MODIFIED EXPOSURE STUDIES IN AQUATIC RISK ASSESSMENTS: HOW USEFUL ARE THEY?

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Regulatory Background

- Modified exposure studies have been included by EFSA in 2013[1] as a refinement option (Tier 2C) under the current guidance for aquatic risk assessments for plant protection products (PPPs).
- They can be a useful refinement option for scenarios where the predicted exposure profile indicates that exposure will not be continuous, and therefore ecotoxicity endpoints based on constant exposure may be over conservative with modified exposure studies aligning more closely to realistic scenarios.
- Although Tier 2C refinements are permitted under the current aquatic guidance, some EU Member States have indicated that they will not readily accept such an approach; for example, the central zone MSs recently concluded that Tier 2C refinements 'should generally not be supported at zonal level, considering that implementation in ERA is complex and linked to high uncertainties'.

→ Aims

The review of EFSA conclusions for active substance submitted and evaluated at the EU level in the last 7 years (allowing 2 years implementation of the 2013 EFSA guidance) to determine:

- How many substances have attempted to use a modified exposure approach in the risk assessment?
- How many of these modified exposure studies have been accepted?
- Reasons why studies were accepted or rejected? How can regulators' concerns be addressed?
- Is there still a role for modified exposure studies in PPP aquatic risk assessments?
- How do modified exposure and TKTD assessments work together?

12 studies from 10 peer reviews of pesticide risk assessments:

- Cypermethrin
- Phosmet
- Mancozeb
- Pelargonic acid
- Benfluralin
- Spiroxamine
- Benalaxyl
- Methiocarb
- Captan

- **5 studies accepted for risk assessment (Fig.1)**
- 1 'accidental' tier 2C study as there was a lack of consistent exposure concentration throughout tier 1 studies
- 2 only accepted for risk for daphnids but cannot be used to represent all aquatic invertebrates
- 4 studies were not accepted for risk assessment

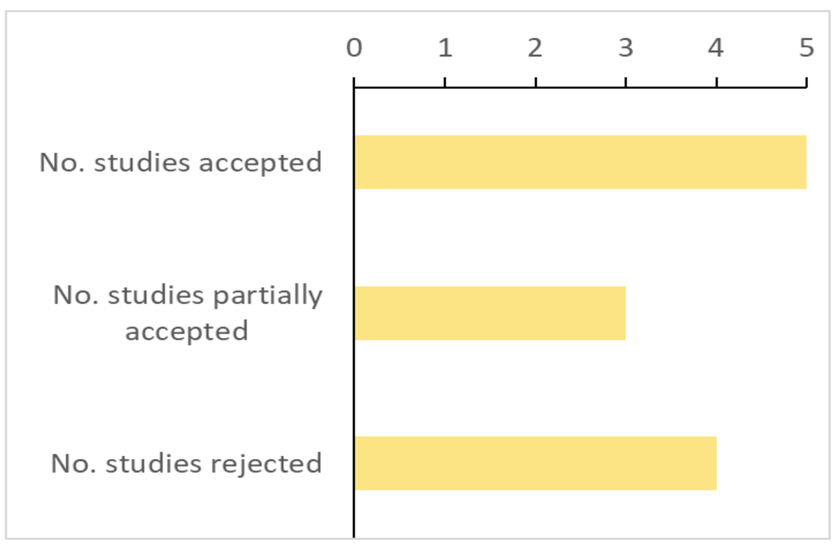


Figure 1: Number of modified exposure studies that were accepted, partially accepted or rejected by the regulators

Accepted studies:

- Modified study covered predicted exposure profile and FOCUS scenario
- Modified exposure study covered most sensitive organisms of a certain group

Accepted studies with caveats (partially accepted):

- Study accepted only for the tested organism but not covering the corresponding group (e.g. the tested species was not the most sensitive organism: *D. magna* & aquatic invertebrates)
- Study accepted but FOCUS scenario deemed inappropriate

Not accepted studies:

- Methodology:
  - Most sensitive life stages were not covered
  - Most sensitive endpoints were not covered (e.g. hatching in fish full life cycle test)
  - Non-specific: Inappropriate test design
- Exposure:
  - GAP was not covered appropriately
  - Lack of information regarding toxicological independence of peaks

→ **Most concerns can be addressed by gathering all information available for the substance and a close collaboration between ecotoxicologists and exposure specialists**

YES, THERE IS:

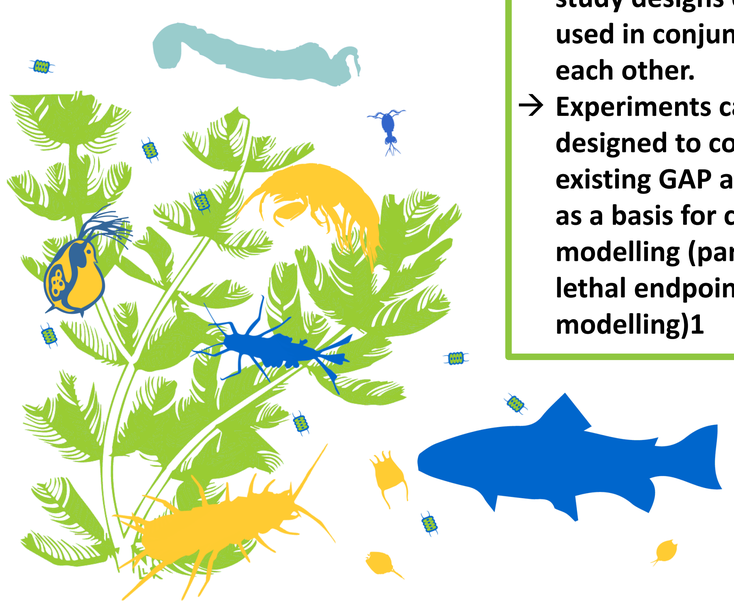
- Studies are accepted if the relevant exposure patterns have been covered
- Studies are accepted if the most sensitive organism of a group has been covered
- Studies are accepted if the most sensitive life stage of this group has been covered
- Studies are accepted if the most sensitive endpoint has been covered.

→ **It is essential that these points are explored before starting a study**
→ **What margin of safety remains after using these experimental results in the risk assessment?**

Modified exposure and TKTD modelling:

- Experimental requirements for TKTD modelling can be addressed by modified exposure studies
- Studies can be used to calibrate or validate models in future
- Modified exposure experiments usually require less experimental effort than calibration and validation experiments.

→ **TKTD and modified exposure studies do not exclude each other but with the appropriate study designs could be used in conjunction with each other.**
→ **Experiments can be designed to cover an existing GAP and be used as a basis for calibration in modelling (particularly, for lethal endpoints GUTs modelling)1**



Recommendations for successful modified exposure studies

- Thorough exploration of the GAP that will ultimately be sought.
- Use current exposure models and efate input parameters and adjust experimental design accordingly (e.g. Fig. 2) but we are aware of possible future changes that may impact exposure profiles (e.g., FOCUS surface water repair).
- Knowledge of the most representative sensitive and/or vulnerable species for each organism group if possible, including knowledge on life stage and endpoint sensitivity.

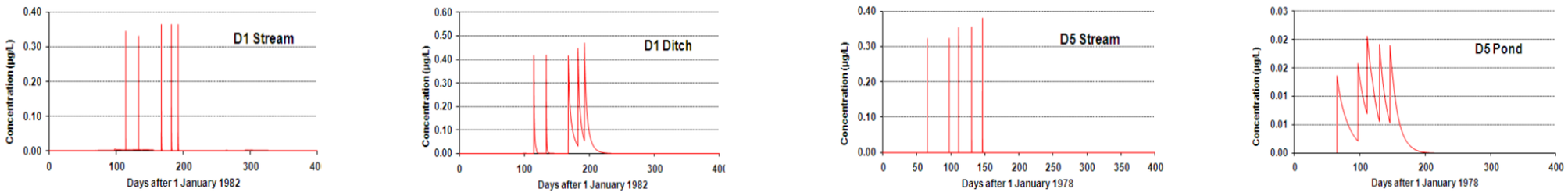


Figure 2: Example exposure scenarios for different water body types[1] illustrating the range of exposure patterns any modified exposure experimental design will need to cover

Conclusions

- Modified exposure studies can be a useful option for refining risk assessment in the EU.
- Reasons regulators reject or accept modified exposure studies were consistent across all 10 actives identified.
- Modified exposure and TKTD modelling are not exclusive and can complement each other.

Acknowledgement

Thanks to Steve Brewer for providing the text mining results from the EFSA webpage:

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References: 1 EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues) (2013). Scientific Opinion - Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. EFSA Journal 2013; 11(7): 3290.