The significance of metabolites in the EU registration of pesticides

When making risk assessments under 91/414/EEC, both the parent compound and its metabolites must be considered if a product is to gain annex 1 approval. The term 'metabolites' describes all breakdown products of the parent compound formed after application by both abiotic and biotic processes.

Surface water

Definitions

Metabolites are all breakdown products of the parent compound, whilst **major metabolites** are those that are formed in quantities >10% of the applied product. **Minor metabolites** are those that are formed in quantities <10% parent compound and **ecotoxicologically relevant metabolites** are those that are present in quantities <10% but likely to pose a comparable or greater risk to non target organisms.

Risk Assessment

Consider risks from all relevant metabolites in the water body as well as the risks from major metabolites formed in the soil that might move to water from drainage, runoff or from ground water.

You can minimise your testing needs by making inferences from parent toxicological studies where the metabolite was formed.

Matching the toxicity profile of parent to test species may also be useful as will selecting the single most important metabolite.

Default environmental parameters for model inputs (K_{oc}, DT_{50}); and default toxicity values for minor metabolites (ten times that of the parent) can be used and may reduce laboratory costs.

Groundwater

Is the metabolite 'relevant'? It may well be if in the degradation study one following is true:

1. > 10% is formed
2. > 5% is formed twice
3. Concentrations are rising at end of the study

Follow this sequential approach to risk assessment:

1. Check if it is a metabolite of no concern (e.g. CO_2, small chain aliphatics)
2. Use modelling techniques to establish ground water concentrations
3. If metabolite is toxic, has similar properties to parent or is carcinogenic then same 0.1 µg/L limit applies as with parent
4. Otherwise 0.75 µg/L maximum applies unless exposure can be assessed

Summary

Risk assessments usually require modelling calculations. Failure of a risk assessment means that a higher tier assessment must be performed. The experience of Enviresearch has shown that many higher tier questions can be answered by using advanced modelling. This is often more cost effective than higher tier toxicity testing.

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