FINAL REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: SHA 076127 A

Product name: PROSIM

Chemical active substances:

Propamocarb hydrochloride, 400 g/L

Cymoxanil, 50 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: SHARDA Cropchem España S.L.

Submission date: October 2020

MS Finalisation date: November 2022; March 2023

Version history

When	What
December 2020	Updated by Applicant
November 2022	Assessment by expert
March 2023	The final Registration Report

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10 Relevance of metabolites in groundwater

10.1 General information

Propamocarb

Propamocarb doesn't produce metabolites in soil and the Cymoxanil metabolites IN-U3204, IN-W3595, IN-JX915 and IN-KQ960 are predicted to occur in groundwater at concentrations below 0.1 µg/L (see dRR section 8, Chapter 8.8.2.2).

Cymoxanil

In soil under aerobic conditions cymoxanil exhibits very low to low persistence forming the major soil metabolites IN-U32045 (maximum occurrence 24.7% applied radioactivity (AR)) and IN-W3595 (maximum occurrence 10.1% AR) and the minor metabolites IN-KQ960 and IN-JX9156 (major metabolite in photolysis study) regarded as relevant for assessment of leaching potential to groundwater. All these metabolites exhibit very low or low persistence in soil. The relevant soil metabolites exhibit very high mobility. There was indication that adsorption of metabolite IN-W3595 was pH dependent.

The potential for groundwater exposure from the applied for intended uses of cymoxanil, IN-U3204, IN-W3595 and IN-JX915 above the parametric drinking water limit of 0.1 µg/L, was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios. Regarding the major soil metabolite IN-U3204 this metabolite exhibits very low or low persistence in soil (0.4 d) and it is unstable in water (hydrolysis DT_{50} 0.5-2.6d and 0.4d in total system), therefore and in agreement with the conclusions and calculations done in dRR Part B 8 chapter 8.8.2.2 the PECgw in all scenarios was below the trigger values of µg/L.

For the metabolite IN-KQ960, in geoclimatic regions represented by Jokioinen and Hamburg FOCUS groundwater scenarios, contaminations of groundwater above the 0.1 µg/L limit cannot be excluded according to the EFSA conclusions. Regarding the calculations done in dRR Part B 8 chapter 8.8.2.2 all metabolites had PECgw lower than 0.1 µg/L with the exception of IN-KQ960.

Indeed, the IN-KQ960 PEC_{gw} exceeded the groundwater trigger of 0.1 µg/L in Jokioinen being the maximum PEC_{gw} is equal to 0.175 µg/L for Jokioinen PELMO scenario at DT_{50} 7.3 d worst case, but when calculations are made with the DT_{50} geomean of 1.2 d, the maximum PEC_{gw} value is equal to 0.117 µg/L for Jokionen PEARL scenario. These values are close to the trigger of 0.1 µg/L.

However, according to EFSA Scientific Report (2008) 167, 1-116, due to the toxicological profile of Cymoxanil, the assessment of IN-KQ960 relevance should be considered, but the RMS point out, that IN-KQ960 is not likely to exceed the trigger of 0.1 µg/L under 'real outdoor conditions' of intended use owing to the following reasons:

- *IN-KQ960 was only observed in the Japanese 'Black Andosol' > 5 % of AR (from which the only valid DegT50 and valid formation fraction used for modelling derive from). IN-KQ960 was never detected > 5 % of AR in any of the eight European or US lab soil studies (maximum confirmed occurrence of IN-KQ960 in these soils 0.6 % of AR). Andosols are considered to represent only a very minor area of soils in Europe (including formally active and still active volcanic areas).*
- *Groundwater modelling of IN-KQ960 is extremely sensitive to the 1/n value used. Since no valid 1/n value is available for INKQ960 (KOC determined by means of HPLC), the PRAPeR 32 agreed default value of 1.0 was used for revised modelling for conservative reasons. However, the great majority of organic compounds exhibit a 1/n value about 0.9 (as indicated by the FOCUS default value).*
- *In the available lysimeter study, representing worst case conditions in terms of precipitation,*

amount of leachate, degradation rate of cymoxanil (acidic lysimeter soil) and application rate (3 x 320 g ai ha-1), no individual leachate compound is considered to exceed 0.1 µg L-1. Taking into account, that (i) the lysimeter soil used ('Borstel' soil) is more or less identical to the soil implemented in the Hamburg groundwater scenario (which resulted in an exceedance of the 0.1 µg L-1 trigger based on the worst case DegT50 of cymoxanil) and that (ii) total precipitation (1170 mm) and the amount of leachate (820 L m-2) in the lysimeter study were distinct higher than modelled in the Hamburg scenario (average precipitation 650 mm, average amount of leachate 183 L m-2), it seems evident that the modelling overpredicts the leaching behaviour of IN-KQ960 or, more likely, modelling input data for INKQ960 are too conservative.

Concluding, the RMS does not expect IN-KQ960 to exceed 0.1 µg/L in shallow groundwater even under more vulnerable conditions.

Furthermore the *PRAPeR 32* decision was agreed under the assumption that the adsorption is lineal since the Kfoc was determined only at one concentration, but for metabolites IN-U3402 and IN-KQ960 due to technical problems in the OECD 106 study no Kfoc nor 1/n reliable values were determined and Koc value was determined using the HPLC method according to OECD 121 guidance. Besides, the IN-KQ960 Koc value from OECD 121 is practically the same than the Koc value calculated by the RMS from water/sediment study, so at 2 different concentrations. Therefore, according to the Generic Guidance for Tier 1 FOCUS Ground Water Assessments v2.2 May 2014:

"….When there is no data, a default value of 0.9 should be used. If a linear relation for sorption has been determined the value may be set to 1[2]."

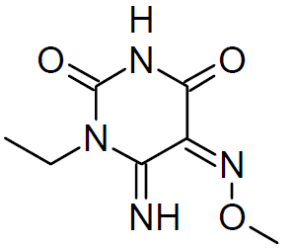
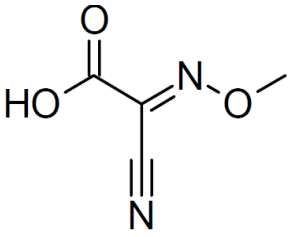
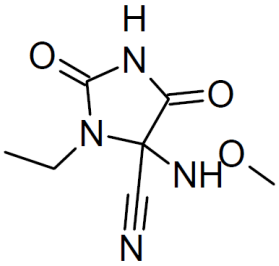
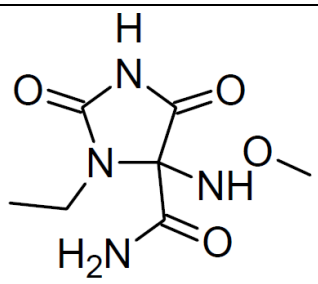
"[2] The origin of the last sentence in this paragraph is the FOCUS Surface Water Scenarios workgroup report. Applicants should be aware that with the aim of harmonising regulatory exposure assessments, Member State fate and behaviour experts from the competent authorities have agreed the following as a practical way of applying." If a linear relation for sorption has been determined the value may be set to 1". They have interpreted this sentence to mean that where an applicant has chosen to carry out a batch adsorption experiment investigating only a single concentration (i.e. just screening experiments in the OECD 106 test guideline), that the applicant has started with the assumption (i.e. text from section 2.4.3 "has determined") that a linear relation for sorption in that soil is reasonable, so a 1/n of 1 should be ascribed for that soil. In the situation where the available experiments investigated the relationship between soil solution concentration and sorption, but it was not possible to determine a reliable 1/n value, (i.e. text from section 2.4.3 "where there is no data") the default value of 0.9 has been ascribed to the pertinent soils."

Therefore, the 1/n value of 1 is not justifiable for metabolite IN-U3402 nor for metabolite IN-KQ960, and the results were that the concentration of IN-KQ960 was below 0.1 µg/L.

Regarding the human health toxicity studies on metabolites, there are only available for IN-U3204 and it was shown to be of low acute oral toxicity and was present in rat metabolism studies (minor amount), concluding that is not to be classified according to EC Council Directive 67/548/EEC nor to CLP Regulation. I relation to the aquatic toxicity all metabolites are less toxic than the parent with the exception of metabolite IN-KQ960 that is more toxic than the parent for aquatic invertebrates only.

According to the EFSA conclusions and our own calculations, the potential for groundwater of Cymoxanil metabolites above the parametric drinking water limit of 0.1 µg/L, was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios, thus the assessment of the relevance of these metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 –rev.10 is not required.

Table 10.1-1: General information on the metabolites

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
Cymoxanil	IN-U3204		Max PEC_{gw} Based on:	<0.001 PELMO and PEARL/potatoes all scenarios
Cymoxanil	IN-W3595		Max PEC_{gw} Based on:	<0.001 PELMO and PEARL/potatoes all scenarios
Cymoxanil	IN-JX915		Max PEC_{gw} Based on:	<0.001 PELMO and PEARL/potatoes all scenarios
Cymoxanil	IN-KQ960		Max PEC_{gw} Based on:	<0.01 PELMO and PEARL/potatoes all scenarios

10.2 Relevance assessment of U3204

10.2.1 STEP 1: Exclusion of degradation products of no concern

Not required. Not relevant.

10.2.2 STEP 2: Quantification of potential groundwater contamination

Not required. Not relevant.

10.2.3 STEP 3: Hazard assessment – identification of relevant metabolites

Not required. Not relevant.

10.2.3.1 STEP 3, Stage 1: screening for biological activity

Not required. Not relevant.

10.2.3.2 STEP 3, Stage 2: screening for genotoxicity

Not required. Not relevant.

10.2.3.3 STEP 3, Stage 3: screening for toxicity

Not required. Not relevant.

10.2.4 STEP 4: Exposure assessment – threshold of concern approach

Not required. Not relevant.

10.2.5 STEP 5: Refined risk assessment

Not required. Not relevant.

10.3 Relevance assessment of IN-W3595

Not required. Not relevant.

10.3.1 STEP 1: Exclusion of degradation products of no concern

Not required. Not relevant.

10.3.2 STEP 2: Quantification of potential groundwater contamination

Not required. Not relevant.

10.3.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.3.3.1 STEP 3, Stage 1: screening for biological activity

Not required. Not relevant.

10.3.3.2 STEP 3, Stage 2: screening for genotoxicity

Not required. Not relevant.

10.3.3.3 STEP 3, Stage 3: screening for toxicity

Not required. Not relevant.

10.3.4 STEP 4: Exposure assessment – threshold of concern approach

Not required. Not relevant.

10.3.5 STEP 5: Refined risk assessment

Not required. Not relevant.

10.4 Relevance assessment of IN-JX915

Not required. Not relevant.

10.4.1 STEP 1: Exclusion of degradation products of no concern

Not required. Not relevant.

10.4.2 STEP 2: Quantification of potential groundwater contamination

Not required. Not relevant.

10.4.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.4.3.1 STEP 3, Stage 1: screening for biological activity

Not required. Not relevant.

10.4.3.2 STEP 3, Stage 2: screening for genotoxicity

Not required. Not relevant.

10.4.3.3 STEP 3, Stage 3: screening for toxicity

Not required. Not relevant.

10.4.4 STEP 4: Exposure assessment – threshold of concern approach

Not required. Not relevant.

10.4.5 STEP 5: Refined risk assessment

Not required. Not relevant

10.5 Relevance assessment of IN-KQ960

Not required. Not relevant.

10.5.1 STEP 1: Exclusion of degradation products of no concern

Not required. Not relevant.

10.5.2 STEP 2: Quantification of potential groundwater contamination

Not required. Not relevant.

10.5.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.5.3.1 STEP 3, Stage 1: screening for biological activity

Not required. Not relevant.

10.5.3.2 STEP 3, Stage 2: screening for genotoxicity

Not required. Not relevant.

10.5.3.3 STEP 3, Stage 3: screening for toxicity

Not required. Not relevant.

10.5.4 STEP 4: Exposure assessment – threshold of concern approach

Not required. Not relevant.

10.5.5 STEP 5: Refined risk assessment

Not required. Not relevant

ACCEPTED

Comment:

cymoxanil

The relevance of the groundwater metabolite IN-K960 has already been assessed and the assessment agreed at EU level (see Final addendum to DAR of Cymoxanil, July-September 2008).

IN-KQ960 is not considered relevant has RMS does not expect IN-KQ960 to exceed 0.1 µg/l in shallow groundwater even under more vulnerable conditions (*EFSA Scientific Report* (2008) 167, 1-116 Conclusion on the peer review of cymoxanil)

Propamocarb

Propamocarb doesn't produce metabolites in soil and the Cymoxanil metabolites IN-U3204, IN-W3595, IN-JX915 and IN-KQ960 are predicted to occur in groundwater at concentrations below 0.1 µg/L

Appendix 1 Lists of data considered in support of the evaluation

Tables considered not relevant can be deleted as appropriate.

MS to blacken authors of vertebrate studies in the version made available to third parties/public.

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

The following tables are to be completed by MS

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

List of data relied on not submitted by the applicant but necessary for evaluation

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner

Appendix 2 Additional information

Comments of zRMS:	Comment on statement; acceptable or not.