: Predicted exposure profiles for FOCUS surface water scenarios Stream D5 and Stream R3

The example has its focus on acute ERA. The standard test species *Daphnia magna* (48-h EC50 = 0.48 µg/L) and *Chironomus riparius* (48-h EC50 = 0.44 µg/L) are the most sensitive standard test species, and standard fish and algae are more than one order of magnitude less sensitive. Applying an Assessment Factor (AF) of 100, the acute Tier-1 Regulatory Acceptable Concentration (RAC) becomes 0.004 µg/L.

Since risks are triggered in Tier-1, the Geometric Mean approach was explored by providing experimental 96-h EC50 values for the crustaceans *D. magna* (0.17 µg/L), *Asellus aquaticus* (3.43 µg/L) and *Gammarus pulex* (0.23 µg/L) and for the insects *C. riparius* (0.18 µg/L), *Cloeon dipterum* (0.31 µg/L) and *Plea minutissima* (1.29 µg/L). The geometric mean EC50 values for these crustaceans and insects are 0.51 and 0.42 µg/L, respectively. Following the procedure described in the Aquatic Guidance Document (*EFSA Journal 213;11(7):3290*), the lowest geometric mean value is selected and an AF of 100 applied. The acute Tier-2A RAC (Geometric mean approach) becomes 0.42/100 = 0.0042 µg/L. The $PEC_{sw;max}$ values are still higher than this acute Tier-2A RAC, so a high environmental risk is still triggered.

To allow the use of te Species Sensitivity Distribution (SSD) approach 96h-EC50 data were provided for two additional crustaceans, viz. *Neocaridina denticulata* (171 µg/L) and *Procambarus* sp. (1.20 µg/L), and for five additional insects, viz. *Anax imperator* (1.63 µg/L), *Notonecta maculata* (2.78 µg/L), *Paraponyx stratiotata* (2.86 µg/L), *Ranatra linearis* (3.33 µg/L) and *Sialis lutaria* (0.96 µg/L). The SSD constructed with the thirteen 96h-EC50 values for the aquatic arthropods mentioned above resulted in a Hazardous Concentration to 5% of the species (HC5) of 0.079 (0.031-0.370) µg/L. According to the EFSA Aquatic Guidance Document an AF of 3 to 6 should be applied to the median HC5, resulting in acute Tier-2B RAC values of 0.0132 – 0.0263 µg/L. Again, these values are lower than the $PEC_{sw;max}$ values, so a high aquatic risk is triggered.

3. Application of validated GUTS models as tools in Tier-2 aquatic risk assessment

To further refine the risks of time-variable exposures validated GUTS-RED-SD (assuming stochastic death) and GUTS-RED-IT (assuming individual tolerance) models were calibrated and validated for the aquatic test species mentioned above. The species and compound-specific GUTS models were used to calculate EP50 values, i.e. the multiplication factor to an entire specific exposure profile (see Figure 1) that causes 50% effect. The calculated EP50 values are presented in Table 1. In the risk assessment, these EP50 values should be higher than the AFs normally used in the corresponding experimental tiers to derive an acute RAC.

Table 1: Calculated EP50's (and 95% uncertainty limits) for the tested aquatic arthropods and exposure profiles for Stream D5 and Stream R3 (see Fig. 1) using the GUTS-RED-SD and GUTS-RED-IT models (see *EFSA Journal 2018;16(8):5377*)

Species		GUTS-RED-SD		GUTS-RED-IT	
		Stream D5	Stream R3	Stream D5	Stream R3
Crustacea	*Daphnia magna*	13 (7-61)	5 (2-33)	122 (97-145)	39 (32-49)
	Asellus aquaticus	762 (250-1285)	391 (92-635)	1445 (1221-1626)	488 (416-671)
	Gammarus pulex	37 (6-62)	13 (1-23)	66 (49-80)	22 (16-37)
	Neocardina denticulata	42500 (29219-63750)	14375 (9883-26504)	50000 (39063-65625)	16875 (12590-26631)
	Procambarus spec.	264 (206-330)	142 (106-174)	352 (264-461)	166 (135-228)
Insecta	*Chironomus riparius*	93 (75-122)	38 (28-52)	93 (70-111)	33 (26-44)
	Anax imperator	469 (432-501)	291 (272-304)	620 (530-673)	347 (280-390)
	Cloeon dipterum	98 (75-110)	57 (40-64)	134 (117-155)	49 (45-62)
	Notonecta maculata	1162 (890-1344)	542 (333-805)	1758 (1636-1978)	605 (563-691)
	Paraponyx stratiotata	557 (533-598)	344 (331-363)	566 (419-743)	352 (286-468)
	Plea minutissima	444 (392-491)	271 (231-299)	576 (514-641)	208 (184-334)
	Ranatra linearis	1709 (1282-2016)	1025 (793-1170)	2031 (1746-2380)	674 (590-1179)
	Sialis lutaria	109 (60-177)	50 (27-100)	264 (204-338)	88 (69-110)

3.1. GUTS models and refining the standard test species approach

In first instance, GUTS models were developed and validated (see *EFSA Journal 2018;16(8):5377*) for the standard test species *D. magna* and *C. riparius* to refine the environmental risks of the time-variable exposure regimes of FOCUS exposure scenarios Stream D5 and Stream R3. From Table 1 it appears that for both exposure scenarios and both types of GUTS models at least one of the Tier-1 test species has an EP50 value lower than 100 (the Tier-1 AF), indicating potential high risks.

3.2. GUTS models and refining the experimental Geometric Mean approach

Besides the GUTS models for the Tier-1 test species, additional GUTS models were developed and validated for the crustaceans *A. aquaticus* and *G. pulex* and for the insects *C. dipterum* and *P. minutissima* (in accordance with the experimental Geometric Mean approach described above). The geometric mean EP50 value for crustaceans was 71.6 for Stream D5 and 29.4 for Stream R3 when using the GUTS-RED-SD model, while for insects these geometric mean EP50 values were 159.4 and 83.7, respectively. When using the GUTS-RED-IT, the geometric mean EP50 values for crustaceans were 226.6 for Stream D5 and 74.8 for Stream R3, while these values for insects were respectively 192.9 (Stream D5) and 69.5 (Stream R3). Only when using the GUTS-RED-IT models and for exposure scenario Stream D5, the aquatic risks are sufficiently low, since the geometric mean EP50 values for both crustaceans and insects were larger than 100 (the AF used in acute Tier-2A). When using the GUTS-RED-SD model the geometric mean EP50 values were lower than 100 for both exposure scenarios, indicating potential risks

3.3. GUTS models and refining the experimental SSD approach

EP50 values for all species mentioned in Table 1 were used to construct exposure scenario-specific SSD curves. On basis of GUTS-RED-SD model calculations, the HP5 (Hazardous exposure Profile to 5% of the species) values derived from the SSD curves were, respectively, 15 (5-80) and 7.3 (2-40) for Stream D5 and Stream R3. Using the GUTS-RED-IT models the HP5 values were 34 (15-120) for Stream D5 and 14 (5.9-54) for Stream R3. Since these median HP5 values all were higher than 3 to 6 (the AF used in the acute SSD approach), estimated risks of the time-variable exposures seem to be sufficiently low when using the GUTS models.

4. Conclusions

It appears that the application of GUTS models in prospective ERA as proposed by EFSA (*EFSA Journal 2018;16(8):5377*) is promising to refine the risk of time-variable exposures. In addition, the Tier-2 assessment based on GUTS models was not in conflict with the principle of the tiered approach that lower tiers should be more conservative than higher-tiers. It is recommended that similar exercises are conducted with a representative number of substances differing in field exposure dynamics and toxic mode of action.