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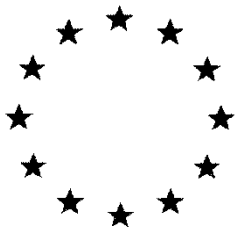

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Napropamide-M

Volume 3 – B.9 (PPP) – D-Devrinol

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B.9. ECOTOXICOLOGY DATA AND ASSESSMENT OF RISKS FOR NON-TARGET SPECIES

Napropamide-M is a herbicide proposed for use in controlling broad-leaved and grass weeds in a range of annual and perennial crops. It is the resolved single isomer version of racemic Napropamide which has been established on the market in plant protection products for a number of years. As such, Napropamide-M is considered a new substance. The applicant has submitted studies that were submitted to support the Annex I inclusion of the the racemic mixture; these have been accepted by the RMS and have not been re-evaluated. Napropamide-M is formulated as a soluable concentrate product 'D-Devrinol 450 SC' containing 450 g Napropamide-M/L.

'D-Devrinol 450 SC' is to be applied pre-sowing (summer-autumn) and pre-planting/ sowing (spring-summer) at a maximum individual rate of 765 g a.s./ha for one application. Applications to winter oilseed rape and brassica vegetable crops are to be made via ground spray and incorporation.

Table B.9-1 Maximum intended use rates for Napropamide-M in the product D-Devrinol 450 SC in Europe (all zones)

Crop group	Application rate (g a.s./ha)	Number of applications	Application type	Application timing
Winter oilseed rape	765	1	Ground spray ± incorporation	Pre-sowing summer-autumn
Brassicas vegetable crop	765	1	Ground spray ± incorporation	Pre-planting / sowing spring-summer

Table B.9-2: Ecotoxicologically identified metabolites

Compartments of relevance	Substance
Soil	None identified
Surface water	Naphthalen-1-ol [1-Naphthol] N, N-diethyl-2-(4-hydroxy-1-naphthyl) propanamide [napropamide isomer I] N, N-diethyl-2-(1-hydroxy-2-naphthyl) propanamide [napropamide isomer II]
Sediment	None identified
Ground water	None identified

B.9.1. EFFECTS ON BIRDS AND OTHER TERRESTRIAL VERTEBRATES

B.9.1.1. Effects on birds

Table B.9.1.1: Critical endpoints used for the risk assessment for birds arising from exposure to Napropamide-M

Experimental endpoint	Test substance	Species	Proposed endpoint
Acute toxicity	Napropamide-M	Bobwhite quail (*Colinus virginianus*)	LD_{50} > 2000 mg a.s./Kg-bw
Reproductive toxicity	Napropamide	Bobwhite quail	NOEL 309 mg a.s./kg bw day

(long-term)		(*Colinus virginianus*)	

The acute toxicity of Napropamide-M was assessed with the Japanese quail ([redacted] 2013), Volume 3 – B9 (AS), section B.9.1.1. No effects were reported at the highest dose tested and therefore the LD_{50} was estimated to be >2000 mg a.s/kg bw.

A comparable endpoint was listed for Napropamide technical (EFSA Journal 2010; 8(4):1565) of LD_{50} >2250 mg a.s/kg bw (Volume B.9)therefore both Napropamide and Napropamide-M are considered to have an equivalent acute toxicity to birds. As a result reproductive toxicity studies with Napropamide-M were not conducted and instead available studies with Napropamide were used to meet the data requirement.

In the EFSA conclusion of Napropamide (EFSA Journal 2010; 8(4):1565) the reproductive toxicity of Napropamide to the mallard duck and bobwhite quail were assessed and the NOAEL values were determined to be 392 mg a.s/kg bw day and 309 mg a.s/kg bw day respectively. The lower endpoint of 309 mg a.s/kg bw ([redacted] 1991) was applied to the reproductive risk assessment of Napropamide-M to provide a protective assessment.

It is noted that in the acute study conducted with Napropamide-M a possible treatment effect was observed for food consumption and body weight (Section B.9 (AS), point B.9.1.1), this was not the case for the study with Napropamide (Volume B.9), this discrepancy does raise some concerns regarding the extrapolation of data to Napropamide-M from Napropamide. However any effect was relatively slight and absent at the end of the study, additionally high variability between individuals could explain the results seen in the study with Napropamide-M. It is also noted that Napropamide-M is structurally similar to Napropamide (Vol.4) therefore a direct comparison between the two is plausible. With the above points considered, the extrapolation of data to Napropamide-M from Napropamide is acceptable.

B.9.1.2. Effects on terrestrial vertebrates other than birds

Table B.9.1.2: Critical endpoints used in the risk assessment for mammals arising from exposure to Napropamide-M

Study type	Test substance	Species	Proposed endpoint
Acute toxicity	Napropamide	Rat	LD_{50} >2000 mg a.s./kg bw
Long-term toxicity (Three generation study)	Napropamide	Rat	NOAEL 30.0 mg a.s./kg bw day

An acute oral toxicity study for Napropamide-M, on rats has been conducted. No significant effects were reported at the test dose and so the LD_{50} was estimated to be >2000 mg a.s/kg bw (Volume 3 – B6, AS).

In the interests of minimising vertebrate testing the reproductive toxicity of napropamide-M was assessed using data from a study available for Napropamide with a reported NOAEL of 30 mg a.s/kg bw (Volume 3 B.9). The RMS mammalian toxicology evaluator has confirmed the acceptability of the read across from Napropamide and the use of the chonic endpoint from this study (Volume 3 – B6 (AS).

B.9.2. RISK ASSESSMENT FOR BIRDS AND OTHER TERRESTRIAL VERTEBRATES

B.9.2.1. Effects on birds

Screening step

Exposure of birds will be predominantly dietary through the consumption of residues on food items. Direct exposure of birds to D-Devrinol 450 SC applications is considered unlikely.

Exposure to birds is calculated according to the EFSA Guidance 'Document on Risk Assessment for Birds and Mammals (2009)'. As D-Devrinol 450 SC is applied to bare soil, the exposure to birds will be the same for each of the intended uses (Winter oilseed rape and brassicas). The risk assessment is therefore based on the maximum intended application rate of 765g a.s/ha and is protective of each of the intended uses.

The screening step crop grouping and critical use pattern relevant to the uses of D-Devrinol 450 SC are given in the table below.

Table B.9.2.1-1 Screening step crop groupings and critical use patterns relevant to the use of D-Devrinol 450 SC

Crop group	Critical GAP crop	Indicator species	Critical use pattern		
			Rate (kg a.s./ha)	No. of apps	App. Interval
Bare soil	Winter oilseed rape/Brassicas	Small granivorous bird	0.765	1	-

Acute assessment

The acute 'daily dietary dose' (DDD) is calculated by multiplying the shortcut value (SV) based on the 90th percentile residues by the application rate in kg as/ha. The multiple application factor is not applicable in this case as there is only one application for the intended use.

DDD = application rate (kg as/ha) x SV x MAF

The daily dietary dose for acute exposure to Napropamide-M following the maximum intended application rate of D-Devrinol 450 SC is given in the table below.

Table B.9.2.1-2 Screening step – estimates of acute exposure to Napropamide-M

Crop group	Indicator species	Shortcut value	App. rate (kg a.s./ha)	No. of apps	DDD (mg a.s./kg bw/ day)
Bare soil	Small granivorous bird	24.7	0.765	1	19.0

The acute risk is assessed by comparing the DDD (Table B.9.2.1-3) with the acute LD_{50} endpoint (Table B.9.2.1-1) to give an acute Toxicity: Exposure Ratio (TER_A):

$$TER_A = \frac{LD_{50}\ (\text{mg/kg bw})}{\text{DDD}}$$

The resulting TER_A values are given in the table below.

Table B.9.2.1-3 Acute risk (TER_A) to birds from Napropamide-M

Test substance	Indicator species	App. rate (kg a.s./ha)	DDD (mg a.s./kg bw/day)	LD_{50} (mg a.s./kg bw/day)	TER_A	Trigger value
Napropamide-M	Small granivorous bird	0.765	19.0	>2000	105	10

The TER_A value based on the maximum intended application rate (and so all application rates) is greater than the regulatory trigger of value of 10, indicating low acute risk to birds from Napropamide-M following application of D-Devrinol 450 SC at the proposed label rates.

Short and Long-term toxicity exposure ratio (TER_{LT})

Derivation of the short-term toxicity exposure ratio is no longer a requirement according to EFSA Guidance (EFSA Journal 2009; 7(12):1438) so a short-term risk assessment is not presented.

The long-term risk assessment is provided below:

The long-term 'daily dietary dose' (DDD) is calculated by multiplying the Shortcut Value (SV) based on the mean residues by the application rate in kg as/ha.

DDD = application rate (kg as/ha) x SV x f_{twa}

The f_{twa} based upon a default DT_{50} of 10 days is 0.53, as given in the EFSA Guidance Document (EFSA Journal 2009; 7(12):1438).

The generic indicator species that is relevant for the proposed worst case use has been used to calculate the long-term DDD values as shown in the table below.

Table B.9.2.1-4 Screening step – estimates of long-term exposure to Napropamide-M

Crop group	Indicator species	Shortcut value	App. rate (kg a.s./ha)	No. of apps	f_{twa}	DDD (mg a.s./kg bw/ day)
Bare soil	Small granivorous bird	11.4	0.765	1	0.53	4.62

Long-term risk is assessed by comparing the long-term DDD with the worst case NOAEL from the reproduction studies, expressed as daily dietary dose, to give a long-term toxicity:exposure ratio (TER_{LT}):

$$TER_{LT} = \frac{NOEL\,(\text{mg/kg bw/day})}{\text{DDD}\,(\text{mg/kg bw/day})}$$

EFSA Guidance (EFSA Journal 2009; 7(12):1438) states that the acute LD_{50}/10 should be used as an endpoint in long-term risk assessment where it is lower than the NOAEL.

For Napropamide-M the lowest acute of LD_{50} >2000 mg a.s/kg bw divided by 10 (200 mg a.s/kg bw) is lower than the lowest NOAEL of 309 mg a.s/kg bw/day from the reproductive studies. Therefore this value is used in calculation of the long-term TER values to provide a conservative assessment.

Table B.9.2.1-5 Long-term risk (TER_{LT}) to birds from Napropamide-M

Test substance	Indicator species	App. rate (kg a.s./ha)	DDD (mg a.s./kg bw/day)	LD_{50}/10 (mg a.s./kg bw/day)	TER_{LT}	Trigger value
Napropamide-M	Small granivorous bird	0.765	4.62	200[a]	43	5

[a] Based on acute endpoint of 2000 mg a.s/kg bw/day /10

The TER_{LT} value exceeds the regulatory trigger value of 5, indicating that the chronic risk to birds is acceptable. This assessment is considered to be protective as it is based on the worst case toxicity endpoint of the acute LD_{50}/10. Using the lowest NOAEL of 309 mg a.s./kg bw/day obtained from the reproductive studies would result in a larger margin of safety.

Risks for birds through drinking water

The EFSA guidance document (2009) requires that the risk to birds from consumption of contaminated drinking water is assessed for the leaf scenario (acute) and puddle scenario (acute and chronic) under certain circumstances. According to the EFSA guidance (2009) the leaf scenario is only relevant for certain crop types and growth stages. These are:

- Leafy vegetables (forming heads) at principle growth stage 4 until harvest;

- Other leafy vegetables at principle growth stage 4 or later with a morphology that facilitates collection of rain/irrigation water in reservoirs that are large enough and easily accessible to attract birds and sufficiently stable over some hours.

Given that the proposed use of Napropamide-M is application to bare soil, only the puddle scenario is considered to be relevant.

Puddle scenario

This is relevant for birds taking water from puddles formed on the soil surface of a field when a (heavy) rainfall event follows the application of a pesticide to a crop or bare soil. This is therefore relevant for all uses of D-Devrinol 450 SC and should be assessed.

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary since the ratio of effective application rate (in g/ha) to acute and long-term endpoint (in mg/kg bw/d) does not exceed 50 (in the case of sorptive substances Koc < 500 L/kg), as specified in EFSA Guidance Document (ref. 5.5, Step 2b).

Table B.9.2.1-6 Ratios of effective application rate (AR_{eff}) to acute and long-term endpoints for Napropamide-M following the use of D-Devrinol 450 SC - puddle scenario

Compound	Koc	AR_{eff} (g/ha)[a]	Acute LD_{50} (mg/kg bw)	Ratio of AR_{eff} / LD_{50}	Long-term NOAEL (mg/kg bw/d)	Ratio of AR_{eff} / NOAEL	Ratio trigger
Napropamide-M	313.09	765	>2000	0.38	309	2.5	50

[a]AR_{eff} = max single application rate as D-Devrinol 450 SC is applied only once per season and a MAF does not need to be considered

The resulting ratios fall below the regulatory trigger value of 50 indicating that further assessment of the acute and long-term risk to birds from drinking water from puddles is not required for Napropamide-M.

Assessment of risk from metabolites formed in potential food items

The table below summarises the plant metabolites identified during residue trials on brassicas, tomatoes and potatoes (section B.7.2.1 Metabolism in plants, Volume CA B.7). No residues in fish were available. These residues were then compared with residues from the hen metabolism study (see section B.7.2.2 Metabolism in poultry, Volume CA B.7) the goat metabolism study (see section B.7.2.3 Metabolism in lactating undulates, Volume CA B.7) and the rat metabolic study (see section B.6.1.1, Volume 3 CA B.6).

Table B.9.2.1-7 Comparison of the occurrence of metabolite residues in plants, mammals and birds, resulting from exposure to napropamide and napropamide-M

Substance	Max % in hen metabolism	Max % in rat or goat metabolism	Max % in plant metabolism
5-hydroxynapropamide	-	-	6.7 (whole cabbage)
Naphthoxypropionamide	-	1.93 (rat urine)	0.2 (whole cabbage)
Desethylnapropamide	4.1 (egg yolk)	0.3% (liver)	2.5 (cabbage heart)
5-hydroxydesethylnapropamide	-	-	4.5 (tomato)
O-phthalic acid	-	-	6.1 (tomato)
1,4- Naphthoxyquinone	-	1.31 (rat urine)	4.9 (whole cabbage)
Naphthoxypropionic acid	-	-	3.0 (cabbage heart)

5-hydroxynaphthoxypropionic acid	-	-	4.2 (tomato)
4-hydroxynapropamide	-	-	0.6 (tomato)
Naphthoxypropionic acid	13.7 (liver)	1.42 (rat urine)	3.0 (cabbage heart)
4-hydroxynaphtoxypropionic acid	-	-	1.2 (tomato)
1-naphthol	-	-	< 0.01 (potatoes)

Many of the metabolites identified in plant tissues, have not been identified in mammalian or avian metabolism studies. However, as napropamide-M is to be applied to pre-emergence and incorporated into the soil, the RMS considers the plant metabolites identified above are not relevant. It is noted that while application is pre-emergence, given the systemic properites of Napropamide-M, uptake into seedlings and residues in weeds could occur. However in the soil, Napropamide-M is quickly degraded to carbon dioxide (see section B.7.2.1, Metabolism in plants, Volume 3 CA B-7), and no relevant soil metabolites have been identified in the Environmental fate section (see section B.8.1, Fate and behaviour in soil, Volume 3 CA B-8). Therefore, the RMS considers that the risk from plant metabolites to mammals and birds is acceptable, based on negligible exposure.

Bioaccumulation and food chain transfer risk assessment

According to EFSA Guidance (2009) substances with a log K_{ow} greater than 3 have potential for bioaccumulation and should be assessed for the risk of biomagnification in terrestrial food chains. Napropamide-M has a log P_{OW} value of 3.27 (section B.2.7, partition coefficient N-octanol/water, Volume CA B.2) therefore, the risk from secondary poisoning to worm-eating birds and fish-eating birds has been carried out and is presented below.

Risk to earthworm-eating birds

A simple worst-case assessment of the risk to earthworm-eating birds, e.g. a 100 g blackbird (*Turdus merula*), is conducted using the following equation:

$$TER = \frac{NOEL\,(mg/kg\ bw/day)}{PEC_{worm}\,(mg/kg) \times 1.05}$$

Where:
PEC_{worm} = 21 d time-weighted average PEC_{soil} × BCF
$BCF = C_{worm}/C_{soil} = (0.84 + 0.012\ Kow)\ /(foc \times Koc)$
K_{OW} = Octanol water partition coefficient
K_{OC} = Organic carbon adsorption coefficient
f_{OC} = Organic carbon content of soil (0.02 taken as a default value)
1.05 is a constant used to convert the PEC_{worm} to a daily dose and is based on a 100g bird eating 104.6 g of worms per day (Smit 2005[1]).
To consider the worst case scenario the accumulation PEC_{soil} value of 1.5979 mg/kg soil was used to assess the risk from secondary poisoning to birds via earthworms. For details of soil PEC calculations, see section B.8.1, Fate and behaviour in soil, Volume 3 CA B-8.
The resulting TER values are given in the table below

Table B.9.2.1-8 Long-term risk from secondary poisoning to earthworm-eating birds from Napropamide-M

Crop	Accumulation PEC	Kow	Foc	Koc	BCF	PEC_{worm} (mg/kg)	DDD (mg/kg	$LD_{50}/10$ (mg/kg	TER_{worm}

[1] Smit CE (2005). Energy and moisture content and assimilation efficiency of bird and mammal food. RIVM report 601516013, 99. 55-71

	(mg a.s./kg)						bw/d)	bw/d)	
Winter oilseed rape/leafy vegetables	1.5979	1887.22	0.02	313.09	3.75	5.4	5.67	200	35.2

The TER is greater than the regulatory trigger value of 5 indicating low risk to birds feeding on earthworms.

Risk to fish-eating birds

A simple worst-case assessment of the risk to fish-eating birds is conducted using the following equation:

TER = long-term NOAEL/ (PEC_{fish} x 0.159)

Where: $PEC_{fish} = PEC_{water} * BCF_{(whole\ body)}$

The multiplicator 0.159 is based on a 1000-g bird eating 159 g per day (Smit, 2005), and converts the PEC_{fish} to a daily dietary dose (DDD).

To provide a conservative and protective assessment, the maximum initial FOCUS Step 3 PECsw value of 23.40 µg a.s/L resulting from application to winter oilseed rape (worst case) was used. For details of the PEC calculations refer to see section B.8.1, Fate and behaviour in soil, Volume 3 CA B-8.

The resulting TER values are given in the table below:

Table B.9.2.1-9 Napropamide-M – long-term risk from secondary poisoning to fish-eating birds

Crop	PEC_{water} Maximum initial FOCUS Step 3 PECsw (mg/L)	BCF	PEC_{fish} (mg/kg)	DDD (mg/kg/bw/day)	LD_{50}/10 (mg/kg bw/d)	TER_{fish}
Winter oilseed rape	0.0234	98	2.29	0.365	200	547.9

Based on the maximum initial PEC_{SW} at FOCUS Step 3 the TER value exceeds the regulatory trigger of 5 indicating acceptable risk for fish eating birds.

It is noted that the BCF of 98 used in the table above is derived from a study with Napropamide ([redacted] 1995), this is considered acceptable because the log K_{ow} of Napropamide-M (=3.27) and Napropamide (=3.3) are comparable and Napropamide-M is structurally similar to Napropamide (B.2.7, partition coefficient N-octanol/water, Volume CA B.2).

Metabolites

Risk to earthworm-eating Birds

No relevant soil metabolites have been identified in the Environmental fate section (see section B.8.1, Fate and behaviour in soil, Volume 3 CA B-8). Therefore an assessment of the risk to earthworm eating birds is not required.

Risk to fish-eating Birds

The surface water metabolites identified by Environmental Fate (section B.8.2.1, Fate and behaviour in soil, Volume 3 CA B-8) are summarised below.

Table B.9.2.1-10 relevant surface water metabolites and log K

Surface water metabolite	Log K_{ow}
Naphthalen-1-ol	2.83

N, N-diethyl-2-(4-hydroxy-1-naphthyl) propanamide [napropamide isomer I]	3.08
N, N-diethyl-2-(1-hydroxy-2-naphthyl) propanamide [napropamide isomer II]	2.52

According to EFSA Guidance (2009) substances with a log K_{ow} greater than 3 have the potential for bioaccumulation and should be assessed for the risk of secondary poisoning. Napropamide isomer I has a log P_{OW} of 3.08 therefore further consideration of the risk is required. Naphthalen-1-ol and Napropamide isomer II have log K_{ow} values of 2.83 and 2.52 respectively which are below the trigger value of 3, however with reference to section B.2.7, partition coefficient N-octanol/water, Volume CA B.2, the experimental determination for Napropamide isomer II cannot be relied upon therefore further consideration of the risk is also required.

As toxicity data has not been provided for Napropamide isomer I or Napropamide isomer II reference is made to the active substance assessment (Table B.9.2.1-9). The LD50/10 of 200 mg/kg bw/d will be used in the risk assessment with a correction factor of 10 to account for any uncertainty. This is considered to be conservative as the log K_{ow} of Napropamide-M is 3.27 which is higher than that of both Napropamide isomer I and Napropamide isomer II. It is also noted that the BCF of 98 used in the table below is derived from a study with Napropamide (Sankey et al, 1995), this is considered acceptable because the log K_{ow} of Napropamide (=3.3). As log K_{ow} values of Napropamide isomer I (3.08) and Napropamide isomer II (2.52) are lower, this read accross is considered acceptable.

Table B.9.2.2-10 Risk from secondary poisoning to fish-eating birds for Napropamide isomer I and Napropamide isomer I

Crop	PEC_{water} Maximum initial FOCUS Step 3 PECsw (mg/L)	BCF	PEC_{fish} (mg/kg)	DDD (mg/kg/bw/day)	LD_{50}/10 (mg/kg bw/d)	TER_{fish}
Winter oilseed rape	0.0234	98	2.29	0.365	20	54.79

The TER_{fish} exceeds the regulatory trigger value of 5 indicating acceptable risk for fish eating birds from Napropamide isomer I and Napropamide isomer II. The margin of safety obtained in the risk assessment is sufficient to address any concerns about the reliability of the experimental determination for Napropamide isomer II.

B.9.2.2 Effects on terrestrial vertebrates other than birds

Screening step

The screening step crop grouping and critical use patters relevant to the uses of D-Devrinol 450 SC are given in the table below.

Table B.9.2.2-1 Screening step crop groupings and critical use patterns relevant to the use of D-Devrinol 450 SC

Crop group	Critical GAP crop	Indicator species	Critical use pattern		
			Rate (kg a.s./ha)[a]	No. of apps	App. Interval
Bare soil	Winter oilseed rape/Brassicas	Small granivorous mammal	0.765	1	-

[a] Maximum application rate. As all applications are to bare soil, this rate is protective of all intended uses.

Acute assessment

The acute 'daily dietary dose' (DDD) is calculated by multiplying the Shortcut value (SV) based on the 90th percentile residues by the application rate in kg as/ha.

DDD = application rate (kg as/ha) x SV

Daily dietary doses for acute exposure to Napropamide-M following use of D-Devrinol 450 SC according to the worst case proposed use is given in the table below.

Table B.9.2.2-2 Screening step – estimates of acute exposure to Napropamide-M

Crop group	Critical GAP crop	Indicator species	Shortcut value	App. rate (kg a.s./ha)[a]	No. of apps	DDD (mg a.s./kg bw/ day)
Bare soil	Winter oilseed rape/Brassicas	Small granivorous mammal	14.4	0.765	1	11.0

[a] Maximum application

The acute risk to mammals was assessed by calculation of toxicity exposure ratios (TER_A) according to the following equation:

$$TER_A = \frac{LD_{50}\,(mg/kg\ bw)}{DDD\,(mg/kg\ bw/d)}$$

Acute risk was calculated using the lowest acute LD_{50} values for the active substances. The results are presented below.

Table Table B.9.2.2-3 Screening step - acute risk (TER_A) to mammals

Substance	Indicator species	LD_{50} (mg/kg bw/day)	Acute DDD (mg/kg bw/day)	TER_A	Annex VI trigger
Napropamide-M	Small granivorous mammal	>2000	11.0	181	10

The TER_A value is greater than the regulatory trigger value of 10, indicating that the acute risk to mammals is acceptable according to the proposed use pattern of D-Devrinol 450 SC.

Short and Long-term toxicity exposure ratio (TER_{LT})

Derivation of the short-term toxicity exposure ratio is no longer a requirement according to EFSA Guidance (EFSA Journal 2009; 7(12):1438) so a short-term risk assessment is not presented.

The long-term risk assessment is provided below

The long-term 'daily dietary dose' (DDD) is calculated by multiplying the Shortcut value (SV) based on the mean residues by the application rate in kg as/ha.

DDD = application rate (kg as/ha) x SV x f_{twa}

The f_{twa} based upon a default DT_{50} of 10 days is 0.53, as given in the EFSA Guidance Document (EFSA Journal 2009; 7(12):1438).

The generic indicator species that is relevant for the proposed uses is considered with the worst case application rate to calculate the long-term DDD value as shown in table below.

Table B.9.2.2-4 Screening step – estimates of long-term exposure to Napropamide

Crop group	Critical GAP crop	Indicator species	Shortcut value	App. rate (kg a.s./ha)	No. of apps	f_{twa}	DDD (mg a.s./kg bw/ day)
Bare soil	Winter oilseed rape/Brassicas	Small granivorous mammal	6.6	0.765	1	0.53	2.68

The long-term risk to mammals was assessed from long-term TER values, calculated according to the following equation:

$$TER_{LT} = \frac{NOEL\,(mg/kg\ bw/day)}{Long\text{-}term\,DDD\,(mg/kg\ bw/day)}$$

The NOAEL value for Napropamide was used to calculate the TER values in order to provide a worst-case scenario. The resulting TER_{LT} values are given below.

Table B.9.2.2-5 Screening step – long-term risk (TER_{LT}) to mammals

Crop group	Critical GAP crop	Indicator species	NOAEL (mg/kg bw/day)	DDD (mg a.s./kg bw/ day)	TER_{LT}	Trigger value
Bare soil	Winter oilseed rape/Brassicas	Small granivorous mammal	30	2.68	11	5

The TER_{LT} value for the maximum intended use is greater than the regulatory trigger value of 5, indicating acceptable long-term risk to mammals.

Risk assessment to mammals through drinking water

Only the puddle scenario is relevant for risk assessment for mammals through drinking water.

Puddle scenario

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary since the ratio of effective application rate (in g/ha) to acute and long-term endpoint (in mg/kg bw/d) does not exceed 50 (in the case of more sorptive substances Koc <500 L/kg), as specified in EFSA Guidance Document (EFSA Journal 2009; 7(12):1438, ref. 5.5, Step 2b).

Table B.9.2.2-6 Ratios of effective application rate (AR_{eff}) to acute and long-term endpoints for Napropamide-M following the use of D-Devrinol - puddle scenario

Compound	Koc	AR_{eff} (g/ha)[a]	Acute LD_{50} (mg/kg bw)	Ratio of AR_{eff} / LD_{50}	Long-term NOAEL (mg/kg bw/d)	Ratio of AR_{eff} / NOAEL	Ratio trigger
Napropamide-M	313.09	765	>2000	0.38	30	26	50

[a] AR_{eff} = max single application rate as D-Devrinol is applied only once per season. MAF does not need to be considered

The resulting ratios fall below the regulatory trigger of 50 indicating that further assessment of the acute and long-term risk to birds from drinking water from puddles is not required for Napropamide-M.

Assessment of risk from metabolites formed in potential food items

The table below summarises the plant metabolites identified during residue trials on brassicas, tomatoes and potatoes (taken from section B.7.2.1 Metabolism in plants, Volume CA B.7). No residues in fish were available. These residues were then compared with residues from the hen metabolism study (see section B.7.2.2 Metabolism in poultry, Volume CA B.7) the goat metabolism

study (see section B.7.2.3 Metabolism in lactating undulates, Volume CA B.7) and the rat metabolic study (see section B.6.1.1, Volume 3 CA B.6).

Table B.9.2.2-7 Comparison of the occurrence of metabolite residues in plants, mammals and birds, resulting from exposure to napropamide and napropamide-M

Substance	Max % in hen metabolism	Max % in rat or goat metabolism	Max % in plant metabolism
5-hydroxynapropamide	-	-	6.7 (whole cabbage)
Naphthoxypropionamide	-	1.93 (rat urine)	0.2 (whole cabbage)
Desethylnapropamide	4.1 (egg yolk)	0.3% (liver)	2.5 (cabbage heart)
5-hydroxydesethylnapropamide	-	-	4.5 (tomato)
O-phthalic acid	-	-	6.1 (tomato)
1,4- Naphthoxyquinone	-	1.31 (rat urine)	4.9 (whole cabbage)
Naphthoxypropionic acid	-	-	3.0 (cabbage heart)
5-hydroxynaphthoxypropionic acid	-	-	4.2 (tomato)
4-hydroxynapropamide	-	-	0.6 (tomato)
Naphthoxypropionic acid	13.7 (liver)	1.42 (rat urine)	3.0 (cabbage heart)
4-hydroxynaphtoxypropionic acid	-	-	1.2 (tomato)
1-naphthol	-	-	< 0.01 (potatoes)

Many of the metabolites identified in plant tissues, have not been identified in mammalian or avian metabolism studies. However, as napropamide-M is to be applied to pre-emergence and incorporated into the soil, the RMS considers the plant metabolites identified above are not relevant. It is noted that while application is pre-emergence, given the systemic properites of napropamide-M, uptake into seedlings and residues in weeds could occur.). However in the soil, Napropamide-M is quickly degraded to carbon dioxide (see section B.7.2.1, Metabolism in plants, Volume 3 CA B-7), and no relevant soil metabolites have been identified in the Environmental fate section (see section B.8.1, Fate and behaviour in soil, Volume 3 CA B-8). Therefore, the RMS considers that the risk from plant metabolites to mammals and birds is acceptable, based on negligible exposure.

Effects of secondary poisoning

Bioaccumulation and food chain transfer risk assessment

According to EFSA Guidance (2009)[2] substances with a log K_{ow} greater than 3 have potential for bioaccumulation and should be assessed for the risk of secondary poisoning. Napropamide-M has a log P_{OW} of 3.27. Therefore risk assessments have been performed and are presented below

Risk to earthworm-eating mammals

The following equation was used to assess the potential risk to wild mammals feeding on earthworms containing residues.

$$TER = \frac{NOEL\,(mg/kg)}{PEC_{worm}\,(mg/kg)^{(1)} \times 1.28}$$

Where:
PEC_{worm} = 21 d time-weighted average PEC_{soil} × BCF

[2]European Food Safety Authority; Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA. EFSA journal 2009; 7(12):1438. [139 pp.]

$BCF = C_{worm}/C_{soil} = (0.84 + 0.012\ K_{ow}) / f_{oc} \times K_{oc}$
K_{ow} = Octanol water partition coefficient
K_{oc} = Organic carbon adsorption coefficient
f_{oc} = Organic carbon content of soil (0.02 taken as a default value)

The conversion factor of 1.28 is a constant used to convert the PECworm to a daily dose and is based on a 10g mammal eating 12.8 g of worms per day (*Smit 2005*[3]).

In order to consider the worst case scenario the accumulation PEC_{soil} value of 1.5979 mg/kg soil was used to assess the risk from secondary poisoning to mammals via earthworms. The resulting TER value of 4.3 did not meet the long-term trigger value of 5 therefore the risk assessment was refined by using the initial PEC_{soil} value of 1.02 mg a.s./kg (Volume 3 B.8). The resulting TER value is given in the table below:

Table B.9.2.2-8 Risk from secondary poisoning to earthworm-eating mammals

Crop	PEC_{soil} 21-d twa (mg a.s./kg)	K_{ow}	f_{oc}	Koc	BCF	PEC_{worm} (mg/kg)	DDD (mg a.s./kg bw/d)	NOAEL (mg a.s./kg bw/d)	TER_{worm}
Bare soil	1.02	1887	0.02	313	3.75	3.83	4.9	30	6.1

TERs shown in bold fall below the relevant trigger

The resulting TER value exceeds the regulatory long-term trigger value of 5 and so indicates acceptable risk of secondary poisoning to earthworm-eating mammals. This is considered acceptable as the worst case values have also been used for the Kow (Octanol water partition coefficient) and the Koc (Organic carbon adsorption coefficient) parameters.

Risk to fish-eating mammals

A simple worst-case assessment of the risk to fish-eating mammals is conducted using the following equation:

TER = long-term NOAEL / (PEC_{fish} x 0.142)

Where: $PEC_{fish} = PEC_{water} \times BCF_{(whole\ body)}$

The multiplicator 0.142 is based on a 3000 g mammal eating 425 g per fish day (Smit, 2005), and converts the PEC_{fish} to a daily dose.

To provide a conservative and protective assessment, the maximum initial FOCUS Step 3 PECsw value of 23.40 µg a.s/L. For details of the PEC calculations refer to Volume 3 B.8. It is noted that the BCF or 98 used in the table above is derived from a study with Napropamide (Voulme 3 B.9, section B.9.2.12.3), this is considered acceptable because the logPow Napropamide-M (=3.27) and Napropamide (=3.3) are comparable and Napropamide-M is structurally similar to Napropamide (B.2.7, partition coefficient N-octanol/water, Volume CA B.2).

The resulting TER values are given in the table below:

Table B.9.2.2-9 Risk from secondary poisoning to fish-eating mammals

Crop	PEC_{water} Maximum initial PECsw (mg/L)	BCF	PEC_{fish} (mg/kg)	DDD (mg/kg/bw/day)	Long-term NOAEL (mg/kg bw/day)	TER_{fish}
Bare soil	0.023	98	2.25	0.32	30	93.73

[3] Smit CE (2005). Energy and moisture content and assimilation efficiency of bird and mammal food. RIVM report 601516013, 99. 55-71

The TER value exceeds the regulatory trigger value of 5 indicating acceptable risk for fish eating mammals.

Metabolites

Risk to earthworm-eating mammals

No relevant soil metabolites have been identified in the Environmental fate section (see section B.8.1, Fate and behaviour in soil, Volume 3 CA B-8). Therefore an assessment of the risk to earthworm eating birds is not required.

Risk to fish-eating mammals

The surface water metabolites identified by Environmental Fate (see section B.8.2.1, Fate and behaviour in soil, Volume 3 CA B-8) are summarised below.

Table B.9.2.2-10 relevant surface water metabolites and log K

Surface water metabolite	Log K_{ow}
Naphthalen-1-ol	2.83
N, N-diethyl-2-(4-hydroxy-1-naphthyl) propanamide [napropamide isomer I]	3.08
N, N-diethyl-2-(1-hydroxy-2-naphthyl) propanamide [napropamide isomer II]	2.52

According to EFSA Guidance (2009) substances with a log K_{ow} greater than 3 have the potential for bioaccumulation and should be assessed for the risk of secondary poisoning. Napropamide isomer I has a log P_{OW} of 3.08 therefore further consideration of the risk is required. Naphthalen-1-ol and Napropamide isomer II have log K_{ow} values of 2.83 and 2.52 respectively which are below the trigger value of 3, however with reference to section B.2.7, partition coefficient N-octanol/water, Volume CA B.2, the experimental determination for Napropamide isomer II cannot be relied upon therefore further consideration of the risk is also required.

As toxicity data has not been provided for Napropamide isomer I or Napropamide isomer II reference is made to the active substance assessment (Table B.9.2.1-9). The LD50/10 of 200 mg/kg bw/d will be used in the risk assessment with a correction factor of 10 to account for any uncertainty. This is considered to be conservative as the log K_{ow} of Napropamide-M is 3.27 which is higher than that of both Napropamide isomer I and Napropamide isomer II. It is also noted that the BCF of 98 used in the table below is derived from a study with Napropamide (Sankey et al, 1995), this is considered acceptable because the log K_{ow} of Napropamide (=3.3). As log K_{ow} values of Napropamide isomer I (3.08) and Napropamide isomer II (2.52) are lower, this read accross is considered acceptable.

Table B.9.2.2-11 Risk from secondary poisoning to fish-eating mammals from Napropamide isomer I and Napropamide isomer I

Crop	PEC_{water} Maximum initial PECsw (mg/L)	BCF	PEC_{fish} (mg/kg)	DDD (mg/kg/bw/day)	Long-term NOAEL (mg/kg bw/day)	TER_{fish}
Bare soil	0.023	98	2.25	0.32	3	9.375

The TER_{fish} exceeds the regulatory trigger value of 5 indicating acceptable risk for fish eating mammals from Napropamide isomer I and Napropamide isomer II. The margin of safety obtained in the risk assessment is sufficient to address any concerns about the reliability of the experimental determination for Napropamide isomer II.

Higher tier data on mammals

No higher tier data on mammals is required as the risk assessment presented above indicates an acceptable risk from the supported uses of D-Devrinol 450 SC.

Assessment of risk from metabolites formed in potential food items

The majority of plant metabolites can also be found in animals as intermediates. The metabolites observed in plant tissues were arranged in three metabolic chains, all three (and an additional fourth) being found in animal metabolism as well (details see avian risk assessment). Thus, the toxicity of all except three of the metabolites identified in the plant metabolism studies have already been assessed during animal metabolism studies of Napropamide itself. The only metabolites not recorded in the rat but recorded in plants were NQ (2-hydroxy-1,4-naphthoquinone) (t*, c, p), PA (o-phthalic acid) (t, c), and 1-Naphtol (p). They were present in very small amounts in crops (≤0.003 mg/kg) and are not considered of toxicological relevance, particularly considering the long-term NOAEL of 30 mg/kg bw /day that was determined for the parent, Napropamide.

Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)

There is no relevant scientifically peer-reviewed open literature on the effects of Napropamide-M or its major metabolites on amphibian and reptile species. In addition, there is currently no guidance addressing terrestrial life stages of amphibians and reptiles in ecotoxicological risk assessments. Therefore, the risk assessment provided above for birds and mammals is considered to be protective of terrestrial amphibian and reptile species.

Acute oral toxicity

In accordance with Commission Regulation 284/2013 an acute toxicity study with the product is not necessary when toxicity can be predicted from the active substance. D-Devrinol 450 SC contains only one active substance, Napropamide-M and the toxicity of the product is considered to result entirely from the active substance. It is therefore considered relevant to assess the acute toxicity of D-Devrinol 450 SC on the toxicity of Napropamide-M alone.

B.9.3. EFFECTS ON AQUATIC ORGANISMS

B.9.3.1. Studies to determine the toxicity of D-Devrinol 450 SC to fish, *Daphnia magna*, algae and *Lemna gibba* were conducted. The study summaries are provided below

B.9.3.1. Acute toxicity to fish

[redacted] (2011b) D-Devrinol 450 SC: Acute toxicity to Rainbow Trout (Oncorhynchus mykiss) in a 96-hour test. [redacted], Unpublished report No.: D03572

Guidelines

Directive 92/69/EEC, C.1; OECD 203 (1992), USA EPA OPPTS 850.1075

GLP

Yes (certified laboratory)

Materials and Methods

Test material	D-Devrinol 450 SC.
Description:	Light brown crystalline powder.
Lot/Batch #:	JM230.
Content:	D-Napropamide: 458 g/L (Purity 97.2%)
Stability of test compound:	Stable under test conditions.
Reference substance:	N/A.

Test organisms

Species:	*Oncorhynchus mykiss*
Description:	Mean body length was 5.1 ± 0.28 cm, mean body wet weight was 1.3 ± 0.15 g.
Source:	[redacted]

Experimental dates**:** 13th of December 2010 – 6th January 2011.

Test Design

The fish used for the study were reared within the laboratory. Prior to the study they were acclimatised for one week to test conditions, during holding and acclimatisation, no fish died in the test batch and all fish were healthy. Before the difinitive test 10 individuals were measured, the mean body length was 5.1±0.28 cm and mean body weight was 1.3 ±0.15 g.

To determine the sensitivity of the test system a range finding test was conductd (non GLP). As a result of this the following nominal concentrations of D-Devrinol 450 SC were tested in under a static non-renewal regime; 3.0, 6.0, 12, 24 and 48 mg/L. Additionally a control (test water without test item) was run in parallel. For the determination of the test item concentrations, duplicate samples were taken from each treatment before the start of the test and at the end of the test (after 96 hrs) and analysed by HPLC with UV/VIS detection.

The test units consisted of one glass vessel (36 cm length x 23 cm width x 26 cm height) filled with 15 litres of test water. The water temperature within the test units was maintained at 14 ºC and a 16 hr light to 8 hr dark photoperiod used (Lux 140-480). Reconstituted test water was used in the study which consisted of analytical grade salts dissolved in purified water. Fish were not fed during the exposure period.

At the start of the exposure 7 fish were introduced into each test vessel in a random order, to give a loading rate of 0.58 g fish w/w per litre. The test fish were observed for mortality and visible abnormalities after approximately 3, 24, 48, 72 and 96 hours test duration. Dead fish were removed at least once daily.

The 96 hour LC_{50} and the 95%-confidence interval at the observation dates after 72 and 96 hours were calculated by Probit Analysis. The NOEC and LOEC were determined directly from the raw data.

Results and Discussion

All of the validity criteria were met. The mortality in the control was 0%. Constant conditions were maintained throughout the test. The dissolved oxygen concentration was always above 60% of the air saturation value which corresponded to 8.6 mg/L throughout the test.

Analytical results

The measured concentrations of D-Devrinol 450 SC (based on the active substance D-Napropamide) in the test media concentrations of 12, 24 and 48 mg/L were between 109 and 112 % of the nominal values at the start of the test. At the highest concentration of 48 mg/L no further measurements were performed since all fish were dead after 3 hours. The values measured at the end of the test media of the concentrations of 12 and 24 mg/L were 90 – 97 % of the nominal respectively. The active substance was therefore considered to be stable in the test media over the exposure period of 96 hours. Therefore, the results are expressed as nominal concentrations.

Biological results

In the control and at the test concentrations up to and including 12 mg/L all fish survived until the end of the study and there were no visible abnormalities. At the next higher concentration of 24 mg/L all test fish showed abnormalities and one fish had to be sacrificed in the interests of animal welfare after

72 hours exposure. This was taken into account as a mortality for LC_{50} value calculation. At the highest concentration of 48 mg/L all fish were dead after 3 hours exposure.

Table B.9.3.1-1 Summary of effects on fish following 96 hours exposure to D-Devrinol 450 SC

Test item concentration (mg/L)	Number of dead fish				
	Observation time				
	3 hours	24 hours	48 hours	72 hours	96 hours
Control	0	0	0	0	0
3.0	0	0	0	0	0
6.0	0	0	0	0	0
12	0	0	0	0	0
24	0	0	0	1[b]	1
48	7[a]	-	-	-	-
LC_{50} (95 % C.I)	34 (24-48)	34 (24-48)	34 (24-48)	30 (23-40)	30 (23-40)

[a] All fish died at 3 hours.
[b] Test fish sacrificed for reasons of animal welfare. Counted as a mortality.
(The NOEC and LOEC were determined directly from the raw data, the LC50 using Probit Analysis)

Conclusion

The 96 hour LC_{50} was calculated to be 30 mg/L with a 95 % confidence interval of 23-40 mg/L, equivalent to 12.3 mg a.s/L .The 96 hr NOEC was determined to be 12 mg test item/L, equivalent to 4.92 mg a.s/L.

RMS Comments

The study was conducted inline with OECD guideline 203 and under GLP compliance. All validity criteria were met, The RMS considers that this study is suitable for use in the risk assessment. The LC_{50} is 30 mg product/L (equivalent to 12.3 mg a.s./L) and the NOEC is 12.0 mg product/L (equivalent to 4.92 mg a.s./L).

It is noted that the guideline suggests an acclimatisation period of at least 12 days however only a 7 day period has been implemented in the study. This is not ideal however as 0% mortality was observed during the acclimation and in the control for the definitive study this is considered acceptable. This study is suitable for use in the risk assessment.

Acute toxicity to aquatic invertebrates

A. Liedtke (2011d) D-Devrinol 450 SC: Acute toxicity to *Daphnia magna* in a 48-hour immobilization test. UPL Europe Ltd, Unpublished report No.: D03561

Guidelines

OECD guideline no. 202.

GLP

Yes (certified laboratory)

Materials and Methods

Test material D-Devrinol 450 SC.
Description: Light brown crystalline powder.
Lot/Batch #: JM230
Content: Napropamide-M 458 g/L (Purity 97.2%)
Stability of test compound: Stable under test conditions.
Reference substance: Potassium dichromate

Test animals

Species:	*Daphnia magna*
Strain:	Straus
Source:	Laboratory cultured, Harlan Laboratories Ltd. Zelgliweg 1 4452 Itingen / Switzerland.
Experimental Dates:	3rd of December 2010 – 10th of December 2010.

Test Design

The study was performed with young daphnids of the species *Daphnia magna* which were bred in the laboratory's own cultures. For the acclimation period the parental daphnids were maintained in test water for at least 48 hours prior to the start of the test, daphnids were fed with an algal suspension of *Desmodesmus subspicatus* three times a week until the test initiation. At the start of the test all daphnids were 6-24 hours old and were not the first brood progeny.

To determine the sensitivity of the test system a range finding test was conductd (non GLP). As a result of this the following nominal concentrations of D-Devrinol 450 SC were tested in under a static non-renewal regime; 4.6, 10, 22, 46 and 100 mg/L. Additionally a control (test water without test item) was run in parallel. For the determination of the test item concentrations, duplicate test media samples of the nominal concentrations of 10 to 100 mg/L from both sampling times (0 and 48 hours) were analysed using HPLC with UV/VIS detection. For evaluation of the quality of the daphnia clone and the experimental conditions, potassium dichromate was tested as a positive control twice a year.

For the test 250 mL glass beakers filled with 125 mL of test medium were used which were covered with glass plates to reduce the loss of water by evaporation. The test was performed in a controlled room with continuous monitoring of temperature. The water temperature was maintained at 20-21 ºC, a 16 hour photoperiod (Lux 520-680) was used and the pH remained in the range of 7.7 – 7.8 throughout the test, the dissolved oxygen was maintained in the range of 8.1-8.4 mg/L in the control and 8.0-8.4 mg/L in the test solutions. pH and dissolved oxygen content were measured at the beginning and end of the test. Reconstituted test water was used in the study however, to meet both the EPA- and OECD-requirements, the hardness was lowered by a factor of 1.7 of the normal hardness. During the test period, the test water was not aerated and the daphnids were not fed.

For each treatment four replicates each containig five daphnids were used. The immobility of the daphnids was determined by visual inspection after 24 and 48 hours of exposure. Those daphnids which were not able to swim within 15 seconds after gentle agitation of the test vessel were considered to be immobilised.

The 48-hour EC_{50} and the 95% confidence limits were calculated by geometric mean and Probit Analysis, respectively. The NOEC and LOEC were determined directly from the raw data.

Results and Discussion

All of the validity criteria were met. The mortality in the control was 0% and no visual signs of stress or abnormality in the test organisms was observed. The dissolved oxygen concentration was always above 8.0 mg/L of the air saturation value throughout the test which meets the criterion of > 3 mg/L.

Analytical results

The measured concentrations of D-Devrinol 450 SC (based on the active substance d-Napropamide) in the test media concentrations of 10 and 100 mg/L were between 102 and 106 % of the nominal values at the start of the test and between 103 and 107 % at the end of the test. Since the test item was shown to be stable during the study, the biological results were based on nominal concentrations.

Biological results

The result of the latest positive control test (with potassium dichromate) gave a 48-hour EC_{50} of 0.56 mg/L indicating that the sensitivity of the test organisms was within the expected range of 0.6 mg/l to 2.1 mg/l with reference to OECD guideline (202)

During the first 24 hours of the test no immobilised test organisms were determined in the control and up to test item concentration of 46 mg/L. At the concentration of 100 mg/L immobilisation was 100 %. At a test item concentration of 46 mg/L, 9 individuals exhibited visual abnormalities such as antennae and spinae which were stuck with algae.

After 48 hours of exposure no immobilised daphnids were determined at the control and up to and including test item concentration of 10 mg/L. The next higher concentration of 22 mg/L one daphnid was immobile. At the two highest concentrations of 46 mg/L and 100 m/L, 5 and 20 daphnids were observed to be immobile, at a test item concentration of 46 mg/L, 7 individuals exhibited visual abnormalities such as antennae and spinae which were stuck with algae. The results are summarised below.

Table B.9.3.1-2 Summary of effects D-Devrinol 450 SC on *Daphnia magna*

Test item concentration (mg/L)	No of daphnids tested	Immobilized daphnids after 24 hours		Immobilized daphnids after 48 hours	
		No.	%	No.	%
Control	20	0	0	0	0
4.6	20	0	0	0	0
10	20	0	0	0	0
22	20	0	0	1	5
46	20	0 (9)	0	5 (7)	25
100	20	20	100	20	100

Value in parenthesis: number of mobile test animals with adverse effects (antennae and spinae were stuck with algae).

Conclusion

The 48 hour EC_{50} was calculated to be 52 mg/L with a 95 % confidence interval of 43-63 mg /L, equivalent to 21.32 mg a.s/L. The NOEC was calculated to be 10 mg test item/L, equivalent to 4.1 mg a.s/L.

RMS Comments

The study was conducted inline with OECD guideline 202 and under GLP compliance. All validity criteria were met, The RMS considers that this study is suitable for use in the risk assessment. The EC_{50} is 52.0 mg product/L (equivalent to 21.32 mg a.s./L) and the NOEC is 10.0 mg product/L (equivalent to 4.1 mg a.s./L).

It is noted that OECD guideline (202) specifies that 'the concentration of the test substance should be measured, as a minimum, at the highest and lowest test concentration, at the beginning and end of the test' however in this study the lowest concentration of 4.6 mg/L was not analysed as this concentration was below the 48-hour NOEC determined in this test. The RMS does not accept this reasoning as it could potentially mean that the test organisms were exposed to below the stated concentration. However as the determined EC_{50} of 52 mg /L was much greater than this, it is accepted that this would not effect the outcome of the study. This study is considered suitable for use in the risk assessment.

Toxicity to algae

M. Kamle (2014) Algal (*Pseudokirchneriella subcapitata*): Growth inhibition test with D-Devrinol 450 SC (HBW03). UPL Europe Ltd, Unpublished report No.: 501-3-07-6180

Guidelines

OECD guideline no. 201.

GLP

Yes (certified laboratory)

Materials and Methods

Test material	D-Devrinol 450 SC
Description:	Cream viscous liquid.
Lot/Batch #:	JM262.
Content:	41.49% w/w napropamide-M.
Stability of test compound:	Stable under test conditions.
Reference substance:	Potassium dichromate.
Test animals	
Species:	*Pseudokirchneriella subcapitata.*
Strain:	ATCC 22662
Source:	American Type Culture Collection, 10801, University of Boulevard, Manassas, Virginia, 20110-2209, USA
Experimental dates:	9th of July 2013 – 10th of August 2013.

Test Design

The study was performed with the algae species *Pseudokirchneriella subcapitata* taken from the laboratory own cultures. The pre-culture was prepared for three days before the study initiation to allow for an adequate density of cells (approximately 5 x 10^3- 10^4/mL).

The difinitive test was conducted with the following six concentrations; 0.09, 0.29, 0.92, 2.93, 9.39 and 30 mg/L and control with three replicates per concentration and six control replications. For analysis of the test concentration 25 mL samples were taken at 0 and 72 hours from the control, the lowest test concentration flasks and highest test concentration flasks from each replicate, analysis was conducted using the HPLC method. The validity and reliability of the test system and incubation conditions were confirmed earlier by conducting a positive control study using potassium dichromate as the reference substance.

Each replicate (250 mL conical flask) was inoculated with 1.0 mL of alga culture to obtain the required concentration of approximately 5 x10^3-10^4 cells/mL and the final volume made up to 150 mL with sterilised culture medium. For the difinitive test the flasks were maintained at 21-24 ºC for 72 hours with continuous illumination of 5257-5567 lux and were constantly agitated at 100 ± 2rpm. The pH was maintained in the range of 7.22 – 7.75.

To determine the algal biomass a volume of 10 mL of the test culture was collected from all replicate flasks at 24, 48 and 72 h. The cell concentration of each sample was determined using a haemocytometer and microscope. The total cell number, growth inhibition and growth rate were calculated from this count.

The 72 hour EC values for growth, growth rate and yield with associated 95% fiducial limits were calculated using the Probit analysis method (Finney, 1971). The NOEC and LOEC were calculated using Bartlett's test to check for homogeneity of variance followed by Dunnett's t-test using the individual replicate values of both control and treated groups. As growth inhibition was the most sensitive parameter for toxicity determination it was used to determine the NOEC and LOEC values.

Results and Discussion

Cell density in the control culture increased by the factor of 61.3 within 72 hours, the coefficient of variation of average growth between control replicates was 0.89% and the coefficient of variation of sectional (daily) growth rate for days 0-1, 1-2 and 2-3 in the control culture was 23.6% therefore all validity criteria were met.

Analytical verification

During the main study the measured concentrations ranged from 90.41 – 93.43 % of the nominal concentrations at test start (0h) and from 82.31- 92.28 % of the nominal at 72 hours. All reported effect concentrations are therefore based on nominal concentrations.

Biological results

The validity and reliability of the test system (*Pseudokirchneriella subcapitata*) and incubation conditions were confirmed earlier by conducting a positive control study using potassium dichromate as the reference substance, the results showed that the E_bC_{50} = 1.5 mg/L and E_rC_{50}= 3.77.

As growth inhibition was the most sensitive parameter for toxicity determination it was used to determine the NOEC and LOEC values. At 0.09 mg/L concentration of D-Devrinol 450 SC no significant effects on algal growth parameters were apparent hence, this concentration was considered the NOEC in the present study.

Table B.9.3.1-3 Summary of effects D-Devrinol 450 SC on algal cell count, biomass and yield

Test item conc (mg/L)	Biomass (mean number of cells counted)/mL			Mean value of specific growth rates				Mean yield value (Iy) at		
	24 hr	48 hr	72 hr	0-1 d	1-2 d	2-3 d	0-3 d	0-24 h	0-48 h	0-72 h
Control	38750	171667	482500	1.54	1.50	1.03	1.36	30556	163472.7	474306
0.09	45000	169167	479167	1.68	1.34	1.04	1.35	36806	160972.7	470972.7
0.29	26667	147500	450833	1.18	1.71	1.12	1.34	18472.67	139306	442639.3
0.92	19167	130000	397500	0.83	1.94	1.12	1.29	10972.67	121806	389306
2.93	18333	117500	340000	0.79	1.87	1.06	1.24	10139.33	109306	331806
9.38	18333	94167	273333	0.74	1.70	1.07	1.17	10139.33	85972.67	265139.3
30.0	15833	4333	87500	0.64	1.02	0.70	0.79	7639.33	35139.33	79306

Table B.9.3.1-4 Summary of effects of D-Devrinol 450 SC on growth inhibition, reduction and yield inhibition.

Test item conc (mg product/L	Growth rate		Yeild
	% inhibition	% reduction	% inhibition
Control	-	-	-
0.09	-0.48	0.18	0.70
0.29	12.08*	1.59	6.68
0.92	24.06*	4.77	17.92
2.93	33.82*	8.66	30.04
9.38	46.96*	13.96	44.10

30.0	80.88*	42.05	83.28

(* = statistically significant, Dunnett's t test with 95% confidence interval, p=<0.05, Growth inhibition was the most sensitive parameter)

The EC_{50} (0 – 72 h) values determined were 6.13 mg/L, 69.43 mg/L and 6.93 mg/L for growth inhibition (EbC_{50}), growth rate reduction (ErC_{50}) and yield inhibition ($E\gamma C_{50}$), respectively. The 95% fiducial limits were 4.48 to 8.38 mg/L for growth inhibition, 36.13 to 133.39 mg/L for growth rate reduction and 4.56 to 10.54 mg/L for yield inhibition.

The endpoint are summarised in the table below:

Table B.9.3.1-5 Summary of calculated effect concentrations

Exposure time	**EbCx value (mg product/L) for growth inhibition**		**95 % fiducial limits (mg/L)**		**Regression equation[a]**
			Lower	**Upper**	**(y = a +b x)**
72 hours	EC_{10}	0.26	0.15	0.47	y =1.45 + 0.94 x
	EC_{20}	0.77	0.51	1.18	
	EC_{50}	6.13	4.48	3.38	
	NOEC	0.09	-	-	-
	LOEC	0.29	-	-	-
Exposure time	**ErCx value (mg product/L) for growth rate reduction**		**95 % fiducial limits (mg/L)**		**Regression equation**
			Lower	**Upper**	**(y = a +b x)**
72 hours	EC_{10}	3.18	2.13	4.74	y =0.37 + 0.96 x
	EC_{20}	9.16	6.43	13.05	
	EC_{50}	69.43	36.13	133.39	
Exposure time	**EyCx value (mg product/L) for yield inhibition**		**95 % fiducial limits (mg/L)**		**Regression equation**
			Lower	**Upper**	**(y = a +b x)**
72 hours	EC_{10}	0.62	0.34	1.14	y =0.31 + 1.22 x
	EC_{20}	1.42	0.89	2.27	
	EC_{50}	6.93	4.56	10.54	

[a] The regression equation is calculated using the Probit mortality (y) vs log concentration of D-Devrinol 450 SC (x)

Conclusion

The 72 hour EC_{50} values were determined to be 6.13 mg/L (2.51 mg a.s./L) , 69.43 mg/L(28.46 mg a.s./L) and 6.93 mg/L (2.84 mg a.s./L) for growth inhibition (E_bC_{50}), growth rate reduction (E_rC_{50}) and yield inhibition (E_yC_{50}) respectively. The NOEC was determined to be 0.09 mg/L.

RMS Comments

It is noted that the applicant has calculated the coefficient of variation of sectional (daily) growth rate for days 0-1, 1-2 and 2-3 in the control culture incorrectly (calculating the coefficient of variation across the individual replicates for each of the time periods rather than across the time periods for each replicate), stating values of 12.99, 11.33 and 9.71, respectively. This has been re-calculated by the RMS and a value of 23.6% was determined, this meets the validity criteria of <35% therefore adhering the requirements. This study is considered suitable for use in the risk assessment.

The study was conducted inline with OECD guideline 201 and under GLP compliance. All validity criteria were met, The RMS considers that this study is suitable for use in the risk assessment. The

ErC_{50} is 69.43 mg product/L (equivalent to 28.46 mg a.s./L) and the NOEC is 0.09 mg product/L (equivalent to 0.037 mg a.s./L).

Toxicity to Aquatic Macrophytes

C. Ramsden (2015) Assessment of the effect of D-Devrinol 450 SC (HBW03) on *Lemna*, growth inhibition test. UPL Europe Ltd, Unpublished report No.: ENV-14-005

Guidelines

OECD guideline no. 221

GLP

Yes (certified laboratory)

Materials and Methods

Test material	D-Devrinol 450 SC
Description:	Cream viscous liquid
Lot/Batch #:	JM267
Content:	45.0% w/w Napropamide-M
Stability of test compound:	Not stable under test conditions.
Reference substance:	Not stated
Test animals	
Species:	*Lemna gibba*
Strain:	Not stated.
Source:	Canadian Phycological Culture Centre (CPCC), University of Waterloo, Canada
Test dates:	16th of June 2013 – 25th of June 2013

Test Design

Lemna gibba used in the study were taken from cultures within the lab and kept in conditions similar to those used for the test period. Colonies used for the study were taken from cultures in the exponential growth phase.

A preliminary range finding test was conducted to determine the sensitivity of the test system and as a result of this the following concentrations were used in the difinitive test; 0 (control), 0.065, 0.163, 0.406, 1.016 and 2.539 mg test item/L. The test was conducted under semi-static conditions with fresh media renewed at days 0, 2 and 4 by dilution of a stock solution. The measured concentrations of the test solutions were determined at the beginning and end of each renewal period. The samples were analysed using HPLC method, for the determination of napropamide-M active substance concentration in test media.

The test vessels consisted of glass jars with 300 mL capacity which contained 120 mL of test item solution. Three colonies comprising of 9 fronds were then added to each test vessel. At renewal new vessels were set up with fresh media and the plants were transferred to the new vessels. The pH was determined in each of the test and control bulk solutions at the start of each renewal period and in a single vessel at each concentration at the end of each renewal period, it was found to be in the range of 7.45 -9.36. Temperature was recorded in a surrogate vessel containing *Lemna* media for the duration of the testand it was found to be in the range of 22. – 23.7^{o}C. Continuous illumination was used and measured on day 0 (7550 lux) and remained within acceptable limits.

The growth of the cultures was assessed by determining the number of fronds at the start of the test, on day 2, 4 and 7 at the end of the test. Changes in plant development e.g. frond size, appearance, indication of necrosis, chlorosis, colony break up or loss of buoyancy and changes in root length or appearance were recorded. At the end of the test dry weight of the plants in each of the test vessels was determined by drying at approximately 60 ^{o}C to a constant weight.

The results were compared statistically using Dunnett's multiple comparison test for dry weight and Wilcoxon/Bonferroni test for frond number with a p-value for significance of 0.05. It was not possible to generate NOEC values for the dry weight endpoints as there were effects observed at all concentrations . To analyse frond count and dry weight and calculate the EC_x values CETIS was used to conduct nonlinear regression analysis; the model used for specific growth rate was a 4 parameter log-logistic and the model used for yield was a 4 parameter cumulative log-normal. The model used for specific growth rate was a 3 parameter cumulative log-normal and the model used for yield was a 4 parameter cumulative log-normal.

Results and Discussion

All validity criteria were met. Doubling time of frond number in the control was 1.6 days and the average specific growth rate in the control was 0.418 d^{-1}.

Analytical results

The analytical verification of the test item showed recovery of between 46 and 61 % of the nominal (Table B.9.3.1-6**)**, therefore effect concentrations were calculated based on geometric mean concentrations. The geometric mean measured concentrations were calculated to be 0.03, 0.086, 0.226, 0.605 and 1.542 mg/L.

Table B.9.3.1-6 Summary table detailing geometric mean test item concentrations and percentage recovery based on HPLC analysis.

Nominal Concentration (mg/L)	Geometric mean test item concentration (mg L^{-1})	Recovery (% of Nominal)
Control	-	-
0.065	0.030	46
0.163	0.086	53
0.406	0.226	56
1.016	0.605	60
2.539	1.542	61

Biological results

In terms of frond count the E_rC_{50} over 7 days exposure was calculated to be 0.096 mg product/L, equivalent to 0.044 mg a.s/L and an E_yC_{50} of 0.076 mg product/L equivalent to 0.035 mg a.s/L. The NOEC value based on frond count for both endpoints was determined to be 0.030 mg test item/L, for example at a concentration of 0.030, by day 2 there was some chlorosis, by day 4 there was some frond death and little root growth. At the end of the test there was some chlorosis, the fronds were small in size compared to controls and there was only a very small amount of root growth.

Table B.9.3.1-7 Summary of effects D-Devrinol 450 SC on mean frond numbers, % inhibition of growth rate (% Ir) and yield (%Iy)

Geometric mean test item concentration (mg/L)	Mean frond number				$\%I_r$	$\%I_y$
	0 days	2 days	4 days	7 days		
Control	9	19	48	169	N/A	N/A
0.03	9	19	43	165	0.82	2.74
0.086	9	15	33	86	23.84*	52.15*
0.226	9	13	23	32	57.25*	85.77*
0.605	9	13	20	28	61.21*	87.96*

1.542	9	13	19	31	58.52*	86.40*

(*= statistically significant, Wilcoxon/Bonferroni, p=<0.05)

For the secondary measurement of dry weight D-Devrinol 450 SC has an E_rC_{50} of > 1.542 mg test item L-1 (> 0.632 mg a.s. L-1) and an E_yC_{50} of 0.0346 mg test item L-1 (0.0141 mg a.s. L-1). It was not possible to generate NOEC values for either endpoint as there were effects observed at all concentrations including the lowest tested concentration.

Table B.9.3.1-8 Summary of effects D-Devrinol 450 SC on mean dry weights (mg total Lemna mass for each group) with mean % inhibition for growth rate (%Ir) and yield (%Iy)

Geometric mean test item concentration (mg/L)	Mean dry weight (mg)		$\%I_r$	$\%I_y$
	0 days	7 days		
Control	0.98	26.67	N/A	N/A
0.03	0.98	18.01	11.87*	33.7*
0.086	0.98	11.95	24.32*	57.3*
0.226	0.98	8.93	33.17*	69.1*
0.605	0.98	7.50	38.37*	74.6*
1.542	0.98	7.79	37.46*	73.5*

(*= statistically significant, Dunnett's multiple comparison test, p=<0.05)

The results of the effects on frond number and dry weight are presented in the following tables:

Table B.9.3.1-9 Frond count EC_{10}, EC_{20} and EC_{50} values for growth rate and yield

Endpoint	Concentration (mg product/L)	95 % confidence limits		Concentration (mg a.s/L)	95 % confidence limits	
		Lower	Upper		Lower	Upper
Growth rate						
E_rC_{10}	0.05281	0.04034	0.06122	0.02429	0.01856	0.02816
E_rC_{20}	0.06592	0.05798	0.07283	0.03032	0.02667	0.0335
E_rC_{50}	0.09629	0.09059	0.1024	0.04429	0.04167	0.0471
Yield						
E_yC_{10}	0.0399	0.03601	0.04327	0.01835	0.01656	0.0199
E_yC_{20}	0.04975	0.04623	0.05311	0.02289	0.02127	0.02443
E_yC_{50}	0.07589	0.07389	0.07794	0.03491	0.03399	0.03585

Table B.9.3.1-10 Dry weight EC_{10}, EC_{20} and EC_{50} values for growth rate and yield

Endpoint	Concentration (mg product/L)	95 % confidence limits		Concentration (mg a.s/L)	95 % confidence limits	
		Lower	Upper		Lower	Upper
Growth rate						
E_rC_{10}	0.004503	0.0000458	0.03454	0.002071	0.0000211	0.01589
E_rC_{20}	0.04749	0.01125	0.1531	0.02185	0.00518	0.07043
E_rC_{50}	>1.542	N/A	N/A	>0.709	N/A	N/A
Yield						
E_yC_{10}	0.00711	0.005418	0.008784	0.00327	0.00249	0.00404
E_yC_{20}	0.01224	0.01032	0.01427	0.00563	0.00475	0.00656

E_yC_{50}	0.0346	0.03228	0.0371	0.01592	0.01485	0.01707

Conclusion

In terms of frond count the E_rC_{50} over 7 days exposure was calculated to be 0.096 mg/L, equivalent to 0.044 mg a.s/L and an E_yC_{50} of 0.076 mg product/L equivalent to 0.035 mg a.s/L. The NOEC value based on frond count for both endpoints was determined to be 0.030 mg test item/L (0.0123 mg a.s./L).

RMS Comments

It is noted that the pH varied by more than 1.5 units during the test in the control group the pH increased by 1.64 units between day 4 and day 7. As the validity criteria were met and the control showed good development this is considered to be a minor deviation.

It was not possible to generate NOEC values based on dry weight as there were effects observed for dry weight at all of the concentrations tested so the EC_{10} values will be used instead (0.004 mg/L equivalent to 0.001 mg a.s./L for growth rate and 0.007 mg/L equivalent to 0.003 mg/L yield). This study is considered suitable for use in the risk assessment.

The study was conducted inline with OECD guideline 221 and under GLP compliance. All validity criteria were met, The RMS considers that this study is suitable for use in the risk assessment. The ErC_{50} is 1.542 mg product/L (equivalent to 0.63 mg a.s./L) and the EC10 is 0.004 mg product/L (equivalent to 0.0016 mg a.s./L).

B.9.3.2 Additional long term testing on fish aquatic invertebrates and sediment dwelling organisms

With reference to EFSA Guidence (2013) toxicological studies with sediment dwelling organisms are not required. The guidance states that if the 'water/sediment study shows >10% of applied radioactivity at or after day 14 present in the sediment and chronic daphnia test (or other comparable study with insects) NOEC <0.1 mg/L' then further studies are required.

With reference to Environmental fate section, (the concentration of Napropamide-M at day 14 was found to be >10% AR for both sediment systems and % AR in the sediment remained high throughout the duration of the experiment/ However the chronic NOEC for *Daphnia magna* was found to be 0.3 mg/L which is above the trigger value of 0.1. Therefore the risk to aquatic invertebrates was shown to be low and risk to sediment dwelling organisms is also likely to be low.

B.9.3.3 Further testing on aquatic organisms

Further studies to refine the risk assessment are not required. Please refer to Volume 3 – B9 (AS), section B.9.2.7. for further details.

B.9.4. RISK ASSESSMENT FOR AQUATIC ORGANISMS

The table below summarises the available toxicity for Napropamide-M, the relevant metabolites and the formulation D-Devrinol 450 SC. The endpoints highlighted in bold are used in the risk assessment.

Table B.9.4-1 Summary of endpoints for aquatic organisms

Test substance	Organism	Endpoint	Value	Reference
Fish				
D-Napropamide (Purity 97.2 %)	Rainbow trout *Oncorhynchus mykiss*	96 hr LC_{50}	**11.2 mg a.s/L**	[redacted] (2011a)
Napropamide-M (Purity 96.1 %)	*Zebrafish* (*Danio rerio*)	ELS NOEC	**>0.4 mg a.s/L**	[redacted] (2015)
D-Devrinol 450 SC	Rainbow trout *Oncorhynchus mykiss*	96 hr LC_{50}	30 mg/L 12.3 mg a.s/L	[redacted] (2011b)
Aquatic invertebrates				
D-Napropamide (Purity 97.2 %)	*Daphnia magna*	48 hr EC_{50}	**19 mg a.s/L**	Liedtke, A (2011c)
Napropamide-M (Purity 96.14 % D-isomer, 3.86 % of L-isomer)	*Daphnia magna*	21-day NOEC	**0.3 mg a.s/L**	Kamile, M.K (2014)
D-Devrinol 450 SC	*Daphnia magna*	48 hr EC_{50}	52 mg/L 21.32 mg a.s/L	Liedtke, A (2011d)
Algae				
Napropamide-M (Purity 97.26 % D-isomer, 3.86 % L-isomer)	*Pseudokirchneriella subcapitata*	72 hr E_rC_{50}	28.18 mg a.s/L NOEC 0.8 mg a.s/L	Kamile, M.K (2014) X
Napropamide (Purity 93.2%)	*Anabaena* sp.	72h E_rC_{50}	55.0 mg a.s./L	Jenkins, (2002)
D-Devrinol 450 SC	*Pseudokirchneriella subcapitata*	72 hr E_rC_{50} NOEC	**30 mg/L** [a] **>12.45 mg a.s/L**[a] 0.09 mg/L 0.037 mg a.s./L	Kamle, M (2014)
Aquatic macrophytes				
Napropamide-M (Purity 96.1 %)	*Lemna gibba*	7-day E_rC_{50}	0.08 mg a.s./L	Ramsden, C (2015)
Isomer I	*Lemna minor*	7-day E_yC_{50} 7-day E_rC_{50}	0.729 mg a.s./L † **>5.81 mg a.s/L**	Juckeland, (2012a)
Isomer II	*Lemna minor*	7-day E_yC_{50} 7-day E_rC_{50}	0.603 mg a.s./L † **>0.321 mg a.s/L**	Juckeland, (2012b)
Napropamide-M	*Myriophyllum spicatum*	14 day E_rC_{50}	2.35 mg a.s/L	Hermes, H (2015)
D-Devrinol 450 SC	*Lemna gibba*	7-day E_rC_{50} NOEC	0.096 mg/L **0.0443 mg a.s/L** 0.004 mg/L 0.001 mg a.s./L	Ramsden, C (2015)

[a] As effects of >50 % were not reported in the study, an extrapolated E_rC_{50} was calculated using regression analysis to be 69.43 mg product/L (equivalent to 28.81 mg a.s/L) however to provide a conservative assessment the maximum concentration tested of 30 mg product/L (equivalent to 12.45 mg a.s/L) is used in the risk assessment.

† Endpoint not used in risk assessment provided for information only.

X Study not considered suitable for risk assessment.

Bold-values have been used in the risk assessment.

Toxicity of the active substance and the formulation

There is negligible difference between the formulation and active substance endpoints for fish and aquatic invertebrates (Fish: LC_{50}=11.2 (a.s.) and 12.3 mg a.s/L (formulation), aquatic invertebrates: EC_{50}=19 mg a.s/L (a.s.) and EC_{50}=21.32 mg a.s/L (formulation)) therefore the lower value will be used

in the FOCUS assessment. For algae the study with the active substance was found to be unreliable therefore the formulation endpoint (>12.45 mg a.s/L) will be used in the risk assessment. For aquatic macrophytes the formulation and active substance endpoints are considered equivalent (ErC_{50}=0.08 mg a.s/L (a.s.) and ErC_{50}=0.0443 mg a.s/L (formulation) as they are within a factor of two (EFSA Journal 2013;11(7):3290), therefore the lower of the two will be used in the FOCUS risk assessment. As the active substance and formulation endpoints are considered equivalent, no separate spray drift assessment is required for the formulation as the risk will be addressed in the active substance FOCUS assessment.

Fish toxicity endpoints

It is noted that the study [redacted] (2011a) does not consider the lowest two dilutions (1:22 and 1:10) in the analytical verification of the test substance. Therefore, it is not known if these nominal concentrations were maintained within 80-120% throughout the test. This could potentially mean that the test organisms were exposed to below the stated concentrations. As a result, this there is uncertainty in the endpoint proposed by the applicant as the stability of the test item is not known. If all concentrations were not maintained within 80-120% of the nominal at all sampling points then an LC_{50} based on mean measured concentrations could potentially be lower. However as the determined LC_{50} of 11.2 mg a.s/L fell within the three highest concentrations which had been subject to analytical verification (dilutions 1:4.6, 1:2.2 and the undiluted filtrate, equivalent to 7.9, 16.8 and 35.7 mg a.s/L, respectively), the RMS considers that this endpoint is suitable for use in the risk assessment.

The study [redacted] (2015) with Napropamide-M does not meet the validity criteria; the dissolved oxygen concentration fell below 60% of the air saturation value, the water temperature was outside of the specifies range for the test species and varied more than 1.5^{o}C and the post hatch success in the controls was below 75%. Several other deviations to the guideline were also noted. Due to these deviations the RMS has determined that the study isn't fully reliable. However with reference to Article 60 of Directive 1107, in order to minimise vertebrate testing a repeat study is not considered to be necessary as the current study provides sufficient evidence to indicate that fish are not a sensitive group.

Aquatic invertebrate toxicity endpoint

It is noted that the study Liedtke (2011c) does not consider the lowest three dilutions (1.46, 1:22 and 1:10) in the analytical verification of the test substance. Therefore, it is not known if these nominal concentrations were maintained within 80-120% throughout the test. This could potentially mean that the test organisms were exposed to below the stated concentrations. As a result, this there is uncertainty in the endpoint proposed by the applicant as the stability of the test item is not known. If all concentrations were not maintained within 80-120% of the nominal at all sampling points then an EC_{50} based on mean measured concentrations could potentially be lower. However as the determined EC_{50} of 19 mg test item/L fell within the three highest concentrations which had been subject to analytical verification (dilutions 1:4.6, 1:2.2 and the undiluted filtrate, equivalent to 8.5, 17 and 37 mg a.s/L, respectively), the RMS considers that this endpoint is suitable for use in the risk assessment.

In the study Liedtke (2011d) the lowest test concentration of 4.6 mg/L was not analytically verified as this concentration was below the 48-hour NOEC determined in this test. The RMS does not accept this reasoning as it could potentially mean that the test organisms were exposed to below the stated concentration. However as the determined EC_{50} of 52 mg /L was much greater than this, it is accepted that this would not effect the outcome of the study. This study is considered suitable for use in the risk assessment.

Algae toxicity endpoints

The study Kamile (2014) with Napropamide-M is not considered suitable for use in risk assessment as it does not meet the validity criteria; the mean coefficient of variation for section-by-section specific

growth rates exceeded 35%. No further consideration of the results has been made. Instead reference will be made to the study Kamle, M (2014) evaluated for D-Devrinol 450 SC (Volume 3 B.9) for the algal endpoint. It is noted that D-Devrinol 450 SC is a single active formulation. With reference to Volume 4 for the technical specification of D-Devrinol 450 SC, there are no co-formulants of concern to algae. Therefore it is acceptable to assume that the majority of the toxicity to algae from D-Devrinol 450 SC is attributed to the active substance. This endpoint is also more sensitive than the endpoint derived from the study with *Anabaena* sp. for Napropamide, therefore it is considered to sufficiently cover the risk from the active substance.

Aquatic macrophytes

The RMS consideres that the study with *Lemna gibba* for Napropamide-M (Ramsden, C 2015) is suitable for use in the risk assessment. As are the studies for Isomer I (D. Juckeland, 2012a) and Isomer II (D. Juckeland, 2012b) both with *Lemna minor*.

Sediment dwelling organisms

With reference to EFSA Guidence (EFSA Journal 2013;11(7):3290), toxicological studies with sediment dwelling organisms are required when: 'water/sediment study shows >10% of applied radioactivity at or after day 14 present in the sediment and chronic daphnia test (or other comparable study with insects) NOEC <0.1 mg/L'. With reference to Volume 3 B.8 - HSE ref: 001713975, the concentration of Napropamide-M at day 14 was found to be >10% AR for both sediment systems and % AR in the sediment remained high throughout the duration of the experiment, however the chronic NOEC for Daphnia was found to be 0.3 mg/L which is above the trigger value of 0.1. Therefore the risk to aquatic invertebrates was shown to be low and risk to sediment dwelling organisms is also likely to be low.

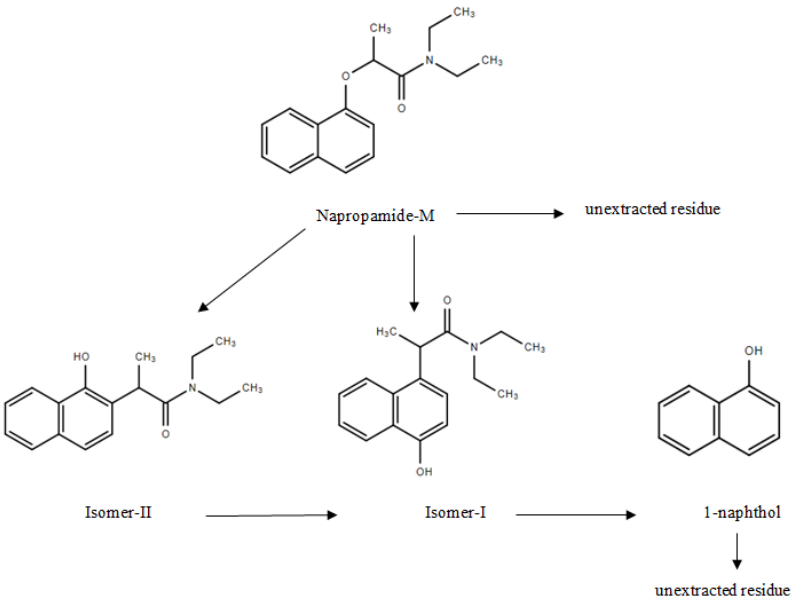
Metabolites of Napropamide-M

Aquatic organisms may be exposed to the relevant metabolites of Napropamide-M; isomer 1, isomer 2 and 1-naphthol (see Environmental fate section), and therefore the risk to aquatic organisms also needs to be assessed.

Aquatic macrophytes were identified as the taxonomic group determining the lowest tier 1 RAC_{SW}-ac for the active substance and so studies were conducted with the metabolites isomer 1 and 2 for *Lemna minor* (with reference to EFSA guidance (EFSA Journal 2013;11(7):3290), the most sensitive group should be defined as 10 times more sensitive than the next most sensitive (*Lemna* ErC_{50}=0.0443 mg a.s./L and fish LC_{50}=11.2 mg a.s/L)). For 1-naphthol an aquatic plant study has not been conducted.

As it is clear that the toxophore has been lost from the isomer I & II studies that are earlier in the degradation pathway than 1-naphthol (Figure B.9.4-1), the active substance toxicity data has been used for 1-naphthol, as recommended for metabolites without the toxophore in the EFSA guidance (2013). The toxixity to fish, aquatic invertebrates and algae will be assessed using the acute and chronic endpoints from studies with the active substance, EFSA guidance (2013) states that 'if it is clear that the toxophore has been lost from the metabolite, in most cases, metabolites are less toxic to the target organisms than the a.s.' therefore this is considered to be an acceptable approach.

Figure B.9.4-1. The aqueous photolysis degradation of Napropamide-M (Volume 3 B.8 - figure B.8.4.3-1)



Risk assessment

The following risk assessment has been conducted according to the EFSA (2013) guidance document "Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters". The acute and long-term risk assessments have been conducted by comparison of FOCUS PEC values with appropriate RAC (Regulatory Acceptable Concentration) values for each group of organisms. Where the PEC exceeds the RAC (shown in bold) the risk is unresolved and further consideration is required.

FOCUS step 3 PECs have been used in the following risk assessment to address the risk from Napropamide-M (Volume 3 B.8). No FOCUS step 1 or 2 risk assessment has been performed given the high toxicity of the active substance to aquatic organisms.

B.9.4.1. Fish

Acute risk

The acute toxicity endpoint for *O. mykiss* (11.2 mg a.s/L) was used to assess the risk from D-Napropamide (active substance); based on the regulatory trigger of 100 the resulting **RAC = 112 µg a.s./L**.

Table B.9.4.1-1 Fish acute, FOCUS step 3, risk assessment for for D-Napropamide

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
Fish (112 µg a.s./L)	Oilseed Rape	Drainage	D2 Ditch	23.40
			D2 Stream	14.67
			D4 Pond	1.10
			D5 Pond	0.33
		Run-off/ erosion	R1 Pond	0.20
			R1 Stream	3.90
			R3 Stream	7.42
		Drift	D3 Ditch	4.90
			D4 stream	4.19

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
			D5 stream	4.52
	Brassicas	Drainage	D4 pond	0.27
		Run off/erosion	R1 pond 1st	0.63
			R1 pond 2nd	0.51
			R1 stream 1st	6.75
			R1 stream 2nd	6.28
			R3 stream 1st	13.82
			R3 stream 2nd	9.02
			R4 stream 1st	4.47
			R4 stream 2nd	16.36
		Drift	D3 ditch 1st	4.85
			D3 ditch 2nd	4.85
			D4 stream	3.80
			D6 ditch	4.75
			R2 stream 1st	4.19
			R2 stream 2nd	4.30

"1st" and "2nd" refer to first and second plantings of brassicas. In some European locations it is possible to grow two cabbage crops per year i.e. two applications of Napropamide-M per year to the same soil environment.

PECsw values are below the RAC for all scenarios for each crop.

Early life risk

The chronic toxicity endpoint for *O. mykiss* (0.4 mg a.s/L) was used to assess the risk from Napropamide-M (active substance); based on the regulatory trigger of 10 the resulting **RAC = 40 µg a.s./L**.

Table B.9.4.1-2 Fish acute, FOCUS step 3, risk assessment for for D-Napropamide

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
Fish (40 µg a.s./L)	Oilseed Rape	Drainage	D2 Ditch	23.40
			D2 Stream	14.67
			D4 Pond	1.10
			D5 Pond	0.33
		Run-off/ erosion	R1 Pond	0.20
			R1 Stream	3.90
			R3 Stream	7.42
		Drift	D3 Ditch	4.90
			D4 stream	4.19
			D5 stream	4.52
	Brassicas	Drainage	D4 pond	0.27
		Run off/erosion	R1 pond 1st	0.63
			R1 pond 2nd	0.51
			R1 stream 1st	6.75
			R1 stream 2nd	6.28
			R3 stream 1st	13.82

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
			R3 stream 2nd	9.02
			R4 stream 1st	4.47
			R4 stream 2nd	16.36
		Drift	D3 ditch 1st	4.85
			D3 ditch 2nd	4.85
			D4 stream	3.80
			D6 ditch	4.75
			R2 stream 1st	4.19
			R2 stream 2nd	4.30

"1st" and "2nd" refer to first and second plantings of brassicas. In some European locations it is possible to grow two cabbage crops per year i.e. two applications of Napropamide-M per year to the same soil environment.

PECsw values are below the RAC for all scenarios for each crop.

B.9.4.2. Aquatic invertebrates

Acute risk

The acute toxicity endpoint for *Daphnia magna* (19 mg a.s/L) was used to assess the risk from D-Napropamide (active substance); based on the regulatory trigger of 100 the resulting **RAC = 190 µg a.s./L**.

Table B.9.4.2-1 Aquatic invertebrate acute, FOCUS step 3, risk assessment for D-Napropamide

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
Daphnia magna (190 µg a.s./L)	Oilseed Rape	Drainage	D2 Ditch	23.40
			D2 Stream	14.67
			D4 Pond	1.10
			D5 Pond	0.33
		Run-off/ erosion	R1 Pond	0.20
			R1 Stream	3.90
			R3 Stream	7.42
		Drift	D3 Ditch	4.90
			D4 stream	4.19
			D5 stream	4.52
	Brassicas	Drainage	D4 pond	0.27
		Run off/erosion	R1 pond 1st	0.63
			R1 pond 2nd	0.51
			R1 stream 1st	6.75
			R1 stream 2nd	6.28
			R3 stream 1st	13.82
			R3 stream 2nd	9.02
			R4 stream 1st	4.47
			R4 stream 2nd	16.36
		Drift	D3 ditch 1st	4.85
			D3 ditch 2nd	4.85

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
			D4 stream	3.80
			D6 ditch	4.75
			R2 stream 1st	4.19
			R2 stream 2nd	4.30

"1st" and "2nd" refer to first and second plantings of brassicas. In some European locations it is possible to grow two cabbage crops per year i.e. two applications of Napropamide-M per year to the same soil environment.

PECsw values are below the RAC for all scenarios for each crop.

Long term risk

The chronic toxicity endpoint for *Daphnia magna* (0.3 mg a.s/L) was used to assess the risk from Napropamide-M (active substance); based on the regulatory trigger of 10 the resulting **RAC = 30 µg a.s./L**.

Table B.9.4.2-2: Aquatic invertebrate chronic, FOCUS step 3, risk assessment for Napropamide-M

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
Daphnia magna (30 µg a.s./L)	Oilseed Rape	Drainage	D2 Ditch	23.40
			D2 Stream	14.67
			D4 Pond	1.10
			D5 Pond	0.33
		Run-off/ erosion	R1 Pond	0.20
			R1 Stream	3.90
			R3 Stream	7.42
		Drift	D3 Ditch	4.90
			D4 stream	4.19
			D5 stream	4.52
	Brassicas	Drainage	D4 pond	0.27
		Run off/erosion	R1 pond 1st	0.63
			R1 pond 2nd	0.51
			R1 stream 1st	6.75
			R1 stream 2nd	6.28
			R3 stream 1st	13.82
			R3 stream 2nd	9.02
			R4 stream 1st	4.47
			R4 stream 2nd	16.36
		Drift	D3 ditch 1st	4.85
			D3 ditch 2nd	4.85
			D4 stream	3.80
			D6 ditch	4.75
			R2 stream 1st	4.19
			R2 stream 2nd	4.30

"1st" and "2nd" refer to first and second plantings of brassicas. In some European locations it is possible to grow two cabbage crops per year i.e. two applications of Napropamide-M per year to the same soil environment.

PECsw values are below the RAC for all scenarios for each crop.

B.9.4.3. Algae

The toxicity endpoint for *Pseudokirchneriella subcapitata*. (12.45 mg a.s/L) obtained from a study with D-Devrinol 450 SC was used to assess the risk from Napropamide (active substance); based on the regulatory trigger of 10 the resulting **RAC = 1245 µg a.s./L**.

Table B.9.4.3-1: Algae, FOCUS step 3, risk assessment for Napropamide

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
Pseudokirchneriella subcapitata (1245 µg a.s./L)	Oilseed Rape	Drainage	D2 Ditch	23.40
			D2 Stream	14.67
			D4 Pond	1.10
			D5 Pond	0.33
		Run-off/ erosion	R1 Pond	0.20
			R1 Stream	3.90
			R3 Stream	7.42
		Drift	D3 Ditch	4.90
			D4 stream	4.19
			D5 stream	4.52
	Brassicas	Drainage	D4 pond	0.27
		Run off/erosion	R1 pond 1st	0.63
			R1 pond 2nd	0.51
			R1 stream 1st	6.75
			R1 stream 2nd	6.28
			R3 stream 1st	13.82
			R3 stream 2nd	9.02
			R4 stream 1st	4.47
			R4 stream 2nd	16.36
		Drift	D3 ditch 1st	4.85
			D3 ditch 2nd	4.85
			D4 stream	3.80
			D6 ditch	4.75
			R2 stream 1st	4.19
			R2 stream 2nd	4.30

"1st" and "2nd" refer to first and second plantings of brassicas. In some European locations it is possible to grow two cabbage crops per year i.e. two applications of Napropamide-M per year to the same soil environment.

PECsw values are below the RAC for all scenarios for each crop. Further consideration by Member States is not required.

B.9.4.4. Aquatic Macrophytes

The toxicity endpoint for *Lemna gibba* (0.0433 mg a.s/L) was used to assess the risk from Napropamide-M (active substance); based on the regulatory trigger of 10 the resulting **RAC = 4.33 µg a.s./L**.

Table B.9.4.4-1: *Lemna gibba*, FOCUS step 3, risk assessment for Napropamide-M

Organism group (RAC, µg a.s./L)	Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max
Lemna (4.33 µg a.s./L)	Oilseed Rape	Drainage	D2 Ditch	**23.40***
			D2 Stream	**14.67***
			D4 Pond	1.10
			D5 Pond	0.33
		Run-off/ erosion	R1 Pond	0.20
			R1 Stream	3.90
			R3 Stream	**7.42***
		Drift	D3 Ditch	**4.90***
			D4 stream	4.19
			D5 stream	**4.52***
	Brassicas	Drainage	D4 pond	0.27
		Run off/erosion	R1 pond 1st	0.63
			R1 pond 2nd	0.51
			R1 stream 1st	**6.75***
			R1 stream 2nd	**6.28***
			R3 stream 1st	**13.82***
			R3 stream 2nd	**9.03***
			R4 stream 1st	**4.47***
			R4 stream 2nd	**16.36***
		Drift	D3 ditch 1st	**4.85***
			D3 ditch 2nd	**4.85***
			D4 stream	3.80
			D6 ditch	**4.75***
			R2 stream 1st	4.19
			R2 stream 2nd	4.30

"1st" and "2nd" refer to first and second plantings of brassicas. In some European locations it is possible to grow two cabbage crops per year i.e. two applications of Napropamide-M per year to the same soil environment.
*Values in bold are greater than the RAC and indicate further refinement is required for the crop/use scenario

PECsw values are above the RAC for the following scenarios: D2 Ditch, D2 Stream, R3 Stream, D3 Ditch and D5 stream (Winter Oilseed Rape) and R1 stream 1st , R1 stream 2nd, R3 stream 1st, R3 stream 1st, R3 stream 2nd, R4 stream 1st, R4 stream 2nd, D3 ditch 1st, D3 Ditch 2nd and D6 Ditch. (Brassica vegetable crops) and these scenarios are considered further at FOCUS step 4. Acceptable risks were demonstrated for all other scenarios for OSR and brassicas.

B.9.4.5 FOCUS step 4 refinement

Based on FOCUS step 3 values, the risk was resolved for all of the aquatic organisms with the exception of *Lemna gibba* for the scenarios summarised in Table B.9.4.4-1. Further refinement using FOCUS step 4 PECs is required for the uses outlined above. The FOCUS step 4 values include a refinement using a 10 and 20 meter buffer zone and vegetative filter strips (and 20 m buffer).

The toxicity endpoint for *Lemna Gibba* (0.0433 mg a.s/L) was used to assess the risk from Napropamide-M (active substance); based on the regulatory trigger of 10, the resulting **RAC = 4.33 µg a.s./L**.

Table B.9.4.5-1: FOCUS step 4 assessment for Napropamide-M.

Crop	Scenario		FOCUS step 3, PEC_{SW} (µg a.s./L) Initial, max	FOCUS step 4, PEC_{SW} (µg a.s./L) Initial, max			
				10 Meter buffer zone	20 meter buffer zone	Vegetative filter strips [a]	Vegetative filter strips [b]
Oilseed Rape	Drainage	D2 Ditch	**23.40***	**23.40***	**23.40***	n/a	n/a
		D2 Stream	**14.67***	**14.67***	**14.67***	n/a	n/a
	Run-off/ erosion	R3 Stream	**7.42***	**7.42***	**7.42***	3.38	-
	Drift	D3 Ditch	**4.90***	0.71	-	-	-
		D5 stream	**4.52***	0.88	-	-	-
Brassicas	Drainage	-	-	-	-	-	-
	Run off/erosion	R1 stream 1st	**6.75***	**6.75***	**6.75***	2.03	-
		R1 stream 2nd	**6.28***	**6.28***	**6.28***	2.86	-
		R3 stream 1st	**13.82***	**13.82***	**13.82***	**6.25***	3.26
		R3 stream 2nd	**9.03***	**9.02***	**9.02***	4.11	-
		R4 stream 1st	**4.47***	**4.47***	**4.47***	2.03	-
		R4 stream 2nd	**16.36***	**16.36***	**16.36***	**7.43***	3.89
	Drift	D3 ditch 1st	**4.85***	0.70	-	-	-
		D3 ditch 2nd	**4.85***	**4.85***	0.36	-	-
		D6 ditch	**4.75***	**4.75***	1.84	-	-

"1st" and "2nd" refer to first and second plantings of brassicas. In some European locations it is possible to grow two cabbage crops per year i.e. two applications of Napropamide-M per year to the same soil environment.
a = 10-12 meter VFS and 20 m buffer
b=18-20 meter VFS and 20 m buffer
*Values in bold are greater than the RAC and indicate further refinement is required for the crop/use scenario

Vegetative filter strips are a potential mitigation measure for run off rather than spray drift or drainage, therefore this mitigation was only applied when the scenarios exceeding the RAC were driven by run off. When the main route of entry to the water body is via drainage and the RAC is exceeded, no mitigation is currently available.

For brassicas, acceptable risk was demonstrated for the D3 Ditch 1st scenario with the includion of a 10 meter buffer zone. For D3 Ditch 2nd and D6 Ditch the risk was resolved with the inclusion of a 20 meter buffer strip and further consideration is not required. For the scenarios R1 stream 1st, R1 stream 2nd, R3 stream 2nd and R4 stream 1st the inclusion of a 20 meter buffer zone was not sufficient to resolve the risk to aquatic macrophytes, however the risk could be resolved with the use of vegetative

filter strips (and 20 m buffer). However it is noted that this method is not accepted as a viable mitigation measure in all Member States.

For OSR, the risk to D3 Ditch and D5 stream could be resolved with the use of a 10 meter buffer zone. For R3 Stream a 20 meter buffer zone was not sufficient to resolve the risk to aquatic macrophytes however the risk could be resolved with the use of vegetative filter strips (and a 20 m buffer). For the D2 ditch and stream scenarios, the inclusion of a 20 meter buffer zone was not sufficient to resolve the risk to aquatic macrophytes for all scenarios and vegetative filter strips are not considered to be a viable mitigation measure. **The relevance of this should also be considered further at the Member State level.**

Metabolites

B.9.4.6. Aquatic Macrophytes

Aquatic organisms may be exposed to the metabolites of Napropamide-M; isomer 1, isomer 2 and 1-naphthol (Volume 3 – B.8). Aquatic macrophytes were identified as the taxonomic group determining the lowest tier 1 RACSW-ac. For isomer I the toxicity endpoint for *Lemna minor* of 5.81 mg a.s/L was used to assess the risk based on the regulatory trigger of 10, the resulting **RAC = 581 µg a.s./L**. For isomer II the toxicity endpoint for *Lemna minor* of >0.321 mg a.s/L was used, the resulting **RAC = 32.1 µg a.s./L.** For 1-naphthol use of the active substance endpoint is considered to provide a conservative assessment therefore the toxicity endpoint for *Lemna gibba* of >0.0433 mg a.s/L was used, the resulting **RAC = 4.33 µg a.s./L.**

Table B.9.4.6-1: Metabolites risk assessment using FOCUS PECs, for Isomer I, Isomer II and 1-naphthol for aquatic macrophytes.

Crop	Water Body	FOCUS, PEC_{SW} (µg a.s./L) Initial, max		
		Isomer I (RAC=581 µg/L)	**Isomer II (RAC = 32.1 µg/L)**	**1-naphthol (RAC=4.33 µg/L)**
Oilseed Rape	D2 ditch	8.66	13.36	2.90
	D2 stream	5.43	8.38	1.82
	D3 ditch	1.81	2.80	0.61
	D4 pond	0.41	0.63	0.14
	D4 stream	1.55	2.39	0.52
	D5 pond	0.12	0.19	0.04
	D5 stream	1.67	2.58	0.56
	R1 pond	0.07	0.12	0.02
	R1 stream	1.44	2.22	0.48
	R3 stream	2.75	4.24	0.92
Brassicas	D3 ditch 1st	1.79	2.77	0.60
	D3 ditch 2nd	1.80	2.77	0.60
	D4 pond	0.10	0.15	0.03
	D4 stream	1.41	2.17	0.47
	D6 ditch	1.76	2.71	0.59
	R1 pond 1st	0.23	0.36	0.08
	R1 pond 2nd	0.19	0.29	0.06
	R1 stream 1st	2.50	3.85	0.84
	R1 stream 2nd	2.32	3.59	0.78
	R2 stream 1st	1.55	2.39	0.52
	R2 stream 2nd	1.59	2.45	0.53
	R3 stream 1st	5.11	7.89	1.71
	R3 stream 2nd	3.34	5.15	1.12
	R4 stream 1st	1.66	2.55	0.55
	R4 stream 2nd	6.05	9.34	2.03

PECsw values are below the RAC for all scenarios for each crop therefore no further consideration is required.

B.9.4.7. Fish

Acute Risk

The acute toxicity endpoint for *O. mykiss* (11.2 mg a.s/L) was used to assess the risk from Isomer I, Isomer II and 1-naphthol; based on the regulatory trigger of 100 the resulting **RAC = 112 µg a.s./L**.

Table B.9.4.7-1: Metabolites risk assessment using FOCUS PECs, for Isomer I, Isomer II and 1-naphthol using the acute toxicity endpoint for *O. mykiss.*

Crop	Water Body	FOCUS, PEC_{SW} (µg a.s./L) Initial, max		
		Isomer I RAC = 112 µg a.s./L.	**Isomer II RAC = 112 µg a.s./L.**	**1-naphthol RAC = 112 µg a.s./L.**
Oilseed Rape	D2 ditch	8.66	13.36	2.90
	D2 stream	5.43	8.38	1.82
	D3 ditch	1.81	2.80	0.61
	D4 pond	0.41	0.63	0.14
	D4 stream	1.55	2.39	0.52
	D5 pond	0.12	0.19	0.04
	D5 stream	1.67	2.58	0.56
	R1 pond	0.07	0.12	0.02
	R1 stream	1.44	2.22	0.48
	R3 stream	2.75	4.24	0.92
Brassicas	D3 ditch 1st	1.79	2.77	0.60
	D3 ditch 2nd	1.80	2.77	0.60
	D4 pond	0.10	0.15	0.03
	D4 stream	1.41	2.17	0.47
	D6 ditch	1.76	2.71	0.59
	R1 pond 1st	0.23	0.36	0.08
	R1 pond 2nd	0.19	0.29	0.06
	R1 stream 1st	2.50	3.85	0.84
	R1 stream 2nd	2.32	3.59	0.78
	R2 stream 1st	1.55	2.39	0.52
	R2 stream 2nd	1.59	2.45	0.53
	R3 stream 1st	5.11	7.89	1.71
	R3 stream 2nd	3.34	5.15	1.12
	R4 stream 1st	1.66	2.55	0.55
	R4 stream 2nd	6.05	9.34	2.03

PECsw values are below the RAC for all scenarios for each crop therefore no further consideration is required.

Early life stage

The chronic toxicity endpoint for *O. mykiss* (0.4 mg a.s/L) was used to assess the risk from Napropamide-M (active substance); based on the regulatory trigger of 10 the resulting **RAC = 40 µg a.s./L.**

Table B.9.4.7-2: Metabolites risk assessment using FOCUS PECs, for Isomer I, Isomer II and 1-naphthol using the chronic toxicity endpoint for *O. mykiss*

Crop	Water Body	FOCUS, PEC_{SW} (µg a.s./L) Initial, max		
		Isomer I RAC = 40 µg a.s./L.	**Isomer II RAC = 40 µg a.s./L..**	**1-naphthol RAC = 40 µg a.s./L.**
Oilseed Rape	D2 ditch	8.66	13.36	2.90
	D2 stream	5.43	8.38	1.82
	D3 ditch	1.81	2.80	0.61
	D4 pond	0.41	0.63	0.14
	D4 stream	1.55	2.39	0.52
	D5 pond	0.12	0.19	0.04
	D5 stream	1.67	2.58	0.56
	R1 pond	0.07	0.12	0.02
	R1 stream	1.44	2.22	0.48
	R3 stream	2.75	4.24	0.92
Brassicas	D3 ditch 1st	1.79	2.77	0.60
	D3 ditch 2nd	1.80	2.77	0.60
	D4 pond	0.10	0.15	0.03
	D4 stream	1.41	2.17	0.47
	D6 ditch	1.76	2.71	0.59
	R1 pond 1st	0.23	0.36	0.08
	R1 pond 2nd	0.19	0.29	0.06
	R1 stream 1st	2.50	3.85	0.84
	R1 stream 2nd	2.32	3.59	0.78
	R2 stream 1st	1.55	2.39	0.52
	R2 stream 2nd	1.59	2.45	0.53
	R3 stream 1st	5.11	7.89	1.71
	R3 stream 2nd	3.34	5.15	1.12
	R4 stream 1st	1.66	2.55	0.55
	R4 stream 2nd	6.05	9.34	2.03

PECsw values are below the RAC for all scenarios for each crop therefore no further consideration is required.

B.9.4.8. Aquatic invertebrates

Acute Risk

The acute toxicity endpoint for *Daphnia magna* (19 mg a.s/L) was used to assess the risk from Isomer I, Isomer II and 1-naphthol; based on the regulatory trigger of 100 the resulting **RAC = 190 µg a.s./L**.

Table B.9.4.8-1: Metabolites risk assessment using FOCUS PECs, for Isomer I, Isomer II and 1-naphthol using the acute toxicity endpoint for *Daphnia magna*

Crop	Water Body	FOCUS, PEC_{SW} (µg a.s./L) Initial, max		
		Isomer I RAC = 190 µg a.s./L	**Isomer II RAC = 190 µg a.s./L**	**1-naphthol RAC = 190 µg a.s./L**
Oilseed Rape	D2 ditch	8.66	13.36	2.90
	D2 stream	5.43	8.38	1.82
	D3 ditch	1.81	2.80	0.61
	D4 pond	0.41	0.63	0.14
	D4 stream	1.55	2.39	0.52
	D5 pond	0.12	0.19	0.04
	D5 stream	1.67	2.58	0.56

	R1 pond	0.07	0.12	0.02
	R1 stream	1.44	2.22	0.48
	R3 stream	2.75	4.24	0.92
Brassicas	D3 ditch 1st	1.79	2.77	0.60
	D3 ditch 2nd	1.80	2.77	0.60
	D4 pond	0.10	0.15	0.03
	D4 stream	1.41	2.17	0.47
	D6 ditch	1.76	2.71	0.59
	R1 pond 1st	0.23	0.36	0.08
	R1 pond 2nd	0.19	0.29	0.06
	R1 stream 1st	2.50	3.85	0.84
	R1 stream 2nd	2.32	3.59	0.78
	R2 stream 1st	1.55	2.39	0.52
	R2 stream 2nd	1.59	2.45	0.53
	R3 stream 1st	5.11	7.89	1.71
	R3 stream 2nd	3.34	5.15	1.12
	R4 stream 1st	1.66	2.55	0.55
	R4 stream 2nd	6.05	9.34	2.03

PECsw values are below the RAC for all scenarios for each crop therefore no further consideration is required.

Chronic Risk

The chronic toxicity endpoint for *Daphnia magna* (0.3 mg a.s/L) was used to assess the risk from Napropamide-M (active substance); based on the regulatory trigger of 10 the resulting **RAC = 30 µg a.s./L.**

Table B.9.4.8-2: Metabolites risk assessment using FOCUS PECs, for Isomer I, Isomer II and 1-naphthol using the chronic toxicity endpoint for *Daphnia magna*

Crop	Water Body	FOCUS, PEC_{SW} (µg a.s./L) Initial, max		
		Isomer I RAC = 30 µg a.s./L.	**Isomer II RAC = 30 µg a.s./L.**	**1-naphthol RAC = 30 µg a.s./L.**
Oilseed Rape	D2 ditch	8.66	13.36	2.90
	D2 stream	5.43	8.38	1.82
	D3 ditch	1.81	2.80	0.61
	D4 pond	0.41	0.63	0.14
	D4 stream	1.55	2.39	0.52
	D5 pond	0.12	0.19	0.04
	D5 stream	1.67	2.58	0.56
	R1 pond	0.07	0.12	0.02
	R1 stream	1.44	2.22	0.48
	R3 stream	2.75	4.24	0.92
Brassicas	D3 ditch 1st	1.79	2.77	0.60
	D3 ditch 2nd	1.80	2.77	0.60
	D4 pond	0.10	0.15	0.03
	D4 stream	1.41	2.17	0.47
	D6 ditch	1.76	2.71	0.59
	R1 pond 1st	0.23	0.36	0.08
	R1 pond 2nd	0.19	0.29	0.06
	R1 stream 1st	2.50	3.85	0.84
	R1 stream 2nd	2.32	3.59	0.78
	R2 stream 1st	1.55	2.39	0.52

	R2 stream 2nd	1.59	2.45	0.53
	R3 stream 1st	5.11	7.89	1.71
	R3 stream 2nd	3.34	5.15	1.12
	R4 stream 1st	1.66	2.55	0.55
	R4 stream 2nd	6.05	9.34	2.03

PECsw values are below the RAC for all scenarios for each crop therefore no further consideration is required.

B.9.4.9. Algae

The toxicity endpoint for *Pseudokirchneriella subcapitata*. (12.45 mg a.s/L) obtained from a study with D-Devrinol 450 SC was used to assess the risk from from Isomer I, Isomer II and 1-naphthol; based on the regulatory trigger of 10 the resulting **RAC = 1245 µg a.s./L**.

Table B.9.4.9-1: Metabolites risk assessment using FOCUS PECs, for Isomer I, Isomer II and 1-naphthol using the toxicity endpoint for *Pseudokirchneriella subcapitata* obtained from a study with D-Devrinol 450 SC.

Crop	Water Body	FOCUS, PEC_{SW} (µg a.s./L) Initial, max		
		Isomer I RAC = 1245 µg a.s./L	**Isomer II RAC = 1245 µg a.s./L**	**1-naphthol RAC = 1245 µg a.s./L**
Oilseed Rape	D2 ditch	8.66	13.36	2.90
	D2 stream	5.43	8.38	1.82
	D3 ditch	1.81	2.80	0.61
	D4 pond	0.41	0.63	0.14
	D4 stream	1.55	2.39	0.52
	D5 pond	0.12	0.19	0.04
	D5 stream	1.67	2.58	0.56
	R1 pond	0.07	0.12	0.02
	R1 stream	1.44	2.22	0.48
	R3 stream	2.75	4.24	0.92
Brassicas	D3 ditch 1st	1.79	2.77	0.60
	D3 ditch 2nd	1.80	2.77	0.60
	D4 pond	0.10	0.15	0.03
	D4 stream	1.41	2.17	0.47
	D6 ditch	1.76	2.71	0.59
	R1 pond 1st	0.23	0.36	0.08
	R1 pond 2nd	0.19	0.29	0.06
	R1 stream 1st	2.50	3.85	0.84
	R1 stream 2nd	2.32	3.59	0.78
	R2 stream 1st	1.55	2.39	0.52
	R2 stream 2nd	1.59	2.45	0.53
	R3 stream 1st	5.11	7.89	1.71
	R3 stream 2nd	3.34	5.15	1.12
	R4 stream 1st	1.66	2.55	0.55
	R4 stream 2nd	6.05	9.34	2.03

PECsw values are below the RAC for all scenarios for each crop therefore no further consideration is required.

B.9.4.11. Risk via groundwater

Exposure of aquatic organisms may occur where groundwater becomes surface water, including indirect exposure via drainage systems. Groundwater PEC values were <0.001 µg/L for all GAP uses and the relevant metabolites (3CA B.8) and therefore a low risk to aquatic organisms from Napropamide-M and relevant metabolites was concluded for groundwater, it is considered that the risk has been sufficiently addressed in the surface water risk assessment.

Table B.9.4.12 Conclusion of the aquatic risk assessment

Based on the FOCUS Step 4 assessment the risk to aquatic organisms is unresolved for the scenarios D2 Ditch and D2 stream (Winter oilseed rape), as summarised in the table below. It is also noted that the addition of the vegetative filter strips successfully resolved the risk for the relevant scenarios for Winter oilseed rape (R3 Stream) and Brassica vegetable crops (R1 Stream 1st, R1 Stream 2nd, R3 stream 2nd and R4 stream 1st, R3 Stream 1st and R4 Stream 2nd) however it is noted that this method is not accepted as a viable mitigation measure in all Member States. The relevance of this should also be considered further at the Member State level. This assessment is driven by the risk to aquatic macrophytes (*Lemna gibba*).

Table B.9.4.12-1 Summary of unresolved FOCUS scenarios

Organism	Crop	Water body	Scenario
Lemna gibba	Winter Oilseed Rape	Drainage	D2 Ditch
			D2 Stream

Provisional Hazard Classification/Labelling of plant protection products according to Regulation (EC) 1272/2008

Pictogram GHS09

Signal word Warning

Hazard statements H410: Very toxic to aquatic life with long lasting effects.

M-factor 10 acute; 10 chronic

Precautionary statements P273 Avoid release to the environment
P391 Collect spillage
P501 Dispose of contents/ container to ... (in accordance with local/ regional/ national/ international regulation (to be specified)

Justification for classification according to Regulation (EC)1272/2008:

Acute category:

Active substance

The lowest acute toxicity endpoint for the active substance is an E_rC_{50} of 0.08 mg a.s./L for toxicity to aquatic macrophytes (fish LC_{50} 11.2 mg a.s./L, aquatic invertebrate EC_{50} 19 mg a.s./L and algae ErC_{50} of 12.45 mg/L). As this is <1 mg/L, acute category 1 applies to the active substance.

Formulation

The lowest acute toxicity endpoint for the formulated product is an E_rC_{50} of 0.096 mg/L for toxicity for aquatic macrophytes (fish LC_{50} 30 mg/L, aquatic invertebrate EC_{50} 52 mg/L and algae E_rC_{50} 30). As this is <1 mg/L, acute category 1 applies to the formulated product.

Chronic category:

Active substance

The lowest chronic toxicity endpoint for the active substance is an NOEC (EC_{10} value taken as true NOEC could not be determined) of 0.003 mg a.s/L for toxicity to aquatic macrophytes (fish NOEC >0.4 mg a.s/L, aquatic invertebrate NOEC 0.3 mg a.s./L and algae NOEC 0.8 mg a.s./L). As this is <0.1 mg/L and the substance is not rapidly degradable, chronic category 1 applies to the active substance.

Formulation

The chronic toxicity endpoints for aquatic macrophytes (NOEC 0.004 mg/L) and algae (NOEC 0.09 mg/L) are the only chronic endpoints considered for the formulation, therefore they been used for classification. The substance is not 'rapidly biodegradable' and as the NOEC for aquatic macrophytes is below the critical value of 0.1, the formulated product is classified as chronic category 1.

In order to determine the chronic classification for fish and aquatic invertebrates for the formulation, active substance endpoints have been used for extrapolation. The fish and aquatic invertebrate NOECs are >0.4 mg a.s/L and 0.3 mg a.s/L, respectively. The active is therefore classified as chronic category 2 based on these species and the assumption of 'not' readily biodegradable (>0.1 to <1 mg/L).

The formulated product D-Devrinol 450 SC contains 41.49% w/w Napropamide-M. The CLP guidance states that for components classified as 'Chronic 2, Chronic 3 or Chronic 4' the relevant concentration is 1% w/w or greater, therefore Napropamide-M (41.49% w/w) is considered to be a relevant component. No Chronic endpoint is required.

- Summation method

w/w of 'chronic category 2'=≥25% then classified as chronic category 2.

= 41.49 therefore chronic category 2.

The summation method determined chronic category 2 for the active substance extrapolation. As the classification for the formulation based on the aquatic macrophytes endpoint (0.004 mg/L) was determined to be chronic category 1, this will be retained as it is worst case.

GHS09 Pictogram	Required for 'aquatic acute category 1' and 'aquatic chronic category 1'
Signal word 'Warning'	Required for 'aquatic acute category 1' and 'aquatic chronic category 1'
P273, P 391, P 501	Required for 'aquatic acute category 1' and 'aquatic chronic category 1'

B.9.5. EFFECTS ON ARTHROPODS

B.9.5.1. Effects on Bees

Acute toxicity studies to bee have been conducted with the lead formulation, D-Devrinol 450 SC.

B.9.5.1.1 Acute oral toxicity to bees

Report

Rana, J.R. (2014a) Acute oral toxicity (LD_{50}) of D-Devrinol 450 SC (HBW03) to the Honey bee, *Apis mellifera* L. UPL Europe Ltd, Unpublished report No.: 523-3-08-6181

Guidelines

OECD 213 (1998)

GLP

Yes (certified laboratory)

Materials and Methods

Test material	D-Devrinol 450 SC
Description:	Cream viscous liquid.
Lot/Batch #:	JM262.
Content:	41.49% w/w Napropamide-M
Toxic reference:	Dimethoate Technical.
Test animals	
Species:	*Apis mellifera* L.
Age/health:	Active young worker bees, taken from healthy and adequately fed hives of a queen-right colony.
Source:	The apiary maintained at Jai Research Foundation Farm, Valvada - 396 108, Gujarat, India
Experimental dates:	11th of July 2013 – 11th of October 2013.

Test Design

Active young worker bees, taken from healthy and adequately fed hives of a queen-right colony, approximately 19 h prior to dosing, were used as test bees. Bees were collected from frames without brood. For the acclimatisation period glass vessels containing the bees were placed under dark conditions in an environmental test chamber for pre-conditioning for approximately 19 h. Bees, which were observed to be abnormal or unduly disoriented, were discarded. Before the experiment the bees were starved for a period of 3 hours before dosing.

The dose level of D-Devrinol 450 SC was selected on the basis of results obtained in the preliminary range finding study. As a result of this the main study was performed as a limit test at single dose of 110 µg a.s. equivalent to 264.9 µg/bee with five replicates, each consisting of 10 bees per cage. The stock solution for the main study was prepared by mixing 264.9 mg D-Devrinol 450 SC (HBW03) in 10 mL 50% sucrose solution to obtain the nominal concentration of 26.49 µg/µL test item which is equivalent to 11.0 µg a.s. (Napropamide-M)/µL. The toxic reference standard/positive control group were offered dimethoate technical at the dose levels of 0.12, 0.14 and 0.16 µg a.s./bee, three replicates were used for each treatment each containing 10 bees. The control group (negative control) was offered 50% sucrose solution. 100 µL of the test solutions were provided in bee feeders to each of the different treatment groups. The weight of feeder was recorded before and after loading treated diet, for each control and treatment group.

After dosing, the honey bees were transferred to the test cages and provided with food in the form of a cotton swab dipped in 50% aqueous sucrose solution. Distilled water was provided in a 60 mL glass tube plugged with absorbent cotton. Thereafter, the cages were placed under dark conditions in an environmental chamber. The temperature and relative humidity of the chamber were maintained at 25 ±2 °C and 61 to 62%, respectively.

All bees were observed for signs of mortality as well as any abnormal behavioural symptoms such as regurgitation, disorientation, lethargy, paralysis, crawling, distended abdomen, erratic movement, aggressiveness, trembling and tumbling at 4, 24 and 48 h post dosing. Dead and moribund bees were recorded and counted as mortalities and removed from the cage.

The mortality data recorded for three dose levels of dimethoate technical (toxic reference standard /positive control) at 24 h and 48 h were subjected to the Probit analysis (Finney, 1997) and the LD_{50} value was calculated along with the 95% fiducial limits (since there was no mortality in the control group, therefore no correction was necessary). As the study with D-Devrinol 450 SC was conducted as a limit study and no mortality was recorded at the selected limit dose level of 110 µg a.s. of D-Devrinol 450 SC(HBW03)/bee, the LD_{50} was not calculated.

Results and Discussion

The mean mortality recorded for the negative control group (50% sucrose solution) was 0.0% throughout the testing period, this meets the criterion of <10%. The LD_{50} of the toxic reference standard was 0.13 µg a.s./bee with the 95% confidence limits ranging between 0.12 and 0.14 µg a.s./bee at 24 h, this is within the range specified for dimethoate for which the reported oral 24 hour LD_{50} is 0.10-0.35 µg a.s./bee.

Biological results

For the control in which bees were fed with untreated 50% aqueous sucrose solution, no mortality was observed at the time of the final assessment. The bees dosed with dimethoate technical (toxic reference standard/positive control) exhibited paralysis, lethargy and crawling at 4 h post dosing. All live bees exhibited normal behaviour at 24 and 48 h post dosing. The bees dosed with the test item exhibited normal behaviour during the testing period. The mean mortality recorded for the group treated with the test item was 0.0% throughout the testing period at 4, 24 and 48 h post exposure.

Table B.9.5.1.1-1 Summary of mortalities observed at 4, 24 and 48 hours post exposure to D-Devrinol 450 SC (HBW03) in acute oral toxicity test

Dose levels		Mean mortalities (%) at		
		4 h	24 h	48 h
D-Devrinol 450 SC (HBW03) (µg a.s./bee) – test item	110.0	0.0 (N)	0.0 (N)	0.0 (N)
Dimethoate Technical (µg a.s./bee) – toxic reference	0.12	0.0 (L,C)	33.3 (N)	36.7 (N)
	0.14	10.0 (P, C)	66.7 (N)	66.7 (N)
	0.16	56.7 (C)	93.3 (N)	93.3 (N)
Negative Control (50 % Sucrose Solution)		0.0 (N)	0.0 (N)	0.0 (N)

Behavioural Symptoms of surviving individuals: (N) = Normal, (P) = Paralysis, (L) = Lethargy and (C) = Crawling

Conclusion

The LD_{50} of D-Devrinol 450 SC was greater than 264.9 µg/bee, equivalent to 110 µg a.s./bee in oral toxicity test.

RMS Comments

The study was carried out in October however the guideline specifies that collection of bees in late Autumn should be avoided as the bees experience a change in physiology at this time. This is not considered to be an issue in this study as the bees were collected in India for which there is a longer active period due to the climate conditions, this is supported by the control and reference item

mortality which were within the expected range. This study is considered suitable for use in the risk assessment.

B.9.5.1.2 Acute contact toxicity to bees

Report

J.R. Rana (2014b) Acute contact toxicity (LD_{50}) of D-Devrinol 450 SC (HBW03) to the Honey bee, *Apis mellifera* L. UPL Europe Ltd, Unpublished report No.: 524-3-08-6182

Guidelines

OECD 214 (1998)

GLP

Yes (certified laboratory)

Materials and Methods

Test material	D-Devrinol 450 SC
Description:	Cream viscous liquid.
Lot/Batch #:	JM262.
Content:	41.49% w/w Napropamide-M
Toxic reference:	Dimethoate Technical.
Test animals	
Species:	*Apis mellifera* L.
Age/health:	Active young worker bees, taken from healthy and adequately fed hives of a queen-right colony with no brood. Taken approximately 19 h prior to dosing.
Source:	The apiary maintained at Jai Research Foundation Farm, Valvada - 396 108, Gujarat, India
Experimental dates:	9th of July 2013 – 27th of July 2013

Test Design

Active young worker bees, taken from healthy and adequately fed hives of a queen-right colony, approximately 19 h prior to dosing, were used as test bees. Bees were collected from frames without brood. For the acclimatisation period glass vessels containing the bees were placed under dark conditions in an environmental test chamber for pre-conditioning for approximately 19 h. Bees, which were observed to be abnormal or unduly disoriented, were discarded. The honeybees were provided with a cotton swab soaked in 50% (w/v) aqueous sucrose solution (sucrose dissolved in deionized water) during acclimatisation and throughout the study period. The food was renewed every 24 hours.
The dose level of D-Devrinol 450 was selected on the basis of results obtained in the preliminary range finding study. As a result of this the main study was performed as a limit test at single dose of 110 µg a.s. equivalent to 264.9 µg D-Devrinol 450 SC/bee with five replicates, each consisting of 10 bees per cage. The stock solution for the main study was prepared by mixing 2649 mg D-Devrinol 450 SC (HBW03) in 10 mL diluent (distilled water containing Tween 80, 0.1 mL/L) to obtain the nominal concentration of 264.9 µg/µL test item which is equivalent to 110 µg a.s. (Napropamide-M)/µL. The stock solutions for dimethoate technical were prepared by dissolving 16, 18 and 20 mg in 100 mL acetone to obtain the required dose levels of 0.14, 0.16 and 0.18 µg a.s./µL. The negative control group was distilled water containing Tween 80 (0.1 mL/L).

The honeybees in the holding vessels were anaesthetized with CO_2 (exposed for approximately 10 seconds) prior to exposure for ease of handling. Each bee was individually treated with test solutions using a micro applicator fitted with a 1 mL Burkard syringe. Each bee was individually treated with 1 µL of the respective test solution on the dorsal side of the thorax. After dosing, the honey bees were

transferred to the test cages and provided with food (cotton swab dipped in 50% aqueous sucrose solution). Distilled water was provided in a glass tube. Thereafter, the cages were placed under dark conditions in an environmental chamber. The temperature and relative humidity of the chamber were maintained at 25 ±2 °C and 61 to 62%, respectively.

All bees were observed for signs of mortality as well as any abnormal behavioural symptoms such as regurgitation, disorientation, lethargy, paralysis, crawling, distended abdomen, erratic movement, aggressiveness, trembling and tumbling at 4, 24 and 48 h post dosing. Dead and moribund bees were recorded and counted as mortalities and removed from the cage.

The mortality data recorded for three dose levels of dimethoate technical (toxic reference standard/positive control) at 24 h and 48 h were subjected to the Probit analysis (Finney, 1997) and the LD_{50} value was calculated along with the 95% fiducial limits (since there was no mortality in the control group, therefore no correction was necessary). As the study with D-Devrinol 450 SC was conducted as a limit study and no mortality was recorded at the selected limit dose level of 110 µg a.s. of D-Devrinol 450 SC(HBW03)/bee, the LD_{50} was not calculated.

Results and Discussion

All of the validity criteria were met. Mortality in the control group was 0%. The LD_{50} value of 15 µg dimethoate/bee for the toxic reference was within the expected range of 0.10 - 0.30 µg a.s./bee.

Biological results

The bees exposed to 264.9 µg D-Devrinol 450 SC (HBW03)/bee, equivalent to 110 µg a.s./bee, exhibited normal behaviour during the testing period of 48 h post exposure. No mortality was recorded in the group exposed to D-Devrinol 450 SC (HBW03) at the dose level of 110 µg a.s./bee. Due to the absence of mortality in the treatment group during the post exposure period of 48 h, the study was terminated after 48 h.

Table B.9.5.1.2-1 Summary of mortalities observed at 4, 24 and 48 hours post exposure to D-Devrinol 450 SC (HBW03) in acute contact toxicity test

Dose levels		Mean mortalities (%) at		
		4 h	24 h	48 h
D-Devrinol 450 SC (HBW03) (µg a.s./bee) – test item	110.0	0.0 (N)	0.0 (N)	0.0 (N)
Dimethoate Technical (µg a.s./bee) – toxic reference	0.14	3.3 (N)	30.0 (N)	30.0 (N)
	0.16	0 (C)	63.3(N)	63.3 (N)
	0.18	6.7 (L, C)	93.3 (N)	93.3 (N)
Negative Control (Distilled water containing Tween 80, 0.1 mL/L)		0.0 (N)	0.0 (N)	0.0 (N)

Behavioural Symptoms of surviving individuals: (N) = Normal, (P) = Paralysis, (L) = Lethargy and (C) = Crawling.

Conclusion

The acute toxicity of D-Devrinol 450 SC (HBW03) to honey bees was tested in contact toxicity test. The median oral lethal dose (LD_{50}) of D-Devrinol 450 SC (HBW03) was greater than 264.9 µg/bee, equivalent to 110 µg a.s./bee in contact toxicity test.

RMS Comments

A negative control of distilled water containing Tween 80, 0.1 mL/L was used in the study, ideally both a negative control containing just distilled water and a dispersant control containing Tween 80,

0.1 mL/L should have been used. However as Tween is not considered toxic to bees and is referred to in the guideline as an acceptable agent to use, it is accepted that this deviation would not adversely affect the study. This study is considered suitable for use in the risk assessment.

B.9.5.1.3 Effects on honey bee development and other honey bee life stages

No data provided.

B.9.5.1.4 Chronic toxicity to bees

No data provided.

B.9.5.1.5 Sub-lethal effects

The risk to bees from the intended use of Napropamide-M is considered to be low and so further studies on the sub-lethal effects on bees are not required.

B.9.5.1.6 Cage and tunnel tests

The risk to bees from the intended use of Napropamide-M is considered to be low and so higher tier studies on the sub-lethal effects on bees are not required.

B.9.5.1.7 Field tests with honeybees

The risk to bees from the intended use of napropamide-M is considered to be low and so higher tier studies on the sub-lethal effects on bees are not required.

B.9.5.2. Effects on non-target arthropods other than bees

Tier I studies with the standard species *Aphidius rhopalosiphi* and *Typhlodromus pyri* have been conducted with D-Devrinol SC.

Report

C. Gamblin (2014) Acute dose-response toxicity of D-Devrinol 450 SC to the parasitic wasp *Aphidius rhopalosiphi* (De Stefani-Perez) (*Hymenoptera, Braxonidae, Aphidiinae*). UPL Europe Ltd, Unpublished report No.: ENV-14-004

Guidelines

Laboratory test for evaluating the effects of plant protection products on the parasitic wasp, *Aphidius rhopalosiphi* (Mead-Briggs *et al*. 2000)

GLP

Yes (certified)

Materials and Methods

Test material	D-Devrinol 450 SC
Description:	Cream viscous liquid.
Lot/Batch #:	JM267.
Content:	45.0% w/w Napropamide-M
Toxic reference:	Dimethoate Technical.
Negative control:	Deionised water
Test animals	
Species:	*Aphidius rhopalosiphi*
Age:	Adults (not over 48 hours old) for the definitive test.
Source:	Katz Biotech AG
Experimental dates:	3rd of June 2014 – 17th of June 2014.

Study Design

The parasitic wasp *Aphidius rhopalosiphi* were obtained as mummies. Wasps, which hatched over a 48-hour period, were used for the test (i.e. adults, not older than 48 hours).

For preration of the test solutions the test item at the highest exposure rate was prepared, serial dilutions were then made from this top concentration to prepare the lower rate treatments which were as follows; 0.11, 0.33, 1.0, 3.0 and 9.0 L D-Devrinol 450 SC/ha. Dimethoate Technical was used as a reference item at a concentration of 0.12 g a.s/ha. For the application of the test item, reference item and control glass slides were sprayed using a calibrated Mardrive Cabinet Track Sprayer with a spray rate of 200 L ha^{-1} +10%. Calibration was made by weight of water using 3 replicates of 5 applications to six petri dishes with an inner diameter of 86 mm.

The test units for the mortality phase consisted of two glass plates (approximately 13 x 13 cm) which were fitted to a square frame made of inert plastic. Each plate had a hole which was plugged with cotton wool soaked in water and honey as a food source after the introduction of the wasps. To prevent a build-up of vapours from the test item, the units were ventilated with humidified air. Four exposure test units (replicates) were used per treatment and each test unit had a minimum of ten wasps (at least five females) added to them. The test units were maintained at a temperature of 18.0-19.3 ºC, relative humidity of 54.8-88.3 %, and light levels of 634-704 lux with a 16 hrs photoperiod.

After 48 hours the fecundity assessment was conducted, this phase was conducted on the three highest concentrations where the mortality was ≤ 50%. The test units consisted of barley seedlings with 10 – 40 per pot that was14 cm in diameter and enclosed in a clear acrylic cylinder with ventilation holes. The plants were 6 days post emergence when used for the study and a minimum of 100 aphids were confirmed as present per pot of seedlings. A single female wasp was added to each of the test units and the units were incubated for 24 hours at the conditions used for the mortality phase. After 24 hours, the wasps were removed, and survival recorded. Only wasps alive at this point were used in the assessment of fecundity. Any wasps found were removed and disposed of.

The test units were incubated for a further 10 – 11 days and after this they were assessed to determine the number of mummies produced per female wasp.The test units were maintained at a temperature of 19.2-21.5 ºC with light levels of 6850-9150 lux with a 16 hrs photoperiod.

The results for the test item treatment groups were compared statistically using a pair-wise comparison to the control group. To assess mortality the analysis was conducted using the Fisher Exact/Bonferoni-Holm test to the level of $p<0.05$. It was not possible to calculate an LR_{50} due to there being less than a 50% effect observed at the highest dose tested. To assess reproduction the untransformed data was analysed using the Wilcoxon/Bonferroni Adj Test to the level of $p< 0.05$.

Results and Discussion:

The study met the validity criteria, mortality in control was 10%, the mortality of the reference item was 100% the mean mummies per female in the control was 26.6 and no wasps in the control produced zero mummies.

Biological results

The statistical analysis showed that there were no significant effect at any of the rates tested therefore it can be concluded that the NOER for mortality is 9.0 L/ha.

The results of the mortality phase are summarised in the following table:

Table B.9.5.2-1 Summary of mortality data for *A. rhopalosiphi*

Treatment	Rate (L/ha)	Mean mortality	% mortality	Corrected
Control	-	1.0	10	0.0
Test item	0.11	0.1	2.5	-8.3
	0.33	1.8	17.5	8.3
	1.0	1.0	10.0	0.0
	30	0.5	5.0	-5.6
	9.0	2.0	20	11.1

Treatment	Rate (L/ha)	Mean mortality	% mortality	Corrected
reference item	0.12 g a.s/ha	10.0	100	100

(*=statistically significant, Fisher Exact/Bonferoni-Holm test, p<0.05)

The results of the fecundity phase are summarised in the table below, this phase was conducted on the three highest concentrations where the mortality was ≤ 50% (dead + moribund wasps). The statistical analysis showed that that there was a significant effect of reproduction at the concentration of 9.0 L/ha-1 (3.69 L a.s./ha).

Table B.9.5.2-2 Summary of fecundity data for *A. rhopalosiphi*

Rate (L ha-1)	Mean mummies per live female	Standard deviation	% Reduction
Control	26.6	24.1	0
1.0	23.3	20.5	12
3.0	13.3	17.4	50
9.0	4.2	6.5	84 *

(* = Significant result, Wilcoxon/Bonferroni Adj Test, p = < 0.05)

Conclusions

Mortality of > 50 % was not reported at 48 hrs at any of the test concentrations. The LR_{50} for mortality was therefore estimated to be > 9.0 L/ha (3.69 L a.s./ha). Significant effects on fecundity were only reported at the maximum rate of 9.0 L/ha (3.69 L a.s./ha).

RMS Comments

It is noted that the report did not specify the time interval between spraying the test units and the introduction of the wasps. The humidity was recorded in the range of 54.8-88.3 % which is outside of the range recommended by the guideline of 60-90% RH. As the validity criteria were met these devations are considered to be minor and would not impact on the reliability of the results. This study is considered suitable for use in the risk assessment.

Report

R. Cockroft (2014) Acute dose-response toxicity of D-Devrinol 450 SC to the predatory mite, *Typhlodromus pyri* Scheuten (Acari: Phytoseiidae). UPL Europe Ltd, Unpublished report No.: ENV-14-006

Guidelines

Laboratory residual contact test with the predatory mite, *Typhlodromus pyri* for regulatory testing of plant protection products, Blumel *et al.* 2000

GLP

Yes (certified)

Materials and Methods

Test material D-Devrinol 450 SC
- Description: Cream viscous liquid.
- Lot/Batch #: JM267.
- Content: 45.0% w/w Napropamide-M
- Toxic reference: Dimethoate Technical.
- Negative control: Deionised water

Test animals
- Species: *Typhlodromus pyri*
- Age: Between 0 and 24 hours old.
- Source: Katz Biotech AG

Experimental dates: 6th of June 2014 – 20th of June 2014.

Study Design

The test was conducted with the predatory mite, *Typhlodromus pyri*. Eggs were obtained as synchronised cohorts, they were then kept on large glass plate arenas and mites were hatched over a 24-hour period prior to the test. Mites in the protonymph stage, between 0 and 24 hours were used.

The test units consisted of two glass slides (approx. 2.2 x 6 cm) joined so that longitudinal slides touched. The test arena was an area on the slides of approximately 10 cm^2 enclosed by Agralan insect barrier glue to prevent mites leaving the area. Test units were placed in petri dishes filled with water with a filter paper in contact with the water and plate to draw up water by capillary action to provide a water source for mites.

The treatments were prepared in distilled water on the day of application with a spray rate of 200 L ha^{-1} ± 10% using a calibrated Mardrive Cabinet track sprayer. Calibration was made by weight of water using 3 replicates of 5 applications to six petri dishes with an inner diameter of 86 mm. Glass slides were sprayed with the control, test item and reference item solutions as applicable and spray drops were visibly uniform. Five treatment rates of 0.11, 0.33, 1.0, 3.0 and 9.0 L D-Devrinol 450 SC/ha were used with 5 replicates for each. The spray was allowed to dry and 20 protonymphs were placed on top of the glass slide with apple pollen for a food source every day. Dimethoate Technical was used as a reference substance to assess the sensitivity of the test system at a rate of 5.0 g a.s/ha.

The test units were transferred to a controlled environment in randomised design, the test conditions were as follows: The recorded temperature was between 20.5 – 26.7°C, the relative humidity was between 51.6 – 94.3% , light levels were recorded at 459 lux and a photoperiod of 16 hours was implemented.

The study consisted of two phases, an exposure phase in which the mortality of the mites was determined and a fecundity phase in which reproduction was assessed, each phase lated seven days. In the mortality phase the number of dead and escaped mites was recorded at 72 hours and on day 7, missing mites were recorded as dead. On day 7 the mites were sexed and the number of males and females recorded, any eggs present at this point were removed. At this point it was confirmed that each test unit had no more than five females per male therefore it was not necessary to transfer mites between test units of the same treatment. For the fecundity assessment the number of eggs and larvae were recorded and removed on days 10, 13 and 14.

For the analysis of the results the NOEC value for mortality was calculated using a pair-wise comparison to the control group with a p-value of 0.05. The analysis was conducted using Fisher's Exact/Bonferroni-Holm Test. The NOER value for fecundity was calculated using the untransformed data which was analysed using Dunnett's multiple comparison test using a p-value for significance of 0.05. For the LR_{50} the mean corrected mortality was observed for a level of 50%. Dimethoate Technical was used as a reference substance to assess the sensitivity of the test system at 24 h the data was subjected to Probit analysis (Finney, 1997) and the LD_{50} value was calculated along with the 95% fiducial limits (no correction was necessary).

Results and Discussion

The study met the validity criteria, the mean mortality in control was 17, the mean mortality in reference treatment was 100% and the cumulative mean number of eggs per female in the control was 8.3.

Biological results

Dimethoate Technical was used as a reference substance to assess the sensitivity of the test system at a rate of 5.0 g a.s/ha.which resulted in 100% mortality at the end of the test period, validating the test system

The results of the mortality phase are summarised in the following table:

Table B.9.5.2-3 Summary of mortality data for *T.pyri*

Treatment group	Rate (L/ha)	Mean mortality	% mortality	Corrected
1	Control	3.4	17	0
2	0.11	6.4	32	18.1
3	0.33	5.0	25	9.6
4	1.0	4.8	24	8.4
5	3.0	3.6	18	1.2
6	9.0	10.4	52	42.2*
7 (reference item)	5.0 g a.s/ha	20.0	100	100

* = significantly different from the control (Fisher's Exact/Bonferroni-Holm Test, p <0.05)

The mean corrected mortality of < 50 % was seen in the highest treatment group therefore the 7-day LR_{50} is determined to be > 9.0 L D-Devrinol 450 SC/ha. Only the lowest and highest rates tested 0.11 and 9.0 L D-Devrinol 450 SC/ha showed a significant effect. The symptoms observed at 0.11 L/ha were not considered to be treatment related as no effects at higher concentrations were reported. The NOER was therefore determined to be 3.0 L D-Devrinol 450 SC/ha.

Table B.9.5.2-4 Summary of reproductive data for *T.pyri*

Treatment group	Rate (L ha-1)	Mean cumulative eggs per female	% Reduction
1	Control	8.3	0
2	0.11	3.0	62
3	0.33	8.1	6
4	1.0	5.6	32
5	3.0	5.8	31
6	9.0	2.5	69 *

* = significantly different from the control (Dunnett's multiple comparison test, p<0.05)

For the fecundity phase the results showed no significant effects for any of the treatment rates except for the highest rate of 9.0 L D-Devrinol 450 SC/ha. Therefore the NOER was determined to be the next highest concentration of 3.0 L D-Devrinol 450 SC/ha.

Conclusions

Mortality of > 50 % was not reported at any of the test concentrations. The LR_{50} for mortality was therefore estimated to be > 9.0 L/ha (3.69 L a.s./ha). Significant effects on fecundity were only reported at the maximum rate of 9.0 L/ha (3.69 L a.s./ha). The NOER for fecundity was therefore taken to be the next highest rate of 3.0 L/ha (1.23 L a.s./ha).

RMS Comments

It is noted that the report did not specify the the time interval between spraying the test units and the introduction of the mites. There were also short term temperature and humitity deviations, for example temperature was recored between 20.5 – 26.7^{o}C (the guideline specifies 25+2 ^{o}C) and the relative humidity was between 51.6 – 94.3% (the guieline specifies 60-90% RH). As the validity criteria were met these deviations were not considered to be an issue.

The RMS does not agree with the proposed NOER of 3.0 L/ha, as notable effects on fecundity were observed at all concentrations (with the exception of 0.33 L/ha). The data set also contains high level of variability. Therefore the RMS has determined that the fecundity data is unreliable, although an assessment of fecundity is not required for first tier a potential issue with fecundity has been highlighted in the study report therefore this must now be considered. This will be considered further in the risk assessment. The mortality findings are acceptable.

B.9.6. RISK ASSESSMENT FOR ARTHROPODS

B.9.6.1. Effects on bees

A summary of the toxicity of Napropamide-M to bees is provided below.

Table B.9.6.1-1 Summary of endpoints for toxicity to bees

Test substance	Organism	Endpoint	Value	Reference
D-Devrinol 450 SC (HBW03) 41.49% w/w Napropamide-M	Honey bee (*Apis mellifera*)	Acute oral LD_{50}	264.9 µg/bee (equivalent to >110 µg a.s/bee)	Rana, J.R (2014a)
		Acute contact LD_{50}	264.9 µg/bee (equivalent to >110 µg a.s/bee)	Rana, J.R (2014b)

Exposure

Applications of pesticides can potentially result in exposure of honeybees either through direct over-spray, or by contact with residues on plants whilst bees are foraging for food. In order to consider a worst-case scenario, the maximum application rate for D-Devrinol 450 SC of 765 g a.s/ha is used for the risk assessment.

Risk assessment

The acute risk to honeybees from use of D-Devrinol 450 SC was assessed using the maximum single application rate of 765 g a.s/ha and the relevant LD_{50} values to calculate hazard quotients (SANCO/10329/2002 rev 2 final) as follows:

$$Hazard\ Quotient = \frac{Maximum\ application\ rate\ (g\ a.s/ha)}{Acute\ LD_{50}\ (\mu g\ a.s/bee)}$$

Hazard quotients were calculated for oral exposure (Q_{HO}) and contact exposure (Q_{HC}). A hazard quotient of less than 50 indicates a low risk to bees.

Table B.6.1-2 Acute oral and contact risk assessment for honeybees from D-Devrinol 450 SC.

Test species	Substance	GAP Crop	Application rate (g a.s./ha)	Exposure route	LD_{50} (µg a.s./bee)	Hazard quotient	Trigger value
Honeybee	D-Devrinol 450 SC (HBW03)	Winter oilseed rape/ Brassicas	765	Oral	>110	<7	50
				Contact	>110	<7	

The HQ values for acute oral and contact exposure based on the maximum intended use of D-Devrinol 450 SC are below the regulatory trigger value of 50 and therefore indicate acceptable acute risk to bees. In addition as D-Devrinol 450 SC is a pre-emergent herbicide applied to bare soil therefore the field sites will not provide an attractive habitat for foraging bees and so exposure should be limited, noting that flowering weeds may be present.

The applicant has not provided oral or contact toxicity studies with the active substance. With reference to SANCO guidance (SANCO/10329/2002 rev 2 final) if honey bees are likely to be exposed to the active substance both acute oral and acute contact toxicity tests must be conducted. It is noted that D-Devrinol 450 SC is a single active formulation. With reference to Volume 4 of the DAR) for the technical specification of D-Devrinol 450 SC, there are no co-formulants of concern to honeybees. Therefore it is acceptable to assume that the majority of the toxicity to bees from D-Devrinol 450 SC is attributed to the active substance.

B.9.6.2 Effects on target arthropods other than bees

Table B.9.6.2-1 Summary of endpoints for toxicity to non-target arthropods

Test substance	Organism	Endpoint	Value	Reference
D-Devrinol SC (HBW03) 46 % w/w Napropamide-M	*Aphidius rhopalosiphi*	LR_{50}	>9 L/ha (equivalent to >4140 g a.s/ha)	Gamblin, C. (2014)
		NOER	1.0 L/ha (equivalent to 460 g a.s/L)	
	Typhlodromus pyri	LR_{50}	>9 L/ha (equivalent to >4140 g a.s/ha)	Cockroft, R. (2014)
		NOER	-	

Effects on arthropods other than bees from the proposed use of D-Devrinol 450 SC have not been previously evaluated. Therefore, all risk assessments and supporting data for D-Devrinol 450 SC with the proposed use pattern are provided here and are considered adequate.

For *Aphidius rhopalosiphi* mortality data indicated there was < 50 % lethal effect at 48hrs for all the rates tested, the LR_{50} was therefore considered to be > 9.0 L/ha (equivalent to 4140 g a.s/ha

For *Typhlodromus pyri* Mortality data indicated that there was < 50 % lethal effect at 48hrs for all the rates tested, the LR_{50} was therefore considered to be > 9.0 L/ha (equivalent to 4140 g a.s/ha). It is noted that a reliable NOER could not be identified in the study with *Typhlodromus pyri* and this was not sufficiently addressed by the applicant. However the margin of safety obtained in the risk assessment is sufficient to address any reproductive concerns. Furthermore as this was a first tier study the LR_{50} is considered to cover the reproductive risk.

In-field exposure

Non-target arthropods living in the crop can be exposed to residues of D-Devrinol 450 SC by direct contact either as a result of overspray or through contact with residues on plants and soil or in food items. D-Devrinol 450 SC is applied at a maximum rate of 765 g a.s/ha on Winter oilseed rape and brassica vegetable crops at pre-emergence. The maximum in-field exposure (Predicted Environmental Residues, PER) to foliar-dwelling or soil-dwelling organisms is therefore 765 g a.s/ha.

The in-field exposure (predicted environmental residue, PER) is calculated according to ESCORT II (Candolfi *et al*. 2001)[4] using the following equation:

$$PER_{in-field} = Application\ rate\ (\text{g a.s./ha}) \times \text{MAF}$$

The MAF is a generic multiple application factor, which is used to take into account the potential build-up of applied substances between applications based on the application interval, the DT_{50} value and number of applications. As D-Devrinol 450 SC is applied once per season, the MAF is not applicable.

The maximum predicted environmental residues (PER) occurring within the field after application of D-Devrinol 450 SC at the maximum application rate are presented below.

Table B.9.6.2-2 In-field PER values for application of D-Devrinol 450 SC

Substance	Application rate	PER (foliar) g a.s/ha	PER (soil) g a.s/ha
D-Devrinol	765 g a.s/ha	765 g a.s/ha	765 g a.s/ha

[4] Candolfi MP, Barrett KL, Campbell PJ, Forster R, Grandy N, Huet M-C, Lewis G, Oomen PA, Schmuck R, Vogt H (2000) 'Guidance Document on regulatory testing procedures for plant protection products with non-target arthropods' From the workshop, European Standard Characteristics of Non-target Arthropod Regulatory Testing (ESCORT 2) 21-23 March 2000.

In-field risk assessment

The risk to non-target arthropods is assessed using the approach recommended in the published ESCORT II document (Candolfi *et al*. 2001)[5] and the EC Guidance Document on Terrestrial Ecotoxicology[6].

The potential risk of D-Devrinol 450 SC to in-field non-target arthropods was assessed by calculation of the hazard quotient (HQ = exposure/toxicity) with the predicted environmental rate (PER) and the lowest lethal rate (LR_{50}) values according to the following formula:

$$\text{In-field HQ} = \frac{\text{In-field PER}}{LR_{50}}$$

The HQ trigger for Tier I laboratory studies is 2, if the HQ value is below 2 then the risk is considered to be acceptable. The resulting $HQ_{in\text{-}field}$ values are presented below.

Table B.9.6.2-3 In-field HQs for non-target arthropods

Species	LR_{50} (g a.s/ha)	PER (g a.s/ha)	HQ	Trigger value
Typhlodromus pyri	>4140	765	<0.18	2
Aphidius rhopalosiphi	>4140	765	<0.18	2

The in-field HQ values for exposure to maximum residues for the representative species are less the regulatory trigger value of 2 for Tier I tests.

The in-field HQ values indicate that D-Devrinol 450 SC poses low risk to in-field non-target arthropods following application according to the proposed use patterns.

The in-field PER is above the NOER for fecundity for *Typhlodromus pyri* which is 46 g a.s/ha and *Aphidius rhopalosiphi* which is 440 g a.s/ha and therefore indicates that the effects on non-target arthropod populations may be a concern. As only two basic first tier glass plate studies have been conducted and no extended studies to investigate reproduction there is some uncertainty in this area.

Off-field exposure

Risk assessment of areas immediately surrounding the crop is considered important since these areas represent a natural reservoir for immigration, emigration and reproduction of arthropod populations and provide increased species diversity. Exposure of non-target arthropods living in off-field areas to D-Devrinol 450 SC will mainly be due to spray drift from field applications. Off-field areas are assumed to be densely vegetated and thus spray drift is unlikely to reach bare ground. Therefore, evaluation of exposure *via* soil residues in off-field areas was not considered. Off-field foliar PER values were calculated from in-field foliar PERs in conjunction with drift values published by the *BBA (2000)*[7] as shown in the following equation:

$$\text{Off-field foliar PER} = \frac{\text{Maximum in-field foliar PER x (\% drift/100)}}{\text{Vegetation distribution factor}}$$

[5] Candolfi MP, Barrett KL, Campbell PJ, Forster R, Grandy N, Huet M-C, Lewis G, Oomen PA, Schmuck R, Vogt H (2000) 'Guidance Document on regulatory testing procedures for plant protection products with non-target arthropods' From the workshop, European Standard Characteristics of Non-target Arthropod Regulatory Testing (ESCORT 2) 21-23 March 2000.

[6] EC Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC, SANCO/10329, 17 October 2002.

Vegetation distribution factor: The model used to estimate spray drift was developed for drift onto a two-dimensional water surface and, as such, does not account for interception and dilution by three-dimensional vegetation in off-crop areas. Therefore, a vegetation distribution or dilution factor is incorporated into the equation when calculating PERs to be used in conjunction with toxicity endpoints derived from two-dimensional (glass plate or leaf disc) studies. A dilution factor of 10 is recommended by ESCORT II (Candolfi *et al*. 2001)[8].

As D-Devrinol 450 SC is applied to bare soil the drift value at 1 m is considered to be 2.77 % of the application rate (90th percentile drift) for the worst case use of D-Devrinol 450 SC. The drift factor (% drift/100) is therefore 2.77/100 = **0.0277**. The resulting $PER_{off\text{-}field}$ values are shown in the table below.

Table B.9.6.2-4 Off-field foliar Predicted Environmental Residues (PER)

Study type	Maximum in-field foliar PER (g a.s/ha)	drift factor (% drift/100)	Vegetation distribution factor	Off-field foliar PER (g a.s/ha)
Glass plate	765	0.0277	10	2.12

Off-field risk assessment

In order to assess the potential risk of D-Devrinol 450 SC to off-field non-target arthropods, the predicted environmental rate is compared with the toxicity endpoints according to the following formula:

$$\text{Off-field HQ} = \frac{PER_{OFF\text{-}FIELD}\ (\text{g ha})}{LR_{50}\ (\text{g ha})} \times \text{Correction factor}$$

The HQ trigger for Tier I laboratory studies is 2.

Correction factor: ESCORT 2 recommends that a correction factor of 10 for Tier I data, to account for extrapolation from testing just 2 standard species as although these species are known to inhabit agricultural crops these species may not be representative of off feild areas.

$HQ_{off\text{-}field}$ values are given in the table below.

Table B.9.6.2-5 Off-field HQ values for non-target arthropods

Species	LR_{50} (g a.s./ha)	Off-field foliar PER (g a.s./ha)	Correction factor	Off-field foliar HQ	Trigger value
Typhlodromus pyri	>4140	2.12	10	<0.0051	2
Aphidius rhopalosiphi	>4140	2.12	10	<0.0051	

[8] EC Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC, SANCO/10329, 17 October 2002.

[8] 90th percentile drift according to BBA (2000): Bundesanzeiger Jg. 52 (Official Gazette), Nr 100, S. 9879-9880 (25.05.2000) Bekanntmachung über die Abtrifteckwerte, die bei der Prüfung und Zulassung von Pflanzenschutzmitteln herangezogen werden

The off-field HQ values for *T. pyri* and *A. rhopalosiphi* fall below the regulatory trigger value of 2 indicating that D-Devrinol 450 SC does not pose an unacceptable risk to non-target arthropods in off-field areas.

Conclusion: D-Devrinol 450 SC poses low in- and off-field risk to non-target arthropods in terms of mortality following application according to the proposed use patterns. The effects on fecundity may be a concern for in-field areas but as no extended laboratory studies were conducted this is uncertain at the moment.

B.9.7. EFFECTS ON NON-TARGET SOIL MESO- AND MACROFAUNA

B.9.7.1. Earthworms- sub-lethal effects

A study with the representative formulation D-Devrinol 450 SC on the chronic toxicity to earthworms has been conducted to meet the data requirements according to Regulation (EU) No. 283/2013.

Report

J.R. Rana (2014) Reproduction toxicity test of D-Devrinol 450 SC (HBW03) to earthworm, *Eisenia foetida foetida*. UPL Europe Ltd, Unpublished report No.: 522-3-08-6183

Guidelines

OECD 222

GLP

Yes (certified laboratory)

Materials and Methods

Test material:	D-Devrinol 450 SC.
Description:	Cream viscous liquid.
Lot/Batch #:	JM262.
Purity:	41.49% w/w.
Solubility:	Water soluble.
Reference substance:	Carbendazim Technical.
Negative control:	De-ionised water.

Test animals:	
Species:	*Eisenia foetida.*
Age:	Approximately 6 months old.
Source:	Institute of Natural Organic Agriculture, Pune - 411 038.
Experimental Dates:	22nd of August 2013 – 29th of January 2014.

Test Design

Adult earthworms *(Eisenia foetida foetida)* were sub-cultured and maintained in recommended breeding/rearing medium (farmyard manure). Mature earthworms (approximate 6 months old) with clitella and body weights between 302.5 and 584.3 mg were selected for the study. For the acclimation period the animals were conditioned for 24 hours in artificial soil and fed with the same feed as in the definitive test.

The artificial soil for use in the study was freshly prepared one day prior to the conduct of the study and was as follows; 10% w/w peat, 20% kaoline clay and 70% industrial sand. The pH of soil was adjusted to 6.0 ± 0.5 using the CaCO3, if needed. A volume of 10 mL distilled water was mixed with 4800 g artificial soil, which served as the control. From these prepared soil samples, 600 g of artificial soil was utilized for each replication (4 replicates per test concentration and 8 replicates for control).

On the day of treatment, the earthworms were separated, washed with distilled water and blotted dry with blotting paper. Earthworms were weighed individually and a group of 10 earthworms (selected at random) were released in respective groups of glass beakers (filled with 600 g artificial soil which is approximate 1/4 volume of the beaker) and covered with perforated and transparent polythene film.
Based on the results of a preliminary range finding study a quantity of 69.4, 117.8, 200.2, 340.3, 578.4, 983.3, 1671.6 and 2841.6 mg of formulation was weighed and dissolved in 10 mL each of distilled water and thoroughly mixed with 2400 g of artificial soil to obtain the test concentrations of 28.9, 49.1, 83.4, 141.8, 241.0, 409.7, 696.5 and 1184.0 mg/kg artificial soil, respectively. Carbendazim technical was tested as a reference item in a separate study under similar exposure conditions at the test concentrations of 0 (control), 0.7, 1.3, 2.4,4.2, 7.6, 13.7, 24.7, 44.4 and 80.0 mg/kg artificial soil.

The test was performed under the following conditions: 16 hours of light per day, the moisture content measured at the start and at the end of the test was 46.5% and 41.6%, respectively (water holding capacity of the soil was 40.75%); the pH of the test medium measured on day 0 and on the 56th day was 6.42 and 6.44 respectively; temperature during study (recorded daily) was 19.2 ± 0.5 °C.

Observations of mortality and sub-lethal effects were made on day 28. Each test beaker with the test medium was emptied on to a tray and earthworms were considered dead when they failed to respond to a mechanical stimulus given at the anterior end. Body weight of earthworms was recorded on day 0 (prior to treatment) and on the 28th day. The number of cocoons were counted on the 28th day and kept for incubation for a further 28 days. The number of juveniles were counted and recorded on the 56th day, by hand sorting of the artificial soil.

The LC_{50} and the EC_{50} of D-Devrinol 450 SC (HBW03) were calculated using the probit analysis (Finney, 1971). Data for cocoons and juveniles were subjected to Bartlett's test to assess the homogeneity of variance before conducting analysis of variance (ANOVA) and Dunnett's t test. The Student's t test was performed to evaluate the data where the data did not meet the homogeneity of variance.

Results and Discussion

All of the validity criteria were met. In the control each replicate produced 43 -51 juveniles, the co-efficient of variation for reproduction was 6% and adult mortality over the initial 4 weeks was 0%.

Biological results

The LC_{50} of carbendazim technical determined on the 28th day was 8.26 mg/kg artificial soil with the 95% confidence limits ranging between 5.42 and 12.58 mg/kg artificial soil. The EC_{50} calculated for cocoon production by the 28th day was 2.15 mg carbendazim technical/kg artificial soil with 95% fiducial limits of 1.94 and 2.39 mg/kg artificial soil. These results are consistent with OECD 222, which indicates that significant effects should be observed between 1 and 5 mg a.s./kg soil.

For the difinitive test the symptom of sluggishness was observed at a concentration of 409.7 mg/kg artificial soil on day 28, no symptoms were observed in any of the other concentrations or the control. 40% mortality was observed at a concentration of 241.0 mg/kg artificial soil and 100% was observed at a concentration of 409.7 mg/kg artificial soil. No mortality was observed at the test concentrations of 28.9, 49.1, 83.4 mg/ kg artificial soil or in the control group.

The mean numbers of cocoons produced on day 28 and the mean numbers of juveniles on day 56 are summarised in the following table. The number of cocoons produced by the 28th day and the number of juveniles produced by the 59th day was significantly reduced at the concentrations of 141.8 and 241.0 mg/kg artificial soil as compared with the control group.

At concentrations of 28.9 and 241.0 mg/kgdry soil significant increases in body weight were observed. These are not considered to be treatment related as no dose response relationship was observed (Table B.9.8.1-1).

Table B.9.7.1-1 Group wise mean cocoons and juveniles production after exposure to D-Devrinol 450 SC (HBW03).

Group and Concentration of D-Devrinol 450 SC (HBW03) (mg/kg artificial soil)	Cocoons on Day 28			Juveniles on Day 56		
	Mean	SD	%	Mean	SD	%
Control	20.00	1.31	-	46.50	2.78	-
28.9	19.25	0.96	3.75	47.75	5.91	-2.69
49.1	18.75	1.71	6.25	47.75	3.30	-2.69
83.4	19.00	1.41	5.00	47.0	3.74	-1.08
141.8	14.25*	3.30	28.75	29.75*	4.65	36.02
241.0	6.0*	1.83	70.00	6.25*	2.22	86.56
409.7	0.00	0.00	100.0	-	-	-
696.5	0.00	0.00	100.0	-	-	-
1184.0	0.00	0.00	100.0	-	-	-

*= Significant result, (ANOVA) and Dunnett's "t" test. The Student's "t" ($p \leq 0.01$), SD= Standard deviation, (-) = Not applicable)

Table B.9.7.1-2 % body weight change, signs of Toxicity and mortality on Day 28

Concentration of D-Devrinol 450 SC (mg/kg soil)	% mortality	Signs of Toxicity	% body weight change, days 0-28
Control	0	Normal	-2.50
28.9	0	Normal	3.46*
49.1	0	Normal	-0.9
83.4	0	Normal	2.83
141.8	10	Normal	2.73
241.0	40	Normal	5.69**
409.7	92.5	Sluggish	-5.50
696.5	100	#	
1184.0	100	#	

Body weight change key: # = Dead. *Significant result *=p<0.05, **=p<0.01 (statistical test not specified).

Conclusion

The 56-day EC_{50} value calculated for juvenile production for D-Devrinol 450 SC (H1BW03) was 161.43 mg formulation/kg artificial soil (66.97 mg a.s/kg) with 95% fiducial limits of 149.85 and 173.90 mg/kg artificial soil. The LC_{50} of D-Devrinol 450 SC (HBW03) was determined to be 244.03 mg/kg artificial soil (100.05 mg a.s/kg) with the 95% confidence limits ranging between 219.27 and 271.59 mg/kg artificial soil. It was concluded that the highest concentration of D-Devrinol 450 SC (HBW03) causes no adverse effect on production of cocoons and juveniles and therefore, the value for the NOEC was determined to be 83.4 mg formulation/kg artificial soil (34.1 mg a.s/kg). The lowest concentration of D-Devrinol 450 SC (HBW03) revealing adverse effect (LOEC) on production of cocoons and juveniles was determined to be 141.8 mg/kg (58.1 mg a.s/kg) artificial soil.

RMS Comments

It is noted that the water content of the soil exceeded 60% of the maximum water holding capacity, this was addressed in the report and was not thought to have an adverse effect and the RMS accepts this. The report does not state if the water content varied more than 10% during the study. As the validity criteria were met, these deviations were considered to be minor. The study is considered suitable for use in the risk assessment.

B.9.7.2. Effects on non-target soil meso- and macrofauna (other than earthworms)

Please refer to the DAR of Napropamide-M, Volume 3 – B9 (AS), section B.9.4.2. for the study summaries for tests with *Hypoaspis aculeifer* and *Folsomia candida.*

B.9.8. RISK ASSESSMENT FOR NON-TARGET SOIL MESO- AND MACROFAUNA

Table B.9.8-1 Summary of endpoints for soil organisms

Test substance	Organism	Endpoint	Value	Reference
D-Devrinol 450 SC (HBW03) 41.49% w/w	Earthworm- *Eisenia foetida*	NOEC	83.4 mg/kg soil, equivalent to - **34.1 mg a.s/kg soil.**	Rana J.R (2014c)
Napropamide-M (96.1 % purity)	Predatory mite *Hypoaspis aculeifer*	NOEC	**>1000 mg a.s/kg soil**	Vinall, S. (2014)
Napropamide-M (96.1 % purity)	Springtail *Folsomia candida*	NOEC	**>95.3 mg a.s/kg soil**	Vinall, S. (2014)

Exposure

The exposure to soil organisms was estimated by calculating the accumulation of predicted environmental concentrations in soil (PEC_S) with reference to Volume 3 – B.8.

Table B.9.8-2 Summary of PEC_{Soil} of Napropamide-M

Crop	Number of applications	Interval (days)	Maximum use rate (g a.s./ha)	Crop interception (%)	Effective soil exposure rate (g a.s./ha)	Initial PEC_S (mg a.s./kg)	Accumulation PEC_S (mg a.s./kg)
Winter oilseed rape	1	-	765	0	1 x 765	1.02	1.5795
Brassicas vegetable crop	1	-	765	0	1 x 765	1.02	1.5795

It was necessary for the RMS to calculate accumulation PEC_{soil} values as the degradation time of the substance was shown to be extended under laboratory conditions. As the substance will accumulate in soil initial PEC_{soil} values will not sufficiently address the risk therefore the accumulation PEC_{soil} values will be used in the risk assessment, for further details please refer to Volume 3 – B.8.

Metabolites

There were no relevant soil metabolites identified for Napropamide-M and so metabolites are not considered in this risk assessment (Volume 3 – B.8,).

Risk assessment for earthworms

An acute risk assessment is no longer required in accordance with the guidance SANCO/11803/2010.

The potential long-term risk of Napropamide- M to earthworms was assessed by calculating long-term TER (TER_{LT}) values by comparing the NOEC resulting from the chronic earthworm study with the accumulation PEC_{Soil} using the following equation:

$$TER_{LT} = \frac{NOEC\,(mg/kg)}{PEC_S\,(mg/kg)}$$

To account for the relatively high organic matter content of the artificial test soil compared to agricultural soils (log Kow=3.27), the NOEC value is reduced by a factor of 2.

The resulting TER_{LT} values are presented below:

Table 8.9.8-3 Long-term TER value for earthworms

GAP crop	Test substance	$NOEC_{corr}$ (mg/kg soil)[a]	Accumulation PEC_S (mg a.s./kg soil)	TER_{LT}	Trigger value
Winter oilseed rape/Brassica vegetables	D-Devrinol 450 SC	17.3	1.5795	10.95	5

[a] Endpoint corrected by a factor of 2 to account for the high organic matter content of the study soil

The TER_{LT} value for Napropamide-M exceeds the long-term trigger value of 5, indicating acceptable chronic risk to earthworms based on the intended uses of D-Devrinol 450 SC.

Earthworms - field studies

Acceptable risk to earthworms has been shown for the intended uses of D-Devrinol 450 SC. Earthworm field studies were therefore not required to refine the risk assessment.

Effects on non-target soil meso- and macrofauna (other than earthworms)

The potential long-term risk of Napropamide-M to non-target soil macro-fauna was assessed by calculating long-term TER_{LT} values by comparing the NOEC values derived for *Hypoaspis aculeifer* and *Folsomia candida* and the accumulation PEC_{soil} value (Volume 3 – B.8) using the following equation:

$$TER_{LT} = \frac{NOEC\,(mg/kg)}{PEC_S\,(mg/kg)}$$

To account for the high organic matter content of the soil used in the studies (log Kow=3.27), the NOEC values are corrected by a factor of 2. The resulting TER values are presented below.

Table B.9.8-4 Long-term TER value for earthworms

GAP crop	Test substance	Organism	$NOEC_{corr}$ (mg/kg soil)[a]	Accumulation PEC_S (mg a.s./kg soil)	TER_{LT}	Trigger value
Winter oilseed rape/Brassica vegetables	Napropamide-M	*Hypoaspis aculeifer*	>500	1.5795	316.56	5
		Folsomia candida	47.7	1.5795	30.20	5

[a] Endpoint corrected by a factor of 2 to account for the high organic matter content of the study soil

The TER_{LT} values for both *Hypoaspis aculeifer* and *Folsomia candida* exceed the trigger value of 5 indicating an acceptable risk to soil macro-organisms from the intended use of D-Devrinol 450 SC.

B.9.9. EFFECTS ON SOIL NITROGEN TRANSFORMATION

A study on the effects of the lead formulation D-Devrinol 450 SC on soil micro-organisms has been conducted to fulfil the current data requirements for Regulation (EU) No. 283/2013.

Report

A. Shrimali (2013) Effect of D-Devrinol 450 SC (HBW03) on soil microorganisms – nitrogen transformation test. UPL Europe Ltd, Unpublished report No.: 608-3-15-6184

Guidelines

OECD 216 (2000)

GLP

Yes (certified laboratory)

Materials and methods

Test material	D-Devrinol 450 SC (HBW03)
Description:	Cream viscous liquid
Lot/Batch #:	JM262
Purity:	41.49% w/w Napropamide-M.
Solubility:	Un-soluble in water.
Reference substance:	N/A.
Negative control:	De-ionised water.
Test animals	
Organism:	Soil Micro-flora (nitrification)
Source:	Nanivahiyal, Gujarat, India. Location: Par river, Vegetation cover: Pasture.
Date of collection:	30th of March 2013.
Experimental dates:	18 June 2013 – 23 July 2013.

Study design

Soil used in this study was obtained from one site in Gujarat, India from a depth of 0 to 25 cm. The area from which the soil collected was pasture land and according to information gathered from the nearest villagers there was no application of crop protection products or biological materials within one year. It was neither flooded nor dried. After transportation to the laboratory, the soil was stored in refrigerator at 4 + 2 ^{o}C and aerobic conditions were ensured during storage.The characteristics of the test soil are summarised below.

Table B.9.9-1 Physico-chemical characteristics of the soils used to investigate the effects of D-Devrinol 450 SC (HBW03) on soil microflora

Soil type	**(EFM-28 (C/N)**
Particle size distribution (DIN 19683) (% Sand (≥ 63 – 2000 µm), Silt (63 µm – ≥ 2 µm), Clay (< 2 µm)	69.83, 13.46, 9.20
Organic carbon (%)	0.67
Initial Nitrate Content (mg/kg soil)	172.27
Total nitrogen (N_{tot}) (%)	0.00616
Cation exchange capacity (meq/100 g of soil)	9.61
pH ($CaCl_2$)	7.37
Bulk density (g/cm^3)	1.5

Maximum water holding capacity (MWC) %	43.52
Minimum Microbial Biomass (mg/kg dry soil)	546.52
Carbon content of microbial biomass (%)	8.16%

Prior to test initiation, the test soil was manually cleared of large objects and was sieved through a 2 mm mesh and adjusted to 40% - 60% of the maximum water-holding capacity (MWC). The soil samples to be used for the nitrification assessments were amended with lucerne-grass-green-meal powder as a source of nitrogen (C/N ratio: 12.8:1). The soil was amended with 5g of powder per 1kg of soil (dry weight). The soil was stored in a refrigerator (2 + 4 ^{o}C, with aerobic conditions) and contained 13.58% moisture content. Prior to application the soil was adjusted to 50 ± 5% maximum water holding capacity.

For the difinitive test three replicates were used for each treatment and the control. A volume of 2 mL of test formulation 1T, formulation 5T and control were added to separate incubated pre-labeled glass beaker (500 ml capacity) containing 320 g of soil with moisture and water holding capacity (250 g dry weight basis) in each container to achieve the dose levels of 15.82 mg test item (product)/kg dry soil for treatment 1T and 79.12 mg test item (product)/kg dry soil for treatment 5T, respectively. The soil was mixed thoroughly using a spatula. Distilled water was added to maintain moisture level at 50 ± 5% water holding capacity. During mixing, care was taken to avoid compacting and balling of the soil. The test containers were covered with perforated polypropylene sheet to prevent water loss and maintain aerobic conditions.

The soils were then incubated at 20 ± 2 °C in the dark for a period of 28 days. Temperature and soil moisture levels were monitored and any loss of moisture was compensated by the addition of distilled water. Soil samples were drawn for nitrate formation on 0, 7, 14 and 28 days of test item application.

The nitrate content in each treated and control sample was determined at each sampling interval. A quantity of 32 g of soil (25 g on a dry weight basis) from the control and treated soil containers were transferred into pre labelled polyethylene bottles in three replicates. A quantity of 125 mL 0.1 M potassium chloride solution was added in each bottle. The mixtures were shaken at 150 + 5 rpm for 60 minutes, then centrifuged at 5000 rpm for 10 minutes and filtered through Whatman N° 1 filter paper in pre labelled glass beaker (150 mL capacity) for analysis. The filtrate solutions were analysed for nitrate content by a pre-calibrated ISE meter using a nitrate electrode. The calibration of the ISE meter was performed using potassium nitrate standard solution. The nitrate concentration was directly recorded using the ISE meter.

Statistical analysis was performed using in-house developed validated statistical Computer software for the data homogeneity (F test for homogeneity of variance). The Student-t test (pair wise comparison, $\alpha = 0.05$) was used for comparison of treated and control values for short-term respiration and nitrification activity.

Results and discussion

The validity criteria was met. The variation between replicate control samples was 0.9 – 4.2%.

Biological results

The mean nitrate content in control soil samples on 0, 7, 14 and 28 days was 316.27, 371.47, 425.73 and 550.13 mg nitrate/kg dry weight soil, respectively. The mean nitrate content on 0, 7, 14 and 28 days at the concentration of 6.48 mg a.s./kg soil dry weight (1T) was 385.73, 405.47, 446.80 and 555.07 mg nitrate/kg dry weight soil, respectively while at the 5 times concentration of 32.40 mg a.s./kg soil dry weight (5T) it was 380.00, 434.53, 379.07 and 515.07 mg nitrate/kg dry weight soil, respectively.

The mean nitrate formation rates between 0 and 7, 7 and 14; and 14 and 28 days interval were 7.89, 3.88 and 4.44 mg nitrate/kg dry weight soil/day, respectively in the control; 2.82, 2.95 and 3.87 mg nitrate/kg dry weight soil/day, respectively at 1T and 7.79, -3.96 and 4.86 mg nitrate/kg dry weight soil/day, respectively at 5T.

The percent deviation of nitrate formation rates between control and treated samples between 0 and 7, 7 and 14; and 14 and 28 days interval were +64.26, +23.97 and +12.84%, respectively at 1T and +1.27, +202.06 and -9.46%, respectively at 5T. The percent deviation of the nitrate contents on 0, 7, 14 and 28 days by D-Devrinol 450 SC (HBW03) at 6.48 mg a.s./kg soil dry weight (1T) was -21.96, -9.15, -4.95 and -0.90%, respectively whereas at 32.40 mg a.s./kg soil dry weight (5T) it was -20.15%, -16.98%, +10.96% and +6.37%, respectively.

Table B.9.9-2Percent Deviation of Nitrate Formation Rates on Different Days duration

mg test item (product)/kg soil dry weight	Nitrate formation rate (mg nitrate/ kg dry weight soil/day)			Percent Deviation of Nitrate Formation Rates compared to the control		
	0 to 7	7 to 14	14 to 28	0 to 7	7 to 14	14 to 28
Control (0)	7.89	3.88	4.44	-	-	-
15.82	2.82	2.95	3.87	+64.26	+23.97	+12.84
79.12	7.79	-3.96	4.86	+1.27	+202.06	-9.46

* = sign shows growth promotion
+ = sign shows growth inhibition

Conclusion

Based on the results of this study, D-Devrinol 450 SC (HBW03) is not harmful to soil microorganism in a nitrogen transformation test at a concentration of 6.48 mg a.s./kg soil dry weight (1T) and another 5 times 1T, 32.40 mg a.s./kg soil dry weight (5T) [15.82 mg test item (product)/kg soil dry weight and at another 5 times concentration of 79.12 mg test item (product)/kg soil dry weight. It can be concluded that D-Devrinol 450 SC (HBW03) exhibited no long term influence on nitrogen transformation in soil.

RMS Comments

It is noted that 172 mg/kg of nitrate has been recorded in the collected soil which increases to 312 - 320.40 mg/kg in the control on day 0 once the lucerne meal is added. Although the nitrate content is not specified in the OECD 216 guideline these concentrations are considered to be very high and are not within the normal ranges based on historical data. There is also no separate control to account for this. This will be considered further in the risk assessment.

B.9.10. RISK ASSESSMENT FOR SOIL NITROGEN TRANSFORMATION

Table B.9.10-1 Summary of endpoints for soil organisms

Test substance	Organism	Endpoint	Value	Reference
D-Devrinol 450 SC (HBW03) 41.49% w/w	Soil microorganisms – nitrogen transformation test.	NOEC	79.12 gm/L 32.4 mg a.s/L	Shrimali A. (2013)

Risk assessment

The NOEC value for Napropamide-M was compared to the accumulation PEC_{soil} value of 1.595 mg a.s./kg (Volume 3 – B8).to determine potential risk to soil microbial activity.

Table B.9.10-1 Risk assessment for effects on soil micro-organisms

Test item	NOEC (mg a.s/kg)	PEC_S (mg a.s./kg)
D-Devrinol 450 SC	32.4	1.5795

D-Devrinol had **no significant effects (<25 %)** on soil-microorganisms at a concentration of 32.4 mg a.s/kg soil. The study had a number of issues, the main one being that the Nitrate content of the collected soil was very high and not within the normal range based on historical data (172 mg/kg of nitrate increasing to 312 -320.40 mg/kg in the control on day 0 once the lucerne meal was added) there was also no separate control to account for this. For further consideration of this issue reference is made to a comparable study that was evaluated for the authorisation of Napropamide (K.H. Reis, 2003) for which no abnormal Nitrate content was reported. With refererence to the EFSA conclusion of Napropamide (EFSA Journal 2010; 8 (4):1565) no effects (of < 25 %) on nitrate formation were shown at 15.92 mg a.s/kg dw soil. With reference to Volume 4 of the DAR for the technical specification of D-Devrinol 450 SC, there are no co-formulants of concern to soil micro-organisms. Therefore it is acceptable to assume that the majority of the toxicity to soil micro-organisms from D-Devrinol 450 SC is attributed to the active substance, as Napropamide and Napropamide-M are structuraly similar (Volume 4) it is considered to make this comparison and assume that the high Nitrate rate had little effect on the outcome of the study.

With the above consideration the NOEC of 32.4 mg a.s/kg soil is approximately 20 times higher than the accumulation PEC_{soil} value of 1.5795. This indicates that the risk to soil micro-organisms is acceptable and a good margin of safety is provided following use of D-Devrinol 450 SC according to the proposed use pattern, therefore an acceptable risk is concluded.

B.9.11. EFFECTS ON TERRESTRIAL NON-TARGET HIGHER PLANTS

B.9.11.1. Summary of screening data

As Napropamide-M is a herbicide, screening data is not required as a full assessment of the toxicity to non-target plants is required.

B.9.11.2. Testing on non-target plants

New studies have been carried out with D-Devrinol 450 SC to assess the effects on seedling emergence and vegetative vigour fulfil the current data requirements for Regulation (EU) No. 283/2013.

Report

R.A. Dickinson (2014a) D-Devrinol 450 SC - Evaluation of the phytotoxicity to non-target terrestrial plant – seedling emergence test. UPL Europe Ltd, Unpublished report No.: ACE-13-164

Guidelines

OECD Guideline 208 (2006)

GLP

Yes (certified laboratory)

Material and Methods

Test material	D-Devrinol 450 SC
Description:	Cream viscous liquid.
Lot/Batch #:	JM267.
Content:	45.0% w/w Napropamide-M.
Toxic reference:	Not stated.
Negative control:	Deionised water
Test animals	
Species:	Monocotyledons · maize *(Zea mays)*[2] · oat *(Avena sativa)*[5] · onion *(Allium cepa)*[2]

· ryegrass *(Lolium perenne)*[1]

Dicotyledons

· radish *(Raphanus sativus)*[2]
· sugar beet *(Beta vulgaris)*[4]
· carrot *(Daucus carota)*[2]
· cucumber *(Cucumis sativus)*[2]
· soybean *(Glycine max)*[3]
· tomato *(Lycopersicon esculentum)*[2]

Variety: Minipop, Dalguise, White Lisbon, N/A, Cherry Belle, Boogie, Early Nantes, Gherkin national, Elena and Money maker - respectively.

Source: 1) Herbiseed Ltd., Twyford, RG10 0NJ, UK.
2) E. W. King & CO. Ltd., Kelvedon, CO5 9PG, UK.
3) Soya UK, Longways House, Burnetts Lane, West End, Southampton, Hampshire, SO30 2HH, UK.
4) Maribo® Hojbygardvej 31, DK-4960, Holeby, Denmark.
5) Senova Ltd, 49 North Road, Great Abington, Cambridge CB21 6AS, UK.

Experimental dates: 27th of September 2013 – 4th of November 2013.

Test Design

The plant species tested included four monocotyledons: maize (*Zea mays*), oat (*Avena sativa*), onion (*Allium cepa*) and ryegrass (*Lolium perenne*); and six dicotyledons: radish (*Raphanus sativus*), sugar beet (*Beta vulgaris*), carrot (*Daucus carota*), cucumber (*Cucumis sativus*), soybean (*Glycine max*) and tomato (*Lycopersicon esculentum*). The seeds had not been pre-treated with fungicides or insecticides and no plant protection products have been used.

All the species were germinated and grown in 8 cm tall non-porous plastic pots. Five replicate pots with four seeds (six for onion) were maintained for each test species per treatment (control and D-Devrinol 450 SC). Seeds were sown directly into the pots at a depth of ca. 1-2 cm. The soil used as support medium in test was characterised as a sandy loam with an organic carbon content of not more than 1.5% and a pH value of 7.8. All pots were placed in saucers filled with enough water to ensure that the pots were kept moist at all times. There were seven treatment groups per species. D-Devrinol 450 SC was applied at following rates: 3.33, 10, 30, 90, 270, 810 and 2430 g a.s. product/ha using acalibrated Mardrive cabinet track sprayer with flat fan nozzle at 200 L/ha, calibration was made by weight of water using 3 replicates of 5 applications to six petri dishes with an inner diameter of 86 mm. The highest concentration of spray solution was prepared by weighing a calculated amount of D-Devrinol 450 SC and diluting with tap water. Lower dose rates were prepared by serial dilution.

The test was performed in a greenhouse, ambient lighting was supplemented by sodium vapour lamps giving at least a 16 hour day. The light level for the duration of the study was well in excess of 2000 lux, giving good growing conditions for the plants. The mean temperature was 21.3 °C (min. 12.6 °C and max. 29.0 °C) and the mean humidity was 67.6% (min. 34.7% and max. 87.2%). The duration of the test was 21 days (after 50% emergence in controls) for emergence, mortality and visual phytotoxicity which were expressed as a percentage of healthy untreated control plants.

The concentration of the formulation D-Devrinol 450 SC was analytically confirmed based on measurements of the active ingredient Napropamide-M by HPLC analysis. For this two aliquots, each approximately 50 ml, were taken from the highest rate of the test item prior to each application.

The ER_{50} values were calculated using audited mean values of final emergence and fresh weight per treatment and simple probit –maximum likelihood estimation method with 95% confidence level. No Observed Effect Rate (NOER) was the highest concentration of the test item at which no adverse effect was observed with 5% significance level.

Results and Discussion

The validity criteria for the test were met, there was at least 80 -100% emergence in the controls, the control seedlings did not exhibit any phytotoxic effects, the mean survival of the emerged control seedlings was at100% and the environmental conditions were identical for all the tested species.

Analytical results

The recovery rates for the active ingredient (Napropamide-M) based on HPLC analysis indicate that the spray solution were prepared to an acceptable level of accuracy (102 – 103% recovery).

Biological results

The final foliar fresh weights of six of the tested species showed decreases with the monocotyledonous species showing the most significant decrease in weight. Onion, oat, ryegrass, maize, carrot and soybean showed decreases of 98%, 99%, 100%, >99%, 60% and 59% in fresh weight (when compared to the controls) at 2430 g a.s./ha, respectively. The most sensitive species with an ER_{50} based on the foliar fresh weight of 76.6 g a.s./ha was ryegrass Table B.9.11.2-1,, the other parameters of emergenge and phytotoxicty are displayed in tables B.9.11.2-2 and B.9.11.2-3 respectivly. The final ER_{50} values are displayed in Table B.9.11.2-4.

Table B.9.11.2-1 Final Mean Plant Foliar Fresh Weight (% of Untreated Control)

Rate d-Devrinol 450 SC g a.s./ha	Oats %	Onion %	Ryegrass %	Sugar beet %	Maize %	Radish %	Cucumber %	Carrot %	Soy bean %	Tomato %
0										
3.33	91	88	89	102	115	98	107	86	100	119
10.0	106	96	86	110	105	102	101	105	96	126
30.0	96	97	83	110	120	110	99	96	87	96
90.0	103	78	53*	97	100	110	99	85	94	116
270	61*	46*	12*	98	84	117	90	87	95	105
810	1*	20*	2*	89	7*	113	77*	76*	59*	107
2430	1*	2*	0*	62*	<1*	103	61*	40*	41*	101

(*= significant result, significance level<0.05)

Table B.9.11.2-2 Final Mean Plant Emergence (% of Total Seeds Sown)

Rate d-Devrinol 450 SC g a.s./ha	Oats %	Onion %	Ryegrass %	Sugar beet %	Maize %	Radish %	Cucumber %	Carrot %	Soy bean %	Tomato %
0	95	93	95	95	80	95	100	80	85	85
3.33	90	90	95	100	95	95	100	90	95	100
10.0	100	93	95	100	85	100	100	90	100	95
30.0	90	100	100	100	95	100	100	80	85	70
90.0	100	100	90	100	90	95	95	85	90	100
270	90	97	50*	100	95	95	95	85	95	85
810	90	100	25*	90	100	100	95	85	90	100
2430	85	97	5*	100	100	95	95	85	80	95

(*= significant result, significance level<0.05)

Table B.9.11.2-3 Final Mean Visual Phytotoxicity Expressed as a percentage

Rate d-Devrinol 450 SC g a.s./ha	Oats %	Onion %	Ryegrass %	Sugar beet %	Maize %	Radish %	Cucumber %	Carrot %	Soy bean %	Tomato %
0	0	0	0	0	0	0	0	0	0	0

3.33	0	0	0	0	0	0	0	0	0	0
10.0	0	11	0	0	0	0	0	0	2	0
30.0	0	0	0	0	5	0	4	0	0	0
90.0	0	13	26	0	0	0	25	5	0	0
270	31	42*	59	0	42	0	32	8	8	0
810	96	58	86	21	92	4	50	18	63	0
2430	97	90	100	47	99	14	67	45	81	12

Onion showed visual symptoms such as stunting and chlorosis, oat showed stunting and necrosis, ryegrass showed slight stunting and slight chlorosis, maize had leaf distortion and necrosis, carrot showed stunting and wilting, radish showed chlorosis, stunting and leaf distortion, sugar beet showed stunting and leaf distortion, cucumber showed chlorosis, leaf distortion and stunting, soybean showed stunting and leaf distortion and tomato showed slight stunting.

Table B.9.11.2-4 The relative sensitivity to D-Devrinol 450 SC for each species tested based on the ER_{50} and the NOER

Test species	ER_{50}		NOER	
	g a.s./ha Fresh weight	g a.s./ha Emergence	g a.s./ha Fresh weight	g a.s./ha Emergence
Onion (*Allium cepa)*	244	>2430	90	2430
Oat (*Avena sativa)*	368	>2430	90	2430
Ryegrass (*Lolium perenne)*	76.6	344	30	90
Maize (*Zea mays)*	321	>2430	270	2430
Carrot (*Daucus carota)*	1776	>2430	270	2430
Radish (*Raphanus sativus)*	>2430	>2430	2430	2430
Sugar beet (*Beta vulgaris)*	>2430	>2430	810	2430
Cucumber (*Cucmuis sativus)*	>2430	>2430	270	2430
Soybean (*Glycine max)*	1506	>2430	270	2430
Tomato (*Lycopersicon esculentum)*	>2430	>2430	2430	2430

Conclusion

A study was performed to assess the effect of D-Devrinol 450 SC technical on seedling emergence of ten plant species. The most sensitive species with an ER_{50} based on the foliar fresh weight of 76.6 g a.s./ha was rye grass.

RMS Comments

There were some short term deviations in temperature and humidity, for example temerature was recorded in the range of 12.6-29.0 °C (the guideline states 22°C ± 10°C) and humidity was recorded in the range of 34.7- 87.2% RH (the guideline states 70 % ± 25 % RH), the study does not report the results of a reference substance experiment. As all of the validity criteria were met it is accepted that these devaitions would not effect the outcome of the study. This study is considered suitable for use in the risk assessment.

Report

R.A. Dickinson (2014b) D-Devrinol 450 SC - Evaluation of the phytotoxicity to non-target terrestrial plant - vegetative vigour test. UPL Europe Ltd, Unpublished report No.: ACE-13-165

Guidelines

OECD Guideline 227 (2006)

GLP

Yes (certified laboratory)

Material and Methods

Test material	D-Devrinol 450 SC
Description:	Cream viscous liquid.
Lot/Batch #:	JM267.
Content:	45.0% w/w Napropamide-M.
Toxic reference:	Not stated.
Negative control:	Deionised water
Test animals	
Species:	Monocotyledons · maize *(Zea mays)*[2] · oat *(Avena sativa)*[1] · onion *(Allium cepa)*[2] · ryegrass *(Lolium perenne)*[1] Dicotyledons · radish *(Raphanus sativus)*[2] · sugar beet *(Beta vulgaris)*[4] · carrot *(Daucus carota)*[2] · cucumber *(Cucumis sativus)*[2] · soybean *(Glycine max)*[3] · tomato *(Lycopersicon esculentum)*[2]
Age:	2 to 4 true leaf stage.
Variety:	Minipop, Ascot, White Lisbon, N/A, Cherry Belle, Boogie, Early Nantes, Gherkin national, Elena and Money maker - respectively.
Source:	1) Herbiseed Ltd., Twyford, RG10 0NJ, UK. 2) E. W. King & CO. Ltd., Kelvedon, CO5 9PG, UK. 3) Soya UK, Longways House, Burnetts Lane, West End, Southampton, Hampshire, SO30 2HH, UK. 4) Maribo® Hojbygardvej 31, DK-4960, Holeby, Denmark.
Experimental dates:	27th of September 2013 – 28th of October 2013.

Test Design

The plant species tested included four monocotyledons: maize (*Zea mays*), oat (*Avena sativa*), onion (*Allium cepa*) and ryegrass (*Lolium perenne*); and six dicotyledons: radish (*Raphanus sativus*), sugar beet (*Beta vulgaris*), carrot (*Daucus carota*), cucumber (*Cucumis sativus*), soybean (*Glycine max*) and tomato (*Lycopersicon esculentum*).The seeds had not been pre-treated with fungicides or insecticides and no plant protection products have been used.

All the species were germinated and grown in 8 cm tall non-porous plastic pots. Five replicate pots with four plants (six for onion) were maintained for each test species per treatment (control and D-Devrinol 450 SC). This method was consistent and repeatable and it ensured 100% healthy plants in the five replicates prior to the application. This study design has been shown to cause no overcrowding effect for the duration of studies lasting 21 days. Plants used for the vegetative vigour test were 2 to 4 leaves at the time of application and grown on for a further 21 days until final assessment. The soil

used as support medium in test was characterised as a sandy loam with an organic carbon content of not more than 1.5% and a pH value of 7.8. Slow release fertiliser (100 g) was incorporated into soil mix (30 litres). All pots were placed in saucers filled with enough water to ensure that the pots were kept moist at all times.

There were seven treatment groups per species. D-Devrinol 450 SC was applied at following rates: 3.33, 10, 30, 90, 270, 810, and 2430 g a.s/ha using a calibrated Mardrive cabinet track sprayer with flat fan nozzle at 65 cm above the soil surface. The sprayer was calibrated to deliver200 l/ha +/-10%. Calibration was made by weight of water using 3 replicates of 5 applications to six petri dishes with an inner diameter of 86 mm. The highest concentration of spray solution was prepared by weighing a calculated amount of D-Devrinol 450 SC and diluting with tap water. Lower dose rates were prepared by serial dilution. The concentration of the formulation D-Devrinol 450 SC was analytically confirmed based on measurements of the active ingredient Napropamide-M by HPLC. For this two aliquots, each approximately 50 ml, were taken from the highest rate of the test item prior to each application.

The test was performed in a greenhouse, ambient lighting was supplemented by sodium vapour lamps giving at least a 16 hour day. The light level for the duration of the study was well in excess of 2000 lux, giving good growing conditions for the plants. The mean temperature was 19.8 °C (min. 11.6 °C and max. 31.5 °C) and the mean humidity was 71.5% (min. 31.1% and max. 94.6%).

The duration of the test was 21 days. The plants were assessed at 7, 14, and 21 days after application for mortality and visual phytotoxicity and fresh weight (on day 21) which were expressed as a percentage of healthy untreated control plants.

The ER_{50} values were calculated using audited mean values of final fresh weight per treatment using simple probit – maximum likelihood estimation method with 95% confidence level. The NOERwas the highest concentration of the test item at which no adverse effect was observed with 5% significance level.

Results and Discussion

The control plants did not exhibit phytotoxic effects, the mean plant survival was 95-100% for the duration of the study. Environmental conditions for each species were identified and growing media contained the same amount of soil matrix, support media or substrate from the same source. The study report does not state seedling emergence in the control therefore it is an uncertainty as to whether this validity criterion was met.

Analytical results

The results of the HPLC analysis indicate that the recovery rates for the active ingredient (Napropamide-M) was within an acceptable range and therefore the endpoints can be based on nominal concentrations (102 – 103% recovery)

Biological results

The final foliar fresh weights of seven of the tested species showed decreases with the monocotyledonous species showing the most significant decreases. Onion, oat, ryegrass and maize showed decreases of 56%, 81%, 58% and 66% in fresh weight (when compared to the controls) at 2430 g a.s./ha, respectively. Carrot, radish and sugar beet showed no significant decrease in fresh weight (when compared to the controls) at 2430 g a.s./ha. Cucumber, soybean and tomato showed lower decreases in fresh weight when compared to the controls. The decreases were 23% for cucumber, 37% for soybean and 26% for tomato at the highest rate tested. The decrease in final foliar fresh weight for tomato at 2430 g a.s/ha was not identified as statistically significantly different from the control. However as the decrease was 26% it was considered biologically relevant (Table B.9.11.2-5).

Table B.9.11.2-5 Final Mean Plant Foliar Fresh Weight (% of Untreated Control)

Rate	Oats	Onion	Ryegrass	Sugar	Maize	Radish	Cucumber	Carrot	Soy	Tomato

d-Devrinol 450 SC g a.s./ha	%	%	%	beet %	%	%	%	%	bean %	%
0	-	-	-	-	-	-	-	-	-	-
3.33	81	99	100	98	103	97	105	119	104	95
10.0	83	108	106	106	97	104	100	130	100	90
30.0	84	106	109	100	105	88	97	150*	114*	99
90.0	93	113	116	88	106	102	91	152*	92	94
270	72*	95	88	92	89	69	83*	158*	72*	78
810	19*	60*	44*	94	63*	102	87	115	74*	104
2430	19*	44*	42*	83	34*	97	77*	116	63*	74

(*= significant result, significance level<0.05)

Onion showed visual symptoms such as stunting and slight chlorosis, oat showed stunting and chlorosis and slight distortion, ryegrass showed stunting, maize had leaf distortion and stunting, carrot showed no visual symptoms, radish showed slight stunting and slight chlorosis, sugar beet showed no visual symptoms, cucumber showed slight chlorosis and stunting, soybean showed stunting and leaf distortion and chlorosis and tomato showed stunting.

Table Table B.9.11.2-6 Final Mean Visual Phytotoxicity Expressed as percent

Rate d-Devrinol 450 SC g a.s./ha	Oats %	Onion %	Ryegrass %	Sugar beet %	Maize %	Radish %	Cucumber %	Carrot %	Soy bean %	Tomato %
0	0	0	0	0	0	0	0	0	0	0
3.33	0	0	0	0	0	0	0	0	0	0
10.0	0	0	0	0	0	0	0	0	0	0
30.0	2	0	0	0	0	0	1	0	0	0
90.0	0	0	0	0	0	0	0	0	8	0
270	24	0	6	0	0	3	1	0	54	4
810	69	18	34	0	60	6	2	0	60	5
2430	72	34	42	0	80	18	28	0	68	23

Table B.9.11.2-7 Relative sensitivity to D-Devrinol 450 SC for each species tested

Test species	ER_{50}	NOER
	D-Devrinol 450 SC g a.s./ha Fresh weight	D-Devrinol 450 SC g a.s/ha Fresh weight
Onion (*Allium cepa)*	1631	270
Oat (*Avena sativa)*	521	90
Ryegrass (*Lolium perenne)*	1159	270
Maize (*Zea mays)*	1408	270
Carrot (*Daucus carota)*	>2430	2430
Radish (*Raphanus sativus)*	>2430	2430
Sugar beet (*Beta vulgaris)*	>2430	2430

Cucumber (*Cucmuis sativus)*	>2430	810
Soybean (*Glycine max)*	>2430	90
Tomato (*Lycopersicon esculentum)*	>2430	810

Conclusion

A study was performed to assess the effect of D-Devrinol 450 SC technical on vegetative vigour of ten plant species. The most sensitive species affected by D-Devrinol 450 SC with an ER_{50} based on the foliar fresh weight of 521 g a.s./ha was oats, the NOER was determined to be 90 g a.s./ha.

RMS Comments

The RMS has considered the validity criteria and concluded that all have been met except for control emergence. The applicant provided addition information to address this point: '*The validity criteria with regard to seedling emergence is not considered to be relevant to this vegetative vigour study due to the way the treatment groups are set up at the start of the study. The seeds are sown into a compost suitable for germination of the seeds and once the seedlings reach growth stage 10, the required number of seedlings are transferred into several pots containing the test soil. These are then continued onto growth stage 12-14 at which point only those pots containing healthy plants of a similar size are selected to be used in the study'*. The RMS does not consider that the applicant has fully addressed the concern as the study design should be such that the validity criteria can be assessed. However it is accepted that this deviation would not be cause to invalidate the study. There were some short term deviations in temperature and humidity, for example temerature was recorded in the range of 11.6 -31.5 °C (the guideline states 22 ^{o}C ± 10 ^{o}C) and humidity was recorded in the range of 31.1-94.6%RH (the guideline states 70 % ± 25 % RH).

B.9.11.3. Extended laboratory studies on non-target plants

No studies were submitted with the representative product as an acceptable risk was demonstrated in a tier 2 risk assessment with appropriate risk mitigation.

B.9.11.4. Semi-field and field tests on non-target plants

No studies were submitted with the representative product as an acceptable risk was demonstrated in a teir 2 risk assessment with appropriate risk mitigation.

B.9.12. RISK ASSESSMENT FOR TERRESTRIAL NON-TARGET HIGHER PLANTS

Table B.9.12-1 Summary of effect of D-Devrinol 450 SC of seedling emergence and vegetative vigour

Test species	**Seedling emergence**	**Vegetative vigour**
	ER_{50} g a.s./ha	**ER_{50} g a.s./ha**
Onion (*Allium cepa)*	244	1631
Oat (*Avena sativa)*	368	**521**
Ryegrass (*Lolium perenne)*	**76.6**	1159
Maize (*Zea mays)*	321	1408

Carrot (*Daucus carota)*	1776	>2430
Radish (*Raphanus sativus)*	>2430	>2430
Sugar beet (*Beta vulgaris)*	>2430	>2430
Cucumber (*Cucmuis sativus)*	>2430	>2430
Soybean (*Glycine max)*	1506	>2430
Tomato (*Lycopersicon esculentum)*	>2430	>2430

All ER_{50} values are based on fresh weight as this was the most sensitive parameter for all species.

Exposure

Effects on non-target plants are of concern in the off-field environment, where the plants may be exposed to spray drift. The amount of spray drift reaching off-crop habitats is calculated using the 90th percentile estimates derived by the BBA (2000)[9] from the spray-drift predictions of Ganzelmeier and Rautmann (2000)[10] to calculate maximum off-field predicted environmental rates ($PER_{off\text{-}field}$). Only a single application is relevant for the recommended uses of D-Devrinol 450 SC. For a single application to bare soil, 2.77 % of the application rate was assumed to reach areas at 1 m from the edge of the crop (worst-case scenario). 0.57% of the application rate was assumed to reach areas at 5m from the edge of the crop. The $PER_{off\text{-}field}$ is calculated based on the following equation:

$PER_{off\text{-}field}$ = Application rate (g a.s./ha) × drift factor

Table B.9.12-2 $PER_{off\text{-}field}$ values

Application rate (g a.s./ha)	Distance (m)	Drift Value (%)	$PER_{off\text{-}field}$ (g a.s/ha)
765	1	2.77	21.19
765	5	0.57	4.36

Risk assessment

The risk assessment has been carried out as recommended in the Terrestrial Guidance Document[11].

The potential risk to non-target plants associated with the application of D-Devrinol 450 SC was assessed considering the lowest endpoints as shown in Table B.9.12-1, above, and the potential exposure in the off-field area of 21.19 g a.s/ha, according to the following formula:

$$TER = \frac{ER_{50}\ (g/ha)}{PER_{off\text{-}field}\ (g/ha)}$$

[9] 90th percentile drift according to BBA (2000): Bundesanzeiger Jg. 52 (Official Gazette), Nr 100, S. 9879-9880 (25.05.2000) Bekanntmachung über die Abtrifteckwerte, die bei der Prüfung und Zulassung von Pflanzenschutzmitteln herangezogen werden

[10] Ganzelmeier H. and Rautmann D. (2000). Drift, drift-reducing sprayers and sprayer testing. Aspects of Applied Biology, 57, 2000.

[11] Anonymous (2002b). Guidance Document on terrestrial ecotoxicology under Council Directive 91/414/EEC. SANCO/10329/2002. 17 October 2002.

The resulting TER values are presented below.

Table B.9.12-3 TER values for effects of Napropamide-M on non-target plants

Effect	Application rate (g a.s./ha)	Distance (m)	Toxicity endpoint ER_{50} (g a.s./ha)	$PER_{off\text{-}field}$ (g a.s./ha)	TER	Trigger value
Seedling emergence	765	1	76.6	21.19	**3.6**	5
Vegetative vigour			521	21.19	25	
Seedling emergence	765	5	76.6	4.36	17.56	5
Vegetative vigour			521	4.36	119.5	

The TER value for vegetative vigour is above the regulatory trigger value of 5 at a drift distance of 1 m (TER=25), however for seedling emergence the TER value is below the trigger value (TER=3.6). At 5m the TER value for seedling emergence is above the trigger value of 5 (TER=17.56) therefore an acceptable risk is concluded with a 5m buffer zone. Appropriate risk mitigation measures will need to be considedered at MS level.

B.9.13. RISK ASSESSMENT FOR OTHER TERRESTRIAL ORGANISMS (FLORA AND FAUNA)

No further data on other terrestrial organisms is required. Please refer to Volume 3 – B9 (AS), section B.9.7. for further details.

B.9.14. MONITORING DATA

No monitoring studies are available for Napropamide-M.

B.9.15. REFERENCES RELIED ON

Plant protection product D-Devrinol

Data Point	Author(s)	Year	Title Compagny Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
CP 10.2.1/01	[redacted]	2011b	D-Devrinol 450 SC: Acute toxicity to rainbow trout (*Oncorhynchus mykiss*) in a 96 hour test Company Report No. D03572 [redacted] GLP,	Y	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None

			Unpublished **Study submitted to meet data requirements**					
CP 10.2.1/02	Liedtke, A.	2011d	D-Devrinol 450 SC: Acute toxicity to *Daphnia magna* in a 48 hour test Company Report No. D03561 Harlan Laboratories Ltd, Switzerland GLP, Unpublished **Study submitted to meet data requirements**	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CP 10.2.1/03	Kamle, K.	2014	Alga (*Pseudokirchneriella subcapitata*), growth inhibition test with D-Devrinol 450 SC (HBW03) Company Report No. 501-3-07-6180 Jai Research Foundation, India GLP, Unpublished **Study submitted to meet data requirements**	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CP 10.2.1/04	Ramsden, C.	2015	Assessment of the effect of d-Devrinol 450 SC (HBW03) on *Lemna*, growth inhibition test Company Report No. ENV-14-005 AgroChemex Environment	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None

			Ltd, UK GLP, Unpublished **Study submitted to meet data requirements**					
CP 10.3.1.1.1 /01	Rana, J.R.	2014a	Acute oral toxicity (LD_{50}) of D-Devrinol 450 SC (HBW03) to the Honey bee, *Apis mellifera* L Company Report No. 523-3-08-6181 Jai Research Foundation, India GLP, Unpublished **Study submitted to meet data requirements**	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CP 10.3.1.1.2 /01	Rana, J.R.	2014b	Acute contact toxicity (LD_{50}) of D-Devrinol 450 SC (HBW03) to the Honey bee, *Apis mellifera* L Company Report No. 523-3-08-6182 Jai Research Foundation, India GLP, Unpublished **Study submitted to meet data requirements**	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CP 10.3.2.1/ 01	Gamblin, C.	2014	Acute dose-response toxicity of d-Devrinol 450 SC to the parasitic wasp *Aphidius rhopalosiphi* (De Stefani-Perez)	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None

			(*Hymenoptera, Braxonidae, Aphidiinae*) Company Report No. ENV-14-004 AgroChemex Environmental Ltd, UK GLP, Unpublished **Study submitted to meet data requirements**					
CP 10.3.2.1/ 02	Cockroft, R.	2014	Acute dose-response toxicity of d-Devrinol 450 SC to the predatory mite *Typhlodromus pyri* Scheuten (Acari: Phytoseiidae) Company Report No. ENV-14-006 AgroChemex Environmental Ltd, UK GLP, Unpublished **Study submitted to meet data requirements**	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CP 10.4.1.1/ 01	Rana, J.	2014c	Reproduction toxicity test of D-Devrinol 450 SC (HBW03) to earthworm, *Eisenia foetida foetida* Company Report No. 522-3-08-6183 Jai Research Foundation, India GLP, Unpublished **Study submitted to meet data requirements**	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None

CP 10.6.2/01	Dickinson, R.	2014a	d-Devrinol 450 SC- Evaluation of the phytotoxicity to non-target terrestrial plants- Seedling emergence test Company Report No. ACE-13-164 AgroChemex Environmental Ltd, UK GLP, Unpublished **Study submitted to meet data requirements**	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None
CP 10.6.2/02	Dickinson, R.	2014b	d-Devrinol 450 SC- Evaluation of the phytotoxicity to non-target terrestrial plants- Vegetative vigour test Company Report No. ACE-13-165 AgroChemex Environmental Ltd, UK GLP, Unpublished **Study submitted to meet data requirements**	N	Y	Data protection is claimed in accordance with Article 59 of Regulation (EC) No 1107/2009	UPL	None