

REGISTRATION REPORT

Part B

Section 9

Ecotoxicology

Detailed summary of the risk assessment

Product code: HBZ10

Product name: Wizard

Chemical active substances:

Phenmedipham, 125 g/L

Ethofumesate, 125 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(Authorisation - Art. 33 application)

Applicant: UPL Holdings Coöperatief U.A.

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October 2023 (final Core Assessment)

Version history

When	What
October 2021	Part B - Section 9 - Core Assessment - Central Zone, version 1
February 2022	Applicant update
September 2022	Applicant update
December 2022	<p>Initial zRMS assessment</p> <p>The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are struck through and shaded for transparency.</p> <p>Following the evaluation and before sending the document for commenting, all coloured highlighting was removed, from the parts updated by the Applicant, for better legibility.</p>
October 2023	<p>Final report (Core Assessment updated following the commenting period)</p> <p>Following the evaluation after commenting period the parts updated by the Applicant and zRMS was highlighted in yellow, for better legibility. Information no longer relevant is struck through and shaded.</p>

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9	Ecotoxicology (KCP 10)
9.1	Critical GAP and overall conclusions
Table 9.1-1	Table of critical GAPs

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Use-No. *	Member state(s)	Crop and/or situation (crop destination / purpose of crop)	F, Fn, Fpn G, Gn, Gpn or I **	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)	Application				Application rate			PHI (days)	Remarks: e.g. g safener/ synergist per ha	Conclusion						
					Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	L product/ha a) max. rate per appl. b) max. total rate per crop/season	g a.s./ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max			Birds	Mammals	Aquatic organisms	Bees	Non-target arthropods	Soil organisms	Non-target plants
Zonal uses (field or outdoor uses, certain types of protected crops)																				
1	NL	Sugar beet	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 6 b) 6	5	a) 1.2 b) 7.2	a) ETO: 150 PMP: 150 b) ETO: 900 PMP: 900	80-400	-	Max. 7.2 L/ha per year	A	C	R	A	A	C	R
2	NL	Sugar beet	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	6	a) 2.4 b) 7.2	a) ETO: 300 PMP: 300 b) ETO: 900 PMP: 900	80-400	-	Max. 7.2 L/ha per year	A	C	R	A	A	C	R
3	BE CZ PL AT	Sugar beet	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 5 b) 5	7	a) 1.2 b) 6.0	a) ETO: 150 PMP: 150 b) ETO: 750 PMP: 750	80-400 / 200-400 in Poland	-	Max. 6.0 L/ha per year	A	C	R	A	A	C	R
4	NL BE CZ PL AT	Sugar beet	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	6	a) 1.8 b) 5.4	a) ETO: 225 PMP: 225 b) ETO: 675 PMP: 675	80-400 / 200-400 in Poland	-	Max. 5.4 L/ha per year	A	C	R	A	A	C	R
5	BE CZ PL AT	Sugar beet	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	9	a) 2.4 b) 7.2	a) ETO: 300 PMP: 300 b) ETO: 900 PMP: 900	80-400 / 200-400 in Poland	-	Max. 7.2 L/ha per year	A	C	R	A	A	C	R
Use group 1 1, 6, 11, 16-24	NL	Beet-crops (sugar beet, Red beet, yellow beet, fodder beet)	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 6 b) 6	5	a) 1.2 b) 7.2	a) ETO: 150 PMP: 150 b) ETO: 900 PMP: 900	80-400	-	Max 7.2 L/ha per year	A	C	R	A	A	C	R

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Use-No. *	Member state(s)	Crop and/or situation (crop destination / purpose of crop)	F, Fn, Fpn G, Gn, Gpn or I **	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)	Application				Application rate			PHI (days)	Remarks: e.g. g saf-ener/ synergist per ha	Conclusion						
					Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	L product/ha a) max. rate per appl. b) max. total rate per crop/season	g a.s./ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max			Birds	Mammals	Aquatic organisms	Bees	Non-target arthropods	Soil organisms	Non-target plants
Use group 2 2, 7, 12, 17-22	NL	Beet-crops (sugar-beet, Red beet, yellow beet, fodder beet)	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	6	a) 2.4 b) 7.2	a) ETO: 300 PMP: 300 b) ETO: 900 PMP: 900	80-400	-	Max 7.2 L/ha per year	A	C	R	A	A	C	R
Use group 3 3, 8, 13, 18-23	BE, CZ, PL, AT	Beet-crops (sugar-beet, Red beet, yellow beet, fodder beet)	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 5 b) 5	7	a) 1.2 b) 6.0	a) ETO: 150 PMP: 150 b) ETO: 750 PMP: 750	80-400 / 200-400 in Poland	-	Max 6 L/ha per year	A	C	R	A	A	C	R
Use group 4 4, 9, 14, 19-24	NL, BE, CZ, PL, AT	Beet-crops (sugar-beet, Red beet, yellow beet, fodder beet)	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	6	a) 1.8 b) 5.4	a) ETO: 225 PMP: 225 b) ETO: 675 PMP: 675	80-400 / 200-400 in Poland	-	Max 5.4 L/ha per year	A	C	R	A	A	C	R
Use group 5 5, 10, 15, 20-25	BE, CZ, PL, AT	Beet-crops (sugar-beet, Red beet, yellow beet, fodder beet)	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	9	a) 2.4 b) 7.2	a) ETO: 300 PMP: 300 b) ETO: 900 PMP: 900	80-400 / 200-400 in Poland	-	Max 7.2 L/ha per year	A	C	R	A	A	C	R
21	NL	Chard	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 6 b) 6	5	a) 1.2 b) 7.2	a) ETO: 150 PMP: 150 b) ETO: 900 PMP: 900	80-400	-	Max. 7.2 L/ha per year	A	C	R	A	A	C	R

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Use-No. *	Member state(s)	Crop and/or situation (crop destination / purpose of crop)	F, Fn, Fpn G, Gn, Gpn or I **	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group)	Application				Application rate			PHI (days)	Remarks: e.g. g saf-ener/ synergist per ha	Conclusion						
					Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	L product/ha a) max. rate per appl. b) max. total rate per crop/season	g a.s./ha a) max. rate per appl. b) max. total rate per crop/season	Water L/ha min/max			Birds	Mammals	Aquatic organisms	Bees	Non-target arthropods	Soil organisms	Non-target plants
22	NL	Chard	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	6	a) 2.4 b) 7.2	a) ETO: 300 PMP: 300 b) ETO: 900 PMP: 900	80-400	-	Max. 7.2 L/ha per year	A	C	R	A	A	C	R
23	BE CZ PL AT	Chard	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 5 b) 5	7	a) 1.2 b) 6.0	a) ETO: 150 PMP: 150 b) ETO: 750 PMP: 750	80-400 / 200-400 in Poland	-	Max. 6.0 L/ha per year	A	C	R	A	A	C	R
24	NL BE CZ PL AT	Chard	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	6	a) 1.8 b) 5.4	a) ETO: 225 PMP: 225 b) ETO: 675 PMP: 675	80-400 / 200-400 in Poland	-	Max. 5.4 L/ha per year	A	C	R	A	A	C	R
25	BE CZ PL AT	Chard	F	Broadleaf weeds	Overall spray	Spring-summer BBCH 10-39	a) 3 b) 3	9	a) 2.4 b) 7.2	a) ETO: 300 PMP: 300 b) ETO: 900 PMP: 900	80-400 / 200-400 in Poland	-	Max. 7.2 L/ha per year	A	C	R	A	A	C	R

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

Explanation for column 15 – 21 “Conclusion”

A	Acceptable, Safe use
R	Further refinement and/or risk mitigation measures required
C	To be confirmed by CMS

N No safe use

- Remarks table:**
- (1) Numeration necessary to allow references
 - (2) Use official codes/nomenclatures of EU
 - (3) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
 - (4) F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application
 - (5) Scientific names and EPPO-Codes of target pests/diseases/ weeds or when relevant the common names of the pest groups (e.g. biting and sucking insects, soil born insects, foliar fungi, weeds) and the developmental stages of the pests and pest groups at the moment of application must be named
 - (6) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
 - (7) Growth stage at first and last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
 - (8) The maximum number of application possible under practical conditions of use must be provided
 - (9) Minimum interval (in days) between applications of the same product.
 - (10) For specific uses other specifications might be possible, e.g.: g/m³ in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products
 - (11) The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha).
 - (12) If water volume range depends on application equipments (e.g. ULVA or LVA) it should be mentioned under “application: method/kind”.
 - (13) PHI - minimum pre-harvest interval
 - (14) Remarks may include: Extent of use/economic importance/restrictions

9.1.1 Overall conclusions

9.1.1.1 Effects on birds (KCP 10.1.1), Effects on terrestrial vertebrates other than birds (KCP 10.1.2), Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)

The risk assessment for effects on birds and wild mammals is carried out according to the Guidance of EFSA on Risk Assessment for Birds and Mammals (EFSA/2009/1438).

Birds

Acute risk assessment

No acute LD₅₀ values are available for HBZ10. Thus, the acute risk was assessed with the lowest endpoint of the active substances as well as the surrogate LD₅₀ for the formulated product.

The TER_A values at the screening step exceed the Annex VI trigger value of 10 what indicates that HBZ10 applied according to the intended use pattern does not pose an acute risk to birds.

Long-term risk assessment

The EU agreed endpoint of the active substances has been used in the assessment of chronic risk.

The TER_{LT} values at the screening step exceed the Annex VI trigger value of 5 what indicates that HBZ10 applied according to the intended use does not pose a reproductive risk to birds. Based on screening and Tier 1 assessments, the combined long-term risk to birds is demonstrated to be acceptable for the formulated product.

Secondary poisoning

The TER values for secondary poisoning of earthworm-eating birds (dry soil ~~and pore water~~ approach) and fish-eating birds are above the trigger value of 5. There is no risk expected for birds exposed to the active substance through consumption of contaminated water from puddles on soil.

Mammals

Acute risk assessment

No acute LD₅₀ values are available for HBZ10. Thus, the acute risk was assessed with the EU agreed endpoint of the active substances as well as the predicted mixture LD₅₀ for the formulated product.

The TER_A values at the screening step exceed the Annex VI trigger value of 10 what indicates that HBZ10 applied according to the intended use does not pose an acute risk to wild mammals.

Long-term risk assessment

The EU agreed endpoint of the active substances have been used in the assessment of chronic risk. The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable risk for mammals following application of HBZ10 ~~in beet crops~~ **according to the intended use pattern**, except for the active substance Phenmedipham for the generic focal species small insectivorous mammal, large herbivorous mammal, and small omnivorous mammal (growth stage BBCH 10-39).

The refined TER_{LT} values for the active substance Phenmedipham are above the respective trigger value for the focal species small insectivorous mammal “shrew”, large herbivorous mammal “lagomorph”, and small omnivorous mammal “mouse”, indicating an acceptable risk for mammals following application of HBZ10 ~~in beet crops~~ **according to the intended use pattern**.

Based on calculations of combined long-term risk **for all species** the TER_{combi} values are above trigger of 5 indicated an acceptable risk for following Group uses:

- 3 × 1.8 L product/ha, 6-day interval
- 6 × 1.2 L product/ha, 5-day interval
- 5 × 1.2 L product/ha, 7-day interval

In the same time, TER_{combi} values are below trigger of 5 for wood mouse and shrew in Group use: 3 × 2.4 L product/ha, 6-day interval and for wood mouse only in June in Group use: 3 × 2.4 L product/ha, 9-day interval, indicating an unacceptable risk. TU approach was used by zRMS as an option of refinement the combined risk.

Although the TU for phenmedipham is not >90%, it is on the very borderline (89%) and indicates that the long-term toxicity of the mixture will mainly result from the presence of this substance, ethofumesate will

contribute to a small extent. Therefore, the risk assessment based on a.s. phenmedipham is considered by zRMS sufficient to conclude acceptable risk from a mixture for all group uses.

However, zRMS would like to stressed that if the other MSs are different opinion referred to refinement of combined risk assessment used by the zRMS they are considered it further at National level.

Secondary poisoning

The TER values for the active substance Ethofumesate and Phenmedipham (based on refined parameters) for secondary poisoning of earthworm-eating mammals (dry soil and pore water approach) are above the trigger value of 5, indicating an acceptable risk for earthworm-eating mammals after application of HBZ10 in beet crops according to the intended use pattern.

~~The TER values for the active substance Phenmedipham for secondary poisoning of earthworm-eating mammals (dry soil and pore water approach) are below the trigger value of 5, indicating a possible risk for earthworm-eating mammals after application of HBZ10 in beet crops.~~

The TER values for the active substances Ethofumesate and Phenmedipham for secondary poisoning of fish-eating mammals are above the trigger value of 5, indicating an acceptable risk for fish-eating mammals after application of HBZ10 in beet crops according to the intended use pattern.

There is no risk expected for wild mammals exposed to the active substance through consumption of contaminated water from puddles on soil.

9.1.1.2 Effects on aquatic organisms (KCP 10.2)

The evaluation of the risk for aquatic and sediment-dwelling organisms was performed in accordance with the recommendations of the “Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters in the context of Regulation (EC) No 1107/2009”, as provided by the Commission Services (SANTE-2015-00080, 15 January 2015).

Effects of HBZ10 on aquatic organisms were not evaluated as part of the respective EU reviews of Ethofumesate and Phenmedipham.

Based on the available data and the mixture toxicity risk assessment, it can be concluded that Phenmedipham is driving the overall mixture toxicity and that an acceptable risk to aquatic organisms following application of HBZ10 in beet crops for all intended use groups is expected. Moreover, the risk assessment based the single-substance toxicity data of Ethofumesate and Phenmedipham has been performed.

~~Based on~~ According to the results of this the risk assessment based on single-substance toxicity data, a low risk to aquatic organisms can be expected from the use of HBZ10 when applying the following risk mitigation measures:

- For the intended use group 3 in beet crops (early and late applications), to protect aquatic organisms, the implementation of a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is required.
- For all the other intended use groups (1, 2, 4 and 5) in beet crops (early and late application), to protect aquatic organisms, the implementation of a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is required.

~~Based on the results of the mixture toxicity risk assessment, and considering mixture toxicity risk assessment based on step 8 a low risk to aquatic organisms can be expected from the use of HBZ10 when applying the following risk mitigation measures:~~

- ~~— For the intended use groups 1, 3, 4 and 5 (early and late applications), to protect aquatic organisms, the implementation of a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is required.~~
- ~~— For the other intended use group 2 (early and late application), to protect aquatic organisms, the implementation of a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is required.~~

The full mixture toxicity assessment based on STEP 8 is validated by zRMS and the following conclusions can be drawn for the mixture:

Use group 1 (6×1.2 L product/ha, 5-day interval):

- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R3 scenario with 20-meter vegetative buffer zone for early application.
- An acceptable risk for R3 scenario with 10-meter vegetative buffer zone for early application
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

Use group no 2 (3×2.4 L product/ha, 6-day interval):

- Acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for late application.

Use group no 3 (5×1.2 L product/ha, 7-day interval):

- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

1. Use group no 4 (3×1.8 L product/ha, 6-day interval):

- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R3 scenario with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for late application
- Acceptable risk for R3 scenario with 10-meter vegetative buffer zone for late application.

Use group no 5 (3×2.4 L product/ha, 9-day interval):

- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

As the above mitigation measures are related to scenarios R1 and/or R3 stream in STEP 8, decision making for mitigation measures applying in each Member State should however be considered at national level, where relevant.

Such mitigation measures are related to scenarios R1 stream and/or R3 stream and thus, conclusions regarding the mitigation measures should be considered at national level where relevant.

Concerned Member States must decide on applicability of indicated risk mitigation measures in their countries at the product authorisation. Please note that additional aquatic risk assessment may be required by the concerned Member States that do not accept simulations performed according to FOCUS recommendations.

9.1.1.3 Effects on bees (KCP 10.3.1)

The evaluation of the risk for bees was performed in accordance with the recommendations of the EPPO Standard PP 3/10 (3) (2010) covering the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002).

There is no acute oral and contact risk to adult honeybees following application of HBZ10 in beet crops according to the intended use pattern. Following the EPPO (2010) risk assessment scheme, the chronic oral (adult bees) and honeybee larvae toxicity based on the predicted dose of HBZ10 consumed by adult and larval honeybees resulted in high margin of safety values, indicating a low chronic oral risk for adult honeybees and honeybee larvae.

According to EFSA Guidance (2013) there is an indication for a possible chronic oral risk to adult and larval honeybees in treated crop (BBCH 10-39), weeds (BBCH 10-39) and next crop scenario (BBCH 10-

39, chronic oral exposure of adult bees only) following the application of HBZ10. The risk assessment based on the EFSA Guidance (2013) is not yet approved and certain parts are currently under revision. Therefore, the outcome of the risk assessment should not be evaluated based only on the EFSA Guidance (2013). Also, the results based on the decision scheme as described in EPPO (2010) should be taken into consideration.

As no further data is available for refining the EFSA 2013 risk assessment, and in case only the EFSA 2013 risk assessment is considered relevant for decision making, applicant proposes risk mitigation phrase SPe8 from Annex V of 1999/45/EC (still relevant under 1107/2009/EC according to Article 65.1).

“Do not apply when flowering weeds are present / Remove weeds before flowering.”

This issue should be further resolved at the product authorisation in Member States considering indications of the not yet noted EFSA 2013 guidance in their national assessments.

9.1.1.4 Effects on arthropods other than bees (KCP 10.3.2)

Effects of HBZ10 on non-target arthropods were not evaluated as part of the EU review of the active substances Ethofumesate and Phenmedipham. Two laboratory studies on glass plates were conducted with *Aphidius rhopalosiphi* and *Typhlodromus pyri*. Additional extended laboratory tests with *A. rhopalosiphi*, *T. pyri*, *Aleochara bilineata* and *Chrysoperla carnea* were performed.

For the representative species *A. rhopalosiphi* and *T. pyri*, the HQ_{in-field} values at Tier 1 are above the trigger value of 2 indicating a possible risk after exposure to HBZ10 according to the proposed use pattern. ~~in-beet crops.~~

For the representative species *A. rhopalosiphi* and *Typhlodromus pyri* as well as for the additional species *C. carnea* and *Aleochara bilineata*, the in-field PER is below the Tier-2 endpoint indicating low in-field risk for all intended uses.

The off-field HQs are below the trigger value of 2, indicating no risk to non-target arthropods is expected in off-field areas following the application of the product HBZ10 according to the proposed use pattern. ~~in-beet-crops.~~

9.1.1.5 Effects on non-target soil meso- and macrofauna (KCP 10.4), Effects on soil microbial activity (KCP 10.5)

The evaluation of the risk for non-target soil meso- and macrofauna and soil microbial activity was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002).

Effects of HBZ10 on non-target soil meso- and macrofauna and soil microbial activity were not evaluated as part of the EU review of the active substances Ethofumesate and Phenmedipham. Three laboratory studies assessing the effects of HBZ10 on *Eisenia fetida*, *Folsomia candida* and *Hypoaspis aculeifer* were conducted and are also considered in the risk assessment. A study on soil microbial activity has been carried out with the product HBZ10.

When taking into account the more realistic PEC_{soil} value for the formulated product based on single application, the TER values for the active substances Ethofumesate and Phenmedipham are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 for all intended uses. ~~in-beet-crops.~~

~~The TER values for the formulated product HBZ10 are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 for all intended uses in-beet-crops.~~

Mixture risk assessments for earthworms and other non-target soil organisms were also performed based on combi-TER approach and TER calculated as the ratio of the measured toxicity endpoint of the formulation expressed as the sum of the amount of individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

According to these additional calculations and weight of evidence, it can be considered a low long-term risk to soil meso- and macrofauna is expected from the combination of the two active ingredients after application of HBZ10 according to the intended use pattern. However, final acceptance of risk assessment for formulation is left at MSs level.

The TER values for the formulated product HBZ10 following mixture risk assessments for earthworms and other non-target soil organisms are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 according to the intended use pattern.

The risk to soil micro-organisms following the application of HBZ10 was evaluated by comparing the PEC value in soil after application to beet crops according to the intended use pattern with the concentrations for the active substances Ethofumesate and Phenmedipham and their relevant metabolites, as well as for the formulated product HBZ10 at which the adverse effects on the soil microbial activity were below 25%. The results of the comparison expressed as Margin of Safety (MoS) for active substances Ethofumesate and Phenmedipham and their relevant metabolites, as well as for the formulated product HBZ10 indicate an acceptable risk following the application of HBZ10 in beet crops according to the intended use pattern.

Mixture risk assessment for soil microorganisms was also performed based on the combination risk assessment in a way equivalent to the combi-TER approach and the ratio of the maximum test concentration of HBZ10 with effects $\leq 25\%$ expressed as the sum of the amount of individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

As a result, an acceptable combination risk of HBZ10 to soil microorganisms is concluded following the application of HBZ10 according to the intended use pattern.

9.1.1.6 Effects on non-target terrestrial plants (KCP 10.6)

The risk assessment is based on the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002 rev.2 final, 2002).

After refinement of the risk assessment using a probabilistic approach, the TER value is above the trigger of 1 at the drift rate following the application HBZ10 according to the proposed use pattern. Thus, the risk to non-target plants after the application of HBZ10 is considered acceptable.

Based on the deterministic risk assessment it is concluded that the use of the product will not produce unacceptable effects on terrestrial non-target plants growing near treated fields, when considering the following mitigation measures:

- 5 m buffer zone, or alternatively 75% drift reducing spray nozzles for all proposed uses
- Final risk mitigation measures for non-target plants should be decided at MSa level.

9.1.1.7 Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)

The spectrum of the biological activity of HBZ10 is well represented by the results and the risk assessments in this section. Therefore, further data from biological primary screening or other preliminary tests are not considered relevant, as they would not change the ecotoxicological assessment.

9.1.2 Grouping of intended uses for risk assessment

The following table documents the grouping of the intended uses to support application of the risk envelope approach (according to SANCO/11244/2011).

Table 9.1.2-1 Critical use pattern of HBZ10 grouped according to application rate and application time

Group	Intended uses	Relevant use parameters for grouping	Relevant parameter or value for sorting
Birds, Mammals			
Beet crops (sugar beet, red beet, yellow beet, fodder beet and chard)	Beet crops Sugar beet, 6 × 1.2 L product/ha, 5-day application interval, application spring, summer BBCH 10-39 (use 1)	Crop group, application rate, number of applications, interval between applications	Risk assessment is presented for all intended uses
	Beet crops Sugar beet, 3 × 2.4 L product/ha, 6-day or 9-day application interval, application spring, summer BBCH 10-39 (use 2)		
Sugar beet	Beet crops Sugar beet, 5 × 1.2 L product/ha, 7-day application interval, application spring, summer BBCH 10-39 (use 3)		

Group	Intended uses	Relevant use parameters for grouping	Relevant parameter or value for sorting
	Beet crops Sugar beet , 3 × 1.8 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (use 4) Sugar beet , 3 × 2.4 L product/ha, 9-day application interval, application spring, summer BBCH 10-39 (use 5)		
Red beet, yellow beet, fodder beet	Red beet/yellow beet/fodder beet , 6 × 1.2 L product/ha, 5-day application interval, application spring, summer BBCH 10-39 (uses 6, 11, 16) Red beet/yellow beet/fodder beet , 3 × 2.4 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (uses 7, 12, 17) Red beet/yellow beet/fodder beet , 5 × 1.2 L product/ha, 7-day application interval, application spring, summer BBCH 10-39 (uses 8, 13, 18) Red beet/yellow beet/fodder beet , 3 × 1.8 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (uses 9, 14, 19) Red beet/yellow beet/fodder beet , 3 × 2.4 L product/ha, 9-day application interval, application spring, summer BBCH 10-39 (uses 10, 15, 20)	Crop group, application rate, number of applications, interval between applications	Risk assessment is presented for all intended uses
Chard	Chard , 6 × 1.2 L product/ha, 5-day application interval, application spring, summer BBCH 10-39 (use 21) Chard , 3 × 2.4 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (use 22) Chard , 5 × 1.2 L product/ha, 7-day application interval, application spring, summer BBCH 10-39 (use 23) Chard , 3 × 1.8 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (use 24) Chard , 3 × 2.4 L product/ha, 9-day application interval, application spring, summer BBCH 10-39 (use 25)	Crop group, application rate, number of applications, interval between applications	Risk assessment is presented for all intended uses
Aquatic organisms			
Beet crops Sugar beet, red beet, yellow beet, fodder beet and chard	Beet crops Use group 1 , 6 × 1.2 L product/ha, 5-day application interval, application spring, summer BBCH 10-39 (including uses 1, 6, 11, 16, 21) Beet crops Use group 2 , 3 × 2.4 L product/ha, 6-day or 9-day application interval, application spring, summer BBCH 10-39 (including uses 2, 7, 12, 17, 22) Beet crops Use group 3 , 5 × 1.2 L product/ha, 7-day application interval, application spring, summer BBCH 10-39 (including uses 3, 8, 13, 18, 23) Beet crops Use group 4 , 3 × 1.8 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (including uses 4, 9, 14, 19, 24) Use group 5 , 3 × 2.4 L product/ha, 9-day application interval, application spring, summer BBCH 10-39 (including uses 5, 10, 15, 20, 25)	Application rate, number of applications, interval between applications Critical use and modelling/e-fate parameters	Risk assessment is presented for all intended uses
Non-target arthropods, non-target plants			
Beet crops Sugar beet, red beet, yellow beet, fodder beet and chard	Beet crops Use group 1 , 6 × 1.2 L product/ha, 5-day application interval, application spring, summer BBCH 10-39 (including uses 1, 6, 11, 16, 21) Beet crops Use group 2 , 3 × 2.4 L product/ha, 6-day or 9-day application interval, application spring, summer BBCH 10-39 (including uses 2, 7, 12, 17, 22)	Application rate, number of applications	3 × 2.4 L product/ha (equivalent to 300 g Ethofumesate/ha + 300 g Phenmedipham/ha) 3 × 1.8 L product/ha (equivalent to 225 g Ethofumesate/ha + 225 g Phenmedipham/ha)

Group	Intended uses	Relevant use parameters for grouping	Relevant parameter or value for sorting
	Beet crops Use group 3, 5 × 1.2 L product/ha, 7-day application interval, application spring, summer BBCH 10-39 (including uses 3, 8, 13, 18, 23) Beet crops Use group 4, 3 × 1.8 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (including uses 4, 9, 14, 19, 24) Use group 5, 3 × 2.4 L product/ha, 9-day application interval, application spring, summer BBCH 10-39 (including uses 5, 10, 15, 20, 25)		6 × 1.2 L product/ha and 5 × 1.2 L product/ha and (equivalent to 150 g Ethofumesate/ha + 150 g Phenmedipham/ha)
Bees			
Beet crops Sugar beet, red beet, yellow beet, fodder beet and chard	Beet crops Use group 1, 6 × 1.2 L product/ha, 5-day application interval, application spring, summer BBCH 10-39 (including uses 1, 6, 11, 16, 21) Beet crops Use group 2, 3 × 2.4 L product/ha, 6-day or 9-day application interval, application spring, summer BBCH 10-39 (including uses 2, 7, 12, 17, 22) Beet crops Use group 3, 5 × 1.2 L product/ha, 7-day application interval, application spring, summer BBCH 10-39 (including uses 3, 8, 13, 18, 23) Beet crops Use group 4, 3 × 1.8 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (including uses 4, 9, 14, 19, 24) Use group 5, 3 × 2.4 L product/ha, 9-day application interval, application spring, summer BBCH 10-39 (including uses 5, 10, 15, 20, 25)	Single application rate	2.4 L product/ha (equivalent to 300 g Ethofumesate/ha + 300 g Phenmedipham/ha) 1.8 L product/ha (equivalent to 225 g Ethofumesate/ha + 225 g Phenmedipham/ha) 1.2 L product/ha (equivalent to 150 g Ethofumesate/ha + 150 g Phenmedipham/ha)
Soil meso- and macrofauna, soil microbial activity			
Beet crops (sugar beet, red beet, yellow beet, fodder beet and chard)	Beet crops, 6 × 1.2 L product/ha, 5-day application interval, application spring, summer BBCH 10-39 (including uses 1, 6, 11, 16, 21) Beet crops, 3 × 2.4 L product/ha, 6-day or 9-day application interval, application spring, summer BBCH 10-39 (including uses 2, 7, 12, 17, 22) Beet crops, 5 × 1.2 L product/ha, 7-day application interval, application spring, summer BBCH 10-39 (including uses 3, 8, 13, 18, 23) Beet crops, 3 × 1.8 L product/ha, 6-day application interval, application spring, summer BBCH 10-39 (including uses 4, 9, 14, 19, 24) Beet crops, 3 × 2.4 L product/ha, 9-day application interval, application spring, summer BBCH 10-39 (including uses 5, 10, 15, 20, 25)	Application rate, number of applications, interval between applications Critical use and modelling/e-fate parameters	3 × 2.4 L product/ha, 6-day or 9-day application interval (equivalent to 300 g Ethofumesate/ha + 300 g Phenmedipham/ha) 3 × 1.8 L product/ha, 6-day application interval (equivalent to 225 g Ethofumesate/ha + 225 g Phenmedipham/ha) 3 × 2.4 L product/ha, 9-day application interval (equivalent to 300 g Ethofumesate/ha + 300 g Phenmedipham/ha)

For all groups of non-target organisms expect for birds and mammals, the 25 intended uses presented in section B0, can be grouped in five main uses as described in Table 9.1.2-1 of this section, when considering the intended uses ~~on beet crops~~ as a whole (sugar beet, yellow beet, red beet, fodder beet, and chard). Such grouping is used hereafter for a better readability of the calculations results and is described below:

- Use group 1: 6 x 1.2 L prod./ha, 5-days interval (includes uses 1, 6, 11, 16 and 21)
- Use group 2: 3 x 2.4 L prod./ha, 6-days interval (includes uses 2, 7, 12, 17, and 22)
- Use group 3: 5 x 1.2 L prod./ha, 7-days interval (includes uses 3, 8, 13, 18, and 23)
- Use group 4: 3 x 1.8 L prod./ha, 6-days interval (includes uses 4, 9, 14, 19, and 24)
- Use group 5: 3 x 2.4 L prod./ha, 9-days interval (includes uses 5, 10, 15, 20, and 25)

zRMS comments:

zRMS agrees with grouping of the intended uses of HBZ10 proposed in Table 9.1.2-1 above. Therefore, the risk assessment is based on five main uses such as:

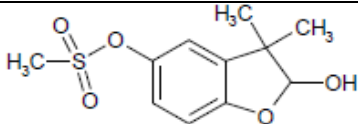
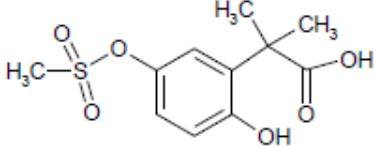
- Use group 1: 6 x 1.2 L prod./ha, 5-days interval (includes uses 1, 6, 11, 16 and 21)

- Use group 2: 3 x 2.4 L prod./ha, 6-days interval (includes uses 2, 7, 12, 17, and 22)
- Use group 3: 5 x 1.2 L prod./ha, 7-days interval (includes uses 3, 8, 13, 18, and 23)
- Use group 4: 3 x 1.8 L prod./ha, 6-days interval (includes uses 4, 9, 14, 19, and 24)
- Use group 5: 3 x 2.4 L prod./ha, 9-days interval (includes uses 5, 10, 15, 20, and 25)

9.1.3 Consideration of metabolites

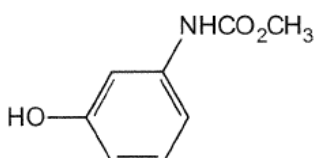
A list of metabolites found in environmental compartments is provided below. The need for conducting a metabolite-specific risk assessment in the context of the evaluation of HBZ10 is indicated in the table below.

Table 9.1.3-1 Metabolites of Ethofumesate

Metabolite	Chemical structure	Molar mass	Maximum occurrence in compartments	Risk assessment required?
NC 8493	 [RS]-2-hydroxy-3,3-dimethyl-2,3-dihydro-1-benzofuran-5-yl methanesulfonate	258.3	Soil: 24.2% Water/sediment: -	Aquatic organisms, soil organisms
NC 20645	 2-{2-hydroxy-5-[(methylsulfonyl)methyl]phenyl}-2-methylpropanoic acid	274.3	Soil: 4.8% Water/sediment: 18.8%	Aquatic organisms

The metabolite CW 35117 determined as major only in the aerobic surface mineralization study, does not need to be considered for exposure assessment.

Table 9.1.3-2 Metabolites of Phenmedipham

Metabolite	Chemical structure	Molar mass	Maximum occurrence in compartments	Risk assessment required?
MHPC		167.2	Soil: 54% Water/Sediment: 70%	Aquatic organisms, soil organisms

zRMS comments:

Information regarding metabolites of ethofumesate provided in Table 9.1.3-1 and Phenmedipham in the Table 9.1.3-2 above are in line with EU agreed data reported in EFSA Journal 2016:14(1):4374 and Review Report (2004), respectively.

9.2 Effects on birds (KCP 10.1.1)

9.2.1 Toxicity data

Avian toxicity studies have been carried out with Ethofumesate and Phenmedipham. Full details of these studies are provided in the respective EU DAR (DAR Ethofumesate, 1998; DAR Phenmedipham, 1999) and related documents (DAR Addendum Ethofumesate, 2000; DAR Addendum Phenmedipham, 2001 and 2003).

Effects on birds of HBZ10 were not evaluated as part of the EU assessment of Ethofumesate and Phenmedipham. However, the provision of further data on HBZ10 is not considered essential, as active substance data on toxicity to birds is available showing low toxicity to birds and so additional formulation data are not considered essential. The risk to birds from HBZ10 can be adequately assessed from risk assessment for the individual active substances.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process. Justifications are provided with respect to the evaluation of mixture toxicity.

Table 9.2.1-1 Endpoints and effect values relevant for the risk assessment for birds - Ethofumesate

Species	Substance	Exposure System	Results	Reference
Mallard duck (<i>Anas platyrhynchos</i>)	Ethofumesate	Oral 14 d Acute	LD ₅₀ > 2000 mg/kg bw	EFSA Conclusion (2016) ¹
Mallard duck (<i>Anas platyrhynchos</i>)	Ethofumesate	Oral 14 d Acute	LD ₅₀ > 3552 mg/kg bw/d	EFSA Conclusion (2016)
Bobwhite quail (<i>Colinus virginianus</i>)	Ethofumesate	Oral 14 d Acute	LD ₅₀ > 2000 mg/kg bw	EFSA Conclusion (2016)
Bobwhite quail (<i>Colinus virginianus</i>)	Ethofumesate	Oral 14 d Acute	LD ₅₀ > 8743mg/kg bw	EFSA Conclusion (2016)
-	Ethofumesate	Acute	LD ₅₀ extrapolated = 3776 mg/kg bw ^{a)}	EFSA Conclusion (2016)
-	Ethofumesate	Long-term	LD ₅₀ /10 = 377.6 mg/kg bw/d	EFSA Conclusion (2016)
Mallard duck (<i>Anas platyrhynchos</i>)	Ethofumesate	Reproductive toxicity	NOEL = 406.0 mg/kg bw/d (reproduction)	EFSA Conclusion (2016)
Bobwhite quail (<i>Colinus virginianus</i>)	Ethofumesate	Reproductive toxicity	NOEL = 265.0 mg/kg bw/d	EFSA Conclusion (2016)

^{a)} LD₅₀ extrapolated according to the EFSA Guidance Document on Birds and Mammals (2009), based on the lowest endpoint for mallard duck and bobwhite quail of 2000 mg a.s./kg bw with an extrapolation factor of 1.888.

Bold written values are used for the risk assessment.

zRMS comments:

Avian toxicity data for ethofumesate are in line with the EU agreed endpoints reported in EFSA Journal 2016;14(1):4374.

Table 9.2.1-2 Endpoints and effect values relevant for the risk assessment for birds - Phenmedipham

Species	Substance	Exposure System	Results	Reference
Mallard duck (<i>Anas platyrhynchos</i>)	Phenmedipham	Oral 14 d Acute	LD ₅₀ > 2100 mg/kg bw	Review Report (2004) ²
Mallard duck (<i>Anas platyrhynchos</i>)	Phenmedipham	Oral 14 d Acute	LD ₅₀ > 2500 mg/kg bw NOEL = 2500 mg/kg ^{a)}	Review Report (2004)
Japanese quail (<i>Coturnix coturnix japonica</i>)	Phenmedipham	Oral 14 d Acute	LD ₅₀ > 2500 mg/kg bw NOEL = 2500 mg/kg ^{a)}	Review Report (2004)
Bobwhite quail (<i>Colinus virginianus</i>)	Phenmedipham	Reproductive toxicity	NOEL = 1200 mg/kg feed (equivalent to 121 mg/kg bw/d)	Review Report (2004)

^{a)} As in the first study with mallard duck no effects were found, the higher NOEL could be used in the risk assessment

Bold written values are used for the risk assessment

zRMS comments:

¹ EFSA (European Food Safety Authority), 2016. Conclusion on the peer review of the pesticide risk assessment of the active substance ethofumesate. EFSA Journal 2016;14(1):4374, 141 pp. doi:10.2903/j.efsa.2016.4374

² European Commission, 2004. Review report for the active substance Phenmedipham. SANCO/4060/2001 - final

Avian toxicity data for phenmedipham are in line with the EU agreed endpoints reported in Review Report (2004).

Mixture toxicity

According to EFSA/2009/1438³ combined action of several toxicants must be specifically considered in the risk assessment when it is obvious that such exposure situations will occur for animals.

Avian toxicity tests with HBZ10 are not available. In line with EFSA/2009/1438, for the assessment of acute effects (mortality), the mixture toxicity is adequately assessed based on the surrogate LD₅₀ calculated by assuming dose additivity:

$$LD_{50}(\text{mix}) = \sum_{i=1}^n \left(\frac{X(a.s._i)}{LD_{50}(a.s._i)} \right)^{-1}$$

With:

X (a.s._i) = fraction of active substance [i] in the mixture

LD₅₀ (a.s._i) = acute toxicity value for active substance [i]

The estimation of the LD₅₀ (mix) is showed in **Table 9.2.1-3**.

Table 9.2.1-3 Estimation of LD₅₀ for the mixture assuming dose additivity

Active substance	Concentration of each active substance in formulation [g a.s. _i /L]	X (a.s. _i) in the mixture	LD ₅₀ [mg a.s. _i /kg bw]	1/tox per fraction [X (a.s. _i)/LD ₅₀ (a.s. _i)]	LD ₅₀ (mix) [Σ mg (a.s. _i)/kg bw]
Ethofumesate	125	0.5	3776	0.0001324	3008
Phenmedipham	125	0.5	> 2500	0.00020000	
Total	250	1.0	-	0.00033242	

To achieve a basis for a comparison of single active substance and mixture toxicity in terms of potential risk, a “tox per fraction” quotient can be calculated for each active substance and compared to the corresponding quotient for the mixture:

$$\text{Tox per fraction (a.s.)} = \frac{LD_{50}(a.s._i)}{X(a.s._i)}$$

$$\text{Tox per fraction (mix)} = \frac{LD_{50}(\text{mix})}{\sum_{i=1}^n X(a.s._i)}$$

Table 9.2.1-4 Comparison of “tox per fraction (a.s._i)” and “tox per fraction (mix)”

Active substance	LD ₅₀ (a.s. _i) [mg a.s./kg bw]	X (a.s. _i) in the mixture	Tox per fraction (a.s.): [LD ₅₀ (a.s. _i)/X (a.s. _i)]	Tox per fraction (mix): [LD ₅₀ (mix)/Σ X (a.s. _i)]	Deviation [%] ^a
Ethofumesate	3776	0.5	7552	3008	60.2
Phenmedipham	> 2500	0.5	5000		39.8

^a Deviation [%] = [(tox per fraction (a.s._i) - tox per fraction (mix))/tox per fraction (a.s._i) × 100]

None of the active substances contributes to ≥ 90% to the toxicity of HBZ10. The “tox per fraction” quotient for both active substances deviates > 10% from the “tox per fraction (mix)”. This indicates that there is not one active substance with a more significant impact on the overall predicted risk. Hence, the risk assessment for acute effects will be performed for the individual active substances, as well as for the calculated mixture toxicity.

Since it is not necessary to calculate a mixture (combined) toxicity value for the product in order to compare to a measured formulation endpoint (as reproduction toxicity with formulation is not available), the

³ 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.]

estimation of chronic combined toxicity for formulations containing more than one active substance can be achieved by combining the TERs for the individual active substances, also referred to as the combi-TER (DRAFT EFSA guidance document - Risk Assessment for Birds and Mammals (version 29.09.2021 for public consultation)). In this way, the TU approach is followed, as the environmental exposure patterns for the individual active substances are already accounted for in the TER values calculated for each substance. When for each substance the trigger values are equal, the combined TER value can be calculated according to:

$$\text{combi TER} = 1/((1/\text{TER}_{\text{substance 1}})+(1/\text{TER}_{\text{substance 2}}))$$

Application Rate	Ethofumesate TER _{LT} Screening step	Phenmedipham TER _{LT} Screening STEP step	TER _{combi}
Sugar beet, 3 × 2.4 L product/ha, 6-day interval	12.2	5.6	3.8
Sugar beet, 3 × 2.4 L product/ha, 9-day interval	14.3	6.5	4.7
Sugar beet, 3 × 1.8 L product/ha, 6-day interval	16.3	7.5	5.1
Sugar beet, 6 × 1.2 L product/ha, 5-day interval	17.1	7.8	5.4
Sugar beet, 5 × 1.2 L product/ha, 7-day interval	21.4	9.8	6.7
Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 6-day interval	12.2	5.6	3.8
Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 9-day interval	14.3	6.5	4.7
Red beet/Yellow beet/Fodder beet, 3 × 1.8 L product/ha, 6-day interval	16.3	7.5	5.1
Red beet/Yellow beet/Fodder beet, 6 × 1.2 L product/ha, 5-day interval	17.1	7.8	5.4
Red beet/Yellow beet/Fodder beet, 5 × 1.2 L product/ha, 7-day interval	21.4	9.8	6.7
Chard, 3 × 2.4 L product/ha, 6-day interval	12.2	5.6	3.8
Chard, 3 × 2.4 L product/ha, 9-day interval	14.3	6.5	4.7
Chard, 3 × 1.8 L product/ha, 6-day interval	16.3	7.5	5.1
Chard, 6 × 1.2 L product/ha, 5-day interval	17.1	7.8	5.4
Chard, 5 × 1.2 L product/ha, 7-day interval	21.4	9.8	6.7

Values in **bold** are below the trigger value

An acceptable risk is expected when **combi TER_{combi}** > trigger of 5 based on long-term risk. Based on the screening assessment TER values, the long-term risk to birds is not demonstrated to be acceptable for the 2.4 L product/ha uses.

Based on Tier 1 TER values for the most sensitive generic focal species (~~lark~~) at BBCH 10–19 (~~early spring~~), the **combi TER_{combi}** are:

Application Rate	Ethofumesate TER _{LT} Tier 1	Phenmedipham TER _{LT} Tier 1	TER _{combi}
Sugar beet, 3 × 2.4 L product/ha, 6-day interval	72.8 69.6	33.2 31.8	22.8 21.8
Sugar beet, 3 × 2.4 L product/ha, 9-day interval	84.9 81.2	38.8 37.1	26.6 25.5
Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 6-day interval	69.6	31.8	21.8
Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 9-day interval	81.2	37.1	25.5
Chard, 3 × 2.4 L product/ha, 6-day interval	35.0	16.0	11.0
Chard, 3 × 2.4 L product/ha, 9-day interval	40.8	18.6	12.8

An acceptable long-term risk to birds can be demonstrated for the formulated product. No further consideration is required.

zRMS comments:

Combined acute toxicity

The LD_{50mix} of 3008 mg /kg bw presented in Table 9.2.1-3 has been validated by the zRMS and is confirmed to be correct.

Due to that none of active substances have more significant impact in the toxicity of mixture, the risk assessment for acute effects is performed for the individual active substances, as well as for the calculated mixture toxicity in relevant Tables below.

Combined long-term toxicity

zRMS agrees with the approach of TER_{combi} calculations presented above based on the lowest TER_{LT} values at screening and Tier 1 step.

9.2.1.1 Justification for new endpoints

The EU agreed endpoints for the active substances Ethofumesate and Phenmedipham are used in the risk assessment.

9.2.2 Risk assessment for spray applications

The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438).

For completeness, the risk assessment is presented for all intended uses (please refer to point 9.1.2).

9.2.2.1 First-tier assessment (screening/generic focal species)

The results of the acute and reproductive screening and first-tier risk assessments are summarised in the following tables. The respective risk assessments for all intended uses are presented starting with the worst-case scenario followed by decreasing exposure.

~~Use group no 2:~~ **Sugar beet**, 3 × 2.4 L product/ha, 6-day interval

Table 9.2.2.1-1 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in ~~beet-crops~~ **sugar beet (3 × 2.4 L product/ha, 6-day interval) - Ethofumesate**

Intended use	Beet-crops Sugar beet					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Acute toxicity [mg/kg bw]	3776					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Sugar beet	Small omnivorous bird	158.8	1.7	-	80.99	46.6
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Sugar beet	Small omnivorous bird	64.8	2.1	0.53	21.64	12.2

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-2 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (3×2.4 L product/ha, 6-day interval) - Phenmedipham

Intended use		Beet-crops Sugar beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 2500					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		158.8	1.7	-	80.99	30.9
Reprod. toxicity [mg/kg bw/d]		121					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		64.8	2.1	0.53	21.64	5.6

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-3 Screening assessment of the acute risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (3×2.4 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		$3 \times \sum 0.300 + 0.300$					
Acute toxicity [mg/kg bw] LD _{mix}		3008					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Bulbs and onion-like crops Sugar beet	Small omnivorous bird	158.8	1.7	-	161.98	18.6	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in ~~beet-crops~~ sugar beet at 3×2.4 L product/ha (6-day interval).

zRMS comments:

The screening step risk assessment for active substances at rate 3×0.3 kg ethofumesate/ha and 3×0.3 kg phenmedipham/ha with 6-day interval is validated by the zRMS.

Based on calculations presented in the Tables from 9.2.2.1-1 to 9.2.2.1-2 acceptable acute and long-term risk may be concluded for birds exposed to ethofumesate and phenmedipham in HBZ10.

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.2.2.1-3 is above the respective trigger value of 10, indicating an acceptable risk for birds following application of HBZ10 in beet crops at 3×2.4 L product/ha (6-day interval).

Combined long-term risk assessment:

TER_{combi} approach used by the Applicant for combined risk assessment is validated by zRMS and confirmed be correct.

Screening combined long-term-risk assessment:				
Application Rate	Ethofumesate TER _{LT} Screening step	Phenmedipham TER _{LT} Screening step	TER _{combi}	Trigger
3 × 2.4 L product/ha, 6-day interval	12.2	5.6	3.8	>5

Values in **bold** are below the trigger value

Based on the screening assessment TER_{combi} values, the risk to birds is not demonstrated to be acceptable for the 2.4 L product/ha uses with 6 d interval.

The Tier 1 long-term risk assessment has been added as being necessary for evaluation of the long-term combined risk.

Table 9.2.2.1-4 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in beet-crops sugar beet (3 × 2.4 L product/ha, 6-day interval) - Ethofumesate

Intended use	Beet-crops Sugar beet (BBCH 10-39)					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Sugar beet BBCH 10-19 (early spring)	Small omnivorous bird, lark	10.9	2.1	0.53	3.64	72.8
Sugar beet BBCH 10-19	Small insectivorous bird, wagtail	5.9	2.1	0.53	1.97	134.5
Sugar beet BBCH 20-49	Small insectivorous bird, wagtail ^a	2.8	2.1	0.53	0.93	283.4
Sugar beet BBCH 10-19	Small insectivorous bird, wagtail	5.9	2.1	0.53	1.97	134.5
Sugar beet BBCH 20-49	Small insectivorous bird, wagtail ^b	9.7	2.1	0.53	3.24	81.8
Sugar beet BBCH 30-49 (late, summer/autumn)	Small granivorous bird, finch	11.4	2.1	0.53	3.81	69.6

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

^a feeding on 100% soil dwelling invertebrates

^b feeding on 50% ground arthropods and 50% foliar arthropods

Table 9.2.2.1-5 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in beet-crops sugar beet (3 × 2.4 L product/ha, 6-day interval) - Phenmedipham

Intended use	Beet-crops Sugar beet (BBCH 10-39)					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Sugar beet BBCH 10-19 (early spring)	Small omnivorous bird, lark	10.9	2.1	0.53	3.64	33.2
Sugar beet BBCH 10-19	Small insectivorous bird, wagtail	5.9	2.1	0.53	1.97	61.4

Sugar beet BBCH 20-49	Small insectivorous bird, wagtail ^a	2.8	2.1	0.53	0.93	129.4
Sugar beet BBCH 10-19	Small insectivorous bird, wagtail	5.9	2.1	0.53	1.97	61.4
Sugar beet BBCH 20-49	Small insectivorous bird, wagtail ^b	9.7	2.1	0.53	3.24	37.4
Sugar beet BBCH 30-49 (late, summer/autumn)	Small granivorous bird, finch	11.4	2.1	0.53	3.81	31.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

^a feeding on 100% soil dwelling invertebrates

^b feeding on 50% ground arthropods and 50% foliar arthropods

zRMS comments:

Tier 1 combined long-term risk assessment

Based on Tier 1 TER_{LT} values for rate 3 x 2.4 L/ha with 6-day interval for the most sensitive generic focal species (lark) at BBCH 10-19 (early spring), the TER_{combi} is above trigger of 5.

Application Rate	Ethofumesate TER _{LT}	Phenmedipham TER _{LT}	TER _{combi}
3 x 2.4 L product/ha, 6-day interval	72.8	33.2	22.8

An acceptable long-term risk to birds can be demonstrated for the formulated product.
No further consideration is required.

Use group no 5: **Sugar beet, 3 x 2.4 L product/ha, 9-day interval**

Table 9.2.2.1-6 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (3 x 2.4 L product/ha, 9-day interval) - Ethofumesate

Intended use	Beet-crops Sugar beet					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 x 0.300					
Acute toxicity [mg/kg bw]	3776					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Sugar beet	Small omnivorous bird	158.8	1.5	-	71.46	52.8
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Sugar beet	Small omnivorous bird	64.8	1.8	0.53	18.55	14.3

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-7 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (3×2.4 L product/ha, 9-day interval) - Phenmedipham

Intended use		Beet-crops Sugar beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 2500					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		158.8	1.5	-	71.46	35.0
Reprod. toxicity [mg/kg bw/d]		121					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		64.8	1.8	0.53	18.55	6.5

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-8 Screening assessment of the acute risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (3×2.4 L product/ha, 9-day interval) – surrogate mixture toxicity

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		$3 \times \sum 0.300 + 0.300$					
Acute toxicity [mg/kg bw] LD _{mix}		3008					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird	158.8	1.5	-	142.92	21.0	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in ~~beet-crops~~ sugar beet at 3×2.4 L product/ha (9-day interval).

zRMS comments:

The screening step risk assessment for active substances at rate 3×0.300 kg ethofumesate/ha and 3×0.300 kg phenmedipham/ha with 9-day interval is agreed by the zRMS.

Based on calculations presented in the Tables from 9.2.2.1-6 to 9.2.2.1-7 acceptable acute and long-term risk may be concluded for birds exposed to ethofumesate and phenmedipham in HBZ10.

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.2.2.1-8 is above the respective trigger value of 10, indicating an acceptable risk for birds following application of HBZ10 in beet crops at 3×2.4 L product/ha with (9-day interval).

Combined long-term risk assessment:

TER_{combi} approach used by the Applicant for combined risk assessment is validated by zRMS and confirmed be correct.

Screening combined long-term-risk assessment:				
Application Rate	Ethofumesate TER _{LT} Screening step	Phenmedipham TER _{LT} Screening STEP	TER _{combi}	Trigger
3 × 2.4 L product/ha, 9-day interval	14.3	6.5	4.7	5

Values in **bold** are below the trigger value

Based on the screening assessment TER_{combi} values, the long-term risk to birds is not demonstrated to be acceptable for the 2.4 L product/ha with 9-day interval.

The Tier 1 long-term risk assessment presented below has been added as being necessary for evaluation of the long-term combined risk.

Table 9.2.2.1-9 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in beet-crops sugar beet (3 × 2.4 L product/ha, 9-day interval) - Ethofumesate

Intended use	Beet-crops Sugar beet (BBCH 10-39)					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Sugar beet BBCH 10-19 (early spring)	Small omnivorous bird, lark	10.9	1.8	0.53	3.12	84.9
Sugar beet BBCH 10-19	Small insectivorous bird, wagtail	5.9	1.8	0.53	1.69	156.9
Sugar beet BBCH 20-49	Small insectivorous bird, wagtail ^a	2.8	1.8	0.53	0.80	330.7
Sugar beet BBCH 10-19	Small insectivorous bird, wagtail	5.9	1.8	0.53	1.69	156.9
Sugar beet BBCH 20-49	Small insectivorous bird, wagtail ^b	9.7	1.8	0.53	2.78	95.5
Sugar beet BBCH 30-49 (late, summer/autumn)	Small granivorous bird, finch	11.4	1.8	0.53	3.26	81.2

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

^a feeding on 100% soil dwelling invertebrates

^b feeding on 50% ground arthropods and 50% foliar arthropods

Table 9.2.2.1-10 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in beet-crops sugar beet (3 × 2.4 L product/ha, 9-day interval) - Phenmedipham

Intended use	Beet-crops Sugar beet (BBCH 10-39)					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Sugar beet BBCH 10-19 (early spring)	Small omnivorous bird, lark	10.9	1.8	0.53	3.12	38.8
Sugar beet BBCH 10-19	Small insectivorous bird, wagtail	5.9	1.8	0.53	1.69	71.7
Sugar beet BBCH 20-49	Small insectivorous bird, wagtail ^a	2.8	1.8	0.53	0.80	151.0
Sugar beet BBCH 10-19	Small insectivorous bird, wagtail	5.9	1.8	0.53	1.69	71.7
Sugar beet BBCH 20-49	Small insectivorous bird, wagtail ^b	9.7	1.8	0.53	2.78	43.6
Sugar beet BBCH 30-49 (late, summer/autumn)	Small granivorous bird, finch	11.4	1.8	0.53	3.26	37.1

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

- a feeding on 100% soil dwelling invertebrates
b feeding on 50% ground arthropods and 50% foliar arthropods

Tier 1 combined long-term risk assessment

Based on Tier 1 TER_{LT} values for rate 3 × 2.4 L product/ha, 9-day interval for the most sensitive generic focal species (lark) at BBCH 10-19 (early spring), small granivorous bird small granivorous bird the TERcombi is above trigger of 5.

Application Rate		Ethofumesate TER _{LT}	Phenmedipham TER _{LT}	TER _{combi}	Trigger
3 × 2.4 L product/ha, 9-day interval		81.2	37.1	25.64	>5

An acceptable long-term risk to birds can be demonstrated for the formulated product.
No further consideration is required.

Use-group no 4: Sugar beet, 3 × 1.8 L product/ha, 6-day interval

Table 9.2.2.1-11 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in beet-crops sugar beet (3 × 1.8 L product/ha, 6-day interval) - Ethofumesate

Intended use	Beet-crops Sugar beet					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.225					
Acute toxicity [mg/kg bw]	3776					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird	158.8	1.7	-	60.74	62.2
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird	64.8	2.1	0.53	16.23	16.3

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-12 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in beet-crops sugar beet (3 × 1.8 L product/ha, 6-day interval) - Phenmedipham

Intended use	Beet-crops Sugar beet					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × 0.225					
Acute toxicity [mg/kg bw]	> 2500					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird	158.8	1.7	-	60.74	41.2
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}

Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird	64.8	2.1	0.53	16.23	7.5
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SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-13 Screening assessment of the acute risk for birds due to the use of HBZ10 in **sugar beet (3×1.8 L product/ha, 6-day interval) – surrogate mixture toxicity**

Intended use	Beet-crops Sugar beet					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$3 \times \sum 0.225 + 0.225$					
Acute toxicity [mg/kg bw] LD_{50mix}	3008					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crop: Sugar beet	Small omnivorous bird	158.8	1.7	-	121.48	24.8

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in **sugar beet** at 3×1.8 L product/ha (6-day interval).

zRMS comments:

The screening step risk assessment for active substances at rate 3×0.225 kg ethofumesate/ha and 3×0.225 kg phenmedipham/ha with 6-day interval is validated by the zRMS.

Based on calculations presented in the Tables from 9.2.2.1-11 to 9.2.2.1-12 acceptable acute and long-term risk may be concluded for birds exposed to ethofumesate and phenmedipham in HBZ10.

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.2.2.1-13 is above the respective trigger value of 10, indicating an acceptable risk for birds following application of HBZ10 in **sugar beet** at 3×1.8 L product/ha (6-day interval).

Combined long-term risk assessment:

TER_{combi} approach used by the Applicant for combined long-term risk assessment is validated by zRMS and confirmed be correct.

Screening combined long-term-risk assessment:

Application Rate	Ethofumesate TER _{LT} Screening sSTEP	Phenmedipham TER _{LT} Screening STEP	TER _{combi}	Trigger
3×1.8 L product/ha, 6-day interval	16.3	7.5	5.1	>5

Based on the screening assessment TER_{combi} values, the long-term risk to birds is demonstrated to be acceptable for 1.8 L product/ha with 6-day interval.

Use-group no-1: **Sugar beet**, 6×1.2 L product/ha, 5-day interval

Table 9.2.2.1-14 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (6×1.2 L product/ha, 5-day interval) - Ethofumesate

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		3776					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		158.8	2.2	-	52.40	72.1
Reprod. toxicity [mg/kg bw/d]		265.0					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		64.8	3.0	0.53	15.45	17.1

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-15 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (6×1.2 L product/ha, 5-day interval) - Phenmedipham

Intended use		Beet-crops Sugar beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		> 2500					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		158.8	2.2	-	52.40	47.7
Reprod. toxicity [mg/kg bw/d]		121					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		64.8	3.0	0.53	15.45	7.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-16 Screening assessment of the acute risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (6×1.2 L product/ha, 5-day interval) – surrogate mixture toxicity

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		$6 \times \sum 0.150 + 0.150$					
Acute toxicity [mg/kg bw] LD50 mix		3008					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird	158.8	2.2	-	104.81	28.7	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the

respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in ~~beet crops~~ **sugar beet** at 6×1.2 L product/ha (5-day interval).

zRMS comments:

The screening step risk assessment for active substances at rate 6×0.150 kg ethofumesate/ha and 6×0.150 kg phenmedipham/ha with 5-day interval is validated by the zRMS.

Based on calculations presented in the Tables from 9.2.2.1-14 to 9.2.2.1-15 acceptable acute and long-term risk may be concluded for birds exposed to ethofumesate and phenmedipham in HBZ10.

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.2.2.1-16 is above the respective trigger value of 10, indicating an acceptable risk for birds following application of HBZ10 in beet crops at 6×1.2 L product/ha (5-day interval).

Combined long-term risk assessment:

TER_{combi} approach used by the Applicant for combined long-term risk assessment is validated by zRMS and confirmed be correct.

Screening combined long-term-risk assessment:

Application Rate	Ethofumesate TER_{LT} Screening STEP	Phenmedipham TER_{LT} Screening STEP	TER_{combi}	Trigger
6×1.2 L product/ha, 5-day interval	17.1	7.8	5.4	>5

Values in **bold** are below the trigger value

Based on the screening assessment TER_{combi} values, the long-term risk to birds is demonstrated to be acceptable for 1.2 L product/ha with 5-day interval.

~~Use group no 3:~~ **Sugar beet**, 5×1.2 L product/ha, 7-day interval

Table 9.2.2.1-17 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in ~~beet crops~~ **sugar beet (5×1.2 L product/ha, 7-day interval) - Ethofumesate**

Intended use		Beet crops Sugar beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		5 × 0.150					
Acute toxicity [mg/kg bw]		3776					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet crops Sugar beet	Small omnivorous bird		158.8	1.9	-	45.26	83.4
Reprod. toxicity [mg/kg bw/d]		265.0					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Beet crops Sugar beet	Small omnivorous bird		64.8	2.4	0.53	12.36	21.4

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-18 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (5×1.2 L product/ha, 7-day interval) - Phenmedipham

Intended use		Beet-crops Sugar beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		5 × 0.150					
Acute toxicity [mg/kg bw]		> 2500					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		158.8	1.9	-	45.26	55.2
Reprod. toxicity [mg/kg bw/d]		121					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird		64.8	2.4	0.53	12.36	9.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-19 Screening assessment of the acute risk for birds due to the use of HBZ10 in ~~beet-crops~~ sugar beet (5×1.2 L product/ha, 7-day interval) – surrogate mixture toxicity

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		$5 \times \sum 0.150 + 0.150$					
Acute toxicity [mg/kg bw] LD50 mix		3008					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Bulbs and onion-like crops Beet-crops Sugar beet	Small omnivorous bird	158.8	1.9	-	90.52	33.2	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in ~~beet-crops~~ sugar beet at 5×1.2 L product/ha (7-day interval).

zRMS comments:

The screening step risk assessment for active substances at rate 5×0.150 kg ethofumesate/ha and 5×0.150 kg phenmedipham/ha with 7-day interval is validated by the zRMS.

Based on calculations presented in the Tables from 9.2.2.1-17 to 9.2.2.1-18 acceptable acute and long-term risk may be concluded for birds exposed to ethofumesate and phenmedipham in HBZ10.

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.2.2.1-19 is above the respective trigger value of 10, indicating an acceptable risk for birds following application of HBZ10 in beet crops at 5×1.2 L product/ha (7-day interval).

Combined long-term risk assessment:

TER_{combi} approach used by the Applicant for combined long-term risk assessment is validated by zRMS and confirmed be correct.

Screening combined long-term-risk assessment:

Application Rate	Ethofumesate TER _{LT} Screening step	Phenmedipham TER _{LT} Screening STEP	TER _{combi}	Trigger
5 × 1.2 L product/ha, 7-day interval	21.4	9.8	6.7	>5

Values in **bold** are below the trigger value

Based on the screening assessment TER_{combi} values, the long-term risk to birds is demonstrated to be acceptable for 1.2 L product/ha with 7-d interval.

Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 6-day interval

Table 9.2.2.1-20 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 6-day interval) - Ethofumesate

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Acute toxicity [mg/kg bw]	3776					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	1.7	-	80.99	46.6
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Root and stem vegetables	Small omnivorous bird	64.8	2.1	0.53	21.64	12.2

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-21 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 6-day interval) - Phenmedipham

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Acute toxicity [mg/kg bw]	> 2500					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	1.7	-	80.99	30.9
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Root and stem vegetables	Small omnivorous bird	64.8	2.1	0.53	21.64	5.6

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-22 Screening assessment of the acute risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × ∑ 0.300 + 0.300					
Acute toxicity [mg/kg bw] LD _{mix}	3008					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	1.7	-	161.98	18.6

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in red beet/yellow beet/fodder beet at 3×2.4 L product/ha (6-day interval).

Table 9.2.2.1-23 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3×2.4 L product/ha, 6-day interval) - Ethofumesate

Intended use	Red beet/yellow beet/fodder beet (BBCH 10-39)					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3×0.300					
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Generic focal species	SV_m	MAF_m	TWA	DDD_m [mg/kg bw/d]	TER_{L,T}
Root and stem vegetables BBCH ≥ 20	Small insectivorous bird, wagtail	9.7	2.1	0.53	3.24	81.8
Root and stem vegetables BBCH 10-19	Small insectivorous bird, wagtail	11.3	2.1	0.53	3.77	70.2
Root and stem vegetables BBCH 10-39	Small granivorous bird, finch	11.4	2.1	0.53	3.81	69.6
Root and stem vegetables BBCH 10-39	Small omnivorous bird, lark	10.9	2.1	0.53	3.64	72.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-24 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3×2.4 L product/ha, 6-day interval) - Phenmedipham

Intended use	Red beet/yellow beet/fodder beet (BBCH 10-39)					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3×0.300					
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Generic focal species	SV_m	MAF_m	TWA	DDD_m [mg/kg bw/d]	TER_{L,T}
Root and stem vegetables BBCH ≥ 20	Small insectivorous bird, wagtail	9.7	2.1	0.53	3.24	37.4
Root and stem vegetables BBCH 10-19	Small insectivorous bird, wagtail	11.3	2.1	0.53	3.77	32.1
Root and stem vegetables BBCH 10-39	Small granivorous bird, finch	11.4	2.1	0.53	3.81	31.8
Root and stem vegetables BBCH 10-39	Small omnivorous bird, lark	10.9	2.1	0.53	3.64	33.2

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 9-day interval

Table 9.2.2.1-25 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 9-day interval) - Ethofumesate

Ethofumesate							
Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		3776					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small omnivorous bird	158.8	1.5	-	71.46	52.8	
Reprod. toxicity [mg/kg bw/d]		265.0					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Root and stem vegetables	Small omnivorous bird	64.8	1.8	0.53	18.55	14.3	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-26 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 9-day interval) - Phenmedipham

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 2500					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small omnivorous bird	158.8	1.5	-	71.46	35.0	
Reprod. toxicity [mg/kg bw/d]		121					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Root and stem vegetables	Small omnivorous bird	64.8	1.8	0.53	18.55	6.5	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-27 Screening assessment of the acute risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 9-day interval) – surrogate mixture toxicity

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × ∑ 0.300 + 0.300					
Acute toxicity [mg/kg bw] LD_{mix}		3008					
TER criterion		10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A	
Root and stem vegetables	Small omnivorous bird	158.8	1.5	-	142.92	21.0	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in red beet/yellow beet/fodder beet at 3 × 2.4 L product/ha (9-day interval).

Table 9.2.2.1-28 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 9-day interval) - Ethofumesate

Intended use	Red beet/yellow beet/fodder beet (BBCH 10-39)					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Root and stem vegetables BBCH ≥ 20	Small insectivorous bird, wagtail	9.7	1.8	0.53	2.78	95.5
Root and stem vegetables BBCH 10-19	Small insectivorous bird, wagtail	11.3	1.8	0.53	3.23	81.9
Root and stem vegetables BBCH 10-39	Small granivorous bird, finch	11.4	1.8	0.53	3.26	81.2
Root and stem vegetables BBCH 10-39	Small omnivorous bird, lark	10.9	1.8	0.53	3.12	84.9

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-29 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 9-day interval) - Phenmedipham

Intended use	Red beet/yellow beet/fodder beet (BBCH 10-39)					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Root and stem vegetables BBCH ≥ 20	Small insectivorous bird, wagtail	9.7	1.8	0.53	2.78	43.6
Root and stem vegetables BBCH 10-19	Small insectivorous bird, wagtail	11.3	1.8	0.53	3.23	37.4
Root and stem vegetables BBCH 10-39	Small granivorous bird, finch	11.4	1.8	0.53	3.26	37.1
Root and stem vegetables BBCH 10-39	Small omnivorous bird, lark	10.9	1.8	0.53	3.12	38.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Red beet/Yellow beet/Fodder beet, 3 × 1.8 L product/ha, 6-day interval

Table 9.2.2.1-30 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 1.8 L product/ha, 6-day interval) - Ethofumesate

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.225					
Acute toxicity [mg/kg bw]	3776					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	1.7	-	60.74	62.2
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Root and stem vegetables	Small omnivorous bird	64.8	2.1	0.53	16.23	16.3

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-31 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 1.8 L product/ha, 6-day interval) - Phenmedipham

Intended use	Red beet/yellow beet/fodder beet					
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Active substance/product		Phenmedipham / HBZ10				
Application rate [kg/ha]		3×0.225				
Acute toxicity [mg/kg bw]		> 2500				
TER criterion		10				
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A
Root and stem vegetables	Small omnivorous bird	158.8	1.7	-	60.74	41.2
Reprod. toxicity [mg/kg bw/d]		121				
TER criterion		5				
Crop scenario	Indicator species	SV_m	MAF_m	TWA	DDD_m [mg/kg bw/d]	TER_{LT}
Root and stem vegetables	Small omnivorous bird	64.8	2.1	0.53	16.23	7.5

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-32 Screening assessment of the acute risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (3×1.8 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use		Red beet/yellow beet/fodder beet				
Active substance/product		Ethofumesate + Phenmedipham / HBZ10				
Application rate [kg/ha]		$3 \times \sum 0.225 + 0.225$				
Acute toxicity [mg/kg bw] LD_{mix}		3008				
TER criterion		10				
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A
Root and stem vegetables	Small omnivorous bird	158.8	1.7	-	121.48	24.8

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in red beet/yellow beet/fodder beet at 3×1.8 L product/ha (6-day interval).

Red beet/Yellow beet/Fodder beet, 6×1.2 L product/ha, 5-day interval

Table 9.2.2.1-33 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (6×1.2 L product/ha, 5-day interval) - Ethofumesate

Intended use		Red beet/yellow beet/fodder beet				
Active substance/product		Ethofumesate / HBZ10				
Application rate [kg/ha]		6×0.150				
Acute toxicity [mg/kg bw]		3776				
TER criterion		10				
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A
Root and stem vegetables	Small omnivorous bird	158.8	2.2	-	52.40	72.1
Reprod. toxicity [mg/kg bw/d]		265.0				
TER criterion		5				
Crop scenario	Indicator species	SV_m	MAF_m	TWA	DDD_m [mg/kg bw/d]	TER_{LT}
Root and stem vegetables	Small omnivorous bird	64.8	3.0	0.53	15.45	17.1

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-34 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (6×1.2 L product/ha, 5-day interval) - Phenmedipham

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	6×0.150					
Acute toxicity [mg/kg bw]	> 2500					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	2.2	-	52.40	47.7
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Root and stem vegetables	Small omnivorous bird	64.8	3.0	0.53	15.45	7.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-35 Screening assessment of the acute risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (6×1.2 L product/ha, 5-day interval) – surrogate mixture toxicity

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$6 \times \sum 0.150 + 0.150$					
Acute toxicity [mg/kg bw] LD _{mix}	3008					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	2.2	-	104.81	28.7

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in red beet/yellow beet/fodder beet at 6×1.2 L product/ha (5-day interval).

Red beet/Yellow beet/Fodder beet, 5×1.2 L product/ha, 7-day interval

Table 9.2.2.1-36 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (5×1.2 L product/ha, 7-day interval) - Ethofumesate

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	5×0.150					
Acute toxicity [mg/kg bw]	3776					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	1.9	-	45.26	83.4
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Root and stem vegetables	Small omnivorous bird	64.8	2.4	0.53	12.36	21.4

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-37 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (5×1.2 L product/ha, 7-day interval) - Phenmedipham

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	5×0.150					
Acute toxicity [mg/kg bw]	> 2500					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	1.9	-	45.26	55.2
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Root and stem vegetables	Small omnivorous bird	64.8	2.4	0.53	12.36	9.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-38 Screening assessment of the acute risk for birds due to the use of HBZ10 in red beet/yellow beet/fodder beet (5×1.2 L product/ha, 7-day interval) – surrogate mixture toxicity

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$5 \times \sum 0.150 + 0.150$					
Acute toxicity [mg/kg bw] LDmix	3008					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small omnivorous bird	158.8	1.9	-	90.52	33.2

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in red beet/yellow beet/fodder beet at 5×1.2 L product/ha (7-day interval).

zRMS comment:

The screening step risk assessment for active substances for all application rate for uses in Red beet/yellow beet/fodder beet is validated by zRMS.

Acute combined risk

The screening acute combined TER_A values for all uses in Red beet/Yellow beet/Fodder beet is above the respective trigger value of 10, indicating an acceptable risk for birds following application of HBZ10

Combined long-term risk assessment:

TER_{combi} approach calculated by the Applicant is validated by zRMS and the relevant calculations are as follows:

Application Rate	Ethofumesate TER _{LT} Screening step	Phenmedipham TER _{LT} Screening step	TER _{combi}
Red beet/Yellow beet/Fodder beet, 3×2.4 L product/ha, 6-day interval	12.2	5.6	3.8
Red beet/Yellow beet/Fodder beet, 3×2.4 L product/ha, 9-day interval	14.3	6.5	4.7
Red beet/Yellow beet/Fodder beet, 3×1.8 L product/ha, 6-day interval	16.3	7.5	5.1

Red beet/Yellow beet/Fodder beet, 6 × 1.2 L product/ha, 5-day interval	17.1	7.8	5.4
Red beet/Yellow beet/Fodder beet, 5 × 1.2 L product/ha, 7-day interval	21.4	9.8	6.7

Based on Tier 1 TER values for the most sensitive generic focal species the TER_{combi} are as follow:

Application Rate	Ethofumesate TER _{LT} Tier 1	Phenmedipham TER _{LT} Tier 1	TER _{combi}
Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 6-day interval	69.6	31.8	21.8
Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 9-day interval	81.2	37.1	25.5

The combined long-term risk assessment is considered as acceptable. No further consideration is required.

Chard, 3 × 2.4 L product/ha, 6-day interval

Table 9.2.2.1-39 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (3 × 2.4 L product/ha, 6-day interval) - Ethofumesate

Intended use	Chard					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Acute toxicity [mg/kg bw]	3776					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small omnivorous bird	158.8	1.7	-	80.99	46.6
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables	Small omnivorous bird	64.8	2.1	0.53	21.64	12.2

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-40 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (3 × 2.4 L product/ha, 6-day interval) - Phenmedipham

Intended use	Chard					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Acute toxicity [mg/kg bw]	> 2500					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small omnivorous bird	158.8	1.7	-	80.99	30.9
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables	Small omnivorous bird	64.8	2.1	0.53	21.64	5.6

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-41 Screening assessment of the acute risk for birds due to the use of HBZ10 in chard (3×2.4 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use	Chard					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$3 \times \sum 0.300 + 0.300$					
Acute toxicity [mg/kg bw] LD_{mix}	3008					
TER criterion	10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A
Leafy vegetables	Small omnivorous bird	158.8	1.7	-	161.98	18.6

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in chard at 3×2.4 L product/ha (6-day interval).

Table 9.2.2.1-42 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in chard (3×2.4 L product/ha, 6-day interval) - Ethofumesate

Intended use	Chard (BBCH 10-39)					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3×0.300					
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Generic focal species	SV_m	MAF_m	TWA	DDD_m [mg/kg bw/d]	TER_{LT}
Leafy vegetables BBCH ≥ 20	Small insectivorous bird, wagtail	9.7	2.1	0.53	3.24	81.8
Leafy vegetables BBCH 10-19	Small insectivorous bird, wagtail	11.3	2.1	0.53	3.77	70.2
Leafy vegetables BBCH 10-49	Small granivorous bird, finch	12.6	2.1	0.53	4.21	63.0
Leafy vegetables BBCH 10-49	Small omnivorous bird, lark	10.9	2.1	0.53	3.64	72.8
Leafy vegetables Leaf development BBCH 10-19	Medium herbivorous/granivorous bird, pigeon	22.7	2.1	0.53	7.58	35.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-43 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in chard (3×2.4 L product/ha, 6-day interval) - Phenmedipham

Intended use	Chard (BBCH 10-39)					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3×0.300					
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Generic focal species	SV_m	MAF_m	TWA	DDD_m [mg/kg bw/d]	TER_{LT}
Leafy vegetables BBCH ≥ 20	Small insectivorous bird, wagtail	9.7	2.1	0.53	3.24	37.4
Leafy vegetables BBCH 10-19	Small insectivorous bird, wagtail	11.3	2.1	0.53	3.77	32.1
Leafy vegetables BBCH 10-49	Small granivorous bird, finch	12.6	2.1	0.53	4.21	28.8
Leafy vegetables BBCH 10-49	Small omnivorous bird, lark	10.9	2.1	0.53	3.64	33.2
Leafy vegetables Leaf development BBCH 10-19	Medium herbivorous/granivorous bird, pigeon	22.7	2.1	0.53	7.58	16.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Chard, 3 × 2.4 L product/ha, 9-day interval

Table 9.2.2.1-44 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (3 × 2.4 L product/ha, 9-day interval) - Ethofumesate

Intended use		Chard					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		3776					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Leafy vegetables	Small omnivorous bird	158.8	1.5	-	71.46	52.8	
Reprod. toxicity [mg/kg bw/d]		265.0					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Leafy vegetables	Small omnivorous bird	64.8	1.8	0.53	18.55	14.3	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-45 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (3 × 2.4 L product/ha, 9-day interval) - Phenmedipham

Intended use		Chard					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 2500					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Leafy vegetables	Small omnivorous bird	158.8	1.5	-	71.46	35.0	
Reprod. toxicity [mg/kg bw/d]		121					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Leafy vegetables	Small omnivorous bird	64.8	1.8	0.53	18.55	6.5	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-46 Screening assessment of the acute risk for birds due to the use of HBZ10 in chard (3 × 2.4 L product/ha, 9-day interval) – surrogate mixture toxicity

Intended use		Chard					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × ∑ 0.300 + 0.300					
Acute toxicity [mg/kg bw] LD_{mix}		3008					
TER criterion		10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A	
Leafy vegetables	Small omnivorous bird	158.8	1.5	-	142.92	21.0	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in chard at 3 × 2.4 L product/ha (9-day interval).

Table 9.2.2.1-47 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in chard (3 × 2.4 L product/ha, 9-day interval) - Ethofumesate

Intended use	Chard (BBCH 10-39)					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables BBCH ≥ 20	Small insectivorous bird, wagtail	9.7	1.8	0.53	2.78	95.5
Leafy vegetables BBCH 10-19	Small insectivorous bird, wagtail	11.3	1.8	0.53	3.23	81.9
Leafy vegetables BBCH 10-49	Small granivorous bird, finch	12.6	1.8	0.53	3.61	73.5
Leafy vegetables BBCH 10-49	Small omnivorous bird, lark	10.9	1.8	0.53	3.12	84.9
Leafy vegetables Leaf development BBCH 10-19	Medium herbivorous/granivorous bird, pigeon	22.7	1.8	0.53	6.50	40.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-48 Tier 1 assessment of the long-term/reproductive risk for birds due to the use of HBZ10 in chard (3 × 2.4 L product/ha, 9-day interval) - Phenmedipham

Intended use	Chard (BBCH 10-39)					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × 0.300					
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables BBCH ≥ 20	Small insectivorous bird, wagtail	9.7	1.8	0.53	2.78	43.6
Leafy vegetables BBCH 10-19	Small insectivorous bird, wagtail	11.3	1.8	0.53	3.23	37.4
Leafy vegetables BBCH 10-49	Small granivorous bird, finch	12.6	1.8	0.53	3.61	33.6
Leafy vegetables BBCH 10-49	Small omnivorous bird, lark	10.9	1.8	0.53	3.12	38.8
Leafy vegetables Leaf development BBCH 10-19	Medium herbivorous/granivorous bird, pigeon	22.7	1.8	0.53	6.50	18.6

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Chard, 3 × 1.8 L product/ha, 6-day interval

Table 9.2.2.1-49 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (3 × 1.8 L product/ha, 6-day interval) - Ethofumesate

Intended use	Chard					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3 × 0.225					
Acute toxicity [mg/kg bw]	3776					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small omnivorous bird	158.8	1.7	-	60.74	62.2
Reprod. toxicity [mg/kg bw/d]	265.0					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables	Small omnivorous bird	64.8	2.1	0.53	16.23	16.3

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-50 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (3 × 1.8 L product/ha, 6-day interval) - Phenmedipham

Intended use	Chard					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × 0.225					
Acute toxicity [mg/kg bw]	> 2500					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small omnivorous bird	158.8	1.7	-	60.74	41.2
Reprod. toxicity [mg/kg bw/d]	121					
TER criterion	5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables	Small omnivorous bird	64.8	2.1	0.53	16.23	7.5

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-51 Screening assessment of the acute risk for birds due to the use of HBZ10 in chard (3 × 1.8 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use	Chard					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × ∑ 0.225 + 0.225					
Acute toxicity [mg/kg bw] LD _{mix}	3008					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small omnivorous bird	158.8	1.7	-	121.48	24.8

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in chard at 3 × 1.8 L product/ha (6-day interval).

Chard 6×1.2 L product/ha, 5-day interval

Table 9.2.2.1-52 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (6×1.2 L product/ha, 5-day interval) - Ethofumesate

Intended use		Chard					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		3776					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Leafy vegetables	Small omnivorous bird	158.8	2.2	-	52.40	72.1	
Reprod. toxicity [mg/kg bw/d]		265.0					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Leafy vegetables	Small omnivorous bird	64.8	3.0	0.53	15.45	17.1	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-53 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (6×1.2 L product/ha, 5-day interval) - Phenmedipham

Intended use		Chard					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		> 2500					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Leafy vegetables	Small omnivorous bird	158.8	2.2	-	52.40	47.7	
Reprod. toxicity [mg/kg bw/d]		121					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{Lt}	
Leafy vegetables	Small omnivorous bird	64.8	3.0	0.53	15.45	7.8	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-54 Screening assessment of the acute risk for birds due to the use of HBZ10 in chard (6×1.2 L product/ha, 5-day interval) – surrogate mixture toxicity

Intended use		Chard					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		$6 \times \sum 0.150 + 0.150$					
Acute toxicity [mg/kg bw] LD _{mix}		3008					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Leafy vegetables	Small omnivorous bird	158.8	2.2	-	104.81	28.7	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in chard at 6×1.2 L product/ha (5-day interval).

Chard, 5 × 1.2 L product/ha, 7-day interval

Table 9.2.2.1-55 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (5 × 1.2 L product/ha, 7-day interval) - Ethofumesate

Intended use		Chard					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		5 × 0.150					
Acute toxicity [mg/kg bw]		3776					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small omnivorous bird		158.8	1.9	-	45.26	83.4
Reprod. toxicity [mg/kg bw/d]		265.0					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{Lt}
Leafy vegetables	Small omnivorous bird		64.8	2.4	0.53	12.36	21.4

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-56 Screening assessment of the acute and long-term/reproductive risk for birds due to the use of HBZ10 in chard (5 × 1.2 L product/ha, 7-day interval) - Phenmedipham

Intended use		Chard					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		5 × 0.150					
Acute toxicity [mg/kg bw]		> 2500					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small omnivorous bird		158.8	1.9	-	45.26	55.2
Reprod. toxicity [mg/kg bw/d]		121					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables	Small omnivorous bird		64.8	2.4	0.53	12.36	9.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.2.2.1-57 Screening assessment of the acute risk for birds due to the use of HBZ10 in chard (5 × 1.2 L product/ha, 7-day interval) – surrogate mixture toxicity

Intended use		Chard					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		5 × ∑ 0.150 + 0.150					
Acute toxicity [mg/kg bw] LD_{mix}		3008					
TER criterion		10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A	
Leafy vegetables	Small omnivorous bird	158.8	1.9	-	90.52	33.2	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening acute and long-term TER values for the active substances Ethofumesate and Phenmedipham and the screening acute TER value for the surrogate mixture toxicity for the formulation are above the respective trigger values, indicating an acceptable risk for birds following application of HBZ10 in chard at 5 × 1.2 L product/ha (7-day interval).

zRMS comments:

The screening step risk assessment for active substances for all application rate for uses in chard is validated by zRMS.

Acute combined risk

The screening acute combined TER_A values for all uses in chard is above the respective trigger value of 10, indicating an acceptable risk for birds following application of HBZ10

Combined long-term risk assessment:

TER_{combi} approach calculated by the Applicant is validated by zRMS and the relevant calculations are as follows.

Application Rate	Ethofumesate TER _{LT} Screening step	Phenmedipham TER _{LT} Screening step	TER _{combi}
Chard, 3 × 2.4 L product/ha, 6-day interval	12.2	5.6	3.8
Chard, 3 × 2.4 L product/ha, 9-day interval	14.3	6.5	4.7
Chard, 3 × 1.8 L product/ha, 6-day interval	16.3	7.5	5.1
Chard, 6 × 1.2 L product/ha, 5-day interval	17.1	7.8	5.4
Chard, 5 × 1.2 L product/ha, 7-day interval	21.4	9.8	6.7

Values in **bold** are below the trigger value

Based on Tier 1 TER values for the most sensitive generic focal species the TER_{combi} are:

Application Rate	Ethofumesate TER _{LT} Tier 1	Phenmedipham TER _{LT} Tier 1	TER _{combi}
Chard, 3 × 2.4 L product/ha, 6-day interval	35.0	16.0	11.0
Chard, 3 × 2.4 L product/ha, 9-day interval	40.8	18.6	12.8

Based on calculations above the TER_{combi} is above trigger value of 5, indicating an acceptable risk. No further consideration is required.

9.2.2.2 Higher-tier risk assessment

Based on the outcome of the first-tier risk assessments, no higher-tier risk assessment is required.

9.2.2.3 Drinking water exposure

When necessary, the assessment of the risk for birds due to uptake of contaminated drinking water is conducted for a small granivorous bird with a body weight of 15.3 g (*Carduelis cannabina*) and a drinking water uptake rate of 0.46 L/kg bw/d (*cf.* Appendix K of EFSA/2009/1438).

Leaf scenario

Since HBZ10 is not intended to be applied on leafy vegetables forming heads or crop plants with comparable water collecting structures at principal growth stage 4 or later, the leaf scenario does not have to be considered.

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 when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances ($K_{oc} < 500$ L/kg) or 3000 in the case of more sorptive substances ($K_{oc} \geq 500$ L/kg).

With a $K(f)_{oc}$ of 118 mL/g (geometric mean), Ethofumesate belongs to the group of less sorptive substances. With a $K(f)_{oc}$ of 657 mL/g (minimum, $n = 3$), Phenmedipham belongs to the group of more sorptive substances.

For completeness, the risk assessment is presented for all intended uses.

Table 9.2.2.3-1 Drinking water assessment (puddle scenario) - Ethofumesate

Effective application rate [g a.s./ha] =	3 × 300 (use group 2 / use group 5 use No 2, 5, 7, 10, 12, 15, 17, 20, 22, 25) and 6 × 150 (use group 1 use No 1, 6, 11, 16, 21)		
Acute toxicity [mg a.s./kg bw] =	3776	quotient =	0.24
Reproduction toxicity [mg a.s./kg bw/d] =	265	quotient =	3.40
Effective application rate [g a.s./ha] =	3 × 225 (use group 4 use No 4, 9, 14, 19, 24)		
Acute toxicity [mg a.s./kg bw] =	3776	quotient =	0.18
Reproduction toxicity [mg a.s./kg bw/d] =	265	quotient =	2.55
Effective application rate [g a.s./ha] =	5 × 150 (use group 3 use No 3, 8, 13, 18, 23)		
Acute toxicity [mg a.s./kg bw] =	3776	quotient =	0.20
Reproduction toxicity [mg a.s./kg bw/d] =	265	quotient =	2.83

Table 9.2.2.3-2 Drinking water assessment (puddle scenario) - Phenmedipham

Effective application rate [g a.s./ha] =	3 × 300 (use group 2 / use group 5 use No 2, 5, 7, 10, 12, 15, 17, 20, 22, 25) and 6 × 150 (use group 1 use No 1, 6, 11, 16, 21)		
Acute toxicity [mg a.s./kg bw] =	> 2500	quotient =	0.36
Reproduction toxicity [mg a.s./kg bw/d] =	121	quotient =	7.44
Effective application rate [g a.s./ha] =	3 × 225 (use group 4 use No 4, 9, 14, 19, 24)		
Acute toxicity [mg a.s./kg bw] =	> 2500	quotient =	0.27
Reproduction toxicity [mg a.s./kg bw/d] =	121	quotient =	5.58
Effective application rate [g a.s./ha] =	5 × 150 (use group 3 use No 3, 8, 13, 18, 23)		
Acute toxicity [mg a.s./kg bw] =	> 2500	quotient =	0.30
Reproduction toxicity [mg a.s./kg bw/d] =	121	quotient =	6.20

The resulting ratios fall below the trigger of 50 for less sorptive substances or 3000 for more sorptive substances, indicating that further assessment of the acute and long-term risk to birds from drinking water from puddles is not required for Ethofumesate and Phenmedipham.

zRMS comments:

The calculation of the drinking water risk assessment for both active substances presented in the Tables above are validated by the zRMS.
Further assessment of the acute and long-term risk to birds from drinking water from puddles is not required for Ethofumesate and Phenmedipham.

9.2.2.4 Effects of secondary poisoning

The log K_{ow} of Ethofumesate amounts to 2.7 and thus does not exceed the trigger value of 3 indicating a low potential risk to accumulate in the food chain. However, since the BCF > 100, the risk assessment for effects due to secondary poisoning is required.

The log K_{ow} of Phenmedipham amounts to 3.59 and thus exceeds the trigger value of 3. Furthermore, the BCF is > 100. A risk assessment for effects due to secondary poisoning is required.

Risk assessment for earthworm-eating birds via secondary poisoning

According to EFSA/2009/1438, the risk for vermivorous birds is assessed for a bird of 100 g body weight with a daily food consumption of 104.6 g. Bioaccumulation in earthworms is estimated based on predicted concentrations in soil.

To achieve a concise risk assessment, the risk envelope approach is applied in line with the approach followed for PEC_{soil} calculations in dRR Part B8, Point 8.7: The 25 intended uses are grouped in 5 use groups, i.e., Use group 1: 6 x 1.2 L prod./ha, 5-days interval (includes uses 1, 6, 11, 16 and 21); Use group 2: 3 x 2.4 L prod./ha, 6-days interval (includes uses 2, 7, 12, 17, and 22); Use group 3: 5 x 1.2 L prod./ha, 7-days interval (includes uses 3, 8, 13, 18, and 23); Use group 4: 3 x 1.8 L prod./ha, 6-days interval (includes uses 4, 9, 14, 19, and 24); Use group 5: 3 x 2.4 L prod./ha, 9-days interval (includes uses 5, 10, 15, 20, and 25), and PEC_{soil} calculations are performed and presented for use groups 2 (worst-case), 4 and 5. Here, the assessment for the worst-case use group 2 in beet crops (3 × 2.4 L product/ha, 6-day interval), use group 4 (3 × 1.8 L product/ha, 6-day interval) and use group 5 (3 × 2.4 L product/ha, 9-day interval) also covers the risk for birds from the intended use groups 1 & 3 in beet crops (6 × 1.2 L product/ha, 5-day interval and 5 × 1.2 L product/ha, 7-day interval).

Dry soil approach

Table 9.2.2.4-1 Assessment of the risk for earthworm-eating birds due to exposure to Ethofumesate via bioaccumulation in earthworms (secondary poisoning) for the **all** intended **uses** in **beet** **crops**

Parameter	Use group 2	Use group 4	Use group 5	Comments
PEC _{Soil} (two = 21 d) + PEC _{Soil plateau} [mg/kg soil]	0.893 0.9934 0.9513	0.670 0.745 0.714	0.882 0.981 0.94	PEC _{Soil} , dry, two 21 d accumulation + PEC _{Soil plateau} after multiple applications (PEC_{act} + PEC_{Soil plateau}) (Section 8, Point 8.7.2)
log K _{ow} / K _{ow}	2.7 / 501 486			EFSA Conclusion (2016)
K _{oc} [mL/g]	118			Geometric mean (EFSA Conclusion, 2016)
f _{oc}	0.02			Default
BCF _{worm}	2.90 2.83			BCF _{worm} = (0.84 + 0.012 × K _{ow}) / (f _{oc} × K _{oc})
PEC _{worm}	2.59 2.69	2.88 2.02	2.16 2.66	PEC _{worm} = PEC _{Soil} × BCF _{worm}
Daily dietary dose [mg/kg bw/d]	2.72 2.82	3.02 2.12	2.27 2.79	DDD = PEC _{worm} × 1.05
NOEL [mg/kg bw/d]	265.0			EFSA Conclusion (2016)
TER _{LT}	97.3 93.8	87.6 125.0	129.7 95.0	TER _{LT} = NOEL/DDD

TER values shown in bold fall below the relevant trigger.

Use group 2: 3 × 2.4 L product/ha, 6-day interval

Use group 4: 3 × 1.8 L product/ha, 6-day interval

Use group 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.2.2.4-2 Assessment of the risk for earthworm-eating birds due to exposure to Phenmedipham via bioaccumulation in earthworms (secondary poisoning) for the **all** intended **uses** in **beet** **crops**

Parameter	Use group 2	Use group 4	Use group 5	Comments
PEC _{Soil} (two = 21 d) [mg/kg soil]	0.742	0.556	0.709	PEC _{Soil} , dry, two 21 d after multiple applications (Section 8, Point 8.7.2)
log K _{ow} / K _{ow}	3.59 / 3890.5			Review Report (2004)
K _{oc}	657			Minimum (n = 3), Review Report (2004)
f _{oc}	0.02			Default
BCF _{worm}	3.62			BCF _{worm} = (0.84 + 0.012 × K _{ow}) / (f _{oc} × K _{oc})
PEC _{worm}	2.68	2.01	2.56	PEC _{worm} = PEC _{Soil} × BCF _{worm}
Daily dietary dose [mg/kg bw/d]	2.82	2.11	2.69	DDD = PEC _{worm} × 1.05
NOEL [mg/kg bw/d]	121			Review Report (2004)
TER _{LT}	42.9	57.3	44.9	TER _{LT} = NOEL/DDD

TER values shown in bold fall below the relevant trigger.

Use group 2: 3 × 2.4 L product/ha, 6-day interval

Use group 4: 3 × 1.8 L product/ha, 6-day interval

Use group 5: 3 × 2.4 L product/ha, 9-day interval

zRMS comments:

The risk assessment for secondary poisoning is based on the TER calculations for dry soil approach that is the current methodology used at EU level.

The TER_{LT} value for the active substances Ethofumesate and Phenmedipham for secondary poisoning of earthworms-eating birds based on worst case scenarios (groups 2, 4, 5) covering remained groups is above the trigger value of 5, indicating an acceptable risk.

Porewater approach

Table 9.2.2.4-3 — Assessment of the risk for earthworm-eating birds due to exposure to Ethofumesate via bioaccumulation in earthworms (secondary poisoning) for the intended use in crop beet crops

Parameter	Use group 2	Use group 4	Use group 5	Comments
$PEC_{\text{Soil, dry, twa-21-d}}$ [mg/kg]	0.893	0.670	0.882	$PEC_{\text{Soil, dry, twa-21-d}}$ after multiple applications (Section 8, Point 8.7.2)
K_{ow}	501			EFSA Conclusion (2016)
K_{oc}	118			Geometric mean (EFSA Conclusion, 2016)
$RHO_{\text{earthworm}}$	1			Default
BCF_{worm}	6.85			$BCF_{\text{worm}} = (0.84 + 0.012 \times K_{\text{ow}}) / RHO_{\text{earthworm}}$
$K_{\text{soil-water}}$ [m ³ /m ³]	3.74			Eq. 24 of Technical Guidance Document on Risk Assessment Part II; Joint Research Center (2003), EUR 20418 EN/2
$RHO_{\text{Soil, wet}}$ [kg/m ³]	1700			Default
$RHO_{\text{Soil, dry}}$ [kg/m ³]	1500			Default
$C_{\text{porewater}}$ [mg/L]	0.358	0.269	0.354	$C_{\text{porewater}} = (PEC_{\text{Soil, dry}} \times RHO_{\text{Soil, wet}}) / (K_{\text{soil-water}} \times 1000)$
$PEC_{\text{Soil, wet, twa-21-d}}$ [mg/kg]	0.788	0.591	0.778	$PEC_{\text{Soil, wet, twa-21-d}} = PEC_{\text{Soil, dry}} / RHO_{\text{Soil, wet}} \times RHO_{\text{Soil, dry}}$
F_{solid} [m ³ /m ³]	0.60			Default
RHO_{solid} [kg dry weight/m ³]	2500			Default
$CONV_{\text{Soil}}$	1.13			$CONV_{\text{Soil}} = RHO_{\text{Soil, wet}} / (F_{\text{solid}} \times RHO_{\text{solid}})$ (default)
F_{gut}	0.10			Default
C_{worm}	2.29	1.71	2.26	$C_{\text{worm}} = (BCF_{\text{worm}} \times C_{\text{porewater}} + PEC_{\text{Soil, wet}} \times F_{\text{gut}} \times CONV_{\text{Soil}}) / (1 + F_{\text{gut}} \times CONV_{\text{Soil}})$
Daily dietary dose [mg/kg bw/d]	2.40	1.80	2.37	$DDD = C_{\text{worm}} \times 1.05$
NOEL [mg/kg bw/d]	265.0			EFSA Conclusion (2016)
TER_{LT}	110.4	147.2	111.8	$TER_{\text{LT}} = NOEL / DDD$

TER values shown in bold fall below the relevant trigger.

Use group 2: 3 × 2.4 L product/ha, 6-day interval

Use group 4: 3 × 1.8 L product/ha, 6-day interval

Use group 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.2.2.4-4 — Assessment of the risk for earthworm-eating birds due to exposure to Phenmedipham via bioaccumulation in earthworms (secondary poisoning) for the intended use in crop beet crops

Parameter	Use group 2	Use group 4	Use group 5	Comments
$PEC_{\text{Soil, dry, twa-21-d}}$ [mg/kg]	0.742	0.556	0.709	$PEC_{\text{Soil, dry, twa-21-d}}$ after multiple applications (Section 8, Point 8.7.2)
K_{ow}	3890.5			Review Report (2004)
K_{oc}	657			Minimum (n = 3), Review Report (2004)
$RHO_{\text{earthworm}}$	1			Default
BCF_{worm}	47.5			$BCF_{\text{worm}} = (0.84 + 0.012 \times K_{\text{ow}}) / RHO_{\text{earthworm}}$
$K_{\text{soil-water}}$ [m ³ /m ³]	3.74			Eq. 24 of Technical Guidance Document on Risk Assessment Part II, Joint Research Center (2003), EUR-20418-EN/2
$RHO_{\text{Soil, wet}}$ [kg/m ³]	1700			Default
$RHO_{\text{Soil, dry}}$ [kg/m ³]	1500			Default
$C_{\text{porewater}}$ [mg/L]	0.298	0.223	0.284	$C_{\text{porewater}} = (PEC_{\text{Soil, dry}} \times RHO_{\text{Soil, wet}}) / (K_{\text{soil-water}} \times 1000)$
$PEC_{\text{Soil, wet, twa-21-d}}$ [mg/kg]	0.655	0.491	0.626	$PEC_{\text{Soil, wet, twa-21-d}} = PEC_{\text{Soil, dry}} / RHO_{\text{Soil, wet}} \times RHO_{\text{Soil, dry}}$
F_{solid} [m ² /m ³]	0.60			Default
RHO_{solid} [kg dry weight/m ³]	2500			Default
$CONV_{\text{soil}}$	1.13			$CONV_{\text{soil}} = RHO_{\text{Soil, wet}} / (F_{\text{solid}} \times RHO_{\text{solid}})$ (default)
F_{gut}	0.10			Default
C_{worm}	12.8	9.57	12.2	$C_{\text{worm}} = (BCF_{\text{worm}} \times C_{\text{porewater}} + PEC_{\text{Soil, wet}} \times F_{\text{gut}} \times CONV_{\text{soil}}) / (1 + F_{\text{gut}} \times CONV_{\text{soil}})$
Daily dietary dose [mg/kg bw/d]	13.4	10.0	12.8	$DDD = C_{\text{worm}} \times 1.05$
NOEL [mg/kg bw/d]	121			Review Report (2004)
TER_{LT}	9.02	12.0	9.44	$TER_{\text{LT}} = NOEL / DDD$

TER values shown in bold fall below the relevant trigger.

Use group 2: 3 × 2.4 L product/ha, 6-day interval

Use group 4: 3 × 1.8 L product/ha, 6-day interval

Use group 5: 3 × 2.4 L product/ha, 9-day interval

The TER values for the active substances Ethofumesate and Phenmedipham for secondary poisoning of earthworm-eating birds (dry soil and pore water approaches) are above the trigger value of 5, indicating an acceptable risk for earthworm-eating birds after application of HBZ10 for all intended uses in beet crops.

zRMS comment:

The Applicant presented TER_{LT} calculations for ethofumesate and phenmedipham for the pore water approach, as recommended in the EFSA GD (2009). zRMS is of opinion that this approach cannot be correctly estimated due to the lack of information about the way to calculate $PEC_{\text{soil pore water}}$. Therefore, the TER_{LT} calculations presented by the applicant have not been checked by zRMS.

Risk assessment for fish-eating birds via secondary poisoning

According to EFSA/2009/1438, the risk for piscivorous birds is assessed for a bird of 1000 g body weight with a daily food consumption of 159 g. Bioaccumulation in fish is estimated based on predicted concentrations in surface water as a limit value for admissible concentrations of Ethofumesate and Phenmedipham in water.

To achieve a concise risk assessment, the risk envelope approach is applied in line with the approach followed for PEC_{sw} calculations in dRR Part B8, Point 8.9: The 25 intended uses are grouped in 5 use groups, i.e., Use group 1: 6 x 1.2 L prod./ha, 5-days interval (includes uses 1, 6, 11, 16 and 21); Use group 2: 3 x 2.4 L prod./ha, 6-days interval (includes uses 2, 7, 12, 17, and 22); Use group 3: 5 x 1.2 L prod./ha, 7-days interval (includes uses 3, 8, 13, 18, and 23); Use group 4: 3 x 1.8 L prod./ha, 6-days interval (includes uses 4, 9, 14, 19, and 24); Use group 5: 3 x 2.4 L prod./ha, 9-days interval (includes uses 5, 10, 15, 20, and 25), and PEC_{sw} calculations are performed and presented for all use groups.

Table 9.2.2.4-5 Assessment of the risk for fish-eating birds due to exposure to Ethofumesate via bioaccumulation in fish (secondary poisoning) for the all intended uses in beet crops

Parameter	Use group 1/2/5	Use group 3	Use group 4	Comments
PEC _{SW} (twa = 21 d) [mg/L]	0.25531	0.212758	0.191483	PEC _{SW} , twa 21 d after multiple applications at FOCUS Step 1 (Section 8, Point 8.9.2)
BCF _{fish}	144			EFSA Conclusion (2016)
BMF	1			biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	36.76	30.64	25.57	PEC _{fish} = PEC _{water} × BCF _{fish}
Daily dietary dose [mg/kg bw/d]	3.10 5.85	4.87	2.32 4.38	DDD = PEC _{fish} × 0.159
NOEL [mg/kg bw/d]	265.0			EFSA Conclusion (2016)
TER _{LT}	83.3 45.3	54.4	114.1 60.4	TER _{LT} = NOEL/DDD

TER values shown in bold fall below the relevant trigger.

Use group 1: 6 x 1.2 L product/ha, 5-day interval

Use group 2: 3 x 2.4 L product/ha, 6-day interval

Use group 3: 5 x 1.2 L product/ha, 7-day interval

Use group 4: 3 x 1.8 L product/ha, 6-day interval

Use group 5: 3 x 2.4 L product/ha, 9-day interval

Table 9.2.2.4-6 Assessment of the risk for fish-eating birds due to exposure to Phenmedipham via bioaccumulation in fish (secondary poisoning) for the all intended uses in beet crops

Parameter	Use group 1/3	Use group 2/5	Use group 4	Comments
PEC _{SW} (twa = 21 d) [mg/L]	0.00069	0.001377	0.001033	PEC _{SW} , twa 21 d after multiple applications at FOCUS Step 1 (Section 8, Point 8.9.2)
BCF _{fish}	165			Review Report (2004)
BMF	1			biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	0.114	0.227	0.170	PEC _{fish} = PEC _{water} × BCF _{fish}
Daily dietary dose [mg/kg bw/d]	0.0181	0.0191 0.0361	0.0144 0.0271	DDD = PEC _{fish} × 0.159
NOEL [mg/kg bw/d]	121			Review Report (2004)
TER _{LT}	6684	6335 3349	8403 4465	TER _{LT} = NOEL/DDD

TER values shown in bold fall below the relevant trigger.

Use group 1: 6 x 1.2 L product/ha, 5-day interval

Use group 2: 3 x 2.4 L product/ha, 6-day interval

Use group 3: 5 x 1.2 L product/ha, 7-day interval

Use group 4: 3 x 1.8 L product/ha, 6-day interval

Use group 5: 3 x 2.4 L product/ha, 9-day interval

The TER value for the active substances Ethofumesate and Phenmedipham for secondary poisoning of fish-eating birds is above the trigger value of 5, indicating an acceptable risk for fish-eating birds after application of HBZ10 for all intended uses. in beet crops.

zRMS comments:

The Applicants' approach in evaluation of the risk of secondary poisoning is in line with EFSA (2009). Compounds selected for this assessment are agreed by the zRMS. Evaluation was not triggered for metabolites of both active substances due to their log Pow <3.

Consideration of the 21 d PEC_{twa} for soil and surface water exposure is validated by the zRMS as they were agreed in the course of the evaluation in area of Section 8.

The risk assessment based on Group uses such as: Use group 2: 3 x 2.4 L product/ha, 6-day interval, Use group 4: 3 x 1.8 L product/ha, 6-day interval, Use group 5: 3 x 2.4 L product/ha, 9-day interval. These group use covers the risk for remaining Group use 1 and Group use 3.

The TER value for the active substances Ethofumesate and Phenmedipham for secondary poisoning of fish-eating birds is above the trigger value of 5, indicating an acceptable risk for fish-eating birds after application of HBZ10 for all intended uses.

9.2.2.5 Biomagnification in terrestrial food chains

Not relevant, since the evaluation of the ADME studies in the toxicology section (EFSA Journal 2016;14(1):4374 and SANCO/4060/2001) concluded that the potential for bioaccumulation of the active substances is low. Thus, it can be assumed that there is no biomagnification along the food chain.

9.2.3 Risk assessment for baits, pellets, granules, pills or treated seed

Not relevant as HBZ10 is used for spray applications.

9.2.4 Overall conclusions

The risk assessment for effects on birds is carried out according to the Guidance of EFSA on Risk Assessment for Birds and Mammals (EFSA/2009/1438).

The acute and long-term risks of HBZ10 to birds were assessed from toxicity exposure ratios between toxicity endpoints, estimated from studies with the active substance, and predicted exposure based on the maximum residues occurring on food items following the intended application pattern. In addition, the acute risk of formulation to birds was assessed on the basis of the predicted mixture toxicity. Risk of secondary poisoning has also been assessed for both active substances.

Acute risk assessment

No acute LD₅₀ values are available for HBZ10. Thus, the acute risk was assessed with the lowest endpoints of the active substances as well as the predicted mixture LD₅₀ for the formulated product.

The TER_A values at the screening step exceed the Annex VI trigger value of 10 what indicates that formulation applied according to the intended use does not pose an acute risk to birds.

Long-term risk assessment

The EU agreed endpoints of the active substances ~~has~~ have been used in the assessment of chronic risk. The TER_{LT} values at the screening step exceed the Annex VI trigger value of 5 what indicates that formulation applied according to the intended use does not pose a reproductive risk to birds.

Although it is not recommended to conduct a long-term mixture toxicity assessment according to EFSA/2009/1438, a combi-TER_{LT} was calculated according to the ~~DRAFT~~ draft EFSA guidance document - Risk Assessment for Birds and Mammals (version 29.09.2021 for public consultation). Based on screening and Tier 1 assessments, the long-term risk to birds is demonstrated to be acceptable for the formulated product.

Secondary poisoning

The TER values for secondary poisoning of earthworm-eating birds (dry soil ~~and pore-water~~ approach) and fish-eating birds are above the trigger value of 5. There is no risk expected for birds exposed to the active substance through consumption of contaminated water from puddles on soil.

9.3 Effects on terrestrial vertebrates other than birds (KCP 10.1.2)

9.3.1 Toxicity data

Mammalian toxicity studies have been carried out with Ethofumesate and Phenmedipham. Full details of these studies are provided in the respective EU DAR (DAR Ethofumesate, 1998; DAR Phenmedipham, 1999) and related documents (DAR Addendum Ethofumesate, 2000; DAR Addendum Phenmedipham, 2001 and 2003, dRAR Phenmedipham, 2017).

Effects on mammals of HBZ10 were not evaluated as part of the EU assessment of Ethofumesate and Phenmedipham.

However, the provision of further data on HBZ10 is not considered essential, because the toxicity of the plant protection product can be predicted on the basis of the data for the active substance.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process. Justifications are provided with respect to the evaluation of mixture toxicity.

Table 9.3.1-1 Endpoints and effect values relevant for the risk assessment for mammals - Ethofumesate

Species	Substance	Exposure System	Results	Reference
Rat	Ethofumesate	Oral 14 d Acute	LD ₅₀ > 5000 mg/kg bw ^{a)}	EFSA Conclusion (2016)
Rat	Ethofumesate	Reproductive toxicity	NOAEL = 60.9 mg/kg bw/d	EFSA Conclusion (2016)

a) The LD50 values listed in the chapter of Mammalian Toxicology (> 2000 mg/kg bw) and in the Ecotoxicology chapter (> 5000 mg/kg bw) are supported by experimental data from rat studies. As the dose level of 2000 mg/kg bw is the limit dose for Classification & Labelling purposes with regard to human health effects (acute toxicity), this value has been considered as being the most relevant one in the Mammalian Toxicology chapter. In Ecotoxicology, however, the acute toxicity value is used directly for TER calculations. Under this aspect listing of the LD50 >5000 mg/kg bw is considered appropriate in Ecotoxicology. No adverse effects (0% mortality) were observed at 2000 mg a.s./kg bw and 5000 mg a.s./kg bw.

Bold written values are used for the risk assessment.

zRMS comments:

Mammalian toxicity data for ethofumesate are in line with the EU agreed endpoints reported in EFSA Journal 2016;14(1):4374.

Table 9.3.1-2 Endpoints and effect values relevant for the risk assessment for mammals - Phenmedipham

Species	Substance	Exposure System	Results	Reference
Rat	Phenmedipham	Oral 14 d Acute	LD ₅₀ > 8000 mg/kg bw	Review Report (2004)
Rat	Phenmedipham	2-Generation study	NOAEL = 6.8 mg/kg bw/d ^{a)}	Review Report (2004)
Position paper on toxicity endpoint for wild-mammal long-term & reproductive risk assessment			NOEL = 25 mg/kg bw/d ^{b)}	Diesing (2014) as cited in dRAR (2017)

a) Endpoint used for first-tier risk assessment

b) Endpoint used for refined risk assessment

Bold written values are used for the risk assessment.

zRMS comments:

Mammalian toxicity data for phenmedipham are in line with the EU agreed endpoints reported in Review Report (2004).

Mixture toxicity

According to EFSA/2009/1438 combined action of several toxicants must be specifically considered in the risk assessment when it is obvious that such exposure situations will occur for animals.

In line with EFSA/2009/1438, for the assessment of acute effects (mortality), the mixture toxicity is adequately assessed on the basis of the surrogate LD₅₀ calculated by assuming dose additivity:

$$LD_{50}(\text{mix}) = \sum_{i=1}^n \left(\frac{X(a.s._i)}{LD_{50}(a.s._i)} \right)^{-1}$$

With:

X (a.s._i) = fraction of active substance [i] in the mixture

LD₅₀ (a.s._i) = acute toxicity value for active substance [i]

The estimation of the LD₅₀ (mix) is showed in **Table 9.3.1-3**.

Table 9.3.1-3 Estimation of LD₅₀ for the mixture assuming dose additivity

Active substance	Concentration of each active substance in formulation [g a.s./L]	X (a.s. _i) in the mixture	LD ₅₀ [mg a.s./kg bw]	1/tox per fraction [X (a.s. _i)/LD ₅₀ (a.s. _i)]	LD ₅₀ (mix) [Σ mg (a.s. _i)/kg bw]
Ethofumesate	125	0.5	> 5000	0.00010000	6154
Phenmedipham	125	0.5	> 8000	0.00006250	
Total	250	1.0	-	0.00016250	

To achieve a basis for a comparison of single active substance and mixture toxicity in terms of potential risk, a “tox per fraction” quotient can be calculated for each active substance and compared to the corresponding quotient for the mixture:

$$\text{Tox per fraction (a.s.)} = \frac{LD_{50}(a.s._i)}{X(a.s._i)}$$

$$\text{Tox per fraction (mix)} = \frac{LD_{50}(\text{mix})}{\sum_{i=1}^n X(a.s._i)}$$

Table 9.3.1-4 Comparison of “tox per fraction (a.s._i)” and “tox per fraction (mix)”

Active substance	LD ₅₀ (a.s. _i) [mg a.s./kg bw]	X (a.s. _i) in the mixture	Tox per fraction (a.s.): [LD ₅₀ (a.s. _i)/X (a.s. _i)]	Tox per fraction (mix): [LD ₅₀ (mix)/Σ X (a.s. _i)]	Deviation [%] ^a
Ethofumesate	> 5000	0.5	10000	6154	38.5
Phenmedipham	> 8000	0.5	16000		61.5

^a Deviation [%] = [(tox per fraction (a.s._i) - tox per fraction (mix)]/tox per fraction (a.s._i) × 100

None of the active substances contributes to ≥ 90% to the toxicity of HBZ10. The “tox per fraction” quotient for both active substances deviates > 10% from the “tox per fraction (mix)”. This indicates that there is not one active substance with a more significant impact on the overall predicted risk. Hence, the risk assessment for acute effects will be performed for the individual active substances, as well as for the calculated mixture toxicity.

Since it is not necessary to calculate a mixture (combined) toxicity value for the product in order to compare to a measured formulation endpoint (as reproduction toxicity with formulation is not available), the estimation of chronic combined toxicity for formulations containing more than one active substance can be achieved by combining the TERs for the individual active substances, also referred to as the combi-TER (DRAFT EFSA guidance document - Risk Assessment for Birds and Mammals (version 29.09.2021 for public consultation)). In this way, the TU approach is followed, as the environmental exposure patterns for the individual active substances are already accounted for in the TER values calculated for each substance.

When for each substance the trigger values are equal, the combined TER value can be calculated according to:

$$\text{combiTER} = 1/((1/\text{TER}_{\text{substance 1}})+(1/\text{TER}_{\text{substance 2}}))$$

The TER_{combi} calculations presented below are relevant for all uses intended for the formulated product HBZ10, i.e., sugar beet, red beet/yellow beet/fodder beet and chard. Additional calculations based on modified higher tier TER_{LT} values for the active substance Phenmedipham (also relevant for all intended uses) have been conducted by the zRMS and are presented in the relevant grey commenting box.

Based on screening, Tier 1 and higher tier TER values, the TER_{combi} are:

Application Rate	Ethofumesate TER _{LT}	Phenmedipham TER _{LT}	TER _{combi}
Lagomorph (BBCH 10-39)			
3 × 2.4 L product/ha, 6 day interval	12.9*	13**	6.4
3 × 2.4 L product/ha, 9 day interval	14.0*	14.2**	7.3
3 × 1.8 L product/ha, 6 day interval	17.0*	17.4**	8.6
6 × 1.2 L product/ha, 5 day interval	17.0*	24.4**	10.3
5 × 1.2 L product/ha, 7 day interval	22.3*	27**	12.2
Shrew (BBCH 10-19)			
3 × 2.4 L product/ha, 6 day interval	43.4*	6.2**	5.4
3 × 2.4 L product/ha, 9 day interval	50.7*	5.7*	5.1
3 × 1.8 L product/ha, 6 day interval	57.9*	6.5*	5.8
6 × 1.2 L product/ha, 5 day interval	60.8*	6.8*	6.1
5 × 1.2 L product/ha, 7 day interval	76.0*	8.5*	7.6
Mouse (BBCH 10-39)			
3 × 2.4 L product/ha, 6 day interval	23.4*	7.0**	5.4
3 × 2.4 L product/ha, 9 day interval	27.3*	8.0**	6.2
3 × 1.8 L product/ha, 6 day interval	31.2*	9.3**	7.2
6 × 1.2 L product/ha, 5 day interval	32.74*	10.0**	7.7
5 × 1.2 L product/ha, 7 day interval	40.0*	12.4**	9.5
Shrew (BBCH ≥20)			
3 × 2.4 L product/ha, 6 day interval	96.0*	10.7*	9.6
3 × 2.4 L product/ha, 9 day interval	112*	12.5*	11.2
3 × 1.8 L product/ha, 6 day interval	128*	14.3*	12.9
6 × 1.2 L product/ha, 5 day interval	134.4*	15.0*	13.5
5 × 1.2 L product/ha, 7 day interval	168*	18.8*	16.9

Values in **bold** are below the trigger value

* TER_{LT} value from tier 1 risk assessment

** TER_{LT} value from higher tier risk assessment

An acceptable risk is expected when TER_{combi} > trigger of 5 based on long term risk. Based on the tier 1 and higher tier assessment TER values, the long term risk to mammals is demonstrated to be acceptable for all the intended uses.

Therefore, an acceptable long term risk to mammals can be demonstrated for the formulated product. No further consideration is required.

zRMS comments:

Combined acute toxicity

The LD_{50mix} of 6154 mg /kg bw presented in Table 9.3.1-3 has been validated by the zRMS and is confirmed to be correct.

Due to that none of active substances have more significant impact in the toxicity of mixture, the risk assessment for acute effects is performed for the individual active substances, as well as for the calculated mixture toxicity in the Tables below.

Combined long-term toxicity

TER_{combi} calculations based on the lowest TER_{LT} values at Tier 1 step (in case of ethofumesate) and on higher tier (in case of phendemipham) were amended by zRMS and are presented under Point 9.3.2.2 for all Group uses.

9.3.1.1 Justification for new endpoints

The EU agreed endpoints for the active substances Ethofumesate and Phenmedipham are used in the risk assessment.

9.3.2 Risk assessment for spray applications

The risk assessment is based on the methods presented in the Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA/2009/1438).

For completeness, the risk assessment is presented for all intended uses (please refer to point 9.1.2).

9.3.2.1 First-tier assessment (screening/generic focal species)

The results of the acute and reproductive first-tier risk assessments are summarised in the following tables.

~~Use-group no 2:~~ **Sugar beet**, 3 × 2.4 L product/ha, 6-day interval

Table 9.3.2.1-1 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ **sugar beet (3 × 2.4 L product/ha, 6-day interval) - Ethofumesate**

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Sugar beet	Small herbivorous mammal		118.4	1.7	-	60.38	82.8
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario Growth stage	Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Sugar beet BBCH 10-19	Small insectivorous mammal “shrew”		4.2	2.1	0.53	1.40	43.4
Sugar beet BBCH 10-39	Large herbivorous mammal “lagomorph”		14.3	2.1	0.53	4.77	12.8
Sugar beet BBCH 10-39	Small omnivorous mammal “mouse”		7.8	2.1	0.53	2.60	23.4
Sugar beet BBCH ≥ 20	Small insectivorous mammal “shrew”		1.9	2.1	0.53	0.63	96.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-2 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ **sugar beet (3 × 2.4 L product/ha, 6-day interval) - Phenmedipham**

Intended use		Beet-crops Sugar beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A	
Bulbs and onion-like crops Sugar beet	Small herbivorous mammal	118.4	1.7	-	60.38	132.5	

Reprod. toxicity [mg/kg bw/d]		6.8				
TER criterion		5				
Crop scenario	Generic focal species	SV_m	MAF_m	TWA	DDD_m [mg/kg bw/d]	TER_{LT}
Sugar beet BBCH 10-19	Small insectivorous mammal “shrew”	4.2	2.1	0.53	1.40	4.8
Sugar beet BBCH 10-39	Large herbivorous mammal “lagomorph”	14.3	2.1	0.53	4.77	1.4
Sugar beet BBCH 10-39	Small omnivorous mammal “mouse”	7.8	2.1	0.53	2.60	2.6
Sugar beet BBCH ≥ 20	Small insectivorous mammal “shrew”	1.9	2.1	0.53	0.63	10.7

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-3 Screening assessment of the acute risk for mammals due to the use of HBZ10 in beet crops sugar beet (3 × 2.4 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use	Beet crops Sugar beet					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	3 × ∑ 0.300 + 0.300					
Acute toxicity [mg/kg bw]	6154					
LD_{50mix}	10					
TER criterion	10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A
Bulbs and onion-like crops Beet crops Sugar beet	Small herbivorous mammal	118.4	1.7	-	120.77	51.0

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in beet crops sugar beet at 3 × 2.4 L product/ha (6-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable risk for mammals following application of HBZ10 in beet crops sugar beet at 3 × 2.4 L product/ha (6-day interval), except for the active substance Phenmedipham for the generic focal species small insectivorous mammal, large herbivorous mammal, and small omnivorous mammal (growth stage BBCH 10-39).

zRMS comments:

The screening step risk assessment for active substances at rates 3 x 0.3 kg ethofumesate/ha and 3 x 0.3 kg phenmedipham/ha with 6-day interval is validated by the zRMS.

Based on calculations presented in the Table from 9.3.2.1-1 acceptable acute and long-term risk may be concluded for mammals exposed to ethofumesate in HBZ10.

In the same time according to calculation presented in the Table 9.3.2.1-2 acceptable acute risk may be concluded for mammals exposed to Phenmedipham in HBZ10 but in case of long-term risk assessment further refinement is required for generic focal species such as: small insectivorous mammal, large herbivorous mammal, and small omnivorous mammal.

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.3.2.1-3 is above the respective trigger value of 10, indicating an acceptable risk for mammals following application of HBZ10 in beet crops at 3 × 2.4 L product/ha (6-day interval).

Combined long-term risk assessment:

TER_{combi} calculations are provided in zRMS's commenting box under Point 9.3.2.2.

Use-group no 5: **Sugar beet**, 3 × 2.4 L product/ha, 9-day interval

Table 9.3.2.1-4 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ **sugar beet (3 × 2.4 L product/ha, 9-day interval) - Ethofumesate**

Intended use		Ethofumesate Sugar beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small herbivorous mammal		118.4	1.5	-	53.28	93.8
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario Growth stage	Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Sugar beet BBCH 10-19	Small insectivorous mammal “shrew”		4.2	1.8	0.53	1.20	50.7
Sugar beet BBCH 10-39	Large herbivorous mammal “lagomorph”		14.3	1.8	0.53	4.09	14.9
Sugar beet BBCH 10-39	Small omnivorous mammal “mouse”		7.8	1.8	0.53	2.23	27.3
Sugar beet BBCH > 20	Small insectivorous mammal “shrew”		1.9	1.8	0.53	0.54	112.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-5 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ **sugar beet (3 × 2.4 L product/ha, 9-day interval) - Phenmedipham**

Intended use		Beet-crops Sugar beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small herbivorous mammal		118.4	1.5	-	53.28	150.2
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario Growth stage	Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Sugar beet BBCH 10-19	Small insectivorous mammal “shrew”		4.2	1.8	0.53	1.20	5.7
Sugar beet BBCH 10-39	Large herbivorous mammal “lagomorph”		14.3	1.8	0.53	4.09	1.7
Sugar beet BBCH 10-39	Small omnivorous mammal “mouse”		7.8	1.8	0.53	2.23	3.0
Sugar beet BBCH ≥ 20	Small insectivorous mammal “shrew”		1.9	1.8	0.53	0.54	12.5

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-6 Screening assessment of the acute risk for mammals due to the use of HBZ10 in ~~beet crops~~ **sugar beet (3 × 2.4 L product/ha, 9-day interval) – surrogate mixture toxicity**

Intended use		Beet crops Sugar beet				
Active substance/product		Ethofumesate + Phenmedipham / HBZ10				
Application rate [kg/ha]		$3 \times \sum 0.300 + 0.300$				
Acute toxicity [mg/kg bw] LD_{50mix}		6154				
TER criterion		10				
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A
Bulbs and onion like crops Beet crops Sugar beet	Small herbivorous mammal	118.4	1.5	-	53.28	115.5

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in ~~beet crops~~ **sugar beet** at 3 × 2.4 L product/ha (9-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable risk for mammals following application of HBZ10 in ~~beet crops~~ **sugar beet** at 3 × 2.4 L product/ha (9-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal, and small omnivorous mammal (growth stage BBCH 10-39).

zRMS comments:

The screening step risk assessment for active substances at rate 3 x 0.300 kg ethofumesate/ha and 3 x 0.300 kg phenmedipham/ha with 9-day interval is agreed by the zRMS.

Based on calculations presented in the Tables from 9.3.2.1-4 acceptable acute and long-term risk may be concluded for birds exposed to ethofumesate in HBZ10.

In the same time according to calculations presented in the Table 9.3.2.1-5 acceptable acute risk may be concluded for mammals exposed to Phenmedipham in HBZ10 but in case of long-term risk assessment further refinement is required for generic focal species such as: large herbivorous mammal and small omnivorous mammal for growth stage BBCH 10-39.

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.3.2.1-6 is above the respective trigger value of 10, indicating an acceptable risk for **mammals birds** following application of HBZ10 in beet crops at 3 × 2.4 L product/ha with (9-day interval).

Combined long-term risk assessment:

TER_{combi} calculations are provided in zRMS's commenting box under Point 9.3.2.2.

~~Use group no 4:~~ **Sugar beet, 3 × 1.8 L product/ha, 6-day interval**

Table 9.3.2.1-7 Screening assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ sugar beet (3 × 1.8 L product/ha, 6-day interval) - Ethofumesate

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.225					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet	Small herbivorous mammal		118.4	1.7	-	45.29	110.4
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Indicator species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Bulbs and onion-like crops Beet-crops Sugar beet	Small herbivorous mammal		48.3	2.1	0.53	12.10	5.03

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-8 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ sugar beet (3 × 1.8 L product/ha, 6-day interval) - Phenmedipham

Intended use		Beet-crops Sugar beet						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.225						
Acute toxicity [mg/kg bw]		> 8000						
TER criterion		10						
Crop scenario		Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet-crops Sugar beet		Small herbivorous mammal		118.4	1.7	-	45.29	176.6
Reprod. toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Crop scenario Growth stage		Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Sugar beet BBCH 10-19		Small insectivorous mammal “shrew”		4.2	2.1	0.53	1.05	6.5
Sugar beet BBCH 10-39		Large herbivorous mammal “lagomorph”		14.3	2.1	0.53	3.58	1.9
Sugar beet BBCH 10-39		Small omnivorous mammal “mouse”		7.8	2.1	0.53	1.95	3.5
Sugar beet BBCH > 20		Small insectivorous mammal “shrew”		1.9	2.1	0.53	0.48	14.3

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-9 Screening assessment of the acute risk for mammals due to the use of HBZ10 in ~~beet crops~~ sugar beet (3 × 1.8 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × ∑ 0.225 + 0.225					
Acute toxicity [mg/kg bw]		6154					
LD _{50mix}		10					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Bulbs and onion-like crops Beet-crops Sugar beet	Small herbivorous mammal	118.4	1.7	-	90.58	67.9	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in ~~beet crops~~ **sugar beet** at 3 × 1.8 L product/ha (6-day interval).

The screening and first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable risk for mammals following application of HBZ10 in ~~beet crops~~ **sugar beet** at 3 × 1.8 L product/ha (6-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal, and small omnivorous mammal (growth stage BBCH 10-39).

zRMS comments:

The screening step risk assessment for active substances at rate 3 x 0.225 kg ethofumesate/ha and 3 x 0.225 kg phenmedipham/ha with 6-day interval is validated by the zRMS.

Based on calculations presented in the Table from 9.3.2.1-7 acceptable acute and long-term risk may be concluded for mammals exposed to ethofumesate in HBZ10.

In the same time according to calculations presented in the Table 9.3.2.1-8 acceptable acute risk may be concluded for mammals exposed to Phenmedipham in HBZ10 but in case of long-term risk assessment further refinement is required for generic focal species such as: large herbivorous mammal and small omnivorous mammal (at growth stage BBCH 10-39).

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.3.2.1-9 is above the respective trigger value of 10, indicating an acceptable risk for **mammals** following application of HBZ10 in beet crops at 3 × 1.8 L product/ha (6-day interval).

Combined long-term risk

TER_{combi} calculations are provided in zRMS's commenting box under Point 9.3.2.2.

~~Use group no 1:~~ **Sugar beet**, 6 × 1.2 L product/ha, 5-day interval

Table 9.3.2.1-10 Screening/Tier1 assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet crops~~ **sugar beet (6 × 1.2 L product/ha, 5-day interval) - Ethofumesate**

Intended use	Beet crops Sugar beet					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	6 × 0.150					
Acute toxicity [mg/kg bw]	> 5000					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Beet crops Sugar beet	Small herbivorous mammal	118.4	2.2	-	39.07	128.0
Reprod. toxicity [mg/kg bw/d]	60.9					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage						
Sugar beet BBCH 10-19	Small insectivorous mammal "shrew"	4.2	3.0	0.53	1.00	60.80
Sugar beet BBCH 10-39	Large herbivorous mammal "lagomorph"	14.3	3.0	0.53	3.41	17.9
Sugar beet BBCH 10-39	Small omnivorous mammal "mouse"	7.8	3.0	0.53	1.86	32.74

Sugar beet BBCH \geq 20	Small insectivorous mammal “shrew”	1.9	3.0	0.53	0.45	134.4
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SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-11 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ sugar beet (6×1.2 L product/ha, 5-day interval) - Phenmedipham

Intended use	Beet-crops Sugar beet					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	6×0.150					
Acute toxicity [mg/kg bw]	> 8000					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Sugar beet	Small herbivorous mammal	118.4	2.2	-	39.07	204.8
Reprod. toxicity [mg/kg bw/d]	6.8					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage						
Sugar beet BBCH 10-19	Small insectivorous mammal “shrew”	4.2	3.0	0.53	1.00	6.8
Sugar beet BBCH 10-39	Large herbivorous mammal “lagomorph”	14.3	3.0	0.53	3.41	2.0
Sugar beet BBCH 10-39	Small omnivorous mammal “mouse”	7.8	3.0	0.53	1.86	3.7
Sugar beet BBCH \geq 20	Small insectivorous mammal “shrew”	1.9	3.0	0.53	0.23	15.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-12 Screening assessment of the acute risk for mammals due to the use of HBZ10 in ~~beet-crops~~ sugar beet (6×1.2 L product/ha, 5-day interval) – surrogate mixture toxicity

Intended use	Beet-crops Sugar beet					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$6 \times \sum 0.150 + 0.150$					
Acute toxicity [mg/kg bw]	6154					
LD _{50mix}						
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Sugar beet	Small herbivorous mammal	118.4	2.2	-	78.14	78.8

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in ~~beet-crops~~ sugar beet at 6×1.2 L product/ha (5-day interval).

The screening and first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable risk for mammals following application of HBZ10 in ~~beet-crops~~ sugar beet at 6×1.2 L product/ha (5-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal, and small omnivorous mammal (growth stage BBCH 10-39).

zRMS comments:

The screening step risk assessment for active substances at rate 6×0.150 kg ethofumesate/ha and 6×0.150 kg phenmedipham/ha with 5-day interval is validated by the zRMS.

Based on calculations presented in the Tables from 9.3.2.1-10 acceptable acute and long-term risk may be concluded for mammals exposed to ethofumesate in HBZ10.

In the same time according to calculations presented in the Table 9.3.2.1-11 acceptable acute risk may be concluded for mammals exposed to Phenmedipham in HBZ10 but in case of long-term risk assessment further refinement is required for generic focal species such as: large herbivorous mammal and small omnivorous mammal (at growth stage BBCH 10-39).

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.3.2.1-12 is above the respective trigger value of 10, indicating an acceptable risk for **mammals birds** following application of HBZ10 in beet crops at 6 × 1.2 L product/ha (5-day interval).

Combined long-term risk assessment:

TER_{combi} calculations are provided in zRMS's commenting box under Point 9.3.2.2.

Use-group no-3: **Sugar beet**, 5 × 1.2 L product/ha, 7-day interval

Table 9.3.2.1-13 Screening assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet crops~~ **sugar beet (5 × 1.2 L product/ha, 7-day interval) - Ethofumesate**

Intended use		Ethofumesate Beet crops Sugar beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		5 × 0.150					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Sugar beet	Small herbivorous mammal		118.4	1.9	-	33.74	148.2
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage							
Sugar beet BBCH 10-19	Small insectivorous mammal “shrew”		4.2	2.4	0.53	0.80	76.0
Sugar beet BBCH 10-39	Large herbivorous mammal “lagomorph”		14.3	2.4	0.53	2.73	22.3
Sugar beet BBCH 10-39	Small omnivorous mammal “mouse”		7.8	2.4	0.53	1.49	40.9
Sugar beet BBCH > 20	Small insectivorous mammal “shrew”		1.9	2.4	0.53	0.36	168.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-14 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ sugar beet (5 × 1.2 L product/ha, 7-day interval) - Phenmedipham

Intended use		Beet crops Sugar beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Bulbs and onion-like crops Sugar beet	Small herbivorous mammal		118.4	1.9	-	33.74	237.1
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario	Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage							
Sugar beet BBCH 10-19	Small insectivorous mammal “shrew”		4.2	2.4	0.53	0.80	8.5
Sugar beet BBCH 10-39	Large herbivorous mammal “lagomorph”		14.3	2.4	0.53	2.73	2.5
Sugar beet BBCH 10-39	Small omnivorous mammal “mouse”		7.8	2.4	0.53	1.49	4.6
Sugar beet BBCH > 20	Small insectivorous mammal “shrew”		1.9	2.4	0.53	0.36	18.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-15 Screening assessment of the acute risk for mammals due to the use of HBZ10 in ~~beet-crops~~ sugar beet (5 × 1.2 L product/ha, 7-day interval) – surrogate mixture toxicity

Intended use		Beet-crops Sugar beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		5 × ∑ 0.150 + 0.150					
Acute toxicity [mg/kg bw]		6154					
LD _{50mix}							
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Bulbs and onion-like crops Sugar beet	Small herbivorous mammal	118.4	1.9	-	67.49	91.2	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening-TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in ~~beet-crops~~ sugar beet at 5 × 1.2 L product/ha (7-day interval).

The screening and first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable risk for mammals following application of HBZ10 in ~~beet-crops~~ sugar beet at 5 × 1.2 L product/ha (7-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal, and small omnivorous mammal (growth stage BBCH 10-39).

zRMS comments:

The screening step risk assessment for active substances at rate 6 x 0.150 kg ethofumesate/ha and 6 x 0.150 kg phenmedipham/ha with 7-day interval is validated by the zRMS.

Based on calculations presented in the Tables from 9.3.2.1-13 acceptable acute and long-term risk may be concluded for mammals exposed to ethofumesate in HBZ10.

In the same time according to calculations presented in the Table 9.3.2.1-14 acceptable acute risk may be concluded for mammals exposed to Phenmedipham in HBZ10 but in case of long-term risk assessment further

refinement is required for **generic** focal species such as: large herbivorous mammal and small omnivorous mammal (growth stage BBCH 10-39).

Acute combined risk

The screening acute combined TER_A value presented in the Table 9.3.2.1-15 is above the respective trigger value of 10, indicating an acceptable risk for **mammals** **birds** following application of HBZ10 in beet crops at 5 × 1.2 L product/ha (7-day interval).

Combined long-term risk assessment:

TER_{combi} calculations are provided in zRMS's commenting box under Point 9.3.2.2.

Red beet/Yellow beet/Fodder beet, 3 × 2.4 L product/ha, 6-day interval

Table 9.3.2.1-16 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 6-day interval) - Ethofumesate

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.7	-	60.38	82.8	
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Growth stage							
Root and stem vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.1	0.53	1.40	43.4	
Root and stem vegetables BBCH 10-39	Small omnivorous mammal, mouse	7.8	2.1	0.53	2.60	23.4	
Root and stem vegetables BBCH > 20	Small insectivorous mammal, shrew	1.9	2.1	0.53	0.63	96.0	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-17 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 6-day interval) - Phenmedipham

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.7	-	60.38	132.5	
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Growth stage							
Root and stem vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.1	0.53	1.40	4.8	
Root and stem vegetables BBCH 10-39	Small omnivorous mammal, mouse	7.8	2.1	0.53	2.60	2.6	
Root and stem vegetables BBCH > 20	Small insectivorous mammal, shrew	1.9	2.1	0.53	0.63	10.7	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-18 Screening assessment of the acute risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 2.4 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × ∑ 0.300 + 0.300					
Acute toxicity [mg/kg bw]		6154					
LD_{50mix}							
TER criterion		10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.7	-	120.77	51.0	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3 × 2.4 L product/ha (6-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3 × 2.4 L product/ha (6-day interval), except for the active substance Phenmedipham for the generic focal species small omnivorous mammal “mouse” at BBCH growth stage 10-39. As regards the small insectivorous mammal “shrew”, as already noted by zRMS in **Table 9.3.2.2-6**, the TER_{LT} value calculated at higher-tier is only slightly below the trigger of 5 and thus the potential long-term risk could be considered as acceptable. As regards the small omnivorous mammal “mouse”, the identified long-term risk can be considered as already addressed based on the refined risk assessment presented in the additional calculations provided by the zRMS in the relevant grey commenting box (recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for

mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3×2.4 L product/ha (6-day interval) can be concluded.

Red beet/Yellow beet/Fodder beet, 3×2.4 L product/ha, 9-day interval

Table 9.3.2.1-19 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3×2.4 L product/ha, 9-day interval) - Ethofumesate

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.5	-	53.28	93.8	
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Growth stage							
Root and stem vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	1.8	0.53	1.20	50.7	
Root and stem vegetables BBCH 10-39	Small omnivorous mammal, mouse	7.8	1.8	0.53	2.23	27.3	
Root and stem vegetables BBCH > 20	Small insectivorous mammal, shrew	1.9	1.8	0.53	0.54	112.0	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-20 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3×2.4 L product/ha, 9-day interval) - Phenmedipham

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.5	-	53.28	150.2	
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Growth stage							
Root and stem vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	1.8	0.53	1.20	5.7	
Root and stem vegetables BBCH 10-39	Small omnivorous mammal, mouse	7.8	1.8	0.53	2.23	3.0	
Root and stem vegetables BBCH > 20	Small insectivorous mammal, shrew	1.9	1.8	0.53	0.54	12.5	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-21 Screening assessment of the acute risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3×2.4 L product/ha, 9-day interval) – surrogate mixture toxicity

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		$3 \times \sum 0.300 + 0.300$					
Acute toxicity [mg/kg bw]		6154					
LD_{50mix}							
TER criterion		10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.5	-	106.56	57.8	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3×2.4 L product/ha (9-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3×2.4 L product/ha (9-day interval), except for the active substance Phenmedipham for the generic focal species small omnivorous mammal “mouse” at BBCH growth stage 10-39. The identified long-term risk can be considered as already addressed based on the refined risk assessment presented in the additional calculations provided by the zRMS in the relevant grey commenting box (recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3×2.4 L product/ha (9-day interval) can be concluded.

Red beet/Yellow beet/Fodder beet, 3×1.8 L product/ha, 6-day interval

Table 9.3.2.1-22 Screening assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3×1.8 L product/ha, 6-day interval) - Ethofumesate

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.225					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.7	-	45.29	110.4	
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Root and stem vegetables	Small herbivorous mammal	48.3	2.1	0.53	12.10	5.03	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-23 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 1.8 L product/ha, 6-day interval) - Phenmedipham

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.225					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.7	-	45.29	176.6	
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Growth stage							
Root and stem vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.1	0.53	1.05	6.5	
Root and stem vegetables BBCH 10-39	Small omnivorous mammal, mouse	7.8	2.1	0.53	1.95	3.5	
Root and stem vegetables BBCH > 20	Small insectivorous mammal, shrew	1.9	2.1	0.53	0.48	14.3	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-24 Screening assessment of the acute risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (3 × 1.8 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × ∑ 0.225 + 0.225					
Acute toxicity [mg/kg bw]		6154					
LD_{50mix}							
TER criterion		10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.7	-	90.58	67.9	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3 × 1.8 L product/ha (6-day interval).

The screening TER_{LT} value for the active substance Ethofumesate and the first tier TER_{LT} values for the active substance Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3 × 1.8 L product/ha (6-day interval), except for the active substance Phenmedipham for the generic focal species small omnivorous mammal “mouse” at BBCH growth stage 10-39. The identified long-term risk can be considered as already addressed based on the refined risk assessment presented in the additional calculations provided by the zRMS in the relevant grey commenting box (recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 3 × 1.8 L product/ha (6-day interval) can be concluded.

Red beet/Yellow beet/Fodder beet, 6 × 1.2 L product/ha, 5-day interval

Table 9.3.2.1-25 Screening assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (6 × 1.2 L product/ha, 5-day interval) - Ethofumesate

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	2.2	-	39.07	128.0	
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Root and stem vegetables	Small herbivorous mammal	48.3	3.0	0.53	11.52	5.29	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-26 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (6 × 1.2 L product/ha, 5-day interval) - Phenmedipham

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	2.2	-	39.07	204.8	
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Growth stage							
Root and stem vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	3.0	0.53	1.00	6.8	
Root and stem vegetables BBCH 10-39	Small omnivorous mammal, mouse	7.8	3.0	0.53	1.86	3.7	
Root and stem vegetables BBCH > 20	Small insectivorous mammal, shrew	1.9	3.0	0.53	0.45	15.0	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-27 Screening assessment of the acute risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (6 × 1.2 L product/ha, 5-day interval) – surrogate mixture toxicity

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		6 × ∑ 0.150 + 0.150					
Acute toxicity [mg/kg bw] LD_{50mix}		6154					
TER criterion		10					
Crop scenario	Indicator species	SV₉₀	MAF₉₀	TWA	DDD₉₀ [mg/kg bw/d]	TER_A	
Root and stem vegetables	Small herbivorous mammal	118.4	2.2	-	78.14	78.8	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 6×1.2 L product/ha (5-day interval).

The screening TER_{LT} value for the active substance Ethofumesate and the first tier TER_{LT} values for the active substance Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 6×1.2 L product/ha (5-day interval), except for the active substance Phenmedipham for the generic focal species small omnivorous mammal “mouse” at BBCH growth stage 10-39. The identified long-term risk can be considered as already addressed based on the refined risk assessment presented in the additional calculations provided by the zRMS in the relevant grey commenting box (recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 6×1.2 L product/ha (5-day interval) can be concluded.

Red beet/Yellow beet/Fodder beet, 5×1.2 L product/ha, 7-day interval

Table 9.3.2.1-28 Screening assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (5×1.2 L product/ha, 7-day interval) - Ethofumesate

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		5 × 0.150					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.9	-	33.74	148.2	
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Indicator species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Root and stem vegetables	Small herbivorous mammal	48.3	2.4	0.53	9.22	6.61	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-29 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (5×1.2 L product/ha, 7-day interval) - Phenmedipham

Intended use		Red beet/yellow beet/fodder beet					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		5 × 0.150					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Root and stem vegetables	Small herbivorous mammal	118.4	1.9	-	33.74	237.1	
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Growth stage							

Root and stem vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.4	0.53	0.80	8.5
Root and stem vegetables BBCH 10-39	Small omnivorous mammal, mouse	7.8	2.4	0.53	1.49	4.6
Root and stem vegetables BBCH ≥ 20	Small insectivorous mammal, shrew	1.9	2.4	0.53	0.36	18.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-30 Screening assessment of the acute risk for mammals due to the use of HBZ10 in red beet/yellow beet/fodder beet (5×1.2 L product/ha, 7-day interval) – surrogate mixture toxicity

Intended use	Red beet/yellow beet/fodder beet					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$5 \times \sum 0.150 + 0.150$					
Acute toxicity [mg/kg bw] LD _{50mix}	6154					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Root and stem vegetables	Small herbivorous mammal	118.4	1.9	-	67.49	91.2

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 5×1.2 L product/ha (7-day interval).

The screening TER_{LT} value for the active substance Ethofumesate and the first tier TER_{LT} values for the active substance Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 5×1.2 L product/ha (7-day interval), except for the active substance Phenmedipham for the generic focal species small omnivorous mammal “mouse” at BBCH growth stage 10-39. The identified long-term risk can be considered as already addressed based on the refined risk assessment presented in the additional calculations provided by the zRMS in the relevant grey commenting box (recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in red beet/yellow beet/fodder beet at 5×1.2 L product/ha (7-day interval) can be concluded.

Chard, 3×2.4 L product/ha, 6-day interval

Table 9.3.2.1-31 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (3×2.4 L product/ha, 6-day interval) - Ethofumesate

Intended use	Chard					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3×0.300					
Acute toxicity [mg/kg bw]	> 5000					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.7	-	69.56	71.9
Reprod. toxicity [mg/kg bw/d]	60.9					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage						

Leafy vegetables All season	Large herbivorous mammal, lagomorph	14.3	2.1	0.53	4.77	12.8
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.1	0.53	1.40	43.4
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse	7.8	2.1	0.53	2.60	23.4
Leafy vegetables BBCH ≥ 20	Small insectivorous mammal, shrew	1.9	2.1	0.53	0.63	96.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-32 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (3×2.4 L product/ha, 6-day interval) - Phenmedipham

Intended use	Chard					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3×0.300					
Acute toxicity [mg/kg bw]	> 8000					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.7	-	69.56	115.0
Reprod. toxicity [mg/kg bw/d]	6.8					
TER criterion	5					
Crop scenario Growth stage	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables All season	Large herbivorous mammal, lagomorph	14.3	2.1	0.53	4.77	1.4
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.1	0.53	1.40	4.8
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse	7.8	2.1	0.53	2.60	2.6
Leafy vegetables BBCH ≥ 20	Small insectivorous mammal, shrew	1.9	2.1	0.53	0.63	10.7

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-33 Screening assessment of the acute risk for mammals due to the use of HBZ10 in chard (3×2.4 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use	Chard					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$3 \times \sum 0.300 + 0.300$					
Acute toxicity [mg/kg bw] LD _{50mix}	6154					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.7	-	139.13	44.2

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in chard at 3×2.4 L product/ha (6-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in chard at 3×2.4 L product/ha (6-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal “lagomorph” during all season, small insectivorous mammal “shrew” at BBCH growth stage 10-19 and small omnivorous mammal “mouse” at BBCH growth stage 10-49. As regards the small insectivorous mammal “shrew”, as already noted by zRMS in **Table 9.3.2.2-6**, the TER_{LT} value calculated at higher-tier is only slightly below the trigger of 5 and thus the potential long-term risk could be considered as acceptable. As regards the large

herbivorous mammal “lagomorph” and the small omnivorous mammal “mouse” the identified long-term risk can be considered as already addressed based on the refined risk assessments presented in **Table 9.3.2.2-6** as well as the additional calculations provided by the zRMS in the relevant grey commenting box (relevant for “mouse”, based recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in chard at 3×2.4 L product/ha (6-day interval) can be concluded.

Chard, 3×2.4 L product/ha, 9-day interval

Table 9.3.2.1-34 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (3×2.4 L product/ha, 9-day interval) - Ethofumesate

Ethofumesate							
Intended use		Chard					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal		136.4	1.5	-	61.38	81.5
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage							
Leafy vegetables All season	Large herbivorous mammal, lagomorph		14.3	1.8	0.53	4.09	14.9
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew		4.2	1.8	0.53	1.20	50.7
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse		7.8	1.8	0.53	2.23	27.3
Leafy vegetables BBCH > 20	Small insectivorous mammal, shrew		1.9	1.8	0.53	0.54	112.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-35 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (3×2.4 L product/ha, 9-day interval) - Phenmedipham

Intended use		Chard					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		3 × 0.300					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Leafy vegetables	Small herbivorous mammal	136.4	1.5	-	61.38	130.3	
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}	
Leafy vegetables All season	Large herbivorous mammal, lagomorph	14.3	1.8	0.53	4.09	1.7	
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	1.8	0.53	1.20	5.7	
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse	7.8	1.8	0.53	2.23	3.0	
Leafy vegetables BBCH > 20	Small insectivorous mammal, shrew	1.9	1.8	0.53	0.54	12.5	

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-36 Screening assessment of the acute risk for mammals due to the use of HBZ10 in chard (3×2.4 L product/ha, 9-day interval) – surrogate mixture toxicity

Intended use	Chard					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$3 \times \sum 0.300 + 0.300$					
Acute toxicity [mg/kg bw]	6154					
LD _{50mix}						
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.5	-	122.76	50.1

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in chard at 3×2.4 L product/ha (9-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in chard at 3×2.4 L product/ha (9-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal “lagomorph” during all season and small omnivorous mammal “mouse” at BBCH growth stage 10-49. As regards the large herbivorous mammal “lagomorph” and the small omnivorous mammal “mouse” the identified long-term risk can be considered as already addressed based on the refined risk assessments presented in **Table 9.3.2.2-7** as well as the additional calculations provided by the zRMS in the relevant grey commenting box (relevant for “mouse”, based recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in chard at 3×2.4 L product/ha (9-day interval) can be concluded.

Chard, 3×1.8 L product/ha, 6-day interval

Table 9.3.2.1-37 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (3×1.8 L product/ha, 6-day interval) - Ethofumesate

Intended use	Chard					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	3×0.225					
Acute toxicity [mg/kg bw]	> 5000					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.7	-	52.17	95.8
Reprod. toxicity [mg/kg bw/d]	60.9					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables All season	Large herbivorous mammal, lagomorph	14.3	2.1	0.53	3.58	17.0
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.1	0.53	1.05	57.9
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse	7.8	2.1	0.53	1.95	31.2
Leafy vegetables BBCH ≥ 20	Small insectivorous mammal, shrew	1.9	2.1	0.53	0.48	128.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-38 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (3×1.8 L product/ha, 6-day interval) - Phenmedipham

Intended use	Chard					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	3×0.225					
Acute toxicity [mg/kg bw]	> 8000					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.7	-	52.17	153.3
Reprod. toxicity [mg/kg bw/d]	6.8					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables All season	Large herbivorous mammal, lagomorph	14.3	2.1	0.53	3.58	1.9
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.1	0.53	1.05	6.5
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse	7.8	2.1	0.53	1.95	3.5
Leafy vegetables BBCH ≥ 20	Small insectivorous mammal, shrew	1.9	2.1	0.53	0.48	14.3

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-39 Screening assessment of the acute risk for mammals due to the use of HBZ10 in chard (3×1.8 L product/ha, 6-day interval) – surrogate mixture toxicity

Intended use	Chard					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	$3 \times \sum 0.225 + 0.225$					
Acute toxicity [mg/kg bw]	6154					
LD _{50mix}						
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.7	-	104.35	59.0

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in chard at 3×1.8 L product/ha (6-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in chard at 3×1.8 L product/ha (6-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal “lagomorph” during all season and small omnivorous mammal “mouse” at BBCH growth stage 10-49. As regards the large herbivorous mammal “lagomorph” and the small omnivorous mammal “mouse” the identified long-term risk can be considered as already addressed based on the refined risk assessments presented in **Table 9.3.2.2-8** as well as the additional calculations provided by the zRMS in the relevant grey commenting box (relevant for “mouse”, based recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in chard at 3×1.8 L product/ha (6-day interval) can be concluded.

Chard 6×1.2 L product/ha, 5-day interval

Table 9.3.2.1-40 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (6×1.2 L product/ha, 5-day interval) - Ethofumesate

Intended use		Chard					
Active substance/product		Ethofumesate / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		> 5000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal		136.4	2.2	-	45.01	111.1
Reprod. toxicity [mg/kg bw/d]		60.9					
TER criterion		5					
Crop scenario	Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage							
Leafy vegetables All season	Large herbivorous mammal, lagomorph		14.3	3.0	0.53	3.41	17.9
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew		4.2	3.0	0.53	1.00	60.8
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse		7.8	3.0	0.53	1.86	32.7
Leafy vegetables BBCH > 20	Small insectivorous mammal, shrew		1.9	3.0	0.53	0.45	134.4

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-41 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (6 × 1.2 L product/ha, 5-day interval) - Phenmedipham

Intended use		Chard					
Active substance/product		Phenmedipham / HBZ10					
Application rate [kg/ha]		6 × 0.150					
Acute toxicity [mg/kg bw]		> 8000					
TER criterion		10					
Crop scenario	Indicator species		SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal		136.4	2.2	-	45.01	177.7
Reprod. toxicity [mg/kg bw/d]		6.8					
TER criterion		5					
Crop scenario	Generic focal species		SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Leafy vegetables All season	Large herbivorous mammal, lagomorph		14.3	3.0	0.53	3.41	2.0
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew		4.2	3.0	0.53	1.00	6.8
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse		7.8	3.0	0.53	1.86	3.7
Leafy vegetables BBCH ≥ 20	Small insectivorous mammal, shrew		1.9	3.0	0.53	0.45	15.0

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-42 Screening assessment of the acute risk for mammals due to the use of HBZ10 in chard (6 × 1.2 L product/ha, 5-day interval) – surrogate mixture toxicity

Intended use		Chard					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]		6 × Σ 0.150 + 0.150					
Acute toxicity [mg/kg bw] LD _{50mix}		6154					
TER criterion		10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A	
Leafy vegetables	Small herbivorous mammal	136.4	2.2	-	90.02	68.4	

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in chard at 6×1.2 L product/ha (5-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in chard at 6×1.2 L product/ha (5-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal “lagomorph” during all season and small omnivorous mammal “mouse” at BBCH growth stage 10-49. As regards the large herbivorous mammal “lagomorph” and the small omnivorous mammal “mouse” the identified long-term risk can be considered as already addressed based on the refined risk assessments presented in **Table 9.3.2.2-9** as well as the additional calculations provided by the zRMS in the relevant grey commenting box (relevant for “mouse”, based recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in chard at 6×1.2 L product/ha (5-day interval) can be concluded.

Chard, 5×1.2 L product/ha, 7-day interval

Table 9.3.2.1-43 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (5×1.2 L product/ha, 7-day interval) - Ethofumesate

Intended use	Chard					
Active substance/product	Ethofumesate / HBZ10					
Application rate [kg/ha]	5×0.150					
Acute toxicity [mg/kg bw]	> 5000					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.9	-	38.87	128.6
Reprod. toxicity [mg/kg bw/d]	60.9					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage						
Leafy vegetables	Large herbivorous mammal, lagomorph	14.3	2.4	0.53	2.73	22.3
All season						
Leafy vegetables	Small insectivorous mammal, shrew	4.2	2.4	0.53	0.80	76.0
BBCH 10-19						
Leafy vegetables	Small omnivorous mammal, mouse	7.8	2.4	0.53	1.49	40.9
BBCH 10-49						
Leafy vegetables	Small insectivorous mammal, shrew	1.9	2.4	0.53	0.36	168.0
BBCH ≥ 20						

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-44 Screening / First-tier assessment of the acute and long-term/reproductive risk for mammals due to the use of HBZ10 in chard (5×1.2 L product/ha, 7-day interval) - Phenmedipham

Intended use	Chard					
Active substance/product	Phenmedipham / HBZ10					
Application rate [kg/ha]	5×0.150					
Acute toxicity [mg/kg bw]	> 8000					
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.9	-	38.87	205.8
Reprod. toxicity [mg/kg bw/d]	6.8					
TER criterion	5					
Crop scenario	Generic focal species	SV _m	MAF _m	TWA	DDD _m [mg/kg bw/d]	TER _{LT}
Growth stage						

Leafy vegetables All season	Large herbivorous mammal, lagomorph	14.3	2.4	0.53	2.73	2.5
Leafy vegetables BBCH 10-19	Small insectivorous mammal, shrew	4.2	2.4	0.53	0.80	8.5
Leafy vegetables BBCH 10-49	Small omnivorous mammal, mouse	7.8	2.4	0.53	1.49	4.6
Leafy vegetables BBCH ≥ 20	Small insectivorous mammal, shrew	1.9	2.4	0.53	0.36	18.8

SV: shortcut value; MAF: multiple application factor; TWA: time-weighted average factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.3.2.1-45 Screening assessment of the acute risk for mammals due to the use of HBZ10 in chard (5 × 1.2 L product/ha, 7-day interval) – surrogate mixture toxicity

Intended use	Chard					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
Application rate [kg/ha]	5 × ∑ 0.150 + 0.150					
Acute toxicity [mg/kg bw]	6154					
LD _{50mix}						
TER criterion	10					
Crop scenario	Indicator species	SV ₉₀	MAF ₉₀	TWA	DDD ₉₀ [mg/kg bw/d]	TER _A
Leafy vegetables	Small herbivorous mammal	136.4	1.9	-	77.75	79.2

SV: shortcut value; MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

The screening TER_A values for the active substances Ethofumesate, Phenmedipham and for the surrogate mixture toxicity for the formulation are above the trigger value of 10, indicating an acceptable acute risk for mammals following application of HBZ10 in chard at 5 × 1.2 L product/ha (7-day interval).

The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable long-term risk for mammals following application of HBZ10 in chard at 5 × 1.2 L product/ha (7-day interval), except for the active substance Phenmedipham for the generic focal species large herbivorous mammal “lagomorph” during all season and small omnivorous mammal “mouse” at BBCH growth stage 10-49. As regards the large herbivorous mammal “lagomorph” and the small omnivorous mammal “mouse” the identified long-term risk can be considered as already addressed based on the refined risk assessments presented in **Table 9.3.2.2-10** as well as the additional calculations provided by the zRMS in the relevant grey commenting box (relevant for “mouse”, based recalculation of PD and FIR/bw based on diet for wood mouse for each month separately in April, May, June, and July, as well as Toxic Units approach). Therefore, no additional higher-tier risk assessments are therefore required and an acceptable long-term risk for mammals following application of HBZ10 in chard at 5 x 1.2 L product/ha (7-day interval) can be concluded.

9.3.2.2 Higher-tier risk assessment

A higher tier assessment is conducted for the following scenarios and generic focal species: for the generic focal species small insectivorous mammal “shrew” (representative species: *Sorex araneus*) at BBCH 10-19, large herbivorous mammal “lagomorph” (representative species: *Oryctolagus cuniculus*) at BBCH 10-139 (relevant for sugar beet) or all season (relevant for chard), and small omnivorous mammal “mouse” (representative species: *Apodemus sylvaticus*) at growth stage BBCH 10-39 (relevant for sugar beet and red beet/yellow beet/fodder beet) or BBCH 10-49 (relevant for chard).

In the Tier 1 risk assessment following EFSA/2009/1438, the diet for the generic focal species small insectivorous mammals consists of 100% ground arthropods, the diet for large herbivorous mammals consists of 100% crop leaves and the diet for small omnivorous mammals consists of 25% weeds, 50% weed seeds and 25% ground arthropods. In the refined risk assessment, it is still assumed that the generic focal species small insectivorous mammal and large herbivorous mammal consume only the above-mentioned diet composition. To address the long-term/reproductive risk to mammals, four refinement options are available.

1. Refinement of MAF_m and f_{TWA} based on DT₅₀ data from residue trials in sugar beets

2. Refinement of crop interception based on BBCH application stage ~~on sugar beets~~ **of treated crops** (DF)
3. Refinement of wood mouse daily diet proportion obtained in habitat treated with pesticide (PT)
4. Refinement of proportion of different food types in the wood mouse diet (PD)
5. Refinement of the endpoint to be used for the long-term/reproductive risk assessment

1. Refinement of MAF_m and f_{TWA} based on DT_{50} data from residue trials in sugar beets

In the refined risk assessment, the diet of the generic focal species small insectivorous mammal “shrew”, large herbivorous mammal “lagomorph” and small omnivorous mammal “mouse” is still assumed as given in the Tier 1 risk assessment, as this is the worst-case diet composition. The amount of residue and the residue decline of Phenmedipham will be refined, using Phenmedipham-specific residue decline data.

In the dRAR (2017) for Phenmedipham, DT_{50} values from residue decline studies in sugar beets are available. The different trials were performed in Northern European zones, however, the experts agreed that the trials are acceptable also for Central European zones.

An overview of the available field trials and the retrieved DT_{50} values, as well as the calculation of a geometric mean DT_{50} value is given in the table below.

Table 9.3.2.2-1 Overview of available field residue trials and DT_{50} values for Phenmedipham

Crop / portion	Region	Country / trial no.	Application pattern	DT ₅₀ [d]	Reference
Sugar beet Leaf with root collar, body	NEU	GE R 2007 0292/2	2 applications at 0.24 kg PMP/ha (BBCH 10-12 / BBCH 18)	0.2	Schmeer (2008) and Theurig (2009) as cited in dRAR (2017)
		N-FR R 2007 0376/7		N/A	
Sugar beet Leaf with root collar, whole plant with root, body	NEU	GE 14-2139-01	1 × 0.9 kg PMP/ha (BBCH 18)	11.7 ^{a)}	Braune (2015) and Ellerich, Hammel (2014a) as cited in dRAR (2017)
		UK 14-2139-02	1 × 0.9 kg PMP/ha (BBCH 19)	5.9 ^{a)}	
		BE 14-2156-03	1 × 0.6 kg PMP/ha (BBCH 18)	0.8 ^{a)}	
		NL 14-2156-04	1 × 0.6 kg PMP/ha (BBCH 18)	2.6 ^{a)}	
Sugar beet Leaf with root collar, whole plant with root, body	NEU	UK S12-00892-05	3 × 0.16 kg PMP/ha BBCH stage not stated	N/A	Tandy (2014) and Ellerich, Hammel (2014b) as cited in dRAR (2017)
		UK S12-00892-06		N/A	
		GE S12-00892-07		N/A	
		FR S12-00892-08		N/A	
Geometric mean DT ₅₀ [d]				1.96	

a) DT_{50} values were re-calculated based on GLP certified data as requested by RMS

N/A DT_{50} values considered as not reliable following RMS recalculation and expert's consultation during Phenmedipham renewal process

A geometric mean DT_{50} over all reliable trials ($n = 5$) in sugar beet of 1.96 days was calculated. This value is used to refine the risk assessment for large herbivorous mammal “lagomorph” and small omnivorous mammal “mouse”.

Following Appendix H of EFSA/2009/1438, the TWA value were recalculated based on the Phenmedipham-specific DT₅₀ of 1.96 days derived from supervised field trials (see above) and using the default value of 21 days using the following equation:

$$TWA = \frac{1 - e^{-ki}}{ki}$$

With:

$k = \ln(2)/DT_{50}$ (rate constant)

i = averaging interval (21 days as default)

Following Appendix H of EFSA/2009/1438, the build-up of residues on food items is expressed by the number of applications (n) and interval between applications (i). The MAF_m was recalculated for the number of applications and the interval between applications based on the Phenmedipham-specific DT₅₀ of 1.96 days using the following equation:

$$MAF_m = \frac{1 - e^{-nki}}{1 - e^{-ki}}$$

With:

$k = \ln(2)/DT_{50}$ (rate constant)

n = number of applications

i = averaging interval

Table 9.3.2.2-2 Overview of recalculated MAF_m values based on residue data for Phenmedipham

Use group No.	Application rate [kg a.s./ha]	Number of applications	Interval between applications [d]	MAF _m *
2, 7, 12, 17, 22	0.300	3	6	1.13
5, 10, 15, 20, 25	0.300	3	9	1.04
4, 9, 14, 19, 24	0.225	3	6	1.13
1, 6, 11, 16, 21	0.150	6	5	1.21
3, 8, 13, 18, 23	0.150	5	7	1.09

* MAF_m: refined multiple application factor based on Phenmedipham-specific DT₅₀ of 1.96 days

The recalculated TER values according to refinement options as detailed above are presented in the following table, showing that the risk to small insectivorous mammal “shrew”, large herbivorous mammal “lagomorph” and small omnivorous mammal “mouse” is acceptable for all intended uses in **beet crops** **sugar beet, red beet/yellow beet/fodder beet and chard.**

As the available residue data used for MAF refinement are only relevant for plant material, they have been only considered to refine MAF and f_{TWA} for the crop itself, non-grass herbs and dicot weeds. Refinement of these two parameters in other food items, such as arthropods and weed seeds was not considered in calculation of the daily dietary doses for the small insectivorous and small omnivorous mammals and thus default values were used.

2. Refinement of crop interception based on BBCH application stage **on sugar beets of treated crops** (DF)

The EFSA Guidance Document proposes a deposition factor of 1 for BBCH growth stages 10 to 39. It has to be considered that the use of a deposition factor of 1 for the BBCH stages 10 to 39 is an unrealistic worst-case.

The growth stages for sugar beet between BBCH 10 to 39 consist of the principal growth stage 1 and 3. The principal growth stage 1 describes the leaf development from unfolding of the cotyledon leaves (BBCH 10) up to unfolding of leaves when 9 and more leaves are visible (BBCH 19). As can be seen

from Figure 9.3.2.2-1 the beet plant has already well developed leaves (seven leaves according to Meier (2001)⁴) which can indeed intercept the spray application.

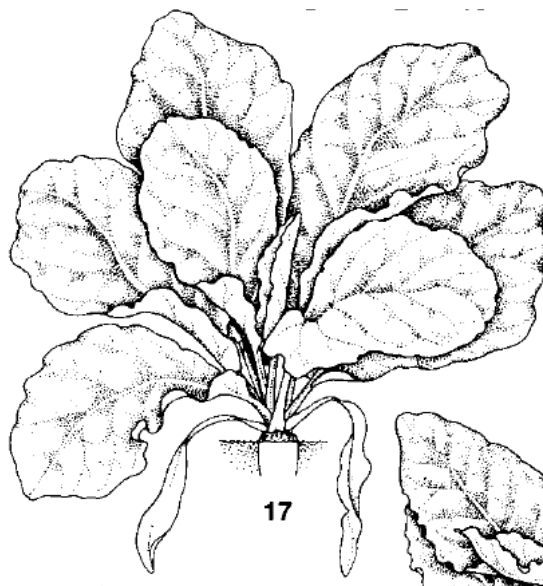


Figure 9.3.2.2-1 Development of beet plants at BBCH 17 following Meier (2001)

As agreed during the Southern Zone Steering Committee dated February 2020, the new interception value used for risk assessment is based on Appendix C of EFSA guidance to obtain DegT₅₀ values (EFSA Journal 2014;12(5):3662), where sugar beet interception from BBCH 10-19 to BBCH 20-39 is set from 20% to 70%, respectively. In the context of a higher-tier assessment, the more detailed values of the FOCUS groundwater report (FOCUS, 2000) may also be used.

Since the intended stage of application is from BBCH 10 to 39, a conservative interception value of 20% is considered for the higher-tier risk assessment, meaning a DF value of 0.80.

Consideration of refined deposition factors in line with EFSA Journal 2014;12(5):3662 could be also relevant for the other two crop groups included in the GAP table, i.e., red beet/yellow beet/fodder beet and chard. However, following zRMS evaluation (please refer to the relevant grey commenting box), crop interception refinement for sugar beet at BBCH growth stages < 40 is not applicable in line with EFSA GD (2009; Appendix E, Table 1). As regards root and stem vegetables (representing red beet/yellow beet/fodder beet) and leafy vegetables (representing chard), according to EFSA GD (2009), refinement of crop interception should not be applicable for BBCH growth stages < 41 and < 51, respectively. Therefore, refinement of crop interception is not considered in the higher tier risk assessments for red beet/yellow beet/fodder beet and chard presented in the following tables.

3. Refinement of wood mouse daily diet proportion obtained in habitat treated with pesticide (PT)

Consistently it is shown by radio-tracking studies, as guidance requested method for PT estimates, that wood mice do not spend their entire time in agricultural habitats. In a study conducted by Todd et al. (2000), 23 wood mice were radio-tracked in winter and spring (November – March) and 56 in summer (June – August) in arable habitat. The preferred “habitats” of wood mice in arable land were hedgerows. In another study conducted by Tew et al. (2000), 48 wood mice were radio-tracked and habitats were recorded. In this study, it was found that wood mice avoided foraging in areas with a high abundance of bare soil areas.

A third field study was conducted to track wood mice on winter cereals and potatoes by Crocker and Irving (2003). Within this CRD sponsored FERA study, animals were trapped using trap grids set in the field as well as in field margins and hedges. Most animals were caught in the hedgerow, but a special effort was made to track animals caught within the crop because they might be expected to spend more time there. Animals were fitted with radio-collars and were released close to their capture locations. Trapping and tracking were not carried out on the same night so that trapping would not

⁴ Meier, U. E. 2001. Growth stages of mono- and dicotyledonous plants. Federal Biological Research Centre for Agriculture and Forestry.

affect tagged animals" behaviour and the bait traps contained. A total of 94 wood mice were caught and radio-tagged in cereal fields in autumn and winter and in potato fields in summer. For 58 mice, median contact time was more than 6 hours. According to the study, wood mice spend on average 26% of their active time in all cropped habitats. Crocker (2005) presented similar data from 22 radio-tracked wood mice (presented in another paper) during the reproductive season in arable habitats which indicate a mean portion of time spent in all cropped habitats of 38%.

Prosser (2010) used all PT data from FERA's previous projects for a variety of bird and mammal species and estimated PT distributions for specific crops which have been fitted to these data, to give more accurately calculated 90th, 95th or other percentiles from the different data sets. The data have been filtered to include only animals (or animal-days) for which a quantity of data is likely to give robust estimates of PT. The paper presents worst-case 90th PT data for wood mice feeding in potatoes (n=7). The 90th percentile PT value for the wood mouse in potato fields is 0.82 (Prosser, 2010) for the summer. Although, the data are derived from potato fields, growth habit of the plants and the structure of potato fields resemble beet (i.e., sugar beet, red beet, yellow beet, fodder beet) fields and chard fields and PT data derived from potato fields can give a good estimate for beet and chard fields.

As a conservative approach of the long-term exposure assessment for the wood mouse in sugar beet, red beet, yellow beet, fodder beet and chard, it is proposed to use a PT value of 0.9 in the higher-tier risk assessment.

4. Refinement of proportion of different food types in the wood mouse diet (PD)

The wood mouse is considered as an opportunist concerning its diet, taking generally green plant matter, seeds as well as invertebrates. The detailed composition of diet of wood mice was investigated in a comprehensive multi-annual study conducted on farmland in Germany (Pelz, 1989; cited in Gurney et al., 1998) where data were collected from 346 individuals trapped over a 7-year period. In the study area a three-year crop rotation system with sugar beet, winter wheat and winter barley was employed, i.e. every year cultivation in each of the studied fields changed from sugar beet to winter wheat, from winter wheat to winter barley and from winter barley to sugar beet. According to the results of this study, the diet of wood mice (based on % volume of stomach contents) in spring consists of three basic food types: animals (insects and earthworms), seeds/cereal grains, and vegetative plant tissue. However, it is well noted that the composition of the diet strongly depends on the food items available in the in-field area and on the timing of the year.

HBZ10 is intended to be applied to sugar and fodder beet, red beet, yellow beet, fodder beet and chard. Although the study by Pelz (1989) was conducted in a typical sugar beet growing area, study findings could be extrapolated to other beet crops (i.e., red beet, yellow beet, fodder beet) and chard as the growth habit of the plants, the crop structure and the maintenance is very similar.

According to the results of the Tier-1 risk assessment presented above an unacceptable long-term risk cannot be excluded for small omnivorous mammals exposed in post emergence BBCH 10-49. Thus, an application timeframe from March to July in accordance with the application scheme detailed in the e-fate modelling is considered as most representative. Based on the data from mouse established from March to July which is relevant for a post-emergence use in sugar and fodder beet, red beet, yellow beet, fodder beet and chard (BBCH 10-49), the diet of the wood mice consists of average of 10.4 % dicot seeds (as surrogate for sugar beet seeds), 26.6 % insects, 19.6 % earthworms, 27.6 % cereal grains and 15.8 % vegetative plant tissue (especially weeds).

Such proportion of different food types in the wood mouse diet will be considered in the higher-tier risk assessment.

FIR/bw calculation for the wood mouse:

According to the EFSA guidance (2009), the FIR has to be adjusted to reflect the actual contribution of each food item to the daily energy expenditure of the species of concern.

Relationship between body weight (b.w. in g) and daily energy expenditure (DEE in kJ) can be described by the equation $\log DEE = \log a + b \times \log b.w.$, using the relevant constants for the species group (mammals) from Appendix G of the EFSA guidance (2009). The energy expenditure of a wood

mouse with a body weight of 21.7 g according to the EFSA guidance (2009) results in a DEE of 58.8 kJ/day.

Considering the fractions (PDi) of individual food items in a mixed diet together with data on their respective moisture and energy content the specific energy content of the mixed diet was calculated (Table 9.3.2.2-3).

The food energy of total mixed diet is used to estimate the required amount of the mixed diet to satisfy the energy expenditure of the wood mouse. The calculation of food intake rate (FIR) per body weight regarding the DEE of the wood mouse is given in Table 9.3.2.2-4.

Table 9.3.2.2-3 Calculation of food energy of total mixed diet for the wood mouse

Parameter	Unit	Weeds	Weed seeds	Cereal grain	Earthworms	Ground arthropods
Fraction of food item in mixed diet	PDi fresh (%)	15.80	10.40	27.60	19.60	26.60
Food energy of food item [i] in mixed diet	FE (kJ/dry g)	17.60	21.70	18.40	19.40	22.70
Moisture content of food item [i] in mixed diet	MC (%)	76.40	9.90	14.70	84.30	68.80
Assimilation efficiency of food item [i] in mixed diet	AE (%)	0.47	0.84	0.84	0.87	0.87
Food energy of food item in diet	FEitem,fresh (kJ/g fresh weight)	0.31	1.71	3.64	0.52	1.64
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	7.81				

Table 9.3.2.2-4 Calculation of food intake rate per body weight for wood mice in beet-crops all intended uses

Parameter	Unit	March to July
Daily energy expenditure	DEE (kJ/day)	58.8
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	7.81
Food intake rate of total mixed diet	FIRtotal, fresh (g fresh weight/d)	7.53
	FIR/bw	0.35

Considering the calculation above, the FIR/b.w. of 0.35 for applications in beet-crops all intended uses at BBCH 10-39 will be used in the refined TER calculations below.

Calculation of residue value for the food item “earthworms”

According to the EFSA guidance (2009), the estimated residues in earthworms are calculated as

$$PEC_{\text{earthworm}} = PEC_{\text{soil}} * BCF_{\text{earthworm}}$$

where the BCF is calculated as $(0.84 + 0.012 * Kow) / (foc * Koc)$

This formula is derived from chapter 5.6 of the current EFSA guidance document (2009) and calculation is provided in table 9.3.2.2-5 below. In order to assume worst-case assessment, overall maximal PEC_{soil} value (from use 1 as a worst-case) is considered in the calculation below and will be applied to the relevant refined TER calculations.

Table 9.3.2.2-5 PEC_{earthworm} calculation – dry soil approach according to GD (EFSA 2009)

Parameter	Phenmedipham	Reference / comments
PEC _{soil, initial}	0.874	Maximal initial PEC _{soil} value for the worst-case use group 1 (covering use groups 2, 3, 4 and 5)
K _{ow}	3890.5	Review Report (2004)
K _{oc}	657	Mean (n = 3), Review Report (2004)
F _{oc}	0.02	Default (EFSA, 2009)
BCF	3.62	BCF = (0.84 + 0.012 * K _{ow}) / f _{oc} * K _{oc}
PEC _{earthworm}	3.16	

The PEC_{earthworm} of 3.16 will be used in the refined TER calculations for the food item “earthworms”.

Use-group 2: Use No 2, 7, 12, 17, 22: 3 × 2.4 L product/ha (6-day interval)

Table 9.3.2.2-6 Higher-tier assessment of the long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ **sugar beet, red beet/yellow beet/fodder beet and chard – refined parameters (*) are further described and justified in the text**

Intended use		Beet-crops Sugar beet, red beet/yellow beet/fodder beet, chard						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Common shrew (<i>Sorex araneus</i>)	Arthropods, 100%	0.55	7.5 × 0.8	2.1	0.53	1	1.37 1.10	4.96* 6.2
Rabbit (<i>Oryctolagus cuniculus</i>)	Non-grass herbs, 100%	0.50	28.7 × 0.8	1.13	0.134	1	0.65 0.52	10.5 13.0
Wood mouse (<i>Apodemus sylvaticus</i>)	Weeds, 15.8%	0.35	28.7 × 0.8	1.13	0.134	1 0.9	0.057 0.052	-
	Earthworms, 19.6%	0.35	3.16*	1**	1**	1 0.9	0.071 0.059	-
	Cereal grain, 27.6%	0.35	15 × 0.8	2.1	0.53	1 0.9	0.60 0.348	-
	Weed seeds, 10.4%	0.35	40.2 × 0.8	2.1	0.53	1 0.9	0.39 0.352	-
	Ground arthropods, 26.6%	0.35	7.5 × 0.8	2.1	0.53	1 0.9	0.18 0.168	-
	Whole diet						1.3 0.98	5.23 7.0

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; DF: deposition factor (considering possible interception of 20% by the crop as a conservative approach); MAF_m: refined multiple application factor based on Phenmedipham-specific DT₅₀ of 1.96 days and an interval between applications of 6 days (only applies to plant material food category); f_{twa}: refined time weighted average factor based on Phenmedipham-specific DT₅₀ of 1.96 days and a default value of 21 days (only applies to plant material food category); DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

* PEC_{earthworm} value as calculated above

** MAF_m and f_{twa} not considered as already included in the PEC_{soil} calculation

*TER_{LT} closed to trigger of 5 and considered as acceptable risk by zRMS.

The refined TER_{LT} values for the active substance Phenmedipham are closed to trigger of 5 in case of shrew and above the trigger values for the focal species small insectivorous mammal “shrew”, large herbivorous mammal “lagomorph” and small omnivorous mammal “mouse”, indicating an acceptable risk for mammals following the application of HBZ10 in beet crops all intended crops at 3 × 2.4 L product/ha (6-day interval).

~~Use group 5:~~ Use No 5, 10, 15, 20, 25: 3 × 2.4 L product/ha (9-day interval)

Table 9.3.2.2-7 Higher-tier assessment of the long-term/reproductive risk for mammals due to the use of HBZ10 in beet crops sugar beet, red beet/yellow beet/fodder beet and chard – refined parameters (*) are further described and justified in the text

Intended use		Beet crops: Sugar beet, red beet/yellow beet/fodder beet, chard						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Rabbit (<i>Oryctolagus cuniculus</i>)	Non-grass herbs, 100%	0.50	28.7 × 0.8	1.04	0.134	1	0.6 0.48	11.33 14.2
Wood mouse (<i>Apodemus sylvaticus</i>)	Weeds, 15.8%	0.35	28.7 × 0.8	1.04	0.134	0.9	0.053 0.048	-
	Earthworms, 19.6%	0.35	3.16*	1**	1**	0.9	0.06 0.059	-
	Cereal grain, 27.6%	0.35	15 × 0.8	1.8	0.53	0.9	0.33 0.299	-
	Weed seeds, 10.4%	0.35	40.2 × 0.8	1.8	0.53	0.9	0.335 0.302	-
	Ground arthropods, 26.6%	0.35	7.5 × 0.8	1.8	0.53	0.9	0.16 0.144	-
	Whole diet						0.93 0.85	7.31 8.0

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; DF: deposition factor (considering possible interception of 20% by the crop); MAF_m: refined multiple application factor based on Phenmedipham-specific DT₅₀ of 1.96 days and an interval between applications of 9 days (only applies to plant material food category); f_{twa}: refined time-weighted average factor based on Phenmedipham-specific DT₅₀ of 1.96 days and a default value of 21 days (only applies to plant material food category); DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

* PECearthworm value as calculated above

** MAF_m and f_{twa} not considered as already included in the PECsoil calculation

The refined TER_{LT} values for the active substance Phenmedipham are above the trigger values for the focal species large herbivorous mammal “lagomorph” and small omnivorous mammal “mouse”, indicating an acceptable risk for mammals following the application of HBZ10 in beet crops all intended crops at 3 × 2.4 L product/ha (9-day interval).

Use-group 4 Use No 4, 9, 14, 19, 24: 3 × 1.8 L product/ha (6-day interval)

Table 9.3.2.2-8 Higher-tier assessment of the long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet crops~~ **sugar beet, red beet/yellow beet/fodder beet and chard** – refined parameters (*) are further described and justified in the text

Intended use		Beet crops Sugar beet, red beet/yellow beet/fodder beet, chard						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.225						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Rabbit (<i>Oryctolagus cuniculus</i>)	Non-grass herbs, 100%	0.50	28.7 × 0.8	1.13	0.134	1	0.5 0.391	13.6 17.4
Wood mouse (Apodemus sylvaticus)	Weeds, 15.8%	0.35	28.7 × 0.8	1.13	0.134	1 0.9	0.043 0.039	-
	Earthworms, 19.6%	0.35	3.16*	1**	1**	1 0.9	0.048 0.044	-
	Cereal grain, 27.6%	0.35	15 × 0.8	2.1	0.53	1 0.9	0.290 0.261	-
	Weed seeds, 10.4%	0.35	40.2 × 0.8	2.1	0.53	1 0.9	0.29 0.264	-
	Ground arthropods, 26.6%	0.35	7.5 × 0.8	2.1	0.53	1 0.9	0.139 0.126	-
	Whole diet						0.81 0.73	8.39 9.3

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; DF: deposition factor (considering possible interception of 20% by the crop); MAF_m: refined multiple application factor based on Phenmedipham specific DT₅₀ of 1.96 days and an interval between applications of 6 days (only applies to plant material food category); f_{twa}: refined time weighted average factor based on Phenmedipham specific DT₅₀ of 1.96 days and a default value of 21 days (only applies to plant material food category); DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

* PEC_{earthworm} value as calculated above

** MAF_m and f_{twa} not considered as already included in the PEC_{soil} calculation

The refined TER_{LT} values for the active substance Phenmedipham are above the trigger values for the focal species large herbivorous mammal “lagomorph” and ~~small omnivorous mammal “mouse”~~, indicating an acceptable risk ~~for mammals~~ following the application of HBZ10 in ~~beet crops~~ **all intended crops** at 3 × 1.8 L product/ha (6-day interval).

Use-group 1: Use No 1, 6, 11, 16, 21: 6 × 1.2 L product/ha (5-day interval)

Table 9.3.2.2-9 Higher-tier assessment of the long-term/reproductive risk for mammals due to the use of HBZ10 in ~~beet-crops~~ sugar beet, red beet/yellow beet/fodder beet and chard – refined parameters (*) are further described and justified in the text

Intended use		Beet-crops Sugar beet, red beet/yellow beet/fodder beet, chard						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		6 × 0.150						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Rabbit (<i>Oryctolagus cuniculus</i>)	Non-grass herbs, 100%	0.50	28.7 × 0.8	1.21	0.134	1	0.35 0.279	19.42 24.4
Wood mouse (Apodemus sylvaticus)	Weeds, 15.8%	0.35	28.7 × 0.8	1.21	0.134	1	0.03 0.028	-
	Earthworms, 19.6%	0.35	3.16*	1**	1**	1	0.032 0.029	-
	Cereal grain, 27.6%	0.35	15 × 0.8	3.0	0.53	1	0.276 0.249	-
	Weed seeds, 10.4%	0.35	40.2 × 0.8	3.0	0.53	1	0.28 0.251	-
	Ground arthropods, 26.6%	0.35	7.5 × 0.8	3.0	0.53	1	0.13 0.120	-
	Whole diet						0.75 0.68	9.06 10.0

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; DF: deposition factor (considering possible interception of 20% by the crop); MAF_m: refined multiple application factor based on Phenmedipham-specific DT₅₀ of 1.96 days and an interval between applications of 5 days (only applies to plant material food category); f_{twa}: refined time-weighted average factor based on Phenmedipham-specific DT₅₀ of 1.96 days and a default value of 21 days (only applies to plant material food category); DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

* PECearthworm value as calculated above

** MAF_m and f_{TWA} not considered as already included in the PECsoil calculation

The refined TER_{LT} values for the active substance Phenmedipham are above the trigger values for the focal species large herbivorous mammal “lagomorph” and small omnivorous mammal “mouse”, indicating an acceptable risk for mammals following the application of HBZ10 in ~~beet-crops~~ all intended crops at 6 × 1.2 L product/ha (5-day interval).

Use-group 3: Use No 3, 8, 13, 18, 23: 5 × 1.2 L product/ha (7-day interval)

Table 9.3.2.2-10 Higher-tier assessment of the long-term/reproductive risk for mammals due to the use of HBZ10 in beet-crops sugar beet, red beet/yellow beet/fodder beet and chard – refined parameters (*) are further described and justified in the text

Intended use		Beet-crops Sugar beet, red beet/yellow beet/fodder beet, chard						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		6 × 0.150						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Rabbit (<i>Oryctolagus cuniculus</i>)	Non-grass herbs, 100%	0.50	28.7 × 0.8	1.09	0.134	1	0.31 0.252	21.93 27.0
Wood mouse (<i>Apodemus sylvaticus</i>)	Weeds, 15.8%	0.35	28.7 × 0.8	1.09	0.134	± 0.9	0.28 0.025	-
	Earthworms, 19.6%	0.35	3.16*	1**	1**	± 0.9	0.0325 0.029	-
	Cereal grain, 27.6%	0.35	15 × 0.8	2.4	0.53	± 0.9	0.22 0.199	-
	Weed seeds, 10.4%	0.35	40.2 × 0.8	2.4	0.53	± 0.9	0.022 0.201	-
	Ground arthropods, 26.6%	0.35	7.5 × 0.8	2.4	0.53	± 0.9	0.106 0.096	-
	Whole diet						0.66 0.55	10.3 12.4

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; DF: deposition factor (considering possible interception of 20% by the crop); MAF_m: refined multiple application factor based on Phenmedipham specific DT₅₀ of 1.96 days and an interval between applications of 7 days (only applies to plant material food category); f_{twa}: refined time weighted average factor based on Phenmedipham specific DT₅₀ of 1.96 days and a default value of 21 days (only applies to plant material food category); DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

* PEC_{earthworm} value as calculated above

** MAF_m and f_{twa} not considered as already included in the PEC_{soil} calculation

The refined TER_{LT} values for the active substance Phenmedipham are above the trigger values for the focal species large herbivorous mammal “lagomorph” and small omnivorous mammal “mouse”, indicating an acceptable risk for mammals following the application of HBZ10 in beet-crops all intended crops at 5 × 1.2 L product/ha (7-day interval).

2. Refined endpoint for the long-term/reproductive risk assessment

The endpoint for reproductive toxicity to mammals of 6.8 mg/kg bw/day (100 ppm) as stated in the Review Report (2004), is based on minor reductions in body weight at 500 ppm. However, these reductions were not sustained throughout the study period and were therefore transient effects of a non-adverse nature. A position paper is available on the relevant ecotoxicological NOEL that should be used for the long-term and reproductive risk assessment (Diesing, 2014, KCP 10.1.2.2/01).

During evaluation of the current application, zRMS legitimately raised that the refined NOEL of 25 mg/kg bw/d has not been agreed as a relevant endpoint for Phenmedipham evaluation following expert’s consultation at Pesticides Peer Review Meeting 169. Below risk assessments are therefore removed and considered not relevant anymore. However, applicant would like to highlight that a new extended one-

generation reproduction toxicity study on rats has been submitted and considered as acceptable by RMS Finland in the context of the Phenmedipham renewal to address this data gap. According to RMS calculations, the lowest NOAEL of the study is 60 mg/kg bw/d based on the decreased weights of male reproductive organs and related changes in histopathology including degenerated seminiferous tubules of testes and decreased sperm counts.

Waiting for final acceptance of this chronic endpoint, RMS already considers this endpoint as agreed, allowing for finalisation of the chronic risk assessment for mammals. As for the previous endpoint refinement from Diesing (2014), new generated data for deriving a chronic endpoint in the context of Phenmedipham renewal show significantly higher values compared to the current EU agreed endpoint of 6.8 mg/kg bw/d. Therefore, in light of the new data available for Phenmedipham chronic toxicity, the current endpoint of 6.8 mg/kg bw/d should be considered as highly overestimated and therefore, leading to a highly conservative risk assessment.

zRMS comments:

Based on calculations provided in the Tables above the risk assessment for shrew and rabbit is considered as acceptable. The ~~higher~~ higher risk assessment for wood mouse is not validated by zRMS. The Applicants' calculations were struck through as being based on not agreed assumptions.

Further refinement of the risk is still needed for small omnivorous mammal - wood mouse.

In order to refine the long-term risk assessment, the following refined parameters were validated by zRMS.

1. Refinement of MAF_m and f_{TWA} based on DT_{50} data from residue trials in sugar beets

The amount of residue and the residue decline of Phenmedipham was refined, using Phenmedipham-specific residue decline data obtained ~~from studies~~ from studies evaluated in the DRAR 2017 for sugar beet. The different trials were performed in Northern European zones (GE, NL, BE, UK) however, the experts agreed during PRAPER 169 that the trials are acceptable also for Central European zones. The application rates used in the valid studies were as follows: 2 x 0.24 kg a.s./ha, BBCH 10-12 /BBCH18 (DE), 1 x 0.6 g a.s./ha, BBCH 18 (UK), 1 x 0.9 kg a.s./ha, BBCH 19 (NL, BE). It was noted that the application rate was lower than the EU GAP in some trials in addition also one application was done (proposed no of applications in the GAP: 1-3).

However, this was considered by experts acceptable for the assessment of the decline rate. Finally, the experts agreed with the RMS's conclusion concerning the acceptability of the trials.

zRMS decided to use the new data of DT_{50} values in the current evaluation of HBZ10 to finalise the long-term risk assessment for mammals.

Overview of reliable field residue trials and DT_{50} values for Phenmedipham is the Table presented below:

Crop / portion	Region	Country / trial no.	Application pattern	DT ₅₀ [d]	Reference
Sugar beet Leaf with root collar, body	NEU	GE R 2007 0292/2	2 applications at 0.24 kg PMP/ha (BBCH 10-12 / BBCH 18)	0.2	Schmeer (2008) and Theurig (2009) as cited in dRAR (2017)
		N-FR R 2007 0376/7		N/A	
Sugar beet Leaf with root collar, whole plant with root, body	NEU	GE 14-2139-01	1 × 0.9 kg PMP/ha (BBCH 18)	11.7 ^{a)}	Braune (2015) and Ellerich, Hammel (2014a) as cited in dRAR (2017)
		UK 14-2139-02	1 × 0.9 kg PMP/ha (BBCH 19)	5.9 ^{a)}	
		BE 14-2156-03	1 × 0.6 kg PMP/ha (BBCH 18)	0.8 ^{a)}	
		NL 14-2156-04	1 × 0.6 kg PMP/ha (BBCH 18)	2.6 ^{a)}	
Geometric mean DT ₅₀ [d]				1.96	

The kinetic analysis of DT_{50} value in sugar beet based on the data from studies above were available in the DRAR, 2017. Based on the results of DT_{50} from residue decline studies, the geomean DT_{50} value of 1.96 d was calculated by the applicant, which is relevant to refine MAF and f_{TWA} for the crop itself, non-grass herbs and dicot weeds.

This value is validated by zRMS and as well as refined MAF_m values included in the Table below.

Use group No.	Application rate [kg a.s./ha]	Number of applications	Interval between applications [d]	MAF _m *
2	0.300	3	6	1.13
5	0.300	3	9	1.04
4	0.225	3	6	1.13
1	0.150	6	5	1.21
3	0.150	5	7	1.09

* MAF_m: refined multiple application factor based on Phenmedipham-specific DT₅₀ of 1.96 days

2. Refinement of crop interception based on BBCH application stage on sugar beets (DF).

We do not agree with the refinement of crop interception provided by the applicant for BBCH 10-39. According to EFSA GD the crop interception > BBCH 40 for sugar beet is only applicable. Therefore, the DF factor of 0.8 was crossed out from calculations presented by the Applicant and was not considered further.

3. Refinement of proportion of different food types (PD) and FIR/bw

Shrew and Rabbit

PD and FIR/bw values for rabbit and shrew were considered in the risk assessment according to the diet given in Appendix A of EFSA (2009) and then was validated by zRMS.

Wood mouse:

zRMS doesn't agree with applicant's PD parameter for wood mouse based on studies by Pelz, 1989; cited in Gurney et al., 1998 calculated as average amount of 10.4 % dicot seeds, 26.6 % insects, 19.6 % earthworms, 27.6 % cereal grains and 15.8 % vegetative plant tissue from March and July.

zRMS provided the own calculations of PD based on diet for wood mouse comes from Pelz 1995 but for each month separately in April, May, June, July, which are relevant for sugar beet at BBCH from 10-39.

The summary of the results is provided in the below:

Wood mice diet in intensive arable land dominated by winter cereals and sugar beet (Pelz 1989)³

Time of year	Food type	Vol.% of diet
March (n=56)	Insect larvae ¹	25
	Earthworms	23
	Vegetative plant tissue ²	22
	Cereal grain	23
	Sugar beet seeds	7
April (n=49)	Insect larvae ¹	45
	Earthworms	26
	Vegetative plant tissue ²	24
	Cereal grain	5
May (n=16)	Insect larvae ¹	10
	Earthworms	40
	Vegetative plant tissue ²	16
	Cereal grain	30
	Dicotyledon seeds (herb)	4
June (n=15)	Insect larvae ¹	25
	Earthworms	9
	Vegetative plant tissue ²	9
	Cereal grain	32
	Dicotyledon seeds (herb)	25
July (n=10)	Insect larvae ¹	28
	Vegetative plant tissue ²	8
	Cereal grain	48
	Dicotyledon seeds (herb)	16

¹ For risk assessment purposes, the insect larvae may be assumed to be picked from the ground.

² Mono- or dicotyledonous, depending on the crop.

³ The Table above comes from diet by Pelz 1985 from GD for North Zone, PESTICIDE RISK ASSESSMENT FOR BIRDS AND MAMMALS, Selection of relevant species and development of standard scenarios for higher tier risk assessment in the Northern Zone in accordance with Regulation EC 1107/2009, December 2020.

It should be indicated that in the first Step zRMS provided the diet according to EFSA GD B&M, 2009 with refinement parameters MAF and twa and then further refinement was presented based on Pelz study 1985 for each month separately.

We would like to stressed out that if the other MSs are different opinion referred to the PD value for wood mouse used in the the risk assessment and agreed by the zRMS they are considered it further at National level.

Calculations of FIR/bw

Various mixed diets were considered depending on the month and in Tables below additional calculations for diets are provided by the zRMS.

Calculation of food energy of total mixed diet for the wood mouse in April

Parameter	Unit	Non-grass herb, leafy crop	Earthworms	Cereal grain	Weed weeds	Ground arthropods
Fraction of food item in mixed diet	PDi fresh (%)	24	26	5	-	45
Food energy of food item [i] in mixed diet	FE (kJ/dry g)	17.8	19.4	18.40	-	22.70
Moisture content of food item [i] in mixed diet	MC (%)	88.1	84.3	14.70	-	68.80
Assimilation efficiency of food item [i] in mixed diet	AE (%)	0.76	0.87	0.84	-	0.87
Food energy of food item in diet	FEitem,fresh (kJ/g fresh weight)	0.38	0.68	0.66	-	2.78
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	4.5				
DEE	58.83					

Calculation of food intake rate per body weight for wood mice in beet crops in April

Parameter	Unit	April
Daily energy expenditure	DEE (kJ/day)	58.83
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	4.5
Food intake rate of total mixed diet	FIRtotal, fresh (g fresh weight/d)	13.07
	FIR/bw	0.6

Calculation of food energy of total mixed diet for the wood mouse in May

Parameter	Unit	Non-grass herb, leafy crop	Earthworms	Cereal grain	Weed weeds	Ground arthropods
Fraction of food item in mixed diet	PDi fresh (%)	16	40	30	4	10
Food energy of food item [i] in mixed diet	FE (kJ/dry g)	17.8	19.4	18.40	21.7	22.70
Moisture content of food item [i] in mixed diet	MC (%)	88.1	84.3	14.70	9.9	68.80
Assimilation efficiency of food item [i] in mixed diet	AE (%)	0.76	0.87	0.84	0.84	0.87
Food energy of food item in diet	FEitem,fresh (kJ/g fresh weight)	0.25	1.05	3.95	0.65	0.616
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	6.51				

Calculation of food intake rate per body weight for wood mice in beet crops in May

Parameter	Unit	May
Daily energy expenditure	DEE (kJ/day)	58.83

Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	6.51
Food intake rate of total mixed diet	FIRtotal, fresh (g fresh weight/d)	8.95
FIR/bw		0.41

Calculation of food energy of total mixed diet for the wood mouse in June

Parameter	Unit	Non-grass herb, leafy crop	Earthworms	Cereal grain	Weed weeds	Ground arthropods
Fraction of food item in mixed diet	PDi fresh (%)	9	9	32	25	25
Food energy of food item [i] in mixed diet	FE (kJ/dry g)	17.8	19.4	18.40	21.7	22.70
Moisture content of food item [i] in mixed diet	MC (%)	88.1	84.3	14.70	9.9	68.80
Assimilation efficiency of food item [i] in mixed diet	AE (%)	0.76	0.87	0.84	0.84	0.87
Food energy of food item in diet	FEitem,fresh (kJ/g fresh weight)	0.14	0.23	4.21	4.10	1.53
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	10.21				

Calculation of food intake rate per body weight for wood mice in beet crops in June

Parameter	Unit	June
Daily energy expenditure	DEE (kJ/day)	58.83
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	10.21
Food intake rate of total mixed diet	FIRtotal, fresh (g fresh weight/d)	5.76
FIR/bw		0.26

Calculation of food energy of total mixed diet for the wood mouse in July

Parameter	Unit	Non-grass herb, leafy crop	Earthworms	Cereal grain	Weed weeds	Ground arthropods
Fraction of food item in mixed diet	PDi fresh (%)	8	-	48	16	28
Food energy of food item [i] in mixed diet	FE (kJ/dry g)	17.8	-	18.40	21.7	22.70
Moisture content of food item [i] in mixed diet	MC (%)	88.1	-	14.70	9.9	68.80
Assimilation efficiency of food item [i] in mixed diet	AE (%)	0.76	-	0.84	0.84	0.87
Food energy of food item in diet	FEitem,fresh (kJ/g fresh weight)	0.13	-	6.32	2.62	1.72
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	10.79				

Calculation of food intake rate per body weight for wood mice in beet crops in July

Parameter	Unit	July
Daily energy expenditure	DEE (kJ/day)	58.83
Food energy of total mixed diet	FEtotal,fresh (kJ/g fresh weight)	10.79
Food intake rate of total mixed diet	FIRtotal, fresh (g fresh weight/d)	5.45
FIR/bw		0.25

4. PT value

The PT value of 0.9 proposed by the applicant was not validated by zRMS. The PT value should not be based on the extrapolation from the other crop such as potato. In addition, the applicant in the context of refinement of PT for wood mouse in sugar beet referred to study by Crooker (2005) which is not submitted to zRMS. Therefore, default value of 1 was considered by zRMS as the worst case.

5. Ecologically relevant endpoints for wild mammals:

For Tier 1 risk assessment the reproductive risk assessment for mammals was evaluated by taking into

In the Tables below the risk assessment based on the diet for wood mouse with PD according Appendix A EFSA GD and refined parameter of MAF and twa are presented by zRMS.

[illegible]

Use group 5 covering uses 10, 15, 20, 25: 3×2.4 L product/ha (9-day interval)

Intended use	Beet crops							
Active substance/product	Phenmedipham / HBZ10							
Application rate [kg/ha]	3×0.300							
Reproduction toxicity [mg/kg bw/d]	6.8							
TER criterion	5							
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Weeds, 25%	0.27	28.7	1.04	0.134	1	0.080	-
	Weed seeds, 50%	0.27	40.2	1.8	0.53	1	1.55	-
	Ground arthropods, 25%	0.27	7.5	1.8	0.53	1	0.273	-
	Whole diet						1.90	3.57

Use group 4 covering uses 9, 14, 19, 24 : 3×1.8 L product/ha (6-day interval)

Intended use	Beet crops
Active substance/product	Phenmedipham / HBZ10
Application rate [kg/ha]	3 × 0.225
Reproduction toxicity [mg/kg bw/d]	6.8

TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m	f _{twa}	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Weeds, 25%	0.27	28.7	1.13	0.134	1	0.066	-
	Weed seeds, 50%	0.27	40.2	2.1	0.53	1	1.35	-
	Ground arthropods, 25%	0.27	7.5	2.1	0.53	1	0.126	-
	Whole diet						1.54	4.41

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; MAF_m: refined multiple application factor based on Phenmedipham-specific DT₅₀ of 1.96 days and an interval between applications of 6 days (only applies to plant material food category); f_{twa}: refined time-weighted average factor based on Phenmedipham-specific DT₅₀ of 1.96 days and a default value of 21 days (only applies to plant material food category); DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Use group 1 covering uses 6, 11, 16, 21: 6 × 1.2 L product/ha (5-day interval)

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		6 × 0.150						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Weeds, 25%	0.27	28.7	1.21	0.134	1	0.047	-
	Weed seeds, 50%	0.27	40.2	3.0	0.53	1	1.29	-
	Ground arthropods, 25%	0.27	7.5	3.0	0.53	1	0.12	-
	Whole diet						1.45	4.68

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; MAF_m: refined multiple application factor based on Phenmedipham-specific DT₅₀ of 1.96 days and an interval between applications of 5 days (only applies to plant material food category); f_{twa}: refined time-weighted average factor based on Phenmedipham-specific DT₅₀ of 1.96 days and a default value of 21 days (only applies to plant material food category); DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Use group 3 covering uses 8, 13, 18, 23: 5 × 1.2 L product/ha (7-day interval)

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		6 × 0.150						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Weeds, 25%	0.27	28.7	1.09	0.134	1	0.042	-
	Weed seeds, 50%	0.27	40.2	2.4	0.53	1	1.03	-
	Ground arthropods, 25%	0.27	7.5	2.4	0.53	1	0.09	-
	Whole diet						1.17	5.81

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; MAF_m: refined multiple application factor based on Phenmedipham-specific DT₅₀ of 1.96 days and an interval between applications of 7 days (only applies to plant material food category); f_{twa}: refined time-weighted average factor based on Phenmedipham-specific DT₅₀ of 1.96

days and a default value of 21 days (only applies to plant material food category); DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Based on calculation of the risk assessment with consideration of PD value for wood mouse according Appendix A of GD B&M, 2009 an unacceptable risk is identified for wood mouse for following uses:

- Use group 2: 3 × 2.4 L product/ha (6-day interval) with TER_{LT} value 3.3
- Use group 5: 3 × 2.4 L product/ha (9-day interval) with TER_{LT} value 3.57
- Use group 4: 3 × 1.8 L product/ha (6-day interval) with TER_{LT} value 4.41
- Use group 1: 6 × 1.2 L product/ha (5-day interval) with TER_{LT} value 4.68

Further refinement of the risk assessment based on the diet for each month relevant for BBCH from 10-39 for sugar beet with consideration refined parameters MAF and ftwa are presented below:

Use group 2: 3 × 2.4 L product/ha (6-day interval)

April

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 24%	0.6	28.7	1.13	0.134	1	0.19	-
	Earthworms 26%	0.6	3.16	1	1	1	0.15	-
	Cereal grain 5 %	0.6	15	2.1	0.53	1	0.152	-
	Ground arthropods 45 %	0.6	7.5	2.1	0.53	1	0.68	-
	Whole diet						1.18	5.76

May

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 16%	0.41	28.7	1.13	0.134		0.085	-
	Earthworms, 40%	0.41	3.16	1	1	1	0.155	-
	Cereal grain, 30%	0.41	15	2.1	0.53	1	0.61	-
	Weed seeds, 4%	0.41	40.2	2.1	0.53	1	0.22	-
	Ground arthropods, 10%	0.41	7.5	2.1	0.53	1	0.10	-
	Whole diet						1.17	5.81

June

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 9%	0.26	28.7	1.13	0.134	1	0.03	-
	Earthworms, 9%	0.26	3.16	1	1	1	0.022	-
	Cereal grain, 32%	0.26	15	2.1	0.53	1	0.41	-
	Weed seeds, 25%	0.26	40.2	2.1	0.53	1	0.87	-
	Ground arthropods, 25%	0.26	7.5	2.1	0.53	1	0.165	-
	Whole diet						1.49	4.56

July:

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 8%	0.25	28.7	1.13	0.134	1	0.026	-
	Cereal grain, 48%	0.25	15	2.1	0.53	1	0.601	-
	Weed seeds, 16%	0.25	40.2	2.1	0.53	1	0.53	-
	Ground arthropods, 28%	0.25	7.5	2.1	0.53	1	0.17	-
	Whole diet						1.32	5.15

Use group 5: 3 × 2.4 L product/ha (9-day interval)

April

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 24%	0.6	28.7	1.04	0.134	1	0.175	-
	Earthworms 26%	0.6	3.16	1	1	1	0.15	-

	Cereal grain 5 %	0.6	15	1.8	0.53	1	0.13	-
	Ground arthropods 45 %	0.6	7.5	1.8	0.53	1	0.617	-
	Whole diet						1.07	6.36
May								
Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m [*]	f _{twa} [*]	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 16%	0.41	28.7	1.04	0.134	1	0.078	
	Earthworms, 40%	0.41	3.16*	1**	1**	1	0.155	
	Cereal grain, 30%	0.41	15	1.8	0.53	1	0.52	
	Weed seeds, 4%	0.41	40.2	1,8	0.53	1	0.188	
	Ground arthropods, 10%	0.41	7.5	1.8	0.53	1	0.09	
	Whole diet						1.031	6.6
June								
Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.300						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m [*]	f _{twa} [*]	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 9%	0.26	28.7	1.04	0.134	1	0.028	-
	Earthworms, 9%	0.26	3.16	1	1	1	0.022	-
	Cereal grain, 32%	0.26	15	1.8	0.53	1	0.357	-
	Weed seeds, 25%	0.26	40.2	1,8	0.53	1	0.747	-
	Ground arthropods, 25%	0.26	7.5	1.8	0.53	1	0.14	-
	Whole diet						1.29	5.3
July								
Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.3						
Reproduction toxicity [mg/kg bw/d]		6.8						

TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 8%	0.25	28.7	1.04	0.134	1	0.0239	-
	Cereal grain, 48%	0.25	15	1.8	0.53	1	0.51	-
	Weed seeds, 16%	0.25	40.2	1.8	0.53	1	0.46	-
	Ground arthropods, 28%	0.25	7.5	1.8	0.53	1	0.15	-
	Whole diet						1.14	6.0

Use group 4: 3 × 1.8 L product/ha (6-day interval)

April

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.225						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 24%	0.6	28.7	1.13	0.134	1	0.143	-
	Earthworms 26%	0.6	3.16	1	1	1	0.11	-
	Cereal grain 5 %	0.6	15	2.1	0.53	1	0.11	-
	Ground arthropods 45 %	0.6	7.5	2.1	0.53	1	0.51	-
	Whole diet						0.873	7.8

May

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.225						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 16%	0.41	28.7	1.13	0.134	1	0.064	
	Earthworms, 40%	0.41	3.16	1	1	1	0.11	
	Cereal grain, 30%	0.41	15	2.1	0.53	1	0.46	
	Weed seeds, 4%	0.41	40.2	2.1	0.53	1	0.165	
	Ground arthropods, 10%	0.41	7.5	2.1	0.53	1	0.077	
	Whole diet						0.876	7.76

June

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.225						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 9%	0.26	28.7	1.13	0.134	1	0.022	-
	Earthworms, 9%	0.26	3.16	1	1	1	0.016	-
	Cereal grain, 32%	0.26	15	2.1	0.53	1	0.312	-
	Weed seeds, 25%	0.26	40.2	2.1	0.53	1	0.654	-
	Ground arthropods, 25%	0.26	7.5	2.1	0.53	1	0.122	-
	Whole diet						1.12	6.07

July

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		3 × 0.225						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 8%	0.25	28.7	1.13	0.134	1	0.019	-
	Cereal grain, 48%	0.25	15	2.1	0.53	1	0.45	-
	Weed seeds, 16%	0.25	40.2	2.1	0.53	1	0.4	-
	Ground arthropods, 28%	0.25	7.5	2.1	0.53	1	0.13	-
	Whole diet						1	6.8

Use group 1: 6 × 1.2 L product/ha (5-day interval)

April

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		6 × 0.150						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 24%	0.6	28.7	1.21	0.134	1	0.102	-
	Earthworms 26%	0.6	3.16	1	1	1	0.075	-

	Cereal grain 5 %	0.6	15	3	0.53	1	0.10	-
	Ground arthropods 45 %	0.6	7.5	3	0.53	1	0.49	-
	Whole diet						0.767	8.86

May

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		6 × 0.150						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 16%	0.41	28.7	1.21	0.134	1	0.045	
	Earthworms, 40%	0.41	3.16	1	1	1	0.077	
	Cereal grain, 30%	0.41	15	3	0.53	1	0.44	
	Weed seeds, 4%	0.41	40.2	3	0.53	1	0.157	
	Ground arthropods, 10%	0.41	7.5	3	0.53	1	0.073	
	Whole diet						0.792	8.58

June

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		6 × 0.150						
Reproduction toxicity [mg/kg bw/d]		6.8						
TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD_m × DF [mg/kg food]	MAF_m *	f_{twa} *	PT	DDD_m [mg/kg bw/d]	TER_{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 9%	0.26	28.7	1.21	0.134	1	0.016	-
	Earthworms, 9%	0.26	3.16	1	1	1	0.1232	-
	Cereal grain, 32%	0.26	15	3	0.53	1	0.297	-
	Weed seeds, 25%	0.26	40.2	3	0.53	1	0.62	-
	Ground arthropods, 25%	0.26	7.5	3	0.53	1	0.116	-
	Whole diet						1.17	5.81

July

Intended use		Beet crops						
Active substance/product		Phenmedipham / HBZ10						
Application rate [kg/ha]		6 × 0.15						
Reproduction toxicity [mg/kg bw/d]		6.8						

TER criterion		5						
Focal species	Food category, % in diet	FIR/bw	RUD _m × DF [mg/kg food]	MAF _m *	f _{twa} *	PT	DDD _m [mg/kg bw/d]	TER _{LT}
Wood mouse (<i>Apodemus sylvaticus</i>)	Non grass herbs, leafy crops 8%	0.25	28.7	1.21	0.134	1	0.013	-
	Cereal grain, 48%	0.25	15	3	0.53	1	0.4293	-
	Weed seeds, 16%	0.25	40.2	3	0.53	1	0.383	-
	Ground arthropods, 28%	0.25	7.5	3	0.53	1	0.125	-
	Whole diet						0.95	7.15

Based on calculations of the long-term risk for wood mouse provided in the Tables above the TER_{LT} values for a.s. - phenmedipham indicated an acceptable risk except Group Use 3 x 2.4 L/ha with 6 days interval in June with TER_{LT} value slight below trigger of 5. In zRMS's opinion as default conservative parameter PT of 1 and lowest available NOEL value of 6.8 mg a.s./kg bw are considered, the long – term risk is considered as acceptable by zRMS.

Combined risk assessment:

The combined risk assessment for all species was calculated by zRMS and the results are presented in the Table below:

Application Rate	Ethofumesate TER _{LT}	Phenmedipham TER _{LT}	TER _{combi}
Lagomorph (BBCH 10-39)			
3 × 2.4 L product/ha, 6-day interval	12.8*	10.5**	5.88
3 × 2.4 L product/ha, 9-day interval	14.9*	11.33**	6.45
3 × 1.8 L product/ha, 6-day interval	17.0*	13.6**	7.7
6 × 1.2 L product/ha, 5-day interval	17.9*	19.42**	9.43
5 × 1.2 L product/ha, 7-day interval	22.3*	21.93**	11.11
Shrew (BBCH 10-19)			
3 × 2.4 L product/ha, 6-day interval	43.4*	4.96*	4.54
3 × 2.4 L product/ha, 9-day interval	50.7*	5.7*	5.1
3 × 1.8 L product/ha, 6-day interval	57.9*	6.5*	5.8
6 × 1.2 L product/ha, 5-day interval	60.8*	6.8*	6.1
5 × 1.2 L product/ha, 7-day interval	76.0*	8.5*	7.6
Mouse (BBCH 10-39)			
3 × 2.4 L product/ha, 6-day interval	23.4*	April 5.76**	4.76
		May 5.81**	4.76
		June 4.56**	3.84
		July 5.15**	4.34
3 × 2.4 L product/ha, 9-day interval	27.3*	April 6.36**	5.26
		May 6.6**	5.55
		June 5.3**	4.54
		July 6.0**	5.0
3 × 1.8 L product/ha, 6-day interval	31.2*	April 7.8 **	6.17
		May 7.76 **	6.17
		June 6.07**	5.1
		July 6.8**	5.58
6 × 1.2 L product/ha, 5-day interval	32.74*	April 8.86**	7.14
		May 8.58**	6.84
		June 5.81 **	5.0
		July 7.15**	5.91
5 × 1.2 L product/ha, 7-day interval	40.9*	5.81 ** ¹	5.26
Shrew (BBCH ≥20)			
3 × 2.4 L product/ha, 6-day interval	96.0*	10.7*	9.6
3 × 2.4 L product/ha, 9-day interval	112*	12.5*	11.2
3 × 1.8 L product/ha, 6-day interval	128*	14.3*	12.9
6 × 1.2 L product/ha, 5-day interval	134.4*	15.0*	13.5
5 × 1.2 L product/ha, 7-day interval	168*	18.8*	16.9

Values in **bold** are below the trigger value

* TER_{LT} value from tier-1 risk assessment

** TER_{LT} value from higher tier risk assessment

¹⁾ diet according to EFSA 2009, Appendix A

Based on calculations of combined long-term risk for all species provided in the Tables above the TER_{combi} values are above trigger of 5 indicated an acceptable risk for following uses:

- 3 × 1.8 L product/ha, 6-day interval
- 6 × 1.2 L product/ha, 5-day interval
- 5 × 1.2 L product/ha, 7-day interval

In the same time, TER_{combi} values are below trigger of 5 for wood mouse and shrew in Group use: 3 × 2.4 L product/ha, 6-day interval and for wood mouse only in June in Group use 3 × 2.4 L product/ha, 9-day interval, indicating an unacceptable risk.

TU approach was used by zRMS as an option of refinement of combined risk and the relevant zRMS's calculations are presented below:

Active substance	Fraction in ppp	Toxicity	Toxic unit	% of total TU
Phenmedipham	0.5	6.8	0.073529412	89.95568685
Ethofumesate	0.5	60.9	0.009210181	10.04431315

Although the TU for phenmedipham is not >90%, it is on the very borderline (89%) and indicates that the long-term toxicity of the mixture will mainly result from the presence of this substance, ethofumesate will contribute to a small extent. Therefore, the risk assessment based on a.s. phenmedipham is considered by zRMS sufficient to conclude acceptable risk from a mixture.

However, zRMS would like to stress out that if the other MSs are different opinion referred to refinement of combined risk assessment used by the zRMS they are considered it further at National level.

Commenting period process:

During commenting period process the Applicant provided the following comments in Reporting Table :

Applicant agrees with zRMS with regards to the Toxic Units approach as a refinement for mammal's risk assessment for use groups 2 and 5.

As the proposed refinements could not be agreed by other CMS, applicant proposes below further information to be considered for acceptability of the mammal's risk assessment and proposes zRMS to include them in the dRR section B9 as additional weight of evidence approach:

Overall, it should be mentioned that the refined TER calculations are still based on conservative exposure assumptions from several points of view. Besides the quantitative parameters used for refined deterministic risk assessment for the different generic focal species, other factors further decreasing the realistic exposure estimates were not taken into account. These parameters provide further confidence in the conclusion that mammals are not at risk from exposure to HBZ10 in beet crops.

Point	Argumentation
Attractiveness / availability of food	In the risk assessments provided in section B9, it was assumed for small omnivorous mammals that the animals satisfy their entire food demand in the exposed area. However, due to the application of HBZ10, a gradual wilting of treated weeds from the day of application onwards can be reasonably assumed. Only a few days after application, the availability of contaminated weeds can be seen as negligible and thus the unattractiveness/gradual disappearance of wilting plant material forces omnivorous animals to search in the untreated off-field area for plant material, which would further reduce the exposure to in-field Phenmedipham residues.
Proportion of diet obtained in the treated area (PT)	According to the available risk assessment and zRMS conclusion, a PT value of 1 was considered for small omnivorous mammal (wood mouse), although it is very likely that animals do not obtain their food exclusively from the treated area. For a refined but still conservative risk assessment for mammals, it seems reasonable to assume that the proportion of diet obtained in the treated area will be lower than 100 %, even though applicant has no data on sugar beet to support this assumption. The study referred to by the applicant in the dRR section 9 for PT refinement (Crocker, 2005), has indeed not been submitted to zRMS. This report is now provided for completeness purposes. It should be recognized that using a PT of 1 is a very conservative and worst-case approach which should be taken into account as a weight of evidence when assessing the acceptability of the determined refined long-term TER values.
Deposition Factor	In the EFSA guidance document (Appendix E – impact of crop interception on residues on plant food items), it is stated that the deposition factors provided for the different crops and growth stages in the guidance document are likely to reflect conservative estimates. In the context of a higher-tier assessment, the more detailed values of the FOCUS groundwater report could therefore be used. Thus, the deposition values reported in the latest 'Generic Guidance for Tier-1 FOCUS Ground Water Assessment' (version 2.3; 2021) could be considered for refinement purposes.

	<p>zRMS refused the refinement on the deposition factor for the currently intended GAP with application between BBCH stage 10 to 39, since crop interception is only applicable from BBCH 40 onwards. However, according to Meier et al. (1993), BBCH stage 10-39 corresponds to beginning of leaf development until rosette growth, for which an increase of ground cover, and thus crop interception, is assumed. Since no interception is considered in the zRMS agreed calculations, this should be recognized as a worst-case and conservative approach be taken into account as a weight of evidence when assessing the acceptability of the determined refined long-term TER values.</p>
Dehusking Factor	<p>No dehusking factor for seeds or grains was considered in the risk assessment for small omnivorous mammals represented by the wood mouse, even though those are part of its diet. However, it is well known that exposure of grain-/seed-eating mammals will be substantially reduced when they dehusk seeds before consumption. █████ studied dehusking by individually caged wood mice and found dehusking efficiencies of 60-80 %. Dehusking efficiency was approximately the same, no matter whether the seed was treated with a fungicide or a generic pigment and no matter whether the mice were starved before the experiment or not. According to SANCO/4145/2002 (final), this behaviour-related exposure reduction can be as high as 85 %, corresponding to a dehusking factor of 0.15. Nevertheless, for a maximum conservative risk assessment, no reduction in pesticide exposure due to dehusking was assumed in the refined risk assessment for the wood mouse. However, it should be recognised that this is a very conservative approach and should be taken into account when assessing the acceptability of the determined refined long-term TER values. The report from █████ referred to in this paragraph is attached to this commenting table for completeness purposes.</p>
Relevance of the current phenmedipham chronic endpoint from EFSA conclusion 2004	<p>Phenmedipham chronic endpoint of 6.8 mg/kg bw/d was used for long-term risk assessment of terrestrial vertebrates other than birds as a worst-case assumption. However, from all available documents present from the EU dossier, it is not clear why the NOAEL of 6.8 mg/kg bw/d is used in the List of Endpoints. The study submitted in the DAR showed that a significant decrease (-15%) in mean body weights of F1a generation males at day 21 was noted at 500 ppm. Decreased offspring survival and growth indices were seen only at the lowest dose level of 20 ppm; in case of weaning survival indices in F2a offspring, there was an increase in weaning survival at 100 and 500 ppm as compared to the control group. The slight but statistically significant changes at the low dose should therefore be considered as incidental in nature. Therefore, a NOAEL for reproductive effects of 500 ppm (25 mg a.s./kg bw/d) has also been proposed, in line with the relevant endpoint in the DAR toxicology section for reproductive NOAEL.</p> <p>These two different endpoints for mammals have been proposed and used in the EU renewal dossier of Phenmedipham (2016): <i>“In the last EU review of phenmedipham the official endpoint for the wild mammal long-term/reproductive risk assessment was set on basis of toxicological data available from three rat reproduction studies. The lowest NOAEL of 100 ppm based on maternal body weight, equivalent to 6.8 mg/kg bw/day, was selected from these data. This value is lower than the one established in the context of the human-health related review of phenmedipham where the overall NOAEL for the rat reproduction studies was set at 25 mg/kg bw/day.”</i></p> <p>In version of October 2017 of the RAR, the expert consultation 5.1 led to the following outcome: <i>“The endpoint of 6.8 mg/kg based on parental effects on males and the NOAEL of 25 mg/kg based on foetal effects, retardation in pup weight. (...) However, it was agreed that the same endpoint has to be used in all the different steps of the risk assessment. In the study by █████ there is a statistically significant effect in male pup’s body weight in the F1a generation (15%) at 500 ppm but not in the other groups. The results do not show a clear effect. Some experts pointed out that another stud █████ shows similar results in terms of reduction in pup’s body weight in both sexes and therefore the NOEL of 25 mg/kg bw/d. The endpoint based on reduced body weight gain for the parental generation was however lower than 25 mg/kg bw/d. In the study by █████ the parental endpoint was also below 25 mg/kg bw/d (22 mg/kg bw/d). The tox experts however set a data gap because, for desmedipham, which is structurally similar, the endpoint from the reproductive study was based on sperm count which has not been measured in the case of phenmedipham. Therefore, some sensitive parameters have not been measured and therefore it is unclear whether the endpoint can change. Overall the experts agreed that based on the data gap set by the tox experts, an endpoint cannot be decided upon before having a complete picture.”</i></p> <p>In May 2022, after provision of new information in the context of the ED assessment of phenmedipham, the RAR LoEP has been updated with the following information: <i>“In EFSA conclusion (2017), a data gap was concluded on the long-term risk assessment for mammals. A new extended one generation reproduction toxicity study on rats has been provided by Applicant. The lowest NOAEL of the study is 60mg/kg bw/d based on the decreased weights of male reproductive organs and related changes in histopathology including degenerated seminiferous tubules of testes and decreased sperm counts. Therefore, the chronic risk assessment for mammals can be finalized now.”</i></p> <p>According to the above information and additional data evaluated during the Phenmedipham renewal process, it should be first noted that the lowest endpoint of 6.8 mg/kg bw/d is not considered anymore as relevant for the long-term risk assessment on mammals. Applicant agrees with zRMS that none of the new proposed/discussed endpoints ranging from 22 to 60 mg/kg bw/d</p>

	are agreed at EU level yet, however, this should be considered as giving further evidence that the chronic risk for mammals is overestimated when risk assessment is based on the 6.8 mg/kg bw/d NOAEL endpoint from the DAR.
<p>With regards to zRMS conclusions, applicant would like to highlight that even based on such overconservative endpoint of 6.8 mg/kg bw/d, only two scenarios are leading to a TER_{LT} value below the relevant trigger of 5 for phenmedipham, with TER_{LT} values of 4.96 and 4.56 for Shrew (BBCH 10-19) with 3 × 2.4 L product/ha, 6-day interval GAP and Mouse (BBCH 10-39) with 3 × 2.4 L product/ha, 6-day interval GAP in June, respectively.</p> <p>Moreover, the theoretical TER_{combitox} risk assessment should also be considered as highly conservative, since the long-term risk assessment fails even with individual active substance TER_{LT} values above the respective trigger of 5 (which is also a conservative trigger value).</p> <p>Finally, when considering the above points not used for refinement, the slight gap between obtained TER_{LT} values and relevant trigger indicating acceptable risk, as well as the safety margins considered globally in the risk assessment, it can be assumed the risk for non-target vertebrates other than birds following the use of HBZ10 is sufficiently covered and won't lead to any unacceptable risk for those organisms.</p> <p>zRMS answer: The final decision of long-term combined risk assessment for mammals is still left at MSs level. zRMS would like to indicated that the study by Crocker, 2005 was not submitted to zRMS.</p>	

9.3.2.3 Drinking water exposure

When necessary, the assessment of the risk for mammals due to uptake of contaminated drinking water is conducted for a small omnivorous mammal with a body weight of 21.7 g (*Apodemus sylvaticus*) and a drinking water uptake rate of 0.24 L/kg bw/d (*cf.* Appendix K of EFSA/2009/1438).

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 when the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances ($K_{oc} < 500$ L/kg) or 3000 in the case of more sorptive substances ($K_{oc} \geq 500$ L/kg).

With a $K(f)_{oc}$ of 118 mL/g (geometric mean), Ethofumesate belongs to the group of less sorptive substances. With a $K(f)_{oc}$ of 657 mL/g (mean minimum, $n = 3$), Phenmedipham belongs to the group of more sorptive substances.

For completeness, the risk assessment is presented for all intended uses.

Table 9.3.2.3-1 Drinking water assessment (puddle scenario) - Ethofumesate

Effective application rate [g/ha] =	3 × 300 (use-group-2-use-group-5 use No 2, 5, 7, 10, 12, 15, 17, 20, 22, 25) and 6 × 150 (use-group-4 use No 1, 6, 11, 16, 21)		
Acute toxicity [mg/kg bw] =	> 5000	quotient =	0.18
Reproduction toxicity [mg/kg bw/d] =	60.9	quotient =	14.8
Effective application rate [g/ha] =	3 × 225 (use-group-4 use No 4, 9, 14, 19, 24)		
Acute toxicity [mg/kg bw] =	> 5000	quotient =	0.14
Reproduction toxicity [mg/kg bw/d] =	60.9	quotient =	11.1
Effective application rate [g/ha] =	5 × 150 (use-group-4 use No 3, 8, 13, 18, 23)		
Acute toxicity [mg/kg bw] =	> 5000	quotient =	0.15
Reproduction toxicity [mg/kg bw/d] =	60.9	quotient =	12.3

The resulting ratios fall below the trigger of 50 for less sorptive substances, indicating that further assessment of the acute and long-term risk to mammals from drinking water from puddles is not required for Ethofumesate.

Table 9.3.2.3-2 Drinking water assessment (puddle scenario) - Phenmedipham

Effective application rate [g/ha] =	3 × 300 (use-group-2 use No 2, 5, 7, 10, 12, 15, 17, 20, 22, 25) and 6 × 150 (use-group-4 use No 1, 6, 11, 16, 21)		
Acute toxicity [mg/kg bw] =	> 8000	quotient =	0.11
Reproduction toxicity [mg/kg bw/d] =	6.8	quotient =	132
Effective application rate [g/ha] =	3 × 225 (use-group-4 use No 4, 9, 14, 19, 24)		
Acute toxicity [mg/kg bw] =	> 8000	quotient =	0.08
Reproduction toxicity [mg/kg bw/d] =	6.8	quotient =	99.3
Effective application rate [g/ha] =	5 × 150 (use-group-3 use No 3, 8, 13, 18, 23)		
Acute toxicity [mg/kg bw] =	> 8000	quotient =	0.09
Reproduction toxicity [mg/kg bw/d] =	6.8	quotient =	110

The resulting ratios fall below the trigger of 3000 for more sorptive substances, indicating that further assessment of the acute and long-term risk to mammals from drinking water from puddles is not required for Phenmedipham.

zRMS comments:

The calculation of the drinking water risk assessment for both active substances presented in the Tables above are validated by the zRMS.
Further assessment of the acute and long-term risk to mammals from drinking water from puddles is not required for Ethofumesate and Phenmedipham.

9.3.2.4 Effects of secondary poisoning

The log K_{OW} of Ethofumesate amounts to 2.7 and thus does not exceed the trigger value of 3 indicating a low potential risk to accumulate in the food chain. However, since the BCF > 100, the risk assessment for effects due to secondary poisoning is required.

The log K_{OW} of Phenmedipham amounts to 3.59 and thus exceeds the trigger value of 3. Furthermore, the BCF is > 100. A risk assessment for effects due to secondary poisoning is required.

Risk assessment for earthworm-eating mammals via secondary poisoning

According to EFSA/2009/1438, the risk for vermivorous mammals is assessed for a small mammal of 10 g body weight with a daily food consumption of 12.8 g. Bioaccumulation in earthworms is estimated based on predicted concentrations in soil.

To achieve a concise risk assessment, the risk envelope approach is applied in line with the approach followed for PEC_{Soil} calculations in dRR Part B8, Point 8.7: The 25 intended uses are grouped in 5 use groups, i.e., Use group 1: 6 × 1.2 L prod./ha, 5-days interval (includes uses 1, 6, 11, 16 and 21); Use group 2: 3 × 2.4 L prod./ha, 6-days interval (includes uses 2, 7, 12, 17, and 22); Use group 3: 5 × 1.2 L prod./ha, 7-days interval (includes uses 3, 8, 13, 18, and 23); Use group 4: 3 × 1.8 L prod./ha, 6-days interval (includes uses 4, 9, 14, 19, and 24); Use group 5: 3 × 2.4 L prod./ha, 9-days interval (includes uses 5, 10, 15, 20, and 25), and PEC_{Soil} calculations are performed and presented for Use groups 2 (worst-case), 4 and 5. Here, the assessment for the worst-case use group 2 in-beet-crops (3 × 2.4 L product/ha, 6-day interval), use group 4 (3 × 1.8 L product/ha, 6-day interval) and use group 5 (3 × 2.4 L product/ha, 9-day interval) also covers the risk for birds from the intended use groups 1 & 3 in-beet-crops (6 × 1.2 L product/ha, 5-day interval and 5 × 1.2 L product/ha, 7-day interval).

Dry soil approach

Table 9.3.2.4-1 Assessment of the risk for earthworm-eating mammals due to exposure to Ethofumesate via bioaccumulation in earthworms (secondary poisoning) for the all intended uses in beet-crops

Parameter	Use group 2	Use group 4	Use group 5	Comments
PEC _{Soil} (two = 21 d) + PEC _{Soil plateau} [mg/kg soil]	0.894 0.903 0.9513	0.676 0.745 0.714	0.882 0.981 0.94	PEC _{Soil} , dry, two 21 d + PEC _{Soil plateau} after multiple applications (PEC _{Soil} + PEC _{Soil plateau}) (Section 8, Point 8.7.2)
log K _{ow} / K _{ow}	2.7 / 561 486			EFSA Conclusion (2016)
K _{oc} [mL/g]	118			Geometric mean (EFSA Conclusion, 2016)
f _{oc}	0.02			Default
BCF _{worm}	0.90 2.83			BCF _{worm/Soil} = (0.84 + 0.012 × K _{ow}) / (f _{oc} × K _{oc})
PEC _{worm}	2.50 2.89 2.69	1.05 2.16 2.02	2.56 2.84 2.66	PEC _{worm} = PEC _{Soil} × BCF _{worm/Soil}
Daily dietary dose [mg/kg bw/d]	3.32 3.69 3.44	2.49 2.77 2.58	3.28 3.64 3.40	DDD = PEC _{worm} × 1.28
NOEL [mg/kg bw/d]	60.9			EFSA Conclusion (2016)
TER _{LT}	18.3 16.5 17.7	24.1 22.0 23.6	18.6 16.7 17.9	TER _{LT} = NOEL/DDD

TER values shown in bold fall below the relevant trigger.

Use group 2: 3 × 2.4 L product/ha, 6-day interval

Use group 4: 3 × 1.8 L product/ha, 6-day interval

Use group 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.3.2.4-2 Assessment of the risk for earthworm-eating mammals due to exposure to Phenmedipham via bioaccumulation in earthworms (secondary poisoning) for the all intended uses in beet-crops

Parameter	Use group 2	Use group 4	Use group 5	Comments
PEC _{Soil} (two = 21 d) [mg/kg soil]	0.742	0.556	0.709	PEC _{Soil} , dry, two 21 d after multiple applications (Section 8, Point 8.7.2)
log K _{ow} / K _{ow}	3.59 / 3890.5			Review Report (2004)
K _{oc}	657			Mean (n = 3), Review Report (2004)
f _{oc}	0.02			Default
BCF _{worm}	3.62			BCF _{worm/Soil} = (0.84 + 0.012 × K _{ow}) / (f _{oc} × K _{oc})
PEC _{worm}	2.68	2.01	2.56	PEC _{worm} = PEC _{Soil} × BCF _{worm/Soil}
Daily dietary dose [mg/kg bw/d]	3.44	2.57	3.28	DDD = PEC _{worm} × 1.28
NOEL [mg/kg bw/d]	6.8 / 25			Review Report (2004) / Position paper (Diesing, 2014)
TER _{LT}	1.98 / 7.28	2.64 / 9.71	2.07 / 7.62	TER _{LT} = NOEL/DDD

TER values shown in bold fall below the relevant trigger.

Use group 2: 3 × 2.4 L product/ha, 6-day interval

Use group 4: 3 × 1.8 L product/ha, 6-day interval

Use group 5: 3 × 2.4 L product/ha, 9-day interval

As shown in Table 9.3.2.4-2, the calculated TER values for the active substance Phenmedipham (dry soil approach) based on the NOAEL of 6.8 mg/kg bw/d are all below the trigger value of 5, indicating a potential long-term risk for earthworm-eating mammals after application of HBZ10 according to the intended use pattern. In order to take into account the scientific and technical knowledge since the first inclusion of Phenmedipham and to more accurately estimate the relevant risk, the above assessment is updated by considering the relevant information from Phenmedipham dRAR, LoEP (2022) and EFSA Journal 2018;16(1):5151 regarding the parameters log P_{ow} and K_{oc}: (i) The geomean K_{oc} for Phenmedipham [same as used in e-fate as input parameter for modelling – recommendation of the new EFSA Guidance on the Risk Assessment for Birds and Mammals (EFSA Journal 2023;21(2):7790)] reported in both dRAR, LoEP (2022) and EFSA Journal 2018;16(1):5151, i.e., 1331 mL/g, instead of the minimum value of the K_{oc} reported in the Review Report (2004), i.e., 657 mL/g (used in e-fate as input parameter for modelling in the submitted dossier) and (ii) the log P_{ow} reported in both dRAR, LoEP (2022) and EFSA Journal 2018;16(1):5151, i.e., 2.7 (=> P_{ow} = 501.2), instead of the log P_{ow}

reported in the Review Report (2004), i.e., 3.59 (\Rightarrow Pow = 3890.5) are used in the risk assessment presented in the table below.

Table 9.3.2.4 3 Revised assessment of the risk for earthworm-eating mammals due to exposure to Phenmedipham via bioaccumulation in earthworms (secondary poisoning) for all intended uses

Parameter	Use group 2	Use group 4	Use group 5	Comments
PEC _{Soil} (twa = 21 d) [mg/kg soil]	0.742	0.556	0.709	PEC _{Soil} , dry, twa 21 d after multiple applications (Section 8, Point 8.7.2)
log K _{ow} / K _{ow}	2.7 / 501.2			dRAR, LoEP (2022) and EFSA Journal 2018;16(1):5151
K _{oc}	1331			Geomean (n = 4); dRAR, LoEP (2022) and EFSA Journal 2018;16(1):5151
f _{oc}	0.02			Default
BCF _{worm}	0.257			$BCF_{worm/Soil} = (0.84 + 0.012 \times K_{ow}) / (f_{oc} \times K_{oc})$
PEC _{worm}	0.191	0.143	0.182	$PEC_{worm} = PEC_{Soil} \times BCF_{worm/Soil}$
Daily dietary dose [mg/kg bw/d]	0.244	0.183	0.233	$DDD = PEC_{worm} \times 1.28$
NOEL [mg/kg bw/d]	6.8			Review Report (2004)
TER _{LT}	27.9	37.2	29.2	$TER_{LT} = NOEL/DDD$

TER values shown in bold fall below the relevant trigger.

Use group 2: 3 × 2.4 L product/ha, 6-day interval

Use group 4: 3 × 1.8 L product/ha, 6-day interval

Use group 5: 3 × 2.4 L product/ha, 9-day interval

zRMS comments:

The risk assessment for secondary poisoning is based on the TER calculations for dry soil approach that is the current methodology used at EU level. The TER_{LT} value for the active substances Ethofumesate and Phenmedipham for secondary poisoning of earthworms-eating mammals with regard to K_{oc} of 1331 mL/g and log K_{ow} 2.7 values from Phenmedipham dRAR, LoEP (2022) and EFSA Journal 2018;16(1):5151 were considered as the refinement option to conclude acceptable risk assessment. It should be noted that these parameters were agreed by the RMS in the course of the ongoing EU renewal process: Although the renewal process is not finalized yet, no changes regarding the derived endpoints are expected. For this reason, the Applicant's approach is validated by zRMS. However, zRMS would like to stressed that if the other MSs are different opinion referred to refinement of revised risk assessment for earthworm-eating mammals due to exposure to Phenmedipham via bioaccumulation in earthworms, they are considered it further at National level.

Based on calculation the TER_{LT} value was above the trigger value of 5, indicating an acceptable risk.

Porewater approach

Table 9.3.2.4-3 — **Assessment of the risk for earthworm-eating mammals due to exposure to Ethofumesate via bioaccumulation in earthworms (secondary poisoning) for the intended use in beet crops**

Parameter	Use group 2	Use group 4	Use group 5	Comments
$PEC_{\text{Soil, dry, twa 21-d}}$ [mg/kg]	0.893	0.670	0.882	$PEC_{\text{Soil, dry, twa 21-d}}$ after multiple applications (Section 8, Point 8.7.2)
K_{ow}	501			EFSA Conclusion (2016)
K_{oc}	118			Geometric mean (EFSA Conclusion, 2016)
$RHO_{\text{earthworm}}$	1			Default
BCF_{worm}	6.85			$BCF_{\text{worm}} = (0.84 + 0.012 \times K_{ow}) / RHO_{\text{earthworm}}$
$K_{\text{soil-water}}$ [m ³ /m ³]	3.74			Eq. 24 of Technical Guidance Document on Risk Assessment Part II, Joint Research Center (2003), EUR 20418 EN/2
$RHO_{\text{Soil, wet}}$ [kg/m ³]	1700			Default
$RHO_{\text{Soil, dry}}$ [kg/m ³]	1500			Default
$C_{\text{porewater}}$ [mg/L]	0.358	0.260	0.354	$C_{\text{porewater}} = (PEC_{\text{Soil, dry}} \times RHO_{\text{Soil, wet}}) / (K_{\text{soil-water}} \times 1000)$
$PEC_{\text{Soil, wet, twa 21-d}}$ [mg/kg]	0.788	0.591	0.778	$PEC_{\text{Soil, wet, twa 21-d}} = PEC_{\text{Soil, dry}} / RHO_{\text{Soil, wet}} \times RHO_{\text{Soil, dry}}$
F_{solid} [m ² /m ²]	0.60			Default
RHO_{solid} [kg dry weight/m ³]	2500			Default
$CONV_{\text{Soil}}$	1.13			$CONV_{\text{Soil}} = RHO_{\text{Soil}} / (F_{\text{solid}} \times RHO_{\text{solid}})$ (default)
F_{gut}	0.10			Default
C_{worm}	2.29	1.71	2.26	$C_{\text{worm}} = (BCF_{\text{worm}} \times C_{\text{porewater}} + PEC_{\text{Soil, wet}} \times F_{\text{gut}} \times CONV_{\text{Soil}}) / (1 + F_{\text{gut}} \times CONV_{\text{Soil}})$
Daily dietary dose [mg/kg bw/d]	2.93	2.19	2.89	$DDD = PEC_{\text{worm}} \times 1.28$
NOEL [mg/kg bw/d]	60.9			EFSA Conclusion (2016)
TER_{LT}	20.8	27.7	21.1	$TER_{LT} = NOEL / DDD$

TER values shown in bold fall below the relevant trigger.

Use group 2: 3 × 2.4 L product/ha, 6-day interval

Use group 4: 3 × 1.8 L product/ha, 6-day interval

Use group 5: 3 × 2.4 L product/ha, 9-day interval

zRMS comment:

The applicant presented TER_{LT} calculations for ethofumesate and phenmedipham for the pore water approach, as recommended in the EFSA GD (2009). zRMS is of opinion that this approach cannot be correctly estimated due to the lack of information about the way to calculate PEC_{soil} pore water. Therefore, the TER_{LT} calculations presented by the applicant have not been checked by zRMS.

Table 9.3.2.4.4 – Assessment of the risk for earthworm-eating mammals due to exposure to Phenmedipham via bioaccumulation in earthworms (secondary poisoning) for the intended uses in beet crops

Parameter	Use-group 2	Use-group 4	Use-group 5	Comments
$PEC_{soil, dry, twa-21-d}$ [mg/kg]	0.745 0.745	0.556 0.556	0.710 0.710	$PEC_{soil, dry, twa-21-d}$ after multiple applications (Section 5, Point 8.7.2)
K_{ow}	2890.5			Review Report (2004)
K_{oc}	659			Mean (n = 3), Review Report (2004)
$RHO_{soil, worm}$	1			Default
BCF_{worm}	47.5			$BCF_{worm} = (0.84 + 0.012 \times K_{ow}) \times RHO_{soil, worm}$
$K_{soil-water}$ [m ³ /m ³]	2.74			Eq. 24 of Technical Guidance Document on Risk Assessment Part II, Joint Research Center (2003), EUR 20418-EN-2
$RHO_{soil, wet}$ [kg/m ³]	1700			Default
$RHO_{soil, dry}$ [kg/m ³]	1500			Default
$C_{porewater}$ [mg/L]	0.508 0.508	0.508 0.508	0.508 0.508	$C_{porewater} = (PEC_{soil, dry} \times RHO_{soil, dry}) / (K_{soil-water} \times 1000)$
$PEC_{soil, wet, twa-21-d}$ [mg/kg]	0.655	0.104	0.626	$PEC_{soil, wet, twa-21-d} = PEC_{soil, dry} \times RHO_{soil, wet} \times RHO_{soil, dry}$
F_{soil} [m ³ /m ³]	0.60			Default
RHO_{soil} [kg-dry-weight/m ³]	2500			Default
$CONV_{soil}$	1.13			$CONV_{soil} = RHO_{soil} / (F_{soil} \times RHO_{soil})$ (default)
F_{air}	0.16			Default
C_{worm}	12.8	0.50	12.3	$C_{worm} = (BCF_{worm} \times C_{porewater} + PEC_{soil, wet} \times F_{air} \times CONV_{soil}) / (1 + F_{air} \times CONV_{soil})$
Daily dietary dose [mg/kg bw/d]	16.3	12.3	15.6	$DDD = PEC_{worm} \times 1.28$
NOEL [mg/kg bw/d]	6.8 / 25			Review Report (2004) + Position paper (Diesing, 2014)
TER _{ET}	0.42 / 1.53	0.56 / 2.04	0.44 / 1.60	$TER_{ET} = NOEL / DDD$

TER values shown in bold fall below the relevant trigger.

Use-group 2: 3 × 2.4 L product/ha, 6-day interval

Use-group 4: 3 × 1.8 L product/ha, 6-day interval

Use-group 5: 3 × 2.4 L product/ha, 9-day interval

The TER values for the active substance Ethofumesate and Phenmedipham for secondary poisoning of earthworm-eating mammals (dry soil and pore-water approaches) are above the trigger value of 5, indicating an acceptable risk for earthworm-eating mammals after application of HBZ10 in beet crops according to the intended use pattern.

The TER values for the active substance Phenmedipham for secondary poisoning of earthworm-eating mammals (dry soil and pore-water approaches) are below the trigger value of 5, indicating a possible risk for earthworm-eating mammals after application of HBZ10 in beet crops.

Risk assessment for fish-eating mammals via secondary poisoning

According to EFSA/2009/1438, the risk for piscivorous mammals is assessed for a mammal of 3000 g body weight with a daily food consumption of 425 g. Bioaccumulation in fish is estimated based on predicted concentrations in surface water as a limit value for admissible concentrations of Ethofumesate and Phenmedipham in water.

To achieve a concise risk assessment, the risk envelope approach is applied in line with the approach followed for PEC_{sw} calculations in dRR Part B8, Point 8.9: The 25 intended uses are grouped in 5 use groups, i.e., Use group 1: 6 × 1.2 L prod./ha, 5-days interval (includes uses 1, 6, 11, 16 and 21); Use group 2: 3 × 2.4 L prod./ha, 6-days interval (includes uses 2, 7, 12, 17, and 22); Use group 3: 5 × 1.2 L prod./ha, 7-days interval (includes uses 3, 8, 13, 18, and 23); Use group 4: 3 × 1.8 L prod./ha, 6-days interval (includes uses 4, 9, 14, 19, and 24); Use group 5: 3 × 2.4 L prod./ha, 9-days interval (includes uses 5, 10, 15, 20, and 25), and PEC_{sw} calculations are performed and presented for all use groups.

Table 9.3.2.4-5 Assessment of the risk for fish-eating mammals due to exposure to Ethofumesate via bioaccumulation in fish (secondary poisoning) for the all intended uses in beet-crops

Parameter	Use group 1/2/5	Use group 3	Use group 4	Comments
PEC _{sw} (twa = 21 d) [mg/L]	0.25531	0.212758	0.191483	PEC _{sw} , twa 21 d after multiple applications at FOCUS Step 1 (Section 8, Point 8.9.2)
BCF _{fish}	144			EFSA Conclusion (2016)
BMF	1			Biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	36.76	30.64	27.57	PEC _{fish} = PEC _{water} × BCF _{fish}
Daily dietary dose [mg/kg bw/d]	5.22	4.35	3.92	DDD = PEC _{fish} × 0.142
NOEL [mg/kg bw/d]	60.9			EFSA Conclusion (2016)
TER _{LT}	11.7	14.0	15.6	TER _{LT} = NOEL/DDD

TER values shown in bold fall below the relevant trigger.

Use group 1: 6 x 1.2 L product/ha, 5-day interval
Use group 2: 3 x 2.4 L product/ha, 6-day interval
Use group 3: 5 x 1.2 L product/ha, 7-day interval
Use group 4: 3 x 1.8 L product/ha, 6-day interval
Use group 5: 3 x 2.4 L product/ha, 9-day interval

Table 9.3.2.4-6 Assessment of the risk for fish-eating mammals due to exposure to Phenmedipham via bioaccumulation in fish (secondary poisoning) for the all intended uses in beet-crops

Parameter	Use group 1/3	Use group 2/5	Use group 4	Comments
PEC _{sw} (twa = 21 d) [mg/L]	0.00069	0.001377	0.001033	PEC _{sw} , twa 21 d after multiple applications at FOCUS Step 1 (Section 8, Point 8.9.2)
BCF _{fish}	165			Review Report (2004)
BMF	1			Biomagnification factor (relevant for BCF ≥ 2000)
PEC _{fish}	0.114	0.227	0.170	PEC _{fish} = PEC _{water} × BCF _{fish}
Daily dietary dose [mg/kg bw/d]	0.0162	0.0323	0.0242	DDD = PEC _{fish} × 0.142
NOEL [mg/kg bw/d]	6.8			Review Report (2004)
TER _{LT}	421	211	281	TER _{LT} = NOEL/DDD

TER values shown in bold fall below the relevant trigger.

The TER values for the active substances Ethofumesate and Phenmedipham for secondary poisoning of fish-eating mammals are above the trigger value of 5, indicating an acceptable risk for fish-eating mammals after application of HBZ10 in beet-crops according to the intended use pattern.

zRMS comments:

The Applicants' approach in evaluation of the risk of secondary poisoning is in line with EFSA (2009). Compounds selected for this assessment are agreed by the zRMS. Evaluation was not triggered for metabolites of both active substances due to their log Pow <3.

Consideration of the 21 d PEC_{twa} for soil and surface water exposure is validated by the zRMS as they were agreed in the course of the evaluation in area of Section 8.

The risk assessment based on Group uses such as: Use group 2: 3 x 2.4 L product/ha, 6-day interval, Use group 4: 3 x 1.8 L product/ha, 6-day interval, Use group 5: 3 x 2.4 L product/ha, 9-day interval. These group use covers the risk for remaining Group use 1 and Group use 3.

9.3.2.5 Biomagnification in terrestrial food chains

Not relevant, since the evaluation of the ADME studies in the toxicology section (Journal 2016;14(1):4374 and SANCO/4060/2001) concluded that the potential for bioaccumulation of active substance is low. Thus, it can be assumed that there is no biomagnification along the food chain.

9.3.3 Risk assessment for baits, pellets, granules, pills or treated seed

Not relevant as HBZ10 is used for spray applications.

9.3.4 Overall conclusions

The risk assessment for effects on wild mammals is carried out according to the Guidance of EFSA on Risk Assessment for Birds and Mammals (EFSA/2009/1438).

The acute and long-term risks of HBZ10 to wild mammals were assessed from toxicity exposure ratios between toxicity endpoints, estimated from studies with the active substances, and predicted exposure based on the maximum residues occurring on food items following the intended application pattern. In addition, the acute risk of formulation to mammals was assessed on the basis of the predicted mixture toxicity. Risk of secondary poisoning has also been assessed for both active substances.

Acute risk assessment

No acute LD₅₀ values are available for HBZ10. Thus, the acute risk was assessed with the EU agreed endpoint of the active substances as well as the predicted mixture LD₅₀ for the formulated product.

The TER_A values at the screening step exceed the Annex VI trigger value of 10 what indicates that HBZ10 applied according to the intended use does not pose an acute risk to wild mammals.

Long-term risk assessment

The EU agreed endpoint of the active substances have been used in the assessment of chronic risk. The first tier TER_{LT} values for the active substances Ethofumesate and Phenmedipham are above the respective trigger value of 5 indicating an acceptable risk for mammals following application of HBZ10 **in-beet-crops according to the intended use pattern**, except for the active substance Phenmedipham for the generic focal species small insectivorous mammal, large herbivorous mammal, and small omnivorous mammal (growth stage BBCH 10-39).

The refined TER_{LT} values for the active substance Phenmedipham are above the respective trigger value for the focal species small insectivorous mammal “shrew”, large herbivorous mammal “lagomorph”, and small omnivorous mammal “mouse”, (except group use: 3 x 2.4 L/ha with 6 days interval, with TER_{LT} value close to trigger of 5) indicating an acceptable risk for mammals following application of HBZ10 **in-beet-crops according to the intended use pattern**. ~~Although it is not recommended to conduct a long-term mixture toxicity assessment according to EFSA/2009/1438, a combi TER_{LT} was calculated according to the DRAFT EFSA guidance document – Risk Assessment for Birds and Mammals (version 29.09.2021 for public consultation). Based on Tier 1 and higher tier assessments, the long-term risk to mammals is demonstrated to be acceptable for the formulated product.~~

Based on calculations of combined long-term risk for all species provided in the Tables above the TER_{combi} values are above trigger of 5 indicated an acceptable risk for following uses:

3 × 1.8 L product/ha, 6-day interval

6 × 1.2 L product/ha, 5-day interval

5 × 1.2 L product/ha, 7-day interval

In the same time, TER_{combi} values are below trigger of 5 for wood mouse and shrew in Group use: 3 × 2.4 L product/ha, 6-day interval and for wood mouse only in June in Group use 3 × 2.4 L product/ha, 9-day interval, indicating an unacceptable risk.

TU approach was used by zRMS to refine combined risk and the relevant zRMS's calculations are below:

Although the TU for phenmedipham is not >90%, it is on the very borderline (89%) and indicates that the long-term toxicity of the mixture will mainly result from the presence of this substance, ethofumesate will contribute to a small extent. Therefore, the risk assessment based on a.s. phendemipham is considered by zRMS sufficient to conclude acceptable risk from a mixture for all group uses.

However, zRMS would like to stressed that if the other MSs are different opinion referred to refinement of combined risk assessment used by the zRMS they are considered it further at National level.

Secondary poisoning

The TER values for the active substance Ethofumesate and Phenmedipham for secondary poisoning of earthworm-eating mammals (dry soil and pore-water approach) are above the trigger value of 5, indicating an acceptable risk for earthworm-eating mammals after application of HBZ10 in beet-crops according to the intended use pattern.

The TER values for the active substance Phenmedipham for secondary poisoning of earthworm-eating mammals (dry soil and pore-water approach) are below the trigger value of 5, indicating a possible risk for earthworm-eating mammals after application of HBZ10 in beet-crops.

The TER values for the active substances Ethofumesate and Phenmedipham for secondary poisoning of fish-eating mammals are above the trigger value of 5, indicating an acceptable risk for fish-eating mammals after application of HBZ10 in beet-crops according to the intended use pattern. There is no risk expected for wild mammals exposed to the active substance through consumption of contaminated water from puddles on soil.

9.4 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)

No relevant data on amphibians and reptiles is available for Ethofumesate and Phenmedipham, consequently no further assessment of potential effects on reptiles and amphibians will be presented in this document.

9.5 Effects on aquatic organisms (KCP 10.2)

9.5.1 Toxicity data

Studies on the toxicity to aquatic organisms have been carried out with Ethofumesate, Phenmedipham and their relevant metabolites. Full details of these studies are provided in the respective EU DAR (DAR Ethofumesate, 1998; DAR Phenmedipham, 1999) and related documents (DAR Addendum Ethofumesate, 2000; DAR Addendum Phenmedipham, 2001 and 2003). One new study on chronic toxicity of the Phenmedipham metabolite MHPC on aquatic invertebrates is submitted with this application, listed in Appendix 1 and summarised in Appendix 2.

Effects on aquatic organisms of HBZ10 were not evaluated as part of the EU assessment of Ethofumesate and Phenmedipham. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

Toxicity testing for HBZ10 has been performed on one species from each three groups of aquatic organisms, i.e., aquatic invertebrates, algae and macrophytes, since the formulation itself may contaminate water.

Acute and chronic studies on fish for HBZ10 were not conducted, since the formulation is less acutely toxic than the active substances by a factor of 10. Thus, it is possible to extrapolate data obtained in the corresponding studies on the a.s. to the formulation.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.5.1-1 Endpoints and effect values relevant for the risk assessment for aquatic organisms – Ethofumesate and relevant metabolites

Species	Substance	Exposure System	Results	Reference
Fish				
<i>Cyprinus carpio</i>	Ethofumesate	96 h, ss	LC ₅₀ = 10.92 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Oncorhynchus mykiss</i>	Ethofumesate	96 h, ss	LC ₅₀ = 11.91 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Lepomis macrochirus</i>	Ethofumesate	96 h, ss	LC ₅₀ = 21.2 mg a.s./L _{nom}	EFSA Conclusion (2016)

Species	Substance	Exposure System	Results	Reference
<i>Cyprinodon variegatus</i>	Ethofumesate	96 h, s	LC ₅₀ = 25.0 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Danio rerio</i>	Ethofumesate	FFLC, f	NOEC = 0.156 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Pimephales promelas</i>	Ethofumesate	ELS, f	NOEC = 4.17 mg a.s./L _{mm}	EFSA Conclusion (2016)
Aquatic invertebrates				
<i>Daphnia magna</i>	Ethofumesate	48 h, s	EC ₅₀ = 13.52 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Americamysis bahia</i>	Ethofumesate	96 h, s	EC ₅₀ = 5.4 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Crassostrea virginica</i>	Ethofumesate	96 h, f	EC ₅₀ = 1.7 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Daphnia magna</i>	NC 8493	48 h, ss	EC ₅₀ > 10 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Daphnia magna</i>	NC 8493	48 h, s	EC ₅₀ > 100 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Daphnia magna</i>	NC 20645	48 h, ss	EC ₅₀ > 10 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Daphnia magna</i>	NC 20645	48 h, s	EC ₅₀ > 100 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Daphnia magna</i>	Ethofumesate	21 d, ss	NOEC = 0.32 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Daphnia magna</i>	Ethofumesate	21 d, ss	NOEC = 0.25 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Daphnia magna</i>	Ethofumesate	21 d, ss	NOEC = 1.06 mg a.s./L _{mm}	EFSA Conclusion (2016)
Sediment-dwelling organisms				
<i>Chironomus riparius</i>	Ethofumesate	28 d, s	NOEC = 3.82 mg a.s./L _{im}	EFSA Conclusion (2016)
<i>Chironomus riparius</i>	Ethofumesate	28 d, s	NOEC = 5.33 mg a.s./L _{im}	EFSA Conclusion (2016)
<i>Chironomus riparius</i>	Ethofumesate	28 d, s	NOEC = 14.05 mg a.s./L _{im}	EFSA Conclusion (2016)
Algae				
<i>Pseudokirchneriella subcapitata</i>	Ethofumesate	72 h, s	E _r C ₅₀ = 16.3 mg a.s./L _{mm} E _y C ₅₀ = 9.68 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Anabaena flos-aquae</i>	Ethofumesate	96 h, s	E _r C ₅₀ > 20 mg a.s./L _{nom} E _b C ₅₀ > 20 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Skeletonema subspicatus</i>	Ethofumesate	72 h, s	E _r C ₅₀ > 20 mg a.s./L _{nom} E _b C ₅₀ = 14.5 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Pseudokirchneriella subcapitata</i>	NC 8493	72 h, s	E _r C ₅₀ = 20.7 mg a.s./L _{nom} E _y C ₅₀ = 0.865 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Desmodesmus subspicatus</i>	NC 8493	72 h, s	E _r C ₅₀ = 4.83 mg a.s./L _{mm} E _y C ₅₀ = 1.87 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Pseudokirchneriella subcapitata</i>	NC 20645	72 h, s	E _r C ₅₀ > 10 mg a.s./L _{nom} E _y C ₅₀ > 10 mg a.s./L _{nom}	EFSA Conclusion (2016)
<i>Desmodesmus subspicatus</i>	NC 20645	72 h, s	E _r C ₅₀ = 52.4 mg a.s./L _{mm} E _y C ₅₀ = 8.83 mg a.s./L _{mm}	EFSA Conclusion (2016)
Higher plant				
<i>Lemna minor</i>	Ethofumesate	14 d, ss	E _r C ₅₀ > 52.8 mg a.s./L _{mm} E _b C ₅₀ = 50.4 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Lemna minor</i>	Ethofumesate	7 d, ss	E _r C ₅₀ > 42.0 mg a.s./L _{mm} E _b C ₅₀ = 35.0 mg a.s./L _{mm}	EFSA Conclusion (2016)
<i>Myriophyllum spicatum</i>	Ethofumesate	14 d, s	E _r C ₅₀ = 0.479 mg a.s./L _{mm} E _y C ₅₀ = 0.25 mg a.s./L _{mm}	EFSA Conclusion (2016)
Higher-tier studies (micro- or mesocosm studies)				
-				

s: static; ss: semi-static; f: flow-through; nom: based on nominal concentrations; mm: based on mean measured concentrations; im: based on initial measured concentrations

Bold written values are used for the risk assessment.

zRMS comments:

Endpoints presented in Table 9.5.1-1 are in line with the EU agreed endpoints reported in EFSA Journal 2016;14(1):4374.

Table 9.5.1-2 Endpoints and effect values relevant for the risk assessment for aquatic organisms – Phenmedipham and relevant metabolites

Species	Substance	Exposure System	Results	Reference
Fish				
<i>Oncorhynchus mykiss</i>	Phenmedipham	96 h	LC ₅₀ = 1.71 mg/L (mm) ⁵	Review Report (2004)
<i>Oncorhynchus mykiss</i>	Phenmedipham	96 h	LC ₅₀ = 1.1 mg/L	Review Report (2004)
<i>Oncorhynchus mykiss</i>	MHPC	96 h	LC ₅₀ = 75 mg/L	Review Report (2004)
<i>Oncorhynchus mykiss</i>	Phenmedipham	21 d	NOEC = 0.32 mg/L	Review Report (2004)
-	MHPC	-	NOEC= 0.032 mg/L (Phenmedipham endpoint/10)	-
Aquatic invertebrates				
<i>Daphnia magna</i>	Phenmedipham	48 h	EC ₅₀ = 0.41 mg/L	Review Report (2004)
<i>Daphnia magna</i>	Phenmedipham	48 h	EC ₅₀ = 0.9 mg/L	Review Report (2004)
<i>Daphnia magna</i>	MHPC	48 h	EC ₅₀ = 14 mg/L	Review Report (2004)
<i>Daphnia magna</i>	Phenmedipham	21 d	NOEC = 0.061 mg/L	Review Report (2004)
<i>Daphnia magna</i>	Phenmedipham	21 d	NOEC = 0.025 mg/L	Review Report (2004)
<i>Daphnia magna</i>	MHPC	21 d, ss	NOEC = 5.00 mg/L _{nom}	Scheerbaum (2021e) KCP 10.2.2/01
Sediment-dwelling organisms				
<i>Chironomus riparius</i>	Phenmedipham	28 d	NOEC = 0.37 mg a.s./L	Review Report (2004)
Algae				
<i>Selenastrum capricornutum</i>	Phenmedipham	72 h	E _r C ₅₀ = 0.192 mg/L _{nom} E _b C ₅₀ = 0.086 mg/L _{nom}	DAR (1999) Review Report (2004)
<i>Pseudokirchneriella subcapitata</i>	MHPC	96 h 72 h	E _b C ₅₀ = 30 mg/L _{nom}	Review Report (2004)
		96 h	E _r C ₅₀ = 79 mg/L _{nom} E _b C ₅₀ = 26 mg/L _{nom}	DAR Addendum (2001)
Higher plant				
<i>Lemna minor</i>	Phenmedipham	14 d	E _r C ₅₀ = 3.9 mg/L _{nom} E _b C ₅₀ = 0.23 mg a.s./L _{nom}	DAR (1999) Review Report (2004)
Higher-tier studies (micro- or mesocosm studies)				
-				

nom: based on nominal concentrations

Bold written values are used for the risk assessment

zRMS comments:

Endpoints presented in Table 9.5.1-2 are in line with the EU agreed endpoints reported in Review Report (2004).

The study on toxicity of MHPC to *Daphnia magna* was evaluated by the zRMS and considered acceptable. For details of evaluation, please refer to Appendix 2. The endpoint reported in Table 9.5.1-3 is confirmed to be correct.

⁵ Endpoint based on geometric mean measured concentrations of phenmedipham

Table 9.5.1-3 Endpoints and effect values relevant for the risk assessment for aquatic organisms – HBZ10

Species	Substance	Exposure System	Results	Reference
<i>Daphnia magna</i>	HBZ10	48 h, ss	EC ₅₀ = 3.96 mg product/L _{geomean}	Scheerbaum (2021a) KCP 10.2.1/01
<i>Pseudokirchneriella subcapitata</i>	HBZ10	72 h, s	ErC ₅₀ = 0.827 mg product/L _{geomean} EyC ₅₀ = 0.175 mg product/L _{geomean}	Scheerbaum (2021b) KCP 10.2.1/02
<i>Lemna gibba</i>	HBZ10	7 d, ss	Frond number ErC ₅₀ = 0.286 mg product/L _{geomean} Dry weight ErC ₅₀ = 0.167 mg product/L _{geomean}	Scheerbaum (2021c) KCP 10.2.1/03
<i>Myriophyllum spicatum</i>	HBZ10	14 d, ss	Shoot length ErC ₅₀ = 1.21 mg product/L _{geomean} Fresh weight ErC ₅₀ = 0.852 mg product/L _{geomean} Dry weight ErC ₅₀ = 1.20 mg product/L _{geomean}	Scheerbaum (2021d) KCP 10.2.1/04
Higher-tier studies (micro- or mesocosm studies)				
-				

s: static; ss: semi-static; nom: based on nominal concentrations; geomean: based on geometric mean measured concentrations

zRMS comments:

Studies on toxicity of HBZ10 to aquatic organisms were evaluated by the zRMS and considered acceptable. For details of evaluation, please refer to Appendix 2. Endpoints reported in Table 9.5.1-3 are confirmed to be correct.

It is accepted for the current dossier to not require an acute test on fish with the formulation considering that the available information permits to conclude that one of the aquatic groups (myriophyllum) is clearly more sensitive to both active substances based on able of endpoint below for Ethofumesate, and also considering the available EU endpoint for Phenmedipham on this species from RAR 2017 from which UPL applicant belongs to the task force (This endpoint is not used in the quantitative risk assessment in the current dossier as not yet in force, but is considered as supportive information for the argument allowing to conclude that an acute test on fish with the formulation is not required according to regulation 284/2013).

Mixture toxicity

In line with EFSA Guidance document (2013), in addition to measured toxicity data, mixture toxicity is assessed on the basis of the concentration addition (CA) model. The CA model is based on the following equation, for deriving a predicted EC₅₀ or NOEC value for a mixture of active substances with known toxicity assuming concentration additivity:

$$EC_{50 \text{ mix-CA}} = \sum_{i=1}^n \left(\frac{p_i}{EC_{x_i}} \right)^{-1}$$

where:

n = number of mixture components

p_i = the ith component as a relative fraction of the mixture composition ($\sum p_i$ must be 1)

EC_{x_i} = concentration of component i provoking a % effect (pragmatically, NOEC_i may be inserted too)

Although EFSA decision scheme for mixture toxicity risk assessment is focusing on effect concentrations (EC_x), it may equally well be applied to NOEC data if these are pragmatically considered as low effect concentrations.

To address the acute mixture toxicity to fish, the endpoint for the active substance Ethofumesate derived from a study with the standard test species *Oncorhynchus mykiss* (LC₅₀ = 11.91 mg a.s./L) was used. Nevertheless, the risk assessment is performed using the lowest endpoint for the active substance Ethofumesate (*Cyprinus carpio*; LC₅₀ = 10.92 mg a.s./L).

To address acute mixture toxicity to aquatic invertebrates, the endpoint for the active substance Ethofumesate derived from a study with the standard test species *Daphnia magna* ($EC_{50} = 13.52$ mg a.s./L) was used. Calculations using the lower endpoint for *Crassostrea virginica* ($EC_{50} = 1.7$ mg a.s./L) would lead to unplausible results as for the second active substance Phenmedipham and the formulated product HBZ10 no endpoints for the species *C. virginica* are available. In contrast, for *Daphnia magna* the dataset is complete for both active substances and the formulated product. Nevertheless, the risk assessment to address acute toxicity to aquatic invertebrates is performed using the lowest endpoint for the active substance Ethofumesate.

To address the mixture toxicity to algae and macrophytes, the endpoints based on growth rate (EC_{50}) for both green algae and aquatic plant species were used.

To address the mixture toxicity to macrophytes, the endpoint for the active substance Ethofumesate derived from a study with the standard test species *Lemna minor* ($EC_{50} = 42$ mg a.s./L) was used since no endpoint for *Myriophyllum* was available for the second active substance Phenmedipham. Nevertheless, the risk assessment to address toxicity to macrophytes is performed using the lowest endpoint for the active substance Ethofumesate (*Myriophyllum spicatum*, $EC_{50} = 0.479$ mg a.s./L).

Table 9.5.1-4 — Estimation of mixture L(E)C₅₀/NOEC for aquatic organism assuming concentration additivity (proportion of active substances in the formulation)

Active substances	Concentration of each active substance in formulation (g a.s./L)	p in the mixture	1/(E)C ₅₀ /NOEC (mg a.s./L)	g/L L ₅₀	$\frac{1}{\sum (p_i / L_i E C_{50})}$	1/(E)C ₅₀ /NOEC (g mix-CA/100 mg a.s./L)
Field acute toxicity						
Ethofumesate	1.25	0.50	11.91 ^a	0.0420	0.402	1.01
Phenmedipham	1.25	0.50	1.4	0.455		
Aquatic invertebrates, acute toxicity						
Ethofumesate	1.25	0.50	13.52 ^a	0.0320	0.26	0.206
Phenmedipham	1.25	0.50	0.44	0.23		
Algae						
Ethofumesate	1.25	0.50	16.3	0.0307	0.43	0.280
Phenmedipham	1.25	0.50	0.192	0.46		
Macrophytes						
Ethofumesate	1.25	0.50	42 ^a	0.0119	0.146	0.14
Phenmedipham	1.25	0.50	3.0	0.128		

^a To address the mixture toxicity, the endpoint for the respective standard test species was used for the calculations

^b Endpoint based on growth rate (EC_{50}) as given in the DAR Phenmedipham (1999)

Step 1 of EFSA decision scheme	Are measured toxicity data ($EC_{x,PP}$) available for the given endpoint?
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For both formulation ($EC_{x,PP}$) and a.s. ($EC_{x,a.s.}$): Go to Step 2
 aquatic invertebrates, algae, macrophytes
 Endpoints only available for the a.s.: Go to Step 2
 acute toxicity to fish

Step 2 of EFSA decision scheme	Check the plausibility of the measured formulation toxicity ($EC_{x,PP}$) against the calculated mixture toxicity $EC_{x,mix-CA}$ (assuming CA) for exactly the mixture composition of the a.s. in the formulation ($EC_{x,PP}$) by means of the model deviation ratio ($MDR = EC_{x,mix-CA} / EC_{x,PP}$)
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Action needed:

In order to determine if the active substances may act more (i.e., synergistically) or less (i.e., antagonistically) than expected by CA, the measured formulation toxicity ($EC_{x,PP}$) is compared against the calculated mixture toxicity $EC_{x,mix-CA}$ for exactly the mixture composition of the active substances in the formulation ($EC_{x,PP}$) by means of the Model Deviation Ratio (MDR):

$$MDR = \frac{ECx_{mix-CA} \text{ (calculated mixture toxicity)}}{ECx_{PP} \text{ (measured mixture toxicity)}}$$

Table 9.5.1-5 Comparison of calculated and measured mixture toxicity for invertebrates, algae and macrophytes

$EC_{50-mix} (L)$ (mg a.s./L)	EC_{50-mix} (mg a.s./L)*	MDR
Aquatic invertebrates, acute toxicity		
0.20	0.01	0.20
Algae		
0.20	0.24	1.20
Macrophytes		
0.4	0.0425	0.68

a) Measured EC_{50-mix} (L, mg a.s./L), expressed in terms of sum of both active substances. The endpoints were calculated assuming 250 g total active substances/L product and a product density of 0.977 g/mL and using endpoints for the standard test species *Daphnia magna* (aquatic invertebrates), *Pseudokirchneriella subcapitata* (algae) and *Lemna minor* (macrophytes).

Based on the calculated MDR values, the observed and calculated mixture toxicities for aquatic invertebrates and algae are in agreement (MDR: 0.2–5). Thus, it can be assumed that CA approximately holds for the mixture and the risk assessment for acute toxicity to aquatic invertebrates and algae could be conducted based on the measured toxicity (EC_{50-mix}). For aquatic macrophytes, the calculated MDR value is > 5, indicating a possible synergistic effect. Thus, the risk assessment for aquatic macrophytes should be based on the measured endpoint for the formulated product.

Answer: If MDR = 0.2–5 (CA approximately holds for the mixture): Go to Step 3 (aquatic invertebrates, algae)
If MDR > 5 (synergistic mixture toxicity is indicated): Go to Step 10 (macrophytes)

Step 3 of EFSA decision scheme	Check whether the mixture composition in the formulation study giving the measured mixture toxicity (EC_{50-mix}) in terms of the relative proportions of the individual a.s. is similar to the mixture composition at the PEC_{mix} . As a direct comparison on the basis of the relative proportions of the a.s. at the EC_{50-mix} with the relative proportion at the PEC_{mix} is not informative as such, the comparison is done based on calculated mixture toxicity (assuming CA) for both mixture compositions. Therefore, calculate $EC_{50-mix, CA}$ for the mixture composition of the a.s. at the PEC_{mix} and compare with the estimate calculated for the formulation (as already done in step 2 above).
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Action needed:

Before using the measured mixture toxicity in the risk assessment for aquatic invertebrates and algae, it is necessary to check whether the mixture composition in the formulation studies giving the measured toxicities (EC_{50-mix}) in terms of the relative proportions of the individual active substances is similar to the mixture composition at the PEC_{mix} . This comparison should be based on calculated mixture toxicity (assuming CA) for both mixture compositions. Thus, the $EC_{50-mix, CA}$ for the mixture composition of the active substances at the PEC_{mix} is calculated and compared with the respective estimate calculated for the formulation.

The mixture toxicity for the mixture composition at the FOCUS Steps 1–3 (considering all relevant exposure scenario) PEC_{mix} is calculated to be 0.80 to 3.51 mg/L for acute toxicity to aquatic invertebrates and 0.38 to 1.92 mg/L for toxicity to algae. The respective $EC_{50-mix, CA}$ (a.s. in PPP)/ $EC_{50-mix, CA}$ (a.s. in PEC_{mix}) ratios are calculated to be 0.23 to 1.0 and 0.20 to 1.0. Table 9.5.1-6 presents the calculated mixture toxicity for the mixture composition at the maximum FOCUS Step 1 PEC_{mix} resulting from the worst-case intended use of HBZ10 in best crops (use group 2–3 + 2.4 L product/ha, 6-day interval), while Table 9.5.1-7 presents the respective $EC_{50-mix, CA}$ (a.s. in PPP)/ $EC_{50-mix, CA}$ (a.s. in PEC_{mix}) ratios.

Table 9.5.1.6 — Estimation of the mixture LC₅₀/NOEC for aquatic organism assuming dose additivity (proportion of active substances at PEC_{mixture})

Active substance	Maximum PEC _{sub} = (mg a.s./L)	as in the mixture (PEC _{mixture})	LC ₅₀ (mg a.s./L)	poT.C ₅₀	Σ(poT.C ₅₀)	LC ₅₀ mixture (a.s.) at PEC _{mixture} (Σ mg a.s./L)
Aquatic invertebrates, acute toxicity						
Ethofenprox	0.267440	0.322	0.32	0.0613	0.424	2.02
Phenmedipham	0.056060	0.128	0.41	0.424		
Algae						
Ethofenprox	0.267440	0.322	0.4	0.0507	0.652	1.08
Phenmedipham	0.056060	0.128	0.102	0.002		

Σ worst-case PEC_{sub} values at step 1 (see groups 3 for both active substances)

Table 9.5.1.7 — Comparison of calculated mixture toxicity for the formulation and at the PEC_{mixture}

EC ₅₀ mixture (a.s.) in PPP (Σ mg a.s./L)	EC ₅₀ mixture (a.s.) (a.s.) at PEC _{mixture} (Σ mg a.s./L)	Ratio EC ₅₀ mixture (a.s.) in PPP/EC ₅₀ mixture (a.s.) (a.s.) at PEC _{mixture})
Aquatic invertebrates, acute toxicity		
0.322	2.02	0.42
Algae		
0.322	1.08	0.42

The calculated ratios for aquatic invertebrates and algae lie not within the recommended range of 0.8–1.2 of the relative proportions of active substances as contained in PPP and at the PEC_{mixture}. Thus, the calculated mixture toxicity (EC₅₀mixture (a.s.)) can be used for assessing the acute risk for aquatic invertebrates and algae.

Answer:	If EC ₅₀ mixture (a.s.) in PPP/EC ₅₀ mixture (a.s.) (a.s.) at PEC _{mixture}) is not within 0.8–1.2 (mixture similar). Go to Step 5 (aquatic invertebrates, algae).
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Step 5 of EFSA decision scheme

The measured mixture toxicity cannot be used directly for assessing the acute risk for aquatic organisms. As an additional step, it is checked if the measured mixture toxicity (EC₅₀measured) is determined by the toxicity of a single component by means of the Toxic Unit (TU) approach:

$$\sum_{i=1}^n TU_i = \sum_{i=1}^n \frac{P_i}{ECx_i}$$

The estimation of TUs for each component and their contribution to the mixture toxicity is shown in Table 9.5.1.8.

Table 9.5.1.8 — Identification of the “driver” of the measured mixture toxicity to HBZ10

TUCL5 scenario	Aquatic invertebrates		Algae	
	Contribution to TU _{measured} (%)		Contribution to TU _{measured} (%)	
	Ethofenprox	Phenmedipham	Ethofenprox	Phenmedipham
Step 1	0.4	99.6	0.4	99.6

Values in bold represent a contribution of more than 90% to the toxicity of formulation. AL SNC LOEC LQ01

As shown in the above Table 9.5.1.8, the active substance Phenmedipham contributes more than 90% to the toxicity of formulation HBZ10 and thus drives the overall mixture toxicity to aquatic invertebrates and algae. The risk assessment for these trophic levels can be based on the single substance toxicity data of Phenmedipham (Step 6 of EFSA decision scheme).

Step 7 of EFSA decision scheme	Fish-acute-toxicity: Is there evidence that synergistic interactions between mixture components might occur (e.g., based on toxicological knowledge from literature or from counter-checking measured and calculated mixture toxicity in other species) which cannot be ruled out for the given species with sufficient certainty?
Answer:	No (mixture toxicity calculation feasible): Go to Step 8 Based on the available data, it can be assumed that there is no evidence for synergistic interactions between mixture components and calculation of mixture toxicity for fish is feasible.
Step 11 of EFSA decision scheme	Macrophytes: Is it possible that co-formulants or metabolites contributed to the toxicity measured in the study with the formulated product?
Answer:	No (synergism as indicated in Step 2 not confirmed): Go to Step 8 Based on the available data, it can be assumed that there is no evidence for synergistic interactions between mixture components and calculation of mixture toxicity for macrophytes is feasible. Available endpoints indicate no higher toxicity of the respective metabolite compared to the respective parent.
Step 8 of EFSA decision scheme	Step 8 (fish and macrophytes) Conduct a mixture RA based on calculated mixture toxicity.

The evaluation of the mixture toxicity risks for aquatic (and sediment-dwelling) organisms was performed in accordance with the “Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters in the context of Regulation (EC) No 1107/2009”, as provided by the Commission Services (SANTE-2015-00080, 15. January 2015) and in EFSA Journal 2013;11(7):3290 (Aquatic Guidance Document, abbreviated as EFSA, 2013). The whole mixture assessment is based on the model of concentration addition (CA) and particularly the decision scheme as provided by EFSA (2013, section 10.3.11) was applied. The calculations were performed with the tool “AGD_AquaMix” version 1.22. To keep the assessment concise the focus of this section of this registration report is on the parts of the assessment leading to the most critical results and to comments raised during commenting period. It does not cover each calculation step for each organism group. Further documentation of the full results is given in the attached mixture risk calculation files as described below:

- “AGD_AquaMix_v1.22 - Use group 1”, for use group 1 (6×1.2 L product/ha, 5-day interval) mixture toxicity risk assessment
- “AGD_AquaMix_v1.22 - Use group 2”, for use group 2 (3×2.4 L product/ha, 6-day interval) mixture toxicity risk assessment
- “AGD_AquaMix_v1.22 - Use group 3”, for use group 3 (5×1.2 L product/ha, 7-day interval) mixture toxicity risk assessment
- “AGD_AquaMix_v1.22 - Use group 4”, for use group 4 (3×1.8 L product/ha, 6-day interval) mixture toxicity risk assessment
- “AGD_AquaMix_v1.22 - Use group 5”, for use group 5 (3×2.4 L product/ha, 9-day interval) mixture toxicity risk assessment

Table Błąd! W dokumencie nie ma tekstu o podanym stylu.1-1: Summary of assessment steps considered for the mixture risk assessment for use groups 1, 2, 3, 4, and 5

Steps	Conclusion on the Steps			
	Fish	Invertebrates	Algae	Macrophytes
Step 1: data available?	Endpoints only available for the a.s., go to Step 7.	Endpoints available for a.s. and the ppp, go to Step 2.	Endpoints available for a.s. and the ppp, go to Step 2.	Endpoints available for a.s. and the ppp, go to Step 2.
Step 2: apparent synergism or antagonism?		The MDR is between 0.2-5. No antagonism or synergism is indicated. Thus, the "concentration addition" concept holds, go to Step 3.	The MDR is between 0.2-5. No antagonism or synergism is indicated. Thus, the "concentration addition" concept holds, go to Step 3.	The MDR is >5. Thus, synergism is indicated, go to Step 10.
Step 3: mixture similar or not?		Different assessment factor or additional data available, go to Step 8.	Mixture sometimes similar. Some scenario can be assessed via product test, go either to Step 4 or 5.	Different assessment factor or additional data available, go to Step 8.
Step 4: ETRmix assessment (ECxPPP)			Acceptable risk have been found in all scenarios in FOCUS step 1-3.	
Step 5: driver available?			There is a driver for algae in all scenarios. Assess driver, go to Step 6.	
Step 6: driver assessment			Risk acceptable for all scenarios in FOCUS step 1-3.	
Step 7: synergism assessment (few data)	Mixture toxicity calculation feasible: go to Step 8			
Step 8b: RQmix assessment	Risk acceptable for all scenarios in FOCUS step 1-3.	Risk acceptable for all scenarios, if risk mitigation is applied (FOCUS Step 4).	Risk acceptable for all scenarios in FOCUS step 1-3.	Risk acceptable for all scenarios in FOCUS step 1-3.
Step 10: synergism assessment				Measured mixture toxicity plausible: go to Step 3

Overview of the assessment steps: Table Błąd! W dokumencie nie ma tekstu o podanym stylu.1-1 gives a summary of the decisions made for each organism group during the mixture risk assessment with respect to the decision scheme as provided by EFSA (2013, section 10.3.11). A discussion of all details of every decision is not intended in this section of this registration report. Further in-depth justification and explanation for the decisions made are documented in the attached mixture risk calculation files as listed above. However, at least data for some important steps are documented in this section of this registration report, beginning with the check for (and potentially assessment of) synergistic or antagonistic effects (Step 2 and Steps 7 and 10) as well as the RQ_{mix} calculation results for the assessed FOCUS Scenarios (Steps 4 and 8b).

Step 2: MDR calculation to check for synergistic or antagonistic effects

Table Błąd! W dokumencie nie ma tekstu o podanym stylu.1-2: Calculated mixture toxicity and MDR for each group of organisms

Species	Active substance	Concentration (C _i) in formulation (g a.s./L)	P _i	EC _{xi} (mg a.s./L)	EC _{xmix- CA} (mg sum a.s. /L)	EC _{xPPP} (mg sum a.s./L)	MDR
Fish, acute toxicity							
<i>Oncorhynchus mykiss</i>	Ethofumesate	125	0.5	11.91 ^{a)}	2.014	-	-
<i>Oncorhynchus mykiss</i>	Phenmedipham	125	0.5	1.1			
Invertebrates, acute toxicity							
<i>Daphnia magna</i>	Ethofumesate	125	0.5	13.52 ^{a)}	0.796	1.013	0.79
<i>Daphnia magna</i>	Phenmedipham	125	0.5	0.41			
Algae							
<i>Pseudokirchneriella subcapitata</i>	Ethofumesate	125	0.5	16.3	0.380	0.212	1.79
<i>Selenastrum capricornutum</i>	Phenmedipham	125	0.5	0.192 [*]			
Macrophytes							
<i>Lemna minor</i>	Ethofumesate	125	0.5	> 42 ^{a)}	7.137	0.043	167.02
<i>Lemna minor</i>	Phenmedipham	125	0.5	3.9 [*]			

Since MDR for invertebrates and algae = 0.2 – 5 → Go to Step 3 for invertebrates and algae (concentration addition (CA) approximately holds for the calculated mixture);

Since MDR for macrophytes > 5 → Go to Step 10 for macrophytes (the calculated mixture is more toxic than CA, i.e. synergistic)

Since no acute toxicity data with the HBZ10 formulation is available for fish → Go to Step 7 for fish

Step 7, Step 9 and Step 10: Assessment of possible synergism effects

Step 7 (for fish):

No acute toxicity data with the HBZ10 formulation is available for fish, triggering possible synergistic interactions between mixture components. Based on the available data, it can be assumed that there is no evidence for synergistic interactions between mixture components and calculation of mixture toxicity for fish is feasible. This organism has therefore been further assessed under Step 8.

Step 10 (for macrophytes):

According to the MDR calculation, a discussion regarding synergism is indicated for macrophytes to check whether co-formulants or metabolites are contributing to the toxicity measured in the study with the formulated product. Based on the available data, it can be assumed that there is no evidence for synergistic interactions between mixture components and calculation of mixture toxicity for macrophytes is feasible. Available endpoints indicate no higher toxicity of the respective metabolite compared to the respective parent. This organism has therefore been further assessed under Step 3.

Step 3 Comparison of mixture composition of PPP and PEC_{mix}

Step 3 (for invertebrates and macrophytes):

According to Step 3 it has to be checked whether the mixture composition in the formulation is similar to the mixture composition at PEC_{mix} (which is the sum of PEC_i of individual active substances). However, additional data have been used in the a.s. assessment for invertebrates and macrophytes ($EC_{50} = 1.7$ mg a.s./L for *Crassostrea virginica* and $E_rC_{50} = 0.479$ mg a.s./L for *Myriophyllum spicatum*). Therefore, it is not appropriate to use product data and not necessary to apply Step 3.

Conclusion:

→ Go directly to Step 8 for invertebrates (even if mixture is similar, Step 3 is not reasonable).

Step 3 (for algae):

According to Step 3 it has to be checked whether the mixture composition in the formulation is similar to the mixture composition at PEC_{mix} (which is the sum of PEC_i of individual active substances). Therefore, the “ $EC_{x_{mix-CA}}$ (a.s. in PPP) / $EC_{x_{mix-CA}}$ (a.s. in PEC_{mix})” ratios were calculated.

In case the ratio is in the range of 0.8–1.2 (mixture similar), the risk assessment can be based on the $EC_{x_{PPP}}$ (Step 4).

In case the ratio is outside the range of 0.8–1.2 (i.e. mixture not similar), the endpoint $EC_{x_{mix-CA}}$ normalized to the mixture composition at PEC_{mix} (reported as “ $EC_{x_{mix-CA}}$ (a.s. in PEC_{mix})” in EFSA, 2013, and the following parts of this report) has to be used to calculate the risk (Step 4/5 or Step 8, respectively).

The decision how the mixture risk assessment is conducted depends on the organism group as well as the assessed FOCUS Scenarios. The overall mixture risk assessment results are given in **Błąd! Nie można znaleźć źródła odwołania.5**, in which it is documented if product or calculated endpoint data (according to Step 3) have to be used. Further in-depth justification and explanation are documented in the attached mixture risk calculation files.

Step 5: Driver detection

The decision how the mixture risk assessment is conducted depends on the organism group as well as the assessed FOCUS Scenarios. The overall driver identification for the risk assessment of particular FOCUS Scenarios is given in **Błąd! Nie można znaleźć źródła odwołania.** and 9.5.1-4, according to Step 5. Further in-depth justification and explanation are documented in the attached mixture risk calculation files.

Table Błąd! W dokumencie nie ma tekstu o podanym stylu.1-3: Summary of assessment steps considered for the mixture risk assessment for use groups 1, 2, and 3

Focus scenarios	Fish		Invertebrates		Algae		Macrophytes	
	Phenmedipham	Ethofumesate	Phenmedipham	Ethofumesate	Phenmedipham	Ethofumesate	Phenmedipham	Ethofumesate
Step 1	-	-	-	-	-	-	-	Driver
Step 2								
N-Europe	-	-	-	-	Driver	-	-	Driver
S-Europe	-	-	-	-	Driver	-	-	Driver
Step 3								
D3/ditc	Driver	-	-	-	Driver	-	-	-

h early								
D4/pond early	-	-	-	-	Driver	-	-	Driver
D4/stream early	Driver	-	-	-	Driver	-	-	-
R1/pond early	-	-	-	-	Driver	-	-	Driver
R1/stream early	-	-	-	-	Driver	-	-	Driver
R3/stream early	-	-	-	-	Driver	-	-	Driver
D3/ditch late	Driver	-	-	-	Driver	-	-	-
D4/pond late	-	-	-	-	Driver	-	-	Driver
D4/stream late	Driver	-	-	-	Driver	-	-	-
R1/pond late	-	-	-	-	Driver	-	-	Driver
R1/stream late	-	-	-	-	Driver	-	-	Driver
R3/stream late	-	-	-	-	Driver	-	-	Driver

Columns in grey should not be considered relevant according to Step 3 decision scheme

Table Błąd! W dokumencie nie ma tekstu o podanym stylu.1-4: Summary of assessment steps considered for the mixture risk assessment for use groups 4, and 5

Focus scenarios	Fish		Invertebrates		Algae		Macrophytes	
	Phenmedipham	Ethofumesate	Phenmedipham	Ethofumesate	Phenmedipham	Ethofumesate	Phenmedipham	Ethofumesate
Step 1	-	-	-	-	Driver	-	-	Driver
Step 2	-	-	-	-		-	-	
N-Europe	-	-	-	-	Driver	-	-	Driver
S-Europe	-	-	-	-	Driver	-	-	Driver
Step 3	-	-	-	-		-	-	
D3/ditch early	-	-	-	-	Driver	-	-	Driver

D4/pond early	-	-	-	-	Driver	-	-	Driver
D4/stream early	-	-	-	-	Driver	-	-	Driver
R1/pond early	-	-	-	-	Driver	-	-	Driver
R1/stream early	-	-	-	-	Driver	-	-	Driver
R3/stream early	-	-	-	-	Driver	-	-	Driver
D3/ditch late	-	-	-	-	Driver	-	-	Driver
D4/pond late	-	-	-	-	Driver	-	-	Driver
D4/stream late	-	-	-	-	Driver	-	-	Driver
R1/pond late	-	-	-	-	Driver	-	-	Driver
R1/stream late	-	-	-	-	Driver	-	-	Driver
R3/stream late	-	-	-	-	Driver	-	-	Driver

Columns in grey should not be considered relevant according to Step 3 decision scheme

Step 4 and Step 8b: Mixture risk assessment based on calculated mixture toxicity

Decisions taken when using the scheme as provided by EFSA (2013, section 10.3.11) lead to several assessment steps, which give a conclusion on the risk of a mixture or provide additional information important for the assessment. Below are given the conclusions of different steps of the mixture risk assessment:

- Step 2** and associated steps, in which the question is answered if concentration addition can be assumed (i.e. a standard mixture toxicity risk assessment is appropriate) or if an antagonism/synergism is possible (more detailed information on Step 2 is given above). This is important to derive if further, specific considerations have to be made in the risk assessment. Associated steps are Step 7 (fish) and Step 10 (macrophytes). Other organisms (invertebrates and algae) were directly assessed under Step 3.
- Step 3** results should only be considered for algae since other organisms (invertebrates and macrophytes) have additional data available. Therefore, algae were further assessed under Step 4 and 5. These two organism groups were thus further evaluated under Step 8.
- Step 4** has been done for algae only, since other organisms (invertebrates and macrophytes) have additional data available. Scenarios passing the risk assessment can be used for performing the mixture risk assessment. Other scenarios are considered relevant for Step 5 assessment.
- Step 5** has been done for algae only, since other organisms (invertebrates and macrophytes) have additional data available. The risk for algae was found to be driven by Phenmedipham in all use groups and all scenarios (see tables 9.5.1-4 and 9.5.1-5 above). Therefore, relevant

- scenarios considered in Step 5 assessment for algae should be based on a Phenmedipham active substance (the driver). These scenarios are marked in grey in Table 9.5.1-5 below (full mixture toxicity assessment). Please refer to the individual a.s. risk assessment for these ones.
- e) **Step 6** has to be considered for algae relevant scenarios, according to previous Steps 4 and 5. The individual Phenmedipham a.s. risk assessment shows acceptable risk without mitigation measures (all acceptable at FOCUS Step 3).
 - f) **Step 7** for fish was finally assessed under Step 8 as no synergism effects were found and thus mixture toxicity calculation was considered feasible.
 - g) **Step 8 (b)** with the assessment results for cases where product data are not usable (according to Step 3), and the risk assessment has to be based on calculated mixture toxicity.
 - h) **Step 10** for macrophytes was finally assessed under Step 3 as no evidence was found regarding synergism effects related to co-formulants or metabolites, and thus mixture toxicity calculation was considered feasible.

The full mixture toxicity risk assessment is presented in **Błąd! Nie można odnaleźć źródła odwołania.-5** below. The assessment is based on the risk quotient (RQ_{mix}); the RQ_{mix} is compared to the trigger value of 1 for RQ_{mix} . Values below the trigger indicating a high risk are marked in **bold**.

Table Błąd! W dokumencie nie ma tekstu o podanym stylu.1-5: Full mixture toxicity risk assessment according to Step 8 for all use groups

Scenario	PEC _{sw} (µg/L)		RQ _{mix}											
	Phenmedipham	Ethofumesate	PEC/RAC Phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Fish	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Invertebrate s	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Algae	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Macroph ytes
Use group 1: 6 × 1.2 L product/ha, 5-day interval; early and late applications														
Step 1	0.028032	0.267494	2.55	2.45	5.00	6.84	15.73	22.57	1.46	0.16	1.62	0.07	5.58	5.66
Step 2														
N-Europe	0.019797	0.031636	1.80	0.29	2.09	4.83	1.86	6.69	1.03	0.02	1.05	0.05	0.66	0.71
S-Europe	0.039594	0.059129	3.60	0.54	4.14	9.66	3.48	13.14	2.06	0.04	2.10	0.10	1.23	1.34
Step 3														
D3/ditch early	0.000463	0.000465	0.04	0.00	0.05	0.11	0.03	0.14	0.02	0.00	0.02	0.00	0.01	0.01
D4/pond early	0.00009	0.000648	0.01	0.01	0.01	0.02	0.04	0.06	0.00	0.00	0.01	0.00	0.01	0.01
D4/stream early	0.000823	0.000641	0.07	0.01	0.08	0.20	0.04	0.24	0.04	0.00	0.04	0.00	0.01	0.02
R1/pond early	0.000275	0.001003	0.03	0.01	0.03	0.07	0.06	0.13	0.01	0.00	0.01	0.00	0.02	0.02
R1/stream early	0.006015	0.008491	0.55	0.08	0.62	1.47	0.50	1.97	0.31	0.01	0.32	0.02	0.18	0.19
R3/stream early	0.005196	0.01378	0.47	0.13	0.60	1.27	0.81	2.08	0.27	0.01	0.28	0.01	0.29	0.30
D3/ditch late	0.000463	0.000465	0.04	0.00	0.05	0.11	0.03	0.14	0.02	0.00	0.02	0.00	0.01	0.01
D4/pond late	0.000108	0.00087	0.01	0.01	0.02	0.03	0.05	0.08	0.01	0.00	0.01	0.00	0.02	0.02
D4/stream late	0.001022	0.000919	0.09	0.01	0.10	0.25	0.05	0.30	0.05	0.00	0.05	0.00	0.02	0.02
R1/pond late	0.000112	0.000841	0.01	0.01	0.02	0.03	0.05	0.08	0.01	0.00	0.01	0.00	0.02	0.02
R1/stream late	0.003455	0.01216	0.31	0.11	0.43	0.84	0.72	1.56	0.18	0.01	0.19	0.01	0.25	0.26
R3/stream late	0.004425	0.009325	0.40	0.09	0.49	1.08	0.55	1.63	0.23	0.01	0.24	0.01	0.19	0.21
Step 4														
R1/stream early 10 m NSB + 10 m VFS	0.002276	0.008491**	0.21	0.08	0.28	0.56	0.50	1.05	0.12	0.01	0.12	0.01	0.18	0.18
R1/stream early 20 m NSB + 20 m VFS	0.001425	0.008491**	0.13	0.08	0.21	0.35	0.50	0.85	0.07	0.01	0.08	0.00	0.18	0.18
R3/stream early 10 m NSB + 10 m VFS	0.002695	0.006285	0.25	0.06	0.30	0.66	0.37	1.03	0.14	0.00	0.14	0.01	0.13	0.14
R3/stream early 20 m NSB + 20 m VFS	0.001413	0.002504	0.13	0.02	0.15	0.34	0.15	0.49	0.07	0.00	0.08	0.00	0.05	0.06
R1/stream late 10 m NSB + 10 m VFS	0.001508	0.005386	0.14	0.05	0.19	0.37	0.32	0.68	0.08	0.00	0.08	0.00	0.11	0.12
R3/stream late 10 m NSB + 10 m VFS	0.00201	0.00425	0.18	0.04	0.22	0.49	0.25	0.74	0.10	0.00	0.11	0.01	0.09	0.09
Use group 2: 3 × 2.4 L product/ha, 6-day interval; early and late applications														
Step 1	0.056064	0.267494	5.10	2.45	7.55	13.67	15.73	29.41	2.92	0.16	3.08	0.14	5.58	5.73
Step 2														
N-Europe	0.021845	0.037379	1.99	0.34	2.33	5.33	2.20	7.53	1.14	0.02	1.16	0.06	0.78	0.84
S-Europe	0.04369	0.06948	3.97	0.64	4.61	10.66	4.09	14.74	2.28	0.04	2.32	0.11	1.45	1.56
Step 3														
D3/ditch early	0.001143	0.001145	0.10	0.01	0.11	0.28	0.07	0.35	0.06	0.00	0.06	0.00	0.02	0.03
D4/pond early	0.00008	0.000528	0.01	0.00	0.01	0.02	0.03	0.05	0.00	0.00	0.00	0.00	0.01	0.01
D4/stream early	0.000959	0.001023	0.09	0.01	0.10	0.23	0.06	0.29	0.05	0.00	0.05	0.00	0.02	0.02

Scenario	PECsw (µg/L)		RQmix											
	Phenmedipham	Ethofumesate	PEC/RAC Phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Fish	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Invertebrates	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Algae	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Macrophytes
R1/pond early	0.000227	0.00049	0.02	0.00	0.03	0.06	0.03	0.08	0.01	0.00	0.01	0.00	0.01	0.01
R1/stream early	0.007108	0.008373	0.65	0.08	0.72	1.73	0.49	2.23	0.37	0.01	0.38	0.02	0.17	0.19
R3/stream early	0.008977	0.01958	0.82	0.18	1.00	2.19	1.15	3.34	0.47	0.01	0.48	0.02	0.41	0.43
D3/ditch late	0.001142	0.001144	0.10	0.01	0.11	0.28	0.07	0.35	0.06	0.00	0.06	0.00	0.02	0.03
D4/pond late	0.000108	0.000836	0.01	0.01	0.02	0.03	0.05	0.08	0.01	0.00	0.01	0.00	0.02	0.02
D4/stream late	0.001001	0.001	0.09	0.01	0.10	0.24	0.06	0.30	0.05	0.00	0.05	0.00	0.02	0.02
R1/pond late	0.000251	0.00188	0.02	0.02	0.04	0.06	0.11	0.17	0.01	0.00	0.01	0.00	0.04	0.04
R1/stream late	0.007059	0.02466	0.64	0.23	0.87	1.72	1.45	3.17	0.37	0.02	0.38	0.02	0.51	0.53
R3/stream late	0.005442	0.01649	0.49	0.15	0.65	1.33	0.97	2.30	0.28	0.01	0.29	0.01	0.34	0.36
Step 4														
R1/stream early 10 m NSB + 10 m VFS	0.003216	0.003797	0.29	0.03	0.33	0.78	0.22	1.01	0.17	0.00	0.17	0.01	0.08	0.09
R1/stream early 20 m NSB + 20 m VFS	0.001682	0.001508	0.15	0.01	0.17	0.41	0.09	0.50	0.09	0.00	0.09	0.00	0.03	0.04
R3/stream early 10 m NSB + 10 m VFS	0.004089	0.008934	0.37	0.08	0.45	1.00	0.53	1.52	0.21	0.01	0.22	0.01	0.19	0.20
R3/stream early 20 m NSB + 20 m VFS	0.002144	0.003558	0.19	0.03	0.23	0.52	0.21	0.73	0.11	0.00	0.11	0.01	0.07	0.08
R1/stream late 10 m NSB + 10 m VFS	0.0032	0.01121	0.29	0.10	0.39	0.78	0.66	1.44	0.17	0.01	0.17	0.01	0.23	0.24
R1/stream late 20 m NSB + 20 m VFS	0.001675	0.00446	0.15	0.04	0.19	0.41	0.26	0.67	0.09	0.00	0.09	0.00	0.09	0.10
R3/stream late 10 m NSB + 10 m VFS	0.002472	0.007514	0.22	0.07	0.29	0.60	0.44	1.04	0.13	0.00	0.13	0.01	0.16	0.16
R3/stream late 20 m NSB + 20 m VFS	0.002472*	0.002992	0.22	0.03	0.25	0.60	0.18	0.78	0.13	0.00	0.13	0.01	0.06	0.07
Use group 3: 5 × 1.2 L product/ha, 7-day interval; early and late applications														
Step 1	0.02803	0.222911	2.55	2.04	4.59	6.84	13.11	19.95	1.46	0.14	1.60	0.07	4.65	4.73
Step 2														
N-Europe	0.016156	0.025986	1.47	0.24	1.71	3.94	1.53	5.47	0.84	0.02	0.86	0.04	0.54	0.58
S-Europe	0.032312	0.049198	2.94	0.45	3.39	7.88	2.89	10.77	1.68	0.03	1.71	0.08	1.03	1.11
Step 3														
D3/ditch early	0.000507	0.000508	0.05	0.00	0.05	0.12	0.03	0.15	0.03	0.00	0.03	0.00	0.01	0.01
D4/pond early	0.000071	0.00051	0.01	0.00	0.01	0.02	0.03	0.05	0.00	0.00	0.00	0.00	0.01	0.01
D4/stream early	0.00065	0.000505	0.06	0.00	0.06	0.16	0.03	0.19	0.03	0.00	0.03	0.00	0.01	0.01
R1/pond early	0.000122	0.000789	0.01	0.01	0.02	0.03	0.05	0.08	0.01	0.00	0.01	0.00	0.02	0.02
R1/stream early	0.003654	0.007698	0.33	0.07	0.40	0.89	0.45	1.34	0.19	0.00	0.20	0.01	0.16	0.17
R3/stream early	0.004127	0.008936	0.38	0.08	0.46	1.01	0.53	1.53	0.21	0.01	0.22	0.01	0.19	0.20
D3/ditch late	0.000507	0.000508	0.05	0.00	0.05	0.12	0.03	0.15	0.03	0.00	0.03	0.00	0.01	0.01
D4/pond late	0.000086	0.000705	0.01	0.01	0.01	0.02	0.04	0.06	0.00	0.00	0.00	0.00	0.01	0.01

Scenario	PECsw (µg/L)		RQmix											
	Phenmedipham	Ethofumesate	PEC/RAC Phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Fish	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Invertebrates	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Algae	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Macrophytes
D4/stream late	0.000815	0.00075	0.07	0.01	0.08	0.20	0.04	0.24	0.04	0.00	0.04	0.00	0.02	0.02
R1/pond late	0.00009	0.000657	0.01	0.01	0.01	0.02	0.04	0.06	0.00	0.00	0.01	0.00	0.01	0.01
R1/stream late	0.002533	0.006682	0.23	0.06	0.29	0.62	0.39	1.01	0.13	0.00	0.14	0.01	0.14	0.15
R3/stream late	0.003292	0.006815	0.30	0.06	0.36	0.80	0.40	1.20	0.17	0.00	0.18	0.01	0.14	0.15
Step 4														
R1/stream early 10 m NSB + 10 m VFS	0.001653	0.007698**	0.15	0.07	0.22	0.40	0.45	0.86	0.09	0.00	0.09	0.00	0.16	0.16
R3/stream early 10 m NSB + 10 m VFS	0.00188	0.008936**	0.17	0.08	0.25	0.46	0.53	0.98	0.10	0.01	0.10	0.00	0.19	0.19
R1/stream late 10 m NSB + 10 m VFS	0.001148	0.006682**	0.10	0.06	0.17	0.28	0.39	0.67	0.06	0.00	0.06	0.00	0.14	0.14
R3/stream late 10 m NSB + 10 m VFS	0.001496	0.006815**	0.14	0.06	0.20	0.36	0.40	0.77	0.08	0.00	0.08	0.00	0.14	0.15
Use group 4: 3 × 1.8 L product/ha, 6-day interval; early and late applications														
Step 1	0.042048	0.20062	3.82	1.84	5.66	10.26	11.80	22.06	2.19	0.12	2.31	0.11	4.19	4.30
Step 2														
N-Europe	0.016384	0.028034	1.49	0.26	1.75	4.00	1.65	5.65	0.85	0.02	0.87	0.04	0.59	0.63
S-Europe	0.032768	0.05211	2.98	0.48	3.46	7.99	3.07	11.06	1.71	0.03	1.74	0.08	1.09	1.17
Step 3														
D3/ditch early	0.000857	0.001181	0.08	0.01	0.09	0.21	0.07	0.28	0.04	0.00	0.05	0.00	0.02	0.03
D4/pond early	0.000057	0.000386	0.01	0.00	0.01	0.01	0.02	0.04	0.00	0.00	0.00	0.00	0.01	0.01
D4/stream early	0.000719	0.000976	0.07	0.01	0.07	0.18	0.06	0.23	0.04	0.00	0.04	0.00	0.02	0.02
R1/pond early	0.000165	0.000351	0.02	0.00	0.02	0.04	0.02	0.06	0.01	0.00	0.01	0.00	0.01	0.01
R1/stream early	0.00517	0.005923	0.47	0.05	0.52	1.26	0.35	1.61	0.27	0.00	0.27	0.01	0.12	0.14
R3/stream early	0.006505	0.01342	0.59	0.12	0.71	1.59	0.79	2.38	0.34	0.01	0.35	0.02	0.28	0.30
D3/ditch late	0.000857	0.001179	0.08	0.01	0.09	0.21	0.07	0.28	0.04	0.00	0.05	0.00	0.02	0.03
D4/pond late	0.000075	0.000614	0.01	0.01	0.01	0.02	0.04	0.05	0.00	0.00	0.00	0.00	0.01	0.01
D4/stream late	0.000713	0.000916	0.06	0.01	0.07	0.17	0.05	0.23	0.04	0.00	0.04	0.00	0.02	0.02
R1/pond late	0.000181	0.001299	0.02	0.01	0.03	0.04	0.08	0.12	0.01	0.00	0.01	0.00	0.03	0.03
R1/stream late	0.005094	0.01694	0.46	0.16	0.62	1.24	1.00	2.24	0.27	0.01	0.28	0.01	0.35	0.37
R3/stream late	0.003939	0.01028	0.36	0.09	0.45	0.96	0.60	1.57	0.21	0.01	0.21	0.01	0.21	0.22
Step 4														
R1/stream early 10 m NSB + 10 m VFS	0.00234	0.007704	0.21	0.07	0.28	0.57	0.45	1.02	0.12	0.00	0.13	0.01	0.16	0.17
R1/stream early 20 m NSB + 20 m VFS	0.00234*	0.001067	0.21	0.01	0.22	0.57	0.06	0.63	0.12	0.00	0.12	0.01	0.02	0.03
R3/stream early 10 m NSB + 10 m VFS	0.002963	0.004685	0.27	0.04	0.31	0.72	0.28	1.00	0.15	0.00	0.16	0.01	0.10	0.11
R1/stream late	0.002308	0.007704	0.21	0.07	0.28	0.56	0.45	1.02	0.12	0.00	0.12	0.01	0.16	0.17

Scenario	PECsw (µg/L)		RQmix											
	Phenmedipham	Ethofumesate	PEC/RAC Phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Fish	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Invertebrates	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Algae	PEC/RAC phenmedipham	PEC/RAC ethofumesate	RQ _{mix} Macrophytes
10 m NSB + 10 m VFS														
R1/stream late 20 m NSB + 20 m VFS	0.002308*	0.003064	0.21	0.03	0.24	0.56	0.18	0.74	0.12	0.00	0.12	0.01	0.06	0.07
R3/stream late 10 m NSB + 10 m VFS	0.001789	0.004685	0.16	0.04	0.21	0.44	0.28	0.71	0.09	0.00	0.10	0.00	0.10	0.10
Use group 5: 3 × 2.4 L product/ha, 9-day interval; early and late applications														
Step 1	0.056064	0.267494	5.10	2.45	7.55	13.67	15.73	29.41	2.92	0.16	3.08	0.14	5.58	5.73
Step 2														
N-Europe	0.020895	0.035177	1.90	0.32	2.22	5.10	2.07	7.17	1.09	0.02	1.11	0.05	0.73	0.79
S-Europe	0.04179	0.06514	3.80	0.60	4.40	10.19	3.83	14.02	2.18	0.04	2.22	0.11	1.36	1.47
Step 3														
D3/ditch early	0.001143	0.001574	0.10	0.01	0.12	0.28	0.09	0.37	0.06	0.00	0.06	0.00	0.03	0.04
D4/pond early	0.000087	0.000584	0.01	0.01	0.01	0.02	0.03	0.06	0.00	0.00	0.00	0.00	0.01	0.01
D4/stream early	0.000959	0.001302	0.09	0.01	0.10	0.23	0.08	0.31	0.05	0.00	0.05	0.00	0.03	0.03
R1/pond early	0.000148	0.000556	0.01	0.01	0.02	0.04	0.03	0.07	0.01	0.00	0.01	0.00	0.01	0.01
R1/stream early	0.004613	0.007831	0.42	0.07	0.49	1.13	0.46	1.59	0.24	0.00	0.25	0.01	0.16	0.18
R3/stream early	0.005708	0.01258	0.52	0.12	0.63	1.39	0.74	2.13	0.30	0.01	0.31	0.01	0.26	0.28
D3/ditch late	0.001142	0.001572	0.10	0.01	0.12	0.28	0.09	0.37	0.06	0.00	0.06	0.00	0.03	0.04
D4/pond late	0.000103	0.000826	0.01	0.01	0.02	0.03	0.05	0.07	0.01	0.00	0.01	0.00	0.02	0.02
D4/stream late	0.000972	0.001223	0.09	0.01	0.10	0.24	0.07	0.31	0.05	0.00	0.05	0.00	0.03	0.03
R1/pond late	0.000146	0.000975	0.01	0.01	0.02	0.04	0.06	0.09	0.01	0.00	0.01	0.00	0.02	0.02
R1/stream late	0.004114	0.01244	0.37	0.11	0.49	1.00	0.73	1.74	0.21	0.01	0.22	0.01	0.26	0.27
R3/stream late	0.005442	0.01376	0.49	0.13	0.62	1.33	0.81	2.14	0.28	0.01	0.29	0.01	0.29	0.30
Step 4														
R1/stream early 10 m NSB + 10 m VFS	0.002087	0.007831**	0.19	0.07	0.26	0.51	0.46	0.97	0.11	0.00	0.11	0.01	0.16	0.17
R3/stream early 10 m NSB + 10 m VFS	0.0026	0.005737	0.24	0.05	0.29	0.63	0.34	0.97	0.14	0.00	0.14	0.01	0.12	0.13
R1/stream late 10 m NSB + 10 m VFS	0.001864	0.005657	0.17	0.05	0.22	0.45	0.33	0.79	0.10	0.00	0.10	0.00	0.12	0.12
R3/stream late 10 m NSB + 10 m VFS	0.002472	0.006273	0.22	0.06	0.28	0.60	0.37	0.97	0.13	0.00	0.13	0.01	0.13	0.14

Please refer to Phenmedipham a.s. risk assessment for cells marked in grey (all have acceptable risk at Step 3)

* 10 m NSB + 10 m VFS value for Phenmedipham

** Step 3 value for Ethofumesate

Table 9.5.1-9 – Estimation of the mixture L(E)C₅₀ / NOEC for aquatic organism assuming dose additivity (proportion of active substances at PEC_{mix})

Proposition of active substances (a.i.)-PEC _{mix}						
Active substance	Maximum PEC _{Sw} # (mg a.s./L)	p _i in the mixture (PEC _{Sw})	LC ₅₀ (mg a.s./L)	p _i /LC ₅₀	Σ (p _i /LC ₅₀)	LC ₅₀ mix-CA (95% at-PEC _{mix}) (Σ mg a.s./L)
Fish						
Ethofumesate	0.01023	0.682	11.017	0.0572	0.347	2.89
Phenmedipham	0.008977	0.313	1.1	0.284		
Macrophytes						
Ethofumesate	0.01023	0.682	12	0.0162	0.0078	10.22
Phenmedipham	0.008977	0.313	3.0	0.0816		

worst case PEC_{Sw} value at step 3 (use group 2-3 → 2.4 L product/ha, 6 day interval), i.e., sum of Step 3 PEC_{Sw} for Ethofumesate, i.e., 19.23 µg/L (R1/stream, late application) and Step 3 PEC_{Sw} for Phenmedipham, i.e., 8.977 µg/L (R3/stream, early application).

Table 9.5.1-9 – Aquatic organisms: acceptability of risk (ETR_{mix-CA} < trigger) to aquatic invertebrates, algae and macrophytes for HBZ10 based on worst case PEC_{mix} calculation

FOCUS scenario	PEC _{mix} (mg a.s./L)	EC _{mix-CA} (based on PEC _{mix}) (mg a.s./L)	ETR _{mix-CA}	ETR trigger
Fish				
Step-3	0.028207	2.38	0.0093	0.4
Macrophytes				
Step-3	0.028207	10.22	0.003	0.4

Values in bold are above the ETR trigger

Table 9.5.1-9 – Aquatic organisms: acceptability of risk (ETR_{mix-CA} < trigger) to, and macrophytes for HBZ10 based on worst case PEC_{mix} calculation

FOCUS scenario	PEC _{mix} # (mg a.s./L)	EC _{mix-CA} (based on PEC _{mix})	ETR _{mix-CA}	ETR trigger
Fish				
STDP3 (R1) scenario late	0.0347	2.38	0.0084	0.4
STDP3 (R1) scenario late	0.03493	2.46	0.0062	0.03
STDP3 (R1) scenario early	0.015441	2.46	0.0074	0.4
STDP3 (R3) scenario early	0.028532	2.61	0.0096	0.03
Macrophytes				
STDP3 (R1) scenario late	0.0347	12.33	0.0025	0.4
STDP3 (R1) scenario late	0.03493	12.33	0.0017	0.4
STDP3 (R1) scenario early	0.015441	2.46	0.0022	0.4
STDP3 (R3) scenario	0.028532	10.22	0.0024	0.4

Values in bold are above the ETR trigger

worst case PEC_{Sw} value at step 3 (use group 2-3 → 2.4 L product/ha, 6 day interval), taking into account sum of Step 3 PEC_{Sw} for Ethofumesate, and Step 3 PEC_{Sw} for Phenmedipham for the worst case scenarios R1 and R3 for early and late application.

The calculated ETR_{mix-CA} ratios at Step 3 for worst case scenario are below the relevant trigger indicating an acceptable risk for both fish and macrophytes. Therefore, no further assessment is necessary.

Based on the available data and the above mixture toxicity risk assessment, it can be concluded that Phenmedipham is driving the overall mixture toxicity for algae and that an acceptable risk to aquatic organisms following application of HBZ10 in beet crops for all intended use groups according to the intended use pattern is expected.

Based on the above performed calculations and full mixture toxicity assessment, the following conclusions can be drawn for the mixture:

2. Use group 1 (6×1.2 L product/ha, 5-day interval):

- a. Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for early application. An acceptable risk for R1 scenario with 10-meter vegetative buffer zone for early application could also be considered as the RQmix exceeds the threshold of 1 by a very small extent (1.05) when using Step 3 PEC_{sw} value for Ethofumesate. Acceptable risk for R3 scenario with 20-meter vegetative buffer zone for early application. An acceptable risk for R3 scenario with 10-meter vegetative buffer zone for early application could also be considered as the RQmix exceeds the threshold of 1 by a very small extent (1.05) when considering conservative approach of mixture toxicity risk assessment.
- b. Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

3. Use group no 2 (3×2.4 L product/ha, 6-day interval):

- a. Acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for early application. An acceptable risk for R1 scenario with 10-meter vegetative buffer zone for early application could also be considered as the RQmix exceeds the threshold of 1 by a very small extent (1.01) when considering conservative approach of mixture toxicity risk assessment.
- b. Acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for late application. An acceptable risk for R3 scenario with 10-meter vegetative buffer zone for late application could also be considered as the RQmix exceeds the threshold of 1 by a very small extent (1.04) when considering conservative approach of mixture toxicity risk assessment.

4. Use group no 3 (5×1.2 L product/ha, 7-day interval):

- a. Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early application.
- b. Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

5. Use group no 4 (3×1.8 L product/ha, 6-day interval):

- a. Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for early application. An acceptable risk for R1 scenario with 10-meter vegetative buffer zone for early application could also be considered as the RQmix exceeds the threshold of 1 by a very small extent (1.02) when considering conservative approach of mixture toxicity risk assessment. Acceptable risk for R3 scenario with 10-meter vegetative buffer zone for early application.
- b. Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for late application. An acceptable risk for R1 scenario with 10-meter vegetative buffer zone for late application could also be considered as the RQmix exceeds the threshold of 1 by a very small extent (1.02) when considering conservative approach of mixture toxicity risk assessment. Acceptable risk for R3 scenario with 10-meter vegetative buffer zone for late application.

6. Use group no 5 (3×2.4 L product/ha, 9-day interval):

- a. Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early application.
- b. Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

Based on the results of the above mixture toxicity risk assessment, and considering mixture toxicity risk assessment based on step 8 is very conservative, applicant propose that a low risk to aquatic organisms can be expected from the use of HBZ10 when applying the following risk mitigation measures:

- For the intended use groups 1, 3, 4 and 5 (early and late applications), to protect aquatic organisms, the implementation of a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is required.
- For the other intended use group 2 (early and late application), to protect aquatic organisms, the implementation of a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is required.

As the above mitigation measures are related to scenarios R1 and/or R3 stream, decision making for mitigation measures applying in each Member State should however be considered at national level, where relevant.

zRMS comments:

Based mixture toxicity risk assessment provided Phenmedipham is driving to aquatic invertebrates, and algae. The risk assessment for these group organisms can be based on the single substance toxicity data of Phenmedipham. The calculated $ETR_{mixture}$ ratios at Step 4 for worst case scenarios were below the relevant trigger indicating an acceptable risk for both fish and macrophytes.

Based on the mixture toxicity risk assessment, it can be concluded that Phenmedipham is driving the overall mixture toxicity for algae and that an acceptable risk to aquatic organisms following application of HBZ10 for all intended use groups according to the intended use pattern is expected.

The full mixture toxicity assessment based on STEP 8 is validated by zRMS and the following conclusions can be drawn for the mixture:

Use group 1 (6×1.2 L product/ha, 5-day interval):

- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R3 scenario with 20-meter vegetative buffer zone for early application.
- An acceptable risk for R3 scenario with 10-meter vegetative buffer zone for early application
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

Use group no 2 (3×2.4 L product/ha, 6-day interval):

- Acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for late application.

Use group no 3 (5×1.2 L product/ha, 7-day interval):

- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

7. Use group no 4 (3×1.8 L product/ha, 6-day interval):

- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R3 scenario with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for late application
- Acceptable risk for R3 scenario with 10-meter vegetative buffer zone for late application.

Use group no 5 (3×2.4 L product/ha, 9-day interval):

- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

As the above mitigation measures are related to scenarios R1 and/or R3 stream in STEP 8, decision making for mitigation measures applying in each Member State should however be considered at national level, where relevant.

9.5.1.1 Justification for new endpoints

According to Regulation (EU) No 284/2013, when a formulated product contains two active substances and the most sensitive taxonomic group for the individual active substance are not the same, testing on all four aquatic groups (fish, aquatic invertebrates, algae and macrophytes) shall be required. In case of HBZ10, there is no clear indication (difference of ≥ 10) of the most sensitive taxonomic group towards either active substance (Ethofumesate, Phenmedipham).

Based on the outcome of the decision scheme for the mixture toxicity risk assessment presented under Point 9.5.1, the acute risk assessment for the formulated product HBZ10 for fish and aquatic invertebrates as well as the risk assessment for algae and macrophytes is covered by the risk assessment presented for the respective active substances.

The aquatic risk assessment for Ethofumesate and Phenmedipham is conducted based on the EU agreed endpoints for the two active substances.

9.5.2 Risk assessment

The evaluation of the risk for aquatic and sediment-dwelling organisms was performed in accordance with the recommendations of the “Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters in the context of Regulation (EC) No 1107/2009”, as provided by the Commission Services (SANTE-2015-00080, 15 January 2015).

The following text is added due to agreements during the Central Zone harmonisation meetings. It should be noted that this text has no impact on the outcome of zonal evaluation of formulation HBZ10 which was performed in line with the EU agreed methodology.

“The endpoint E_rC_{50} is selected in this Core Assessment but there are some uncertainties regarding the level of protection reached for primary producers. This is indicated for macrophytes in the aquatic Guidance Document (EFSA Journal 2013;11(7):3290) that recommends: “... a proper calibration between different tiers (higher and lower tier data) for macrophytes should be performed in the future”. Such calibration should be extended to algae. Until available relevant information on the level of protection reached is considered at EU level, it is recommended to address this uncertainty at each Member State level in the National Addendum if considered necessary, although it would be highly appreciated to have a harmonised approach in the Central zone.”

In line with the approach followed for PEC_{SW} calculations in dRR Part B8, Point 8.9.2, the 25 intended uses are grouped in 5 use groups, i.e., Use group 1: 6 x 1.2 L prod./ha, 5-days interval (includes uses 1, 6, 11, 16 and 21); Use group 2: 3 x 2.4 L prod./ha, 6-days interval (includes uses 2, 7, 12, 17, and 22); Use group 3: 5 x 1.2 L prod./ha, 7-days interval (includes uses 3, 8, 13, 18, and 23); Use group 4: 3 x 1.8 L prod./ha, 6-days interval (includes uses 4, 9, 14, 19, and 24); Use group 5: 3 x 2.4 L prod./ha, 9-days interval (includes uses 5, 10, 15, 20, and 25), and PEC_{SW} calculations are performed and presented for all use groups.

Ethofumesate and relevant metabolites

For Ethofumesate and the relevant metabolites NC 20465 and NC 8493, the relevant global maximum FOCUS Step 1, 2 and relevant worst-case FOCUS Step 3 and 4 PEC_{SW} values for risk assessment for all intended uses **in-beet-groups** (early and late application) and the resulting PEC/RAC ratios are presented in the **Table 9.5.2-1** to **Table 9.5.2-15** and in **Table 9.5.2-26**. All PEC_{SW} values for Ethofumesate and the metabolite NC 20645 at FOCUS Step 3 and Step 4, when necessary, have been recalculated considering a plant update factor of 0. Updated risk assessment is presented in the following tables (worst-case presented from single and multiple application).

Phenmedipham and relevant metabolites

For Phenmedipham and the relevant metabolite MHPC, the relevant global maximum FOCUS Step 1, 2 and relevant worst-case FOCUS Step 3 and 4 PEC_{SW} values for risk assessment for all intended uses (early and late application) and the resulting PEC/RAC ratios are presented in the **Table 9.5.2-16** to **Table 9.5.2-25** and in **Table 9.5.2-27** to **Table 9.5.2-31**.

For details on the PEC_{SW} value calculations please refer to dRR part B, Section 8 (Environmental Fate), Point 8.9.2. According to the assessment of environmental-fate data, multiple applications are considered. In the following table, the ratios between predicted environmental concentrations in surface water bodies (PEC_{SW} , PEC_{SED}) and regulatory acceptable concentrations (RAC) for aquatic organisms are given per intended use for each FOCUS scenario and each organism group.

Active substance Ethofumesate and relevant metabolites

Table 9.5.2-1 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for **Ethofumesate** for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in **beet-crops** –use group no 1 (6 × 1.2 L product/ha, 5-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _r C ₅₀	NOEC	E _r C ₅₀
[µg/L]		10920	156	1700	250	16300	3820	479
AF		100	10	100	10	10	10	10
RAC [µg/L]		109.2	15.6	17.0	25.0	1630.0	382.0	47.9
FOCUS Scenario	PEC _{sw} global max [µg/L]	PEC/RAC ratio						
Step 1								
	267.494	2.450	17.147	15.735	10.700	0.1641	0.7002	5.584
Step 2								
N-Europe/Mar-May	31.636	0.2897	2.028	1.861	1.265	0.0194	0.0828	0.660
N-Europe/Jun-Sep	31.636	0.2897	2.028	1.861	1.265	0.0194	0.0828	0.660
S-Europe/Mar-May	59.129	0.5415	3.790	3.478	2.365	0.0363	0.1548	1.234
S-Europe/Jun-Sep	45.383	0.4156	2.909	2.670	1.815	0.0278	0.1188	0.947
Step 3	Early application							
D3/ditch	0.465	0.0043	0.0298	0.0274	0.0186	0.0003	0.0012	0.0097
D4/pond	0.648	0.0059	0.0415	0.0381	0.0259	0.0004	0.0017	0.0135
D4/stream	0.641	0.0059	0.0411	0.0377	0.0256	0.0004	0.0017	0.0134
R1/pond	1.003	0.0092	0.0643	0.0590	0.0401	0.0006	0.0026	0.0209
R1/stream	8.491	0.0778	0.5443	0.4995	0.3396	0.0052	0.0222	0.1773
R3/stream	13.78	0.1262	0.8833	0.8106	0.5512	0.0085	0.0361	0.2877
Step 3	Late application							
D3/ditch	0.465	0.0043	0.0298	0.0274	0.0186	0.0003	0.0012	0.0097
D4/pond	0.870	0.0080	0.0558	0.0512	0.0348	0.0005	0.0023	0.0182
D4/stream	0.919	0.0084	0.0589	0.0541	0.0368	0.0006	0.0024	0.0192
R1/pond	0.841	0.0077	0.0539	0.0495	0.0336	0.0005	0.0022	0.0176
R1/stream	12.16	0.1114	0.7795	0.7153	0.4864	0.0075	0.0318	0.2539
R3/stream	9.325	0.0854	0.5978	0.5485	0.3730	0.0057	0.0244	0.1947

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-2 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Ethofumesate for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in leaf-crops-use group no 2 (3 × 2.4 L product/ha, 6-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		10920	156	1700	250	16300	3820	479
AF		100	10	100	10	10	10	10
RAC [µg/L]		109.2	15.6	17.0	25.0	1630.0	382.0	47.9
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio						
Step 1								
	267.494	2.450	17.147	15.735	10.700	0.1641	0.7002	5.584
Step 2								
N-Europe/Mar-May	37.379	0.3423	2.396	2.199	1.495	0.0229	0.0979	0.780
N-Europe/Jun-Sep	37.379	0.3423	2.396	2.199	1.495	0.0229	0.0979	0.780
S-Europe/Mar-May	69.480	0.6363	4.454	4.087	2.779	0.0426	0.1819	1.451
S-Europe/Jun-Sep	53.429	0.4893	3.425	3.143	2.137	0.0328	0.1399	1.115
Step 3	Early application							
D3/ditch	1.145	0.0105	0.0734	0.0674	0.0458	0.0007	0.0030	0.0239
D4/pond	0.528	0.0048	0.0338	0.0311	0.0211	0.0003	0.0014	0.0110
D4/stream	1.023	0.0094	0.0656	0.0602	0.0409	0.0006	0.0027	0.0214
R1/pond	0.490	0.0045	0.0314	0.0288	0.0196	0.0003	0.0013	0.0102
R1/stream	8.373	0.0767	0.5367	0.4925	0.3349	0.0051	0.0219	0.1748
R3/stream	19.58	0.1793	1.2551	1.1518	0.7832	0.0120	0.0513	0.4088
Step 3	Late application							
D3/ditch	1.144	0.0105	0.0733	0.0673	0.0458	0.0007	0.0030	0.0239
D4/pond	0.836	0.0077	0.0536	0.0492	0.0334	0.0005	0.0022	0.0175
D4/stream	1.000	0.0092	0.0641	0.0588	0.0400	0.0006	0.0026	0.0209
R1/pond	1.880	0.0172	0.1205	0.1106	0.0752	0.0012	0.0049	0.0392
R1/stream	24.66	0.2258	1.5808	1.4506	0.9864	0.0151	0.0646	0.5148
R3/stream	16.49	0.1510	1.0571	0.9700	0.6596	0.0101	0.0432	0.3443

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-3 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Ethofumesate for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in **leaf-crops use group no 3 (5 × 1.2 L product/ha, 7-day interval)**

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		10920	156	1700	250	16300	3820	479
AF		100	10	100	10	10	10	10
RAC [µg/L]		109.2	15.6	17.0	25.0	1630.0	382.0	47.9
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio						
Step 1								
	222.911	2.041	14.289	13.112	8.916	0.1368	0.5835	4.654
Step 2								
N-Europe/Mar-May	25.986	0.2380	1.666	1.529	1.039	0.0159	0.0680	0.543
N-Europe/Jun-Sep	25.986	0.2380	1.666	1.529	1.039	0.0159	0.0680	0.543
S-Europe/Mar-May	49.198	0.4505	3.154	2.894	1.968	0.0302	0.1288	1.027
S-Europe/Jun-Sep	37.092	0.3397	2.378	2.182	1.484	0.0228	0.0971	0.774
Step 3	Early application							
D3/ditch	0.508	0.0047	0.0326	0.0299	0.0203	0.0003	0.0013	0.508
D4/pond	0.510	0.0047	0.0327	0.0300	0.0204	0.0003	0.0013	0.51
D4/stream	0.505	0.0046	0.0324	0.0297	0.0202	0.0003	0.0013	0.505
R1/pond	0.789	0.0072	0.0506	0.0464	0.0316	0.0005	0.0021	0.789
R1/stream	7.698	0.0705	0.4935	0.4528	0.3079	0.0047	0.0202	7.698 0.1607
R3/stream	8.936	0.0818	0.5728	0.5256	0.3574	0.0055	0.0234	8.936 0.1866
Step 3	Late application							
D3/ditch	0.508	0.0047	0.0326	0.0299	0.0203	0.0003	0.0013	0.508
D4/pond	0.705	0.0065	0.0452	0.0415	0.0282	0.0004	0.0018	0.705
D4/stream	0.750	0.0069	0.0481	0.0441	0.0300	0.0005	0.0020	0.75
R1/pond	0.657	0.0060	0.0421	0.0386	0.0263	0.0004	0.0017	0.657
R1/stream	6.682	0.0612	0.4283	0.3931	0.2673	0.0041	0.0175	6.682 0.1395
R3/stream	6.815	0.0624	0.4369	0.4009	0.2726	0.0042	0.0178	6.815 0.1423

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-4 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Ethofumesate for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in leaf-crops use group no 4 (3 × 1.8 L product/ha, 6-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _r C ₅₀	NOEC	E _r C ₅₀
[µg/L]		10920	156	1700	250	16300	3820	479
AF		100	10	100	10	10	10	10
RAC [µg/L]		109.2	15.6	17.0	25.0	1630.0	382.0	47.9
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio						
Step 1								
	200.62	1.837	12.860	11.801	8.025	0.1231	0.5252	4.188
Step 2								
N-Europe/Mar-May	28.034	0.2567	1.797	1.649	1.121	0.0172	0.0734	0.585
N-Europe/Jun-Sep	28.034	0.2567	1.797	1.649	1.121	0.0172	0.0734	0.585
S-Europe/Mar-May	52.110	0.4772	3.340	3.065	2.084	0.0320	0.1364	1.088
S-Europe/Jun-Sep	40.072	0.3670	2.569	2.357	1.603	0.0246	0.1049	0.837
Step 3	Early application							
D3/ditch	1.181	0.0108	0.0757	0.0695	0.0472	0.0007	0.0031	0.0247
D4/pond	0.386	0.0035	0.0247	0.0227	0.0154	0.0002	0.0010	0.0081
D4/stream	0.976	0.0089	0.0626	0.0574	0.0390	0.0006	0.0026	0.0204
R1/pond	0.351	0.0032	0.0225	0.0206	0.0140	0.0002	0.0009	0.0073
R1/stream	5.923	0.0542	0.3797	0.3484	0.2369	0.0036	0.0155	0.1237
R3/stream	13.42	0.1229	0.8603	0.7894	0.5368	0.0082	0.0351	0.2802
Step 3	Late application							
D3/ditch	1.179	0.0108	0.0756	0.0694	0.0472	0.0007	0.0031	0.0246
D4/pond	0.614	0.0056	0.0394	0.0361	0.0246	0.0004	0.0016	0.0128
D4/stream	0.916	0.0084	0.0587	0.0539	0.0366	0.0006	0.0024	0.0191
R1/pond	1.299	0.0119	0.0833	0.0764	0.0520	0.0008	0.0034	0.0271
R1/stream	16.94	0.1551	1.0859	0.9965	0.6776	0.0104	0.0443	0.3537
R3/stream	10.28	0.0941	0.6590	0.6047	0.4112	0.0063	0.0269	0.2146

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-5 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Ethofumesate for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in leaf-crops use group no 5 (3 × 2.4 L product/ha, 9-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Crassostrea virginica</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		10920	156	1700	250	16300	3820	479
AF		100	10	100	10	10	10	10
RAC [µg/L]		109.2	15.6	17.0	25.0	1630.0	382.0	47.9
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio						
Step 1								
	267.494	2.450	17.147	15.735	10.700	0.1641	0.7002	5.584
Step 2								
N-Europe/Mar-May	35.177	0.3221	2.255	2.069	1.407	0.0216	0.0921	0.734
N-Europe/Jun-Sep	35.177	0.3221	2.255	2.069	1.407	0.0216	0.0921	0.734
S-Europe/Mar-May	65.140	0.5965	4.176	3.832	2.606	0.0400	0.1705	1.360
S-Europe/Jun-Sep	50.159	0.4593	3.215	2.951	2.006	0.0308	0.1313	1.047
Step 3	Early application							
D3/ditch	1.574	0.0144	0.1009	0.0926	0.0630	0.0010	0.0041	0.0329
D4/pond	0.584	0.0053	0.0374	0.0344	0.0234	0.0004	0.0015	0.0122
D4/stream	1.302	0.0119	0.0835	0.0766	0.0521	0.0008	0.0034	0.0272
R1/pond	0.556	0.0051	0.0356	0.0327	0.0222	0.0003	0.0015	0.0116
R1/stream	7.831	0.0717	0.5020	0.4606	0.3132	0.0048	0.0205	0.1635
R3/stream	12.58	0.1152	0.8064	0.7400	0.5032	0.0077	0.0329	0.2626
Step 3	Late application							
D3/ditch	1.572	0.0144	0.1008	0.0925	0.0629	0.0010	0.0041	0.0328
D4/pond	0.826	0.0076	0.0529	0.0486	0.0330	0.0005	0.0022	0.0172
D4/stream	1.223	0.0112	0.0784	0.0719	0.0489	0.0008	0.0032	0.0255
R1/pond	0.975	0.0089	0.0625	0.0574	0.0390	0.0006	0.0026	0.0204
R1/stream	12.44	0.1139	0.7974	0.7318	0.4976	0.0076	0.0326	0.2597
R3/stream	13.760	0.1260	0.8821	0.8094	0.5504	0.0084	0.0360	0.2873

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-6 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 20645 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~leafy crops~~ use group no 1 (6 × 1.2 L product/ha, 5-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		1092 ^{a)}	15.6 ^{a)}	> 100000 *	25.0 ^{a)}	> 10000	382 ^{a)}	47.9 ^{a)}
AF		100	10	100	10	10	10	10
RAC [µg/L]		10.92	1.56	1000	2.50	1000	38.2	4.79
FOCUS Scenario	PEC _{SW global max} [µg/L]	PEC/RAC ratio						
Step 1								
	60.358	5.527	38.691	0.06036	24.143	0.06036	1.580	12.601
Step 2								
N-Europe/Mar-May	6.523	0.59734	4.181	0.00652	2.609	0.00652	0.17076	1.362
N-Europe/Jun-Sep	6.523	0.59734	4.181	0.00652	2.609	0.00652	0.17076	1.362
S-Europe/Mar-May	12.216	1.119	7.831	0.01222	4.886	0.01222	0.31979	2.550
S-Europe/Jun-Sep	9.370	0.858	6.006	0.00937	3.748	0.00937	0.24529	1.956
Step 3	Early application							
D3/ditch	0.001	0.0001	0.0006	0.0000	0.0004	0.0000	0.0000	0.0002
D4/pond	0.020	0.0018	0.0128	0.0000	0.0080	0.0000	0.0005	0.0042
D4/stream	0.002	0.0002	0.0013	0.0000	0.0008	0.0000	0.0001	0.0004
R1/pond	0.050	0.0046	0.0321	0.0001	0.0200	0.0001	0.0013	0.0104
R1/stream	0.026	0.0024	0.0167	0.0000	0.0104	0.0000	0.0007	0.0054
R3/stream	0.115	0.0105	0.0737	0.0001	0.0460	0.0001	0.0030	0.0240
Step 3	Late application							
D3/ditch	0.000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
D4/pond	0.024	0.0022	0.0154	0.0000	0.0096	0.0000	0.0006	0.0050
D4/stream	0.003	0.0003	0.0019	0.0000	0.0012	0.0000	0.0001	0.0006
R1/pond	0.048	0.0044	0.0308	0.0000	0.0192	0.0000	0.0013	0.0100
R1/stream	0.038	0.0035	0.0244	0.0000	0.0152	0.0000	0.0010	0.0079
R3/stream	0.078	0.0071	0.0500	0.0001	0.0312	0.0001	0.0020	0.0163

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-7 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 20645 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in leaf-crops use group no 2 (3 × 2.4 L product/ha, 6-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		1092 ^{a)}	15.6 ^{a)}	> 100000 *	25.0 ^{a)}	> 10000	382 ^{a)}	47.9 ^{a)}
AF		100	10	100	10	10	10	10
RAC [µg/L]		10.92	1.56	1000	2.50	1000	38.2	4.79
FOCUS Scenario	PEC _{SW global max} [µg/L]	PEC/RAC ratio						
Step 1								
	60.358	5.527	38.691	0.06036	24.143	0.06036	1.580	12.601
Step 2								
N-Europe/Mar-May	7.700	0.70513	4.936	0.00770	3.080	0.00770	0.20157	1.608
N-Europe/Jun-Sep	7.700	0.70513	4.936	0.00770	3.080	0.00770	0.20157	1.608
S-Europe/Mar-May	14.347	1.314	9.197	0.01435	5.739	0.01435	0.37558	2.995
S-Europe/Jun-Sep	11.023	1.009	7.066	0.01102	4.409	0.01102	0.28856	2.301
Step 3	Early application							
D3/ditch	0.001	0.0001	0.0006	0.0000	0.0004	0.0000	0.0000	0.0002
D4/pond	0.017	0.0016	0.0109	0.0000	0.0068	0.0000	0.0004	0.0035
D4/stream	0.002	0.0002	0.0013	0.0000	0.0008	0.0000	0.0001	0.0004
R1/pond	0.024	0.0022	0.0154	0.0000	0.0096	0.0000	0.0006	0.0050
R1/stream	0.025	0.0023	0.0160	0.0000	0.0100	0.0000	0.0007	0.0052
R3/stream	0.163	0.0149	0.1045	0.0002	0.0652	0.0002	0.0043	0.0340
Step 3	Late application							
D3/ditch	0.001	0.0001	0.0006	0.0000	0.0004	0.0000	0.0000	0.0002
D4/pond	0.025	0.0023	0.0160	0.0000	0.0100	0.0000	0.0007	0.0052
D4/stream	0.003	0.0003	0.0019	0.0000	0.0012	0.0000	0.0001	0.0006
R1/pond	0.086	0.0079	0.0551	0.0001	0.0344	0.0001	0.0023	0.0180
R1/stream	0.075	0.0069	0.0481	0.0001	0.0300	0.0001	0.0020	0.0157
R3/stream	0.137	0.0125	0.0878	0.0001	0.0548	0.0001	0.0036	0.0286

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-8 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 20645 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~leafy crops~~ use group no 3 (5 × 1.2 L product/ha, 7-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		1092 ^{a)}	15.6 ^{a)}	> 100000 *	25.0 ^{a)}	> 10000	382 ^{a)}	47.9 ^{a)}
AF		100	10	100	10	10	10	10
RAC [µg/L]		10.92	1.56	1000	2.50	1000	38.2	4.79
FOCUS Scenario	PEC _{SW global max} [µg/L]	PEC/RAC ratio						
Step 1								
	50.298	4.606	32.242	0.05030	20.119	0.05030	1.317	10.501
Step 2								
N-Europe/Mar-May	5.357	0.490	3.434	0.00536	2.143	0.00536	0.14024	1.118
N-Europe/Jun-Sep	5.357	0.490	3.434	0.00536	2.143	0.00536	0.14024	1.118
S-Europe/Mar-May	9.956	0.912	6.382	0.00996	3.982	0.00996	0.26063	2.078
S-Europe/Jun-Sep	7.656	0.701	4.908	0.00766	3.062	0.00766	0.20042	1.598
Step 3	Early application							
D3/ditch	0.000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
D4/pond	0.016	0.0015	0.0103	0.0000	0.0064	0.0000	0.0004	0.0033
D4/stream	0.002	0.0002	0.0013	0.0000	0.0008	0.0000	0.0001	0.0004
R1/pond	0.041	0.0038	0.0263	0.0000	0.0164	0.0000	0.0011	0.0086
R1/stream	0.023	0.0021	0.0147	0.0000	0.0092	0.0000	0.0006	0.0048
R3/stream	0.074	0.0068	0.0474	0.0001	0.0296	0.0001	0.0019	0.0154
Step 3	Late application							
D3/ditch	0.000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
D4/pond	0.020	0.0018	0.0128	0.0000	0.0080	0.0000	0.0005	0.0042
D4/stream	0.003	0.0003	0.0019	0.0000	0.0012	0.0000	0.0001	0.0006
R1/pond	0.039	0.0036	0.0250	0.0000	0.0156	0.0000	0.0010	0.0081
R1/stream	0.021	0.0019	0.0135	0.0000	0.0084	0.0000	0.0005	0.0044
R3/stream	0.057	0.0052	0.0365	0.0001	0.0228	0.0001	0.0015	0.0119

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-9 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 20645 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~leafy crops~~ use group no 4 (3 × 1.8 L product/ha, 6-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		1092 ^{a)}	15.6 ^{a)}	> 100000 *	25.0 ^{a)}	> 10000	382 ^{a)}	47.9 ^{a)}
AF		100	10	100	10	10	10	10
RAC [µg/L]		10.92	1.56	1000	2.50	1000	38.2	4.79
FOCUS Scenario	PEC _{SW global max} [µg/L]	PEC/RAC ratio						
Step 1								
	45.268	4.145	29.018	0.04527	18.107	0.04527	1.185	9.451
Step 2								
N-Europe/Mar-May	5.775	0.5288	3.702	0.00578	2.310	0.00578	0.15118	1.206
N-Europe/Jun-Sep	5.775	0.5288	3.702	0.00578	2.310	0.00578	0.15118	1.206
S-Europe/Mar-May	10.76	0.985	6.897	0.01076	4.304	0.01076	0.28168	2.246
S-Europe/Jun-Sep	8.267	0.757	5.299	0.00827	3.307	0.00827	0.21641	1.726
Step 3	Early application							
D3/ditch	0.001	0.0001	0.0006	0.0000	0.0004	0.0000	0.0000	0.0002
D4/pond	0.012	0.0011	0.0077	0.0000	0.0048	0.0000	0.0003	0.0025
D4/stream	0.001	0.0001	0.0006	0.0000	0.0004	0.0000	0.0000	0.0002
R1/pond	0.017	0.0016	0.0109	0.0000	0.0068	0.0000	0.0004	0.0035
R1/stream	0.018	0.0016	0.0115	0.0000	0.0072	0.0000	0.0005	0.0038
R3/stream	0.112	0.0103	0.0718	0.0001	0.0448	0.0001	0.0029	0.0234
Step 3	Late application							
D3/ditch	0.001	0.0001	0.0006	0.0000	0.0004	0.0000	0.0000	0.0002
D4/pond	0.018	0.0016	0.0115	0.0000	0.0072	0.0000	0.0005	0.0038
D4/stream	0.002	0.0002	0.0013	0.0000	0.0008	0.0000	0.0001	0.0004
R1/pond	0.059	0.0054	0.0378	0.0001	0.0236	0.0001	0.0015	0.0123
R1/stream	0.051	0.0047	0.0327	0.0001	0.0204	0.0001	0.0013	0.0106
R3/stream	0.086	0.0079	0.0551	0.0001	0.0344	0.0001	0.0023	0.0180

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-10 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 20645 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~leaf crops~~ use group no 5 (3 × 2.4 L product/ha, 9-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		1092 ^{a)}	15.6 ^{a)}	> 100000 *	25.0 ^{a)}	> 10000	382 ^{a)}	47.9 ^{a)}
AF		100	10	100	10	10	10	10
RAC [µg/L]		10.92	1.56	1000	2.50	1000	38.2	4.79
FOCUS Scenario	PEC _{SW global max} [µg/L]	PEC/RAC ratio						
Step 1								
	60.358	5.527	38.691	0.06036	24.143	0.06036	1.580	12.601
Step 2								
N-Europe/Mar-May	7.247	0.6636	4.646	0.00725	2.899	0.00725	0.18971	1.513
N-Europe/Jun-Sep	7.247	0.6636	4.646	0.00725	2.899	0.00725	0.18971	1.513
S-Europe/Mar-May	13.451	1.232	8.622	0.01345	5.380	0.01345	0.35212	2.808
S-Europe/Jun-Sep	10.349	0.948	6.634	0.01035	4.140	0.01035	0.27092	2.161
Step 3	Early application							
D3/ditch	0.001	0.0001	0.0006	0.0000	0.0004	0.0000	0.0000	0.0002
D4/pond	0.018	0.0016	0.0115	0.0000	0.0072	0.0000	0.0005	0.0038
D4/stream	0.002	0.0002	0.0013	0.0000	0.0008	0.0000	0.0001	0.0004
R1/pond	0.031	0.0028	0.0199	0.0000	0.0124	0.0000	0.0008	0.0065
R1/stream	0.025	0.0023	0.0160	0.0000	0.0100	0.0000	0.0007	0.0052
R3/stream	0.105	0.0096	0.0673	0.0001	0.0420	0.0001	0.0027	0.0219
Step 3	Late application							
D3/ditch	0.001	0.0001	0.0006	0.0000	0.0004	0.0000	0.0000	0.0002
D4/pond	0.024	0.0022	0.0154	0.0000	0.0096	0.0000	0.0006	0.0050
D4/stream	0.003	0.0003	0.0019	0.0000	0.0012	0.0000	0.0001	0.0006
R1/pond	0.045	0.0041	0.0288	0.0000	0.0180	0.0000	0.0012	0.0094
R1/stream	0.034	0.0031	0.0218	0.0000	0.0136	0.0000	0.0009	0.0071
R3/stream	0.115	0.0105	0.0737	0.0001	0.0460	0.0001	0.0030	0.0240

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-11 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 8493 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~beet-crops~~ use group no 1 (6 × 1.2 L product/ha, 5-day interval)

[illegible]

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

a) Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-12 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 8493 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in beet crops — use group no 2 (3 × 2.4 L product/ha, 6-day interval)

[illegible]

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _r C ₅₀	NOEC	E _r C ₅₀
[µg/L]		1092 ^{a)}	15.6 ^{a)}	> 100000 *	25.0 ^{a)}	4830	382 ^{a)}	47.9 ^{a)}
AF		100	10	100	10	10	10	10
RAC [µg/L]		10.92	1.56	1000	2.50	483	38.2	4.79
FOCUS Scenario	PEC _{sw} global max [µg/L]	PEC/RAC ratio						
S-Europe/Jun-Sep	0.00	0.000	0.000	0.000	0.000	0.000	0.000	0.000

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-13 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 8493 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in **best crops— use group no 3 (5 × 1.2 L product/ha, 7-day interval)**

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _r C ₅₀	NOEC	E _r C ₅₀
[µg/L]		1092 ^{a)}	15.6 ^{a)}	> 100000 *	25.0 ^{a)}	4830	382 ^{a)}	47.9 ^{a)}
AF		100	10	100	10	10	10	10
RAC [µg/L]		10.92	1.56	1000	2.50	483	38.2	4.79
FOCUS Scenario	PEC _{sw} global max [µg/L]	PEC/RAC ratio						
Step 1								
	54.432	4.985	34.892	0.0544	21.773	0.1127	1.425	11.364
Step 2								
N-Europe/Mar-May	0.00	0.000	0.000	0.000	0.000	0.000	0.000	0.000
N-Europe/Jun-Sep	0.00	0.000	0.000	0.000	0.000	0.000	0.000	0.000
S-Europe/Mar-May	0.00	0.000	0.000	0.000	0.000	0.000	0.000	0.000
S-Europe/Jun-Sep	0.00	0.000	0.000	0.000	0.000	0.000	0.000	0.000

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-14 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 8493 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~beet-crops~~ use group no 4 (3×1.8 L product/ha, 6-day interval)

[illegible]

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

a) Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Table 9.5.2-15 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for NC 8493 for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~beet crops~~ use group no 5 (3 × 2.4 L product/ha, 9-day interval)

[illegible]

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Cyprinus carpio</i>	<i>Danio rerio</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Myriophyllum spicatum</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _r C ₅₀	NOEC	E _r C ₅₀
[µg/L]		1092 ^{a)}	15.6 ^{a)}	> 100000 *	25.0 ^{a)}	4830	382 ^{a)}	47.9 ^{a)}
AF		100	10	100	10	10	10	10
RAC [µg/L]		10.92	1.56	1000	2.50	483	38.2	4.79
FOCUS Scenario	PEC _{sw global max} [µg/L]	PEC/RAC ratio						
S-Europe/Jun-Sep	0.00	0.000	0.000	0.000	0.000	0.000	0.000	0.000

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent.

* The EC₅₀ > 10 mg/L endpoint from Table 9.5.1-1 is not considered in the risk assessment since it is an artificial “higher than” endpoint. Thus, it is justified to consider the EC₅₀ > 100 mg/L in the risk assessment.

Phenmedipham and relevant metabolite

Table 9.5.2-16 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Phenmedipham for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 ~~in beet crops~~ use group no 1 (6 × 1.2 L product/ha, 5-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _r C ₅₀	NOEC	E _r C ₅₀
[µg/L]		1100	320	410	25.0	192	370	3900
AF		100	10	100	10	10	10	10
RAC [µg/L]		11.0	32.0	4.10	2.50	19.2	37.0	390
FOCUS Scenario	PEC _{sw} global max [µg/L]	PEC/RAC ratio						
Step 1								
	28.032	2.548	0.876	6.837	11.213	1.460	0.758	0.072
Step 2								
N-Europe/Mar-May	19.797	1.800	0.619	4.829	7.919	1.031	0.535	0.051
N-Europe/Jun-Sep	19.797	1.800	0.619	4.829	7.919	1.031	0.535	0.051
S-Europe/Mar-May	39.594	3.599	1.237	9.657	15.838	2.062	1.070	0.102
S-Europe/Jun-Sep	29.696	2.700	0.928	7.243	11.878	1.547	0.803	0.076
Step 3	Early application							
D3/ditch	0.463	0.042	0.014	0.113	0.185	0.024	0.013	0.001
D4/pond	0.090	0.008	0.003	0.022	0.036	0.005	0.002	0.000
D4/stream	0.832 0.823	0.076 0.075	0.026	0.203 0.201	0.333 0.329	0.043	0.022	0.002
R1/pond	0.275	0.025	0.009	0.067	0.110	0.014	0.007	0.001
R1/stream	6.015	0.547	0.188	1.467	2.406	0.313	0.163	0.015
R3/stream	5.196	0.472	0.162	1.267	2.078	0.271	0.140	0.013
Step 3	Late application							
D3/ditch	0.436 0.463	0.040 0.042	0.014	0.106 0.113	0.174 0.185	0.023 0.024	0.012 0.013	0.001
D4/pond	0.108	0.010	0.003	0.026	0.043	0.006	0.003	0.000
D4/stream	1.022	0.093	0.032	0.249	0.409	0.053	0.028	0.003
R1/pond	0.112	0.010	0.004	0.027	0.045	0.006	0.003	0.000
R1/stream	3.455	0.314	0.108	0.843	1.382	0.180	0.093	0.009
R3/stream	4.425	0.402	0.138	1.079	1.770	0.230	0.120	0.011

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-17 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Phenmedipham for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in leaf-crops use group no 2 (3 × 2.4 L product/ha, 6-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		1100	320	410	25.0	192	370	3900
AF		100	10	100	10	10	10	10
RAC [µg/L]		11.0	32.0	4.10	2.50	19.2	37.0	390
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio						
Step 1								
	56.064	5.097	1.752	13.674	22.426	2.920	1.515	0.144
Step 2								
N-Europe/Mar-May	21.845	1.986	0.683	5.328	8.738	1.138	0.590	0.056
N-Europe/Jun-Sep	21.845	1.986	0.683	5.328	8.738	1.138	0.590	0.056
S-Europe/Mar-May	43.690	3.972	1.365	10.656	17.476	2.276	1.181	0.112
S-Europe/Jun-Sep	32.768	2.979	1.024	7.992	13.107	1.707	0.886	0.084
Step 3	Early application							
D3/ditch	1.143	0.104	0.036	0.279	0.457	0.060	0.031	0.003
D4/pond	0.080	0.007	0.003	0.020	0.032	0.004	0.002	0.000
D4/stream	0.959	0.087	0.030	0.234	0.384	0.050	0.026	0.002
R1/pond	0.227	0.021	0.007	0.055	0.091	0.012	0.006	0.001
R1/stream	7.108	0.646	0.222	1.734	2.843	0.370	0.192	0.018
R3/stream	8.977	0.816	0.281	2.190	3.591	0.468	0.243	0.023
Step 3	Late application							
D3/ditch	1.142	0.104	0.036	0.279	0.457	0.059	0.031	0.003
D4/pond	0.108	0.010	0.003	0.026	0.043	0.006	0.003	0.000
D4/stream	1.001	0.091	0.031	0.244	0.400	0.052	0.027	0.003
R1/pond	0.251	0.023	0.008	0.061	0.100	0.013	0.007	0.001
R1/stream	7.059	0.642	0.221	1.722	2.824	0.368	0.191	0.018
R3/stream	5.442	0.495	0.170	1.327	2.177	0.283	0.147	0.014

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-18 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Phenmedipham for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in leaf-crops use group no 3 (5 × 1.2 L product/ha, 7-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		1100	320	410	25.0	192	370	3900
AF		100	10	100	10	10	10	10
RAC [µg/L]		11.0	32.0	4.10	2.50	19.2	37.0	390
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio						
Step 1								
	28.030	2.548	0.876	6.837	11.212	1.460	0.758	0.072
Step 2								
N-Europe/Mar-May	16.156	1.469	0.505	3.940	6.462	0.841	0.437	0.041
N-Europe/Jun-Sep	16.156	1.469	0.505	3.940	6.462	0.841	0.437	0.041
S-Europe/Mar-May	32.312	2.937	1.010	7.881	12.925	1.683	0.873	0.083
S-Europe/Jun-Sep	24.234	2.203	0.757	5.911	9.694	1.262	0.655	0.062
Step 3	Early application							
D3/ditch	0.507	0.046	0.016	0.124	0.203	0.026	0.014	0.001
D4/pond	0.071	0.006	0.002	0.017	0.028	0.004	0.002	0.000
D4/stream	0.650	0.059	0.020	0.159	0.260	0.034	0.018	0.002
R1/pond	0.122	0.011	0.004	0.030	0.049	0.006	0.003	0.000
R1/stream	3.654	0.332	0.114	0.891	1.462	0.190	0.099	0.009
R3/stream	4.127	0.375	0.129	1.007	1.651	0.215	0.112	0.011
Step 3	Late application							
D3/ditch	0.507	0.046	0.016	0.124	0.203	0.026	0.014	0.001
D4/pond	0.086	0.008	0.003	0.021	0.034	0.004	0.002	0.000
D4/stream	0.815	0.074	0.025	0.199	0.326	0.042	0.022	0.002
R1/pond	0.090	0.008	0.003	0.022	0.036	0.005	0.002	0.000
R1/stream	2.533	0.230	0.079	0.618	1.013	0.132	0.068	0.006
R3/stream	3.292	0.299	0.103	0.803	1.317	0.171	0.089	0.008

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-19 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Phenmedipham for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in leaf-crops use group no 4 (3 × 1.8 L product/ha, 6-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _r C ₅₀	NOEC	E _r C ₅₀
[µg/L]		1100	320	410	25.0	192	370	3900
AF		100	10	100	10	10	10	10
RAC [µg/L]		11.0	32.0	4.10	2.50	19.2	37.0	390
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio						
Step 1								
	42.048	3.823	1.314	10.256	16.819	2.190	1.136	0.108
Step 2								
N-Europe/Mar-May	16.384	1.489	0.512	3.996	6.554	0.853	0.443	0.042
N-Europe/Jun-Sep	16.384	1.489	0.512	3.996	6.554	0.853	0.443	0.042
S-Europe/Mar-May	32.768	2.979	1.024	7.992	13.107	1.707	0.886	0.084
S-Europe/Jun-Sep	24.576	2.234	0.768	5.994	9.830	1.280	0.664	0.063
Step 3	Early application							
D3/ditch	0.857	0.078	0.027	0.209	0.343	0.045	0.023	0.002
D4/pond	0.057	0.005	0.002	0.014	0.023	0.003	0.002	0.000
D4/stream	0.719	0.065	0.022	0.175	0.288	0.037	0.019	0.002
R1/pond	0.165	0.015	0.005	0.040	0.066	0.009	0.004	0.000
R1/stream	5.170	0.470	0.162	1.261	2.068	0.269	0.140	0.013
R3/stream	6.505	0.591	0.203	1.587	2.602	0.339	0.176	0.017
Step 3	Late application							
D3/ditch	0.857	0.078	0.027	0.209	0.343	0.045	0.023	0.002
D4/pond	0.075	0.007	0.002	0.018	0.030	0.004	0.002	0.000
D4/stream	0.713	0.065	0.022	0.174	0.285	0.037	0.019	0.002
R1/pond	0.181	0.016	0.006	0.044	0.072	0.009	0.005	0.000
R1/stream	5.094	0.463	0.159	1.242	2.038	0.265	0.138	0.013
R3/stream	3.939	0.358	0.123	0.961	1.576	0.205	0.106	0.010

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-20 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for Phenmedipham for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in leaf-crops use group no 5 (3 × 2.4 L product/ha, 9-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Sediment dwelling prolonged	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Chironomus riparius</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	ErC ₅₀	NOEC	ErC ₅₀
[µg/L]		1100	320	410	25.0	192	370	3900
AF		100	10	100	10	10	10	10
RAC [µg/L]		11.0	32.0	4.10	2.50	19.2	37.0	390
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio						
Step 1								
	56.064	5.097	1.752	13.674	22.426	2.920	1.515	0.144
Step 2								
N-Europe/Mar-May	20.895	1.900	0.653	5.096	8.358	1.088	0.565	0.054
N-Europe/Jun-Sep	20.895	1.900	0.653	5.096	8.358	1.088	0.565	0.054
S-Europe/Mar-May	41.790	3.799	1.306	10.193	16.716	2.177	1.129	0.107
S-Europe/Jun-Sep	31.342	2.849	0.979	7.644	12.537	1.632	0.847	0.080
Step 3	Early application							
D3/ditch	1.143	0.104	0.036	0.279	0.457	0.060	0.031	0.003
D4/pond	0.087	0.008	0.003	0.021	0.035	0.005	0.002	0.000
D4/stream	0.959	0.087	0.030	0.234	0.384	0.050	0.026	0.002
R1/pond	0.148	0.013	0.005	0.036	0.059	0.008	0.004	0.000
R1/stream	4.613	0.419	0.144	1.125	1.845	0.240	0.125	0.012
R3/stream	5.708	0.519	0.178	1.392	2.283	0.297	0.154	0.015
Step 3	Late application							
D3/ditch	1.142	0.104	0.036	0.279	0.457	0.059	0.031	0.003
D4/pond	0.103	0.009	0.003	0.025	0.041	0.005	0.003	0.000
D4/stream	0.972	0.088	0.030	0.237	0.389	0.051	0.026	0.002
R1/pond	0.146	0.013	0.005	0.036	0.058	0.008	0.004	0.000
R1/stream	4.114	0.374	0.129	1.003	1.646	0.214	0.111	0.011
R3/stream	5.442	0.495	0.170	1.327	2.177	0.283	0.147	0.014

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-21 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for MHPC for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~leaf-crops~~ use group no 1 (6 × 1.2 L product/ha, 5-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _b C ₅₀	E _b C ₅₀
[µg/L]		75000	32 ^{a)}	14000	5000	30000	127.98 ^{a)}
AF		100	10	100	10	10	10
RAC [µg/L]		750	3.2	140	500	3000	12.798
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio					
Step 1							
	163.371	0.218	51.053	1.167	0.327	0.054	12.765
Step 2							
N-Europe/Mar-May	12.228	0.016	3.821	0.087	0.024	0.005	0.955
N-Europe/Jun-Sep	12.228	0.016	3.821	0.087	0.024	0.005	0.955
S-Europe/Mar-May	23.420	0.031	7.319	0.167	0.047	0.008	1.830
S-Europe/Jun-Sep	17.824	0.024	5.570	0.127	0.036	0.006	1.393
Step 3	Early application						
D3/ditch	0.116	0.000	0.036	0.001	0.000	0.000	0.009
D4/pond	0.136	0.000	0.043	0.001	0.000	0.000	0.011
D4/stream	0.299	0.000	0.093	0.002	0.001	0.000	0.023
R1/pond	0.256	0.000	0.080	0.002	0.001	0.000	0.020
R1/stream	2.236	0.003	0.699	0.016	0.004	0.001	0.175
R3/stream	2.182	0.003	0.682	0.016	0.004	0.001	0.170
Step 3	Late application						
D3/ditch	0.125	0.000	0.039	0.001	0.000	0.000	0.010
D4/pond	0.147	0.000	0.046	0.001	0.000	0.000	0.011
D4/stream	0.372	0.000	0.116	0.003	0.001	0.000	0.029
R1/pond	0.097	0.000	0.030	0.001	0.000	0.000	0.008
R1/stream	1.780	0.002	0.556	0.013	0.004	0.001	0.139
R3/stream	1.711	0.002	0.535	0.012	0.003	0.001	0.134

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent and considering molecular weight of the metabolite.

Table 9.5.2-22 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for MHPC for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in
use group no 2 (3 × 2.4 L product/ha, 6-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _b C ₅₀	E _b C ₅₀
[µg/L]		75000	32 ^{a)}	14000	5000	30000	127.98 ^{a)}
AF		100	10	100	10	10	10
RAC [µg/L]		750	3.2	140	500	3000	12.798
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio					
Step 1							
	163.371	0.218	51.053	1.167	0.327	0.054	12.765
Step 2							
N-Europe/Mar-May	13.862	0.018	4.332	0.099	0.028	0.005	1.083
N-Europe/Jun-Sep	13.862	0.018	4.332	0.099	0.028	0.005	1.083
S-Europe/Mar-May	26.212	0.035	8.191	0.187	0.052	0.009	2.048
S-Europe/Jun-Sep	20.037	0.027	6.262	0.143	0.040	0.007	1.565
Step 3	Early application						
D3/ditch	0.282	0.000	0.088	0.002	0.001	0.000	0.022
D4/pond	0.134	0.000	0.042	0.001	0.000	0.000	0.010
D4/stream	0.259	0.000	0.081	0.002	0.001	0.000	0.020
R1/pond	0.243	0.000	0.076	0.002	0.000	0.000	0.019
R1/stream	2.664	0.004	0.833	0.019	0.005	0.001	0.208
R3/stream	3.312	0.004	1.035	0.024	0.007	0.001	0.259
Step 3	Late application						
D3/ditch	0.303	0.000	0.095	0.002	0.001	0.000	0.024
D4/pond	0.155	0.000	0.048	0.001	0.000	0.000	0.012
D4/stream	0.364	0.000	0.114	0.003	0.001	0.000	0.028
R1/pond	0.220	0.000	0.069	0.002	0.000	0.000	0.017
R1/stream	2.698	0.004	0.843	0.019	0.005	0.001	0.211
R3/stream	2.104	0.003	0.658	0.015	0.004	0.001	0.164

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent and considering molecular weight of the metabolite.

Table 9.5.2-23 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for MHPC for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in ~~leaf-crops~~ use group no 3 (5 × 1.2 L product/ha, 7-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _b C ₅₀	E _b C ₅₀
[µg/L]		75000	32 ^{a)}	14000	5000	30000	127.98 ^{a)}
AF		100	10	100	10	10	10
RAC [µg/L]		750	3.2	140	500	3000	12.798
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio					
Step 1							
	136.14	0.182	42.544	0.972	0.272	0.045	10.638
Step 2							
N-Europe/Mar-May	10.053	0.013	3.142	0.072	0.020	0.003	0.786
N-Europe/Jun-Sep	10.053	0.013	3.142	0.072	0.020	0.003	0.786
S-Europe/Mar-May	19.187	0.026	5.996	0.137	0.038	0.006	1.499
S-Europe/Jun-Sep	14.620	0.019	4.569	0.104	0.029	0.005	1.142
Step 3	Early application						
D3/ditch	0.132	0.000	0.041	0.001	0.000	0.000	0.010
D4/pond	0.103	0.000	0.032	0.001	0.000	0.000	0.008
D4/stream	0.237	0.000	0.074	0.002	0.000	0.000	0.019
R1/pond	0.167	0.000	0.052	0.001	0.000	0.000	0.013
R1/stream	1.369	0.002	0.428	0.010	0.003	0.000	0.107
R3/stream	1.522	0.002	0.476	0.011	0.003	0.001	0.119
Step 3	Late application						
D3/ditch	0.137	0.000	0.043	0.001	0.000	0.000	0.011
D4/pond	0.113	0.000	0.035	0.001	0.000	0.000	0.009
D4/stream	0.297	0.000	0.093	0.002	0.001	0.000	0.023
R1/pond	0.101	0.000	0.032	0.001	0.000	0.000	0.008
R1/stream	1.188	0.002	0.371	0.008	0.002	0.000	0.093
R3/stream	1.263	0.002	0.395	0.009	0.003	0.000	0.099

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent and considering molecular weight of the metabolite.

Table 9.5.2-24 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for **MHPC** for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in **leaf-crops** use group no 4 (3 × 1.8 L product/ha, 6-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _b C ₅₀	E _b C ₅₀
[µg/L]		75000	32 ^{a)}	14000	5000	30000	127.98 ^{a)}
AF		100	10	100	10	10	10
RAC [µg/L]		750	3.2	140	500	3000	12.798
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio					
Step 1							
	122.528	0.163	38.290	0.875	0.245	0.041	9.574
Step 2							
N-Europe/Mar-May	10.397	0.014	3.249	0.074	0.021	0.003	0.812
N-Europe/Jun-Sep	10.397	0.014	3.249	0.074	0.021	0.003	0.812
S-Europe/Mar-May	19.659	0.026	6.143	0.140	0.039	0.007	1.536
S-Europe/Jun-Sep	15.028	0.020	4.696	0.107	0.030	0.005	1.174
Step 3	Early application						
D3/ditch	0.211	0.000	0.066	0.002	0.000	0.000	0.016
D4/pond	0.088	0.000	0.028	0.001	0.000	0.000	0.007
D4/stream	0.186	0.000	0.058	0.001	0.000	0.000	0.015
R1/pond	0.179	0.000	0.056	0.001	0.000	0.000	0.014
R1/stream	1.938	0.003	0.606	0.014	0.004	0.001	0.151
R3/stream	2.400	0.003	0.750	0.017	0.005	0.001	0.188
Step 3	Late application						
D3/ditch	0.227	0.000	0.071	0.002	0.000	0.000	0.000
D4/pond	0.098	0.000	0.031	0.001	0.000	0.000	0.000
D4/stream	0.259	0.000	0.081	0.002	0.001	0.001	0.000
R1/pond	0.160	0.000	0.050	0.001	0.000	0.000	0.000
R1/stream	1.947	0.003	0.608	0.014	0.004	0.004	0.001
R3/stream	1.523	0.002	0.476	0.011	0.003	0.003	0.001

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent and considering molecular weight of the metabolite.

Table 9.5.2-25 Aquatic organisms: acceptability of risk (PEC/RAC < 1) for MHPC for each organism group based on FOCUS Steps 1, 2 and 3 calculations for the use of HBZ10 in beet-cropps use group no 5 (3 × 2.4 L product/ha, 9-day interval)

Group		Fish acute	Fish prolonged	Invertebrate acute	Invertebrate prolonged	Algae	Higher plant
Test species		<i>Oncorhynchus mykiss</i>	<i>Oncorhynchus mykiss</i>	<i>Daphnia magna</i>	<i>Daphnia magna</i>	<i>Pseudokirchneriella subcapitata</i>	<i>Lemna minor</i>
Endpoint		LC ₅₀	NOEC	EC ₅₀	NOEC	E _b C ₅₀	E _b C ₅₀
[µg/L]		75000	32 ^{a)}	14000	5000	30000	127.98 ^{a)}
AF		100	10	100	10	10	10
RAC [µg/L]		750	3.2	140	500	3000	12.798
FOCUS Scenario	PEC _{SW} global max [µg/L]	PEC/RAC ratio					
Step 1							
	163.371	0.218	51.053	1.167	0.327	0.054	12.765
Step 2							
N-Europe/Mar-May	13.220	0.018	4.131	0.094	0.026	0.004	1.033
N-Europe/Jun-Sep	13.220	0.018	4.131	0.094	0.026	0.004	1.033
S-Europe/Mar-May	25.032	0.033	7.823	0.179	0.050	0.008	1.956
S-Europe/Jun-Sep	19.126	0.026	5.977	0.137	0.038	0.006	1.494
Step 3	Early application						
D3/ditch	0.281	0.000	0.088	0.002	0.001	0.000	0.022
D4/pond	0.141	0.000	0.044	0.001	0.000	0.000	0.011
D4/stream	0.285	0.000	0.089	0.002	0.001	0.000	0.022
R1/pond	0.194	0.000	0.061	0.001	0.000	0.000	0.015
R1/stream	1.729	0.002	0.540	0.012	0.003	0.001	0.135
R3/stream	2.106	0.003	0.658	0.015	0.004	0.001	0.165
Step 3	Late application						
D3/ditch	0.304	0.000	0.095	0.002	0.001	0.000	0.024
D4/pond	0.142	0.000	0.044	0.001	0.000	0.000	0.011
D4/stream	0.354	0.000	0.111	0.003	0.001	0.000	0.028
R1/pond	0.135	0.000	0.042	0.001	0.000	0.000	0.011
R1/stream	1.632	0.002	0.510	0.012	0.003	0.001	0.128
R3/stream	2.104	0.003	0.658	0.015	0.004	0.001	0.164

AF: Assessment factor; PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

^{a)} Endpoint estimated by assuming ten times greater toxicity than the parent and considering molecular weight of the metabolite.

For the active substance Ethofumesate, the calculated PEC/RAC ratios did not indicate an acceptable risk for the more sensitive group of aquatic organisms (risk for fish as characterised by NOEC for *Danio rerio* of 156 µg/L in connection with an assessment factor of 10) in FOCUS Step 3 scenario R3/stream for early application and in FOCUS Step 3 scenario R1/stream for late application for the intended use in beet crops (use group 2 (3 × 2.4 L product/ha, 6-day interval) and for R1 scenario for late application (use group no 4 (3 × 1.8 L product/ha, 6-day interval)). Therefore, further PEC/RAC ratio were calculated based on FOCUS Step 4 PEC_{sw} values considering reduced exposure of surface water bodies.

For the Ethofumesate metabolites NC 20645 and NC 8493, the calculated PEC/RAC ratios indicated an acceptable risk for aquatic organisms in all FOCUS Step 2 and 3 scenarios for the all intended uses of HBZ10 in beet crops.

For the active substance Phenmedipham, the calculated PEC/RAC ratios did not indicate an acceptable risk for the more sensitive group of aquatic organisms (risk for aquatic invertebrates as characterised by NOEC for *Daphnia magna* of 25.0 µg/L in connection with an assessment factor of 10) in FOCUS Step 3 scenario R1/stream and R3/stream for early application and late application for all intended uses of HBZ10 in beet crops. Therefore, the relevant global maximum FOCUS Step 4 PEC_{sw} values and the resulting PEC/RAC ratios are presented in the following tables below.

For the Phenmedipham metabolite MHPC, the calculated PEC/RAC ratios indicated an acceptable risk for aquatic organisms in all FOCUS Step 3 scenarios for the all intended uses of HBZ10 in beet crops except for the R3 stream scenario following the early application in use group 2 (3 × 2.4 L product/ha, 6-day interval). For this scenario, the PEC/RAC ratio is calculated to be slightly above the trigger of 1, i.e., 1.035; however, the risk mitigation measures implemented for this scenario as a result of the unfavourable Tier 1 risk identified for parent compound Phenmedipham (i.e., 20 m no-spray buffer zone including 20 m vegetative filter strip; please refer to **Table 9.5.2-28**), are considered more than adequate to conclude on an acceptable chronic risk to fish also for metabolite MHPC. No additional PEC_{sw} calculations at FOCUS Step 4 for the metabolite MHPC have been performed.

Table 9.5.2-26 Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for Ethofumesate based on FOCUS Step 4 calculations and toxicity data for fish with mitigation of spray drift and run-off for the use of HBZ10 in ~~beet crops~~ use group 2

Intended use		Beet crops: Sugar beet, red beet/yellow beet/fodder beet, chard					
Active substance		Ethofumesate					
Application rate [g/ha]		3 × 300 (6-day interval) – early application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R3/stream	19.58	-	-	-	8.934	-
RAC [µg/L]		15.6					
(Danio rerio)		PEC/RAC ratio					
None	R3/stream	1.2551	-	-	-	0.573	-
Application rate [g/ha]		3 × 300 (6-day interval) – late application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	24.660	-	-	-	11.21	-
None	R3/stream	16.490	-	-	-	7.514	-
RAC [µg/L]		15.6					
(Danio rerio)		PEC/RAC ratio					
None	R1/stream	1.5808	-	-	-	0.719	-
None	R3/stream	1.0571	-	-	-	0.482	-

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

The PEC/RAC values for Ethofumesate for all aquatic organisms are below the trigger value of 1 if a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is considered for the intended use in beet crops indicating an acceptable risk to aquatic organisms following the application of HBZ10 at the proposed use pattern (use group 2).

This mitigation measure is only relevant for the FOCUS scenarios R1/stream (late application) and R3/stream (early and late application).

Table 9.5.2-26a Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for Ethofumesate based on FOCUS Step 4 calculations and toxicity data for fish with mitigation of spray drift and run-off for the use of HBZ10 in ~~beet-crops~~ use group 4

Intended use		Beet-crops Sugar beet, red beet/yellow beet/fodder beet, chard					
Active substance		Ethofumesate					
Application rate [g/ha]		3 × 225 (6-day interval) – late application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	16.94	-	-	-	7.704	-
RAC [µg/L]		15.6					
(Danio rerio)		PEC/RAC ratio					
None	R1/stream	1.0859	-	-	-	0.494	-

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

The PEC/RAC values for Ethofumesate for all aquatic organisms are below the trigger value of 1 if a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is considered for the intended use in beet crops indicating an acceptable risk to aquatic organisms following the application of HBZ10 at the proposed use pattern (use group 4). This mitigation measure is only relevant for the FOCUS scenario R1/stream (late application)

Table 9.5.2-27 Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for Phenmedipham based on FOCUS Step 4 calculations and toxicity data for aquatic invertebrates with mitigation of spray drift and run-off for the use of HBZ10 in beet-crops use group 1

Intended use		<u>Beet-crops</u> Sugar beet, red beet/yellow beet/fodder beet, chard					
Active substance		Phenmedipham					
Application rate [g/ha]		6 × 150 (5-day interval) – early application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	6.015	-	-	-	2.726	1.425
None	R3/stream	5.196	-	-	-	2.695	1.413
RAC [µg/L]		2.50					
(Daphnia magna)		PEC/RAC ratio					
None	R1/stream	2.406	-	-	-	1.090	0.570
None	R3/stream	2.078	-	-	-	1.078	0.565
Application rate [g/ha]		6 × 150 (5-day interval) – late application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	3.455	-	-	-	1.508	-
None	R3/stream	4.425	-	-	-	2.010	-
RAC [µg/L]		2.50					
(Daphnia magna)		PEC/RAC ratio					
None	R1/stream	1.382	-	-	-	0.603	-
None	R3/stream	1.770	-	-	-	0.804	-

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-28 Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for Phenmedipham based on FOCUS Step 4 calculations and toxicity data for aquatic invertebrates with mitigation of spray drift and run-off for the use of HBZ10 in beet-crops use group 2

Intended use		<u>Beet-crops</u> Sugar beet, red beet/yellow beet/fodder beet, chard					
Active substance		Phenmedipham					
Application rate [g/ha]		3 × 300 (6-day interval) – early application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	7.108	-	-	-	3.216	1.682
None	R3/stream	8.977	-	-	-	4.089	2.144
RAC [µg/L]		2.50					
(Daphnia magna)		PEC/RAC ratio					
None	R1/stream	2.843	-	-	-	1.286	0.673
None	R3/stream	3.591	-	-	-	1.636	0.858
Application rate [g/ha]		3 × 300 (6-day interval) – late application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	7.059	-	-	-	3.200	1.675
None	R3/stream	5.442	-	-	-	2.472	-
RAC [µg/L]		2.50					
(Daphnia magna)		PEC/RAC ratio					
None	R1/stream	2.824	-	-	-	1.280	0.670
None	R3/stream	2.177	-	-	-	0.989	-

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-29 Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for Phenmedipham based on FOCUS Step 4 calculations and toxicity data for aquatic invertebrates with mitigation of spray drift and run-off for the use of HBZ10 in beet-crops use group 3

Intended use		<u>Beet-crops</u> Sugar beet, red beet/yellow beet/fodder beet, chard					
Active substance		Phenmedipham					
Application rate [g/ha]		5 × 150 (7-day interval) – early application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	3.654	-	-	-	1.653	-
None	R3/stream	4.127	-	-	-	1.880	-
RAC [µg/L]		2.50					
<i>(Daphnia magna)</i>		PEC/RAC ratio					
None	R1/stream	1.462	-	-	-	0.661	-
None	R3/stream	1.651	-	-	-	0.752	-
Application rate [g/ha]		5 × 150 (7-day interval) – late application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	2.533	-	-	-	1.148	-
None	R3/stream	3.292	-	-	-	1.496	-
RAC [µg/L]		2.50					
<i>(Daphnia magna)</i>		PEC/RAC ratio					
None	R1/stream	1.013	-	-	-	0.459	-
None	R3/stream	1.317	-	-	-	0.598	-

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-30 Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for Phenmedipham based on FOCUS Step 4 calculations and toxicity data for aquatic invertebrates with mitigation of spray drift and run-off for the use of HBZ10 in beet-crops use group 4

Intended use		<u>Beet-crops</u> Sugar beet, red beet/yellow beet/fodder beet, chard					
Active substance		Phenmedipham					
Application rate [g/ha]		3 × 225 (6-day interval) – early application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	5.170	-	-	-	2.340	-
None	R3/stream	6.505	-	-	-	2.963	1.553
RAC [µg/L]		2.50					
<i>(Daphnia magna)</i>		PEC/RAC ratio					
None	R1/stream	2.068	-	-	-	0.936	-
None	R3/stream	2.602	-	-	-	1.185	0.621
Application rate [g/ha]		3 × 225 (6-day interval) – late application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	5.094	-	-	-	2.308	-
None	R3/stream	3.939	-	-	-	1.789	-
RAC [µg/L]		2.50					
<i>(Daphnia magna)</i>		PEC/RAC ratio					
None	R1/stream	2.038	-	-	-	0.923	-
None	R3/stream	1.576	-	-	-	0.716	-

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Table 9.5.2-31 Aquatic organisms: PEC calculation and acceptability of risk (PEC/RAC < 1) for Phenmedipham based on FOCUS Step 4 calculations and toxicity data for aquatic invertebrates with mitigation of spray drift and run-off for the use of HBZ10 in beet-crops – use group 5

Intended use		Beet-crops Sugar beet, red beet/yellow beet/fodder beet, chard					
Active substance		Phenmedipham					
Application rate [g/ha]		3 × 300 (6-day interval) – early application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	4.613	-	-	-	2.087	-
None	R3/stream	5.708	-	-	-	2.600	1.363
RAC [µg/L]		2.50					
(Daphnia magna)		PEC/RAC ratio					
None	R1/stream	1.845	-	-	-	0.835	-
None	R3/stream	2.283	-	-	-	1.040	0.545
Application rate [g/ha]		3 × 300 (6-day interval) – late application					
Drift reduction	Vegetated filter strip [m]	None	None	None	None	10	20
	No-spray buffer [m]	None	10	15	20	10	20
None	R1/stream	4.114	-	-	-	1.864	-
None	R3/stream	5.442	-	-	-	2.472	-
RAC [µg/L]		2.50					
(Daphnia magna)		PEC/RAC ratio					
None	R1/stream	1.646	-	-	-	0.746	-
None	R3/stream	2.177	-	-	-	0.989	-

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

The PEC/RAC values for Phenmedipham for all aquatic organisms are below the trigger value of 1 if a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is considered for the intended use groups 1 and 2 in beet-crops indicating an acceptable risk to aquatic organisms following the application of HBZ10 at the proposed use pattern. This mitigation measure is only relevant for the FOCUS scenarios R1/stream and R3/stream.

The PEC/RAC values for Phenmedipham for all aquatic organisms are below the trigger value of 1 if a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is considered for the intended use group 3 in beet-crops indicating an acceptable risk to aquatic organisms following the application of HBZ10 at the proposed use pattern. This mitigation measure is only relevant for the FOCUS scenarios R1/stream and R3/stream.

The PEC/RAC values for Phenmedipham for all aquatic organisms are below the trigger value of 1 if a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is considered for the intended use groups 4 and 5 in beet-crops indicating an acceptable risk to aquatic organisms following the application of HBZ10 at the proposed use pattern. This mitigation measure is only relevant for the FOCUS scenarios R1/stream and R3/stream where a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is required for R1 stream, and a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is required for R3 stream.

zRMS comments:

The aquatic risk assessment presented above for the active substances has been validated by zRMS.

Ethofumesate

Based on the performed calculations following conclusions may be derived:

1. Use group 1 (6×1.2 L product/ha, 5-day interval)
 - Etofumesate: acceptable risk with no need for risk mitigation measures
2. Use group no 2 (3×2.4 L product/ha, 6-day interval)
 - Etofumesate: acceptable risk with no need for risk mitigation measures except R1 (stream) and R3 (stream) scenarios for early application and R1 (stream) scenario for late application.
 - Etofumesate: acceptable risk for R1 scenario with 10-meter vegetative buffer zone for early application.
 - Etofumesate: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.
3. Use group no 3 (5×1.2 L product/ha, 7-day interval)
 - Etofumesate: acceptable risk with no need for risk mitigation measures.
4. Use group no 4 (3×1.8 L product/ha, 6-day interval)
 - Etofumesate: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) scenario for late application.
 - Etofumesate: acceptable risk for R1 (stream) scenario with 10-meter vegetative buffer zone for late application.
5. Use group no 5 (3×2.4 L product/ha, 9-day interval)
 - Etofumesate: acceptable risk with no need for risk mitigation measures.

For the Ethofumesate metabolites NC 20645 and NC 8493, the calculated PEC/RAC ratios indicated an acceptable risk for aquatic organisms in all FOCUS Step 2 and 3 scenarios for the intended use in beet crops.

Phenmedipham

1. Use group 1 (6×1.2 L product/ha, 5-day interval)
 - Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) and R3 (stream) scenarios for early and late application
 - Phenmedipham: acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for early application
 - Phenmedipham: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application
2. Use group no 2 (3×2.4 L product/ha, 6-day interval)
 - Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) and R3 (stream) scenarios for early and late application
 - Phenmedipham: acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for early application
 - Phenmedipham: acceptable risk for R1 scenarios with 20-meter vegetative buffer zone and 10-meter vegetative buffer zone for R3 scenario for late application
3. Use group no 3 (5×1.2 L product/ha, 7-day interval)
 - Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) and R3 (stream) scenarios for early and late application
 - Phenmedipham: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early and late application
4. Use group no 4 (3×1.8 L product/ha, 6-day interval)
 - Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) and R3 (stream) scenarios for early and late application
 - Phenmedipham: acceptable risk for R1 scenario with 10-meter vegetative buffer zone and for R3 scenarios with 20-meter vegetative buffer zone for early application
 - Phenmedipham: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application

5. Use group no 5 (3×2.4 L product/ha, 9-day interval)

- Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except: R1 (stream) and R3 (stream) scenarios for early and late application
- Phenmedipham: acceptable risk for R1 stream with 10-meter vegetative buffer zone and R3 stream scenarios with 20-meter vegetative buffer zone for early application
- Phenmedipham: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application

Based on mixture toxicity assessment it was indicated that the active substance Phenmedipham contributes more than 90% to the toxicity of formulation HBZ10 and thus drives the overall mixture toxicity to aquatic invertebrates, and algae. The risk assessment for these groups of organisms was based on the single-substance toxicity data of Phenmedipham (Step 6 of EFSA decision scheme).

For the Phenmedipham metabolite MHPC (assumed 10 x more than the parent), the calculated PEC/RAC ratios indicated an acceptable risk for aquatic organisms in all FOCUS Step 3 scenarios for the all intended uses of HBZ10 in beet crops except for the R3 stream scenario following the early application in use group 2 (3×2.4 L product/ha, 6-day interval). For this scenario, the PEC/RAC ratio was 1.035; however, the risk mitigation measures implemented for this scenario as a result of the Tier 1 risk identified for parent compound Phenmedipham (i.e., 20 m no-spray buffer zone including 20 m vegetative filter strip is considered sufficient to conclude the acceptable risk for this metabolite.

Based on the results of this risk assessment, a low risk to aquatic organisms can be expected from the use of HBZ10 when applying the following risk mitigation measures:

- For the intended use group 3 in beet crops (early and late applications, 5×1.2 L product/ha with 7 day interval), to protect aquatic organisms, the implementation of a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is required.

- For all the other intended use groups (1, 2, 4 and 5) in beet crops (early and late application), to protect aquatic organisms, the implementation of a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is required.

Such mitigation measures are related to scenarios R1 stream and/or R3 stream and thus, conclusions regarding the mitigation measures should be considered at national level where relevant.

Concerned Member States must decide on applicability of indicated risk mitigation measures in their countries at the product authorisation.

Please note that additional aquatic risk assessment may be required by the concerned Member States that do not accept simulations performed according to FOCUS recommendations.

9.5.3 Overall conclusions

The evaluation of the risk for aquatic and sediment-dwelling organisms was performed in accordance with the recommendations of the “Guidance document on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters in the context of Regulation (EC) No 1107/2009”, as provided by the Commission Services (SANTE-2015-00080, 15 January 2015).

Effects of HBZ10 on aquatic organisms were not evaluated as part of the respective EU reviews of Ethofumesate and Phenmedipham.

Based on the available data and the mixture toxicity risk assessment, it can be concluded that Phenmedipham is driving the overall mixture toxicity and that an acceptable risk to aquatic organisms following application of HBZ10 in beet crops for all intended use groups is expected. Moreover, the risk assessment based the single-substance toxicity data of Ethofumesate and Phenmedipham has been performed.

Based on According to the results of this the risk assessment based on single-substance toxicity data, a low risk to aquatic organisms can be expected from the use of HBZ10 when applying the following risk mitigation measures:

- For the intended use group 3 **in-beet-crops** (early and late applications), to protect aquatic organisms, the implementation of a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is required.
- For all the other intended use groups (1, 2, 4 and 5) **in-beet-crops** (early and late application), to protect aquatic organisms, the implementation of a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is required.

According to the results of the mixture risk assessment, and considering mixture toxicity risk assessment based on step 8 is very conservative, applicant propose that a low risk to aquatic organisms can be expected from the use of HBZ10 when applying the following risk mitigation measures:

- For the intended use groups 1, 3, 4 and 5 (early and late applications), to protect aquatic organisms, the implementation of a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is required.
- For the other intended use group 1 (early and late application), to protect aquatic organisms, the implementation of a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is required.

Such mitigation measures are related to scenarios R1 stream and/or R3 stream and thus, conclusions regarding the mitigation measures should be considered at national level where relevant.

zRMS comments:

The aquatic risk assessment presented above has been validated by zRMS.

Ethofumesate

Based on the performed calculations following conclusions may be derived:

1. Use group 1 (6×1.2 L product/ha, 5-day interval)
 - Ethofumesate: acceptable risk with no need for risk mitigation measures
2. Use group no 2 (3×2.4 L product/ha, 6-day interval)
 - Ethofumesate: acceptable risk with no need for risk mitigation measures except R1 (stream) and R3 (stream) scenarios for early application and R1 (stream) scenario for late application.
 - Ethofumesate: acceptable risk for R1 scenario with 10-meter vegetative buffer zone for early application.
 - Ethofumesate: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.
3. Use group no 3 (5×1.2 L product/ha, 7-day interval)
 - Ethofumesate: acceptable risk with no need for risk mitigation measures.
4. Use group no 4 (3×1.8 L product/ha, 6-day interval)
 - Ethofumesate: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) scenario for late application.
 - Ethofumesate: acceptable risk for R1 (stream) scenario with 10-meter vegetative buffer zone for late application.
5. Use group no 5 (3×2.4 L product/ha, 9-day interval)
 - Ethofumesate: acceptable risk with no need for risk mitigation measures.

For the Ethofumesate metabolites NC 20645 and NC 8493, the calculated PEC/RAC ratios indicated an acceptable risk for aquatic organisms in all FOCUS Step 2 and 3 scenarios for the intended use in beet crops.

Phenmedipham

1. Use group 1 (6×1.2 L product/ha, 5-day interval)

- Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) and R3 (stream) scenarios for early and late application
- Phenmedipham: acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for early application
- Phenmedipham: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application

2. Use group no 2 (3×2.4 L product/ha, 6-day interval)

- Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) and R3 (stream) scenarios for early and late application
- Phenmedipham: acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for early application
- Phenmedipham: acceptable risk for R1 scenarios with 20-meter vegetative buffer zone and 10-meter vegetative buffer zone for R3 scenario for late application

3. Use group no 3 (5×1.2 L product/ha, 7-day interval)

- Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) and R3 (stream) scenarios for early and late application
- Phenmedipham: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early and late application

4. Use group no 4 (3×1.8 L product/ha, 6-day interval)

- Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except R1 (stream) and R3 (stream) scenarios for early and late application
- Phenmedipham: acceptable risk for R1 scenario with 10-meter vegetative buffer zone and for R3 scenarios with 20-meter vegetative buffer zone for early application
- Phenmedipham: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application

5. Use group no 5 (3×2.4 L product/ha, 9-day interval)

- Phenmedipham: acceptable risk with no need for risk mitigation measures for all scenarios except: R1 (stream) and R3 (stream) scenarios for early and late application
- Phenmedipham: acceptable risk for R1 stream with 10-meter vegetative buffer zone and R3 stream scenarios with 20-meter vegetative buffer zone for early application
- Phenmedipham: acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application

Based on mixture toxicity assessment it was indicated that the active substance Phenmedipham contributes more than 90% to the toxicity of formulation HBZ10 and thus drives the overall mixture toxicity to aquatic invertebrates, and algae. The risk assessment for these groups of organisms was based on the single-substance toxicity data of Phenmedipham (Step 6 of EFSA decision scheme).

Based on the results of this risk assessment, a low risk to aquatic organisms can be expected from the use of HBZ10 when applying the following risk mitigation measures:

- For the intended use group 3 in beet crops (early and late applications, 5×1.2 L product/ha with 7day interval), to protect aquatic organisms, the implementation of a vegetated filter strip of 10 m including a no-spray buffer zone of 10 m is required.
- For all the other intended use groups (1, 2, 4 and 5) in beet crops (early and late application), to protect aquatic organisms, the implementation of a vegetated filter strip of 20 m including a no-spray buffer zone of 20 m is required.

Based on the mixture toxicity risk assessment, it can be concluded that Phenmedipham is driving the overall mixture toxicity for algae and that an acceptable risk to aquatic organisms following application of HBZ10 for all intended use groups according to the intended use pattern is expected.

The full mixture toxicity assessment based on STEP 8 is validated by zRMS and the following conclusions can be drawn for the mixture:

Use group 1 (6×1.2 L product/ha, 5-day interval):

- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R3 scenario with 20-meter vegetative buffer zone for early application.
- An acceptable risk for R3 scenario with 10-meter vegetative buffer zone for early application
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

Use group no 2 (3×2.4 L product/ha, 6-day interval):

- Acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 20-meter vegetative buffer zone for late application.

Use group no 3 (5×1.2 L product/ha, 7-day interval):

- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

8. Use group no 4 (3×1.8 L product/ha, 6-day interval):

- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for early application.
- Acceptable risk for R3 scenario with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 scenario with 20-meter vegetative buffer zone for late application
- Acceptable risk for R3 scenario with 10-meter vegetative buffer zone for late application.

Use group no 5 (3×2.4 L product/ha, 9-day interval):

- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for early application.
- Acceptable risk for R1 and R3 scenarios with 10-meter vegetative buffer zone for late application.

As the above mitigation measures are related to scenarios R1 and/or R3 stream in STEP 8, decision making for mitigation measures applying in each Member State should however be considered at national level, where relevant.

Such mitigation measures are related to scenarios R1 stream and/or R3 stream and thus, conclusions regarding the mitigation measures should be considered at national level where relevant.

Concerned Member States must decide on applicability of indicated risk mitigation measures in their countries at the product authorisation.

Please note that additional aquatic risk assessment may be required by the concerned Member States that do not accept simulations performed according to FOCUS recommendations.

Please note that Additional calculations may be required by cMS that do not accept surface water exposure derived using FOCUS models.

The acceptability and applicability of the indicated risk mitigation measures has to be confirmed at the cMS level.

The following text is added due to agreements during the Central Zone harmonisation meetings. It should be noted that this text has no impact on the outcome of zonal evaluation of formulation HBZ10, which was performed in line with the EU agreed methodology.

“The endpoint E_rC_{50} is selected in this Core Assessment but there are some uncertainties regarding the level of protection reached for primary producers. This is indicated for macrophytes in the aquatic Guidance Document (EFSA Journal 2013;11(7):3290) that recommends: “... a proper calibration between different tiers (higher and lower tier data) for macrophytes should be performed in the future”. Such calibration should be extended to algae. Until available relevant information on the level of protection reached is considered at EU level, it is recommended to address this uncertainty at each Member State level in the National Addendum if considered necessary, although it would be highly appreciated to have a harmonised approach in the Central zone.”

9.6 Effects on bees (KCP 10.3.1)

9.6.1 Toxicity data

Studies on the toxicity to bees have been carried out with Ethofumesate and Phenmedipham. Full details of these studies are provided in the respective EU DAR (DAR Ethofumesate, 1998; DAR Phenmedipham, 1999) and related documents (DAR Addendum Ethofumesate, 2000; DAR Addendum Phenmedipham, 2001 and 2003).

Effects on bees of HBZ10 were not evaluated as part of the EU assessment of Ethofumesate and Phenmedipham. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment is deviating the results of the EU review process. Justifications are provided below.

Table 9.6.1-1 Endpoints and effect values relevant for the risk assessment for bees - Ethofumesate

Species	Substance	Exposure System	Results	Reference
<i>Apis mellifera</i>	Ethofumesate	Oral, 48 h	LD ₅₀ > 106.3 µg a.s./bee	EFSA Conclusion (2016)
<i>Apis mellifera</i>	Ethofumesate	Oral, 48 h	LD ₅₀ > 50 µg a.s./bee	EFSA Conclusion (2016)
<i>Apis mellifera</i>	Ethofumesate	Oral, 48 h	LD ₅₀ > 100 µg a.s./bee	EFSA Conclusion (2016)
<i>Apis mellifera</i>	Ethofumesate	Contact, 48 h	LD ₅₀ > 100 µg a.s./bee	EFSA Conclusion (2016)
<i>Apis mellifera</i>	Ethofumesate	Contact, 48 h	LD ₅₀ > 50 µg a.s./bee	EFSA Conclusion (2016)
<i>Apis mellifera</i>	Ethofumesate	Contact, 48 h	LD ₅₀ > 100 µg a.s./bee	EFSA Conclusion (2016)
<i>Apis mellifera</i>	Ethofumesate	Oral, 10 d	LDD ₅₀ > 4.4 µg a.s./bee/d	EFSA Conclusion (2016)

Higher-tier studies (tunnel test, field studies)

Field tests (EFSA Conclusion 2016)

Ethofol 500 SC:

Bee brood feeding field study in Germany performed with *Apis mellifera*. Study performed to Oomen (1992) but did not account for the medications to the methodology given in EFSA (2013).

Single dose of 2.9 g product fed in 1 L of sugar solution. Three colonies per treatment group. Untreated control fed only sugar solution. Reference item was Insegar at 0.75 g a.s./L. Observations were made for 21 days after the start of feeding. Parameters assessed: mortality, bee brood terminations rate of eggs, young larvae and old larvae, mortality of pupae) and behavioural abnormalities. Statistical analysis performed. No assessment of the statistical power of the study was available.

11.5% difference between in the termination rate of eggs between the test item and the untreated control. The difference was not statistically different. No other adverse effects were noted.

Ethofumesate 500 SC

Bee brood feeding field study in Germany performed with *Apis mellifera*. Study performed to Oomen (1992) but did not account for the medications to the methodology given in EFSA (2013).

Single dose of 5.64 g product fed in 1 L of sugar solution (= 2.5 g a.s./L). Three colonies per treatment group. Untreated control fed only sugar solution. Reference item was Insegar at 0.75 g a.s./L. Observations were made for 21 days after the start of feeding. Parameters assessed: mortality, bee brood terminations rate of eggs, young larvae and old larvae, mortality of pupae) and behavioural abnormalities. Statistical analysis performed. No assessment of the statistical power of the study was available.

10.0% difference between in the termination rate of eggs between the test item and the untreated control. The difference was not statistically different. No other adverse effects were noted.

Bold written values are used for the risk assessment.

zRMS comments:

Endpoints presented in Table 9.6.1-1 are in line with the EU agreed endpoints reported in EFSA Journal 2016;14(1):4374.

Table 9.6.1-2 Endpoints and effect values relevant for the risk assessment for bees - Phenmedipham

Species	Substance	Exposure System	Results	Reference
<i>Apis mellifera</i>	Phenmedipham	Oral, 48 h	LD ₅₀ > 16 µg a.s./bee	Review Report (2004)
<i>Apis mellifera</i>	Phenmedipham	Contact, 48 h	LD ₅₀ = 50 µg a.s./bee	Review Report (2004)

Bold written values are used for the risk assessment.

Table 9.6.1-3 Endpoints and effect values relevant for the risk assessment for bees – HBZ10

Species	Substance	Exposure System	Results	Reference
<i>Apis mellifera</i>	HBZ10	Oral, 48 h	LD ₅₀ > 787 µg product/bee	Klix (2021a) KCP 10.3.1.1.1/01
<i>Bombus terrestris</i>	HBZ10	Oral, 48 h	LD ₅₀ > 1516.7 µg product/bumblebee	Klix (2021b) KCP 10.3.1.1.1/02
<i>Apis mellifera</i>	HBZ10	Contact, 48 h	LD ₅₀ = 317 µg product/bee	Klix (2021c) KCP 10.3.1.1.2/01
<i>Bombus terrestris</i>	HBZ10	Contact, 48 h	LD ₅₀ > 781.6 µg product/bumblebee	Klix (2021d) KCP 10.3.1.1.2/02
<i>Apis mellifera</i>	HBZ10	Chronic oral, 10 d	LDD ₅₀ = 29.6 µg product/bee/day LC ₅₀ = 1640 mg product/kg food NOEDD = 24.2 µg product/bee/day	Klix (2021e) KCP 10.3.1.2/01
<i>Apis mellifera</i>	HBZ10	Larvae, 22 d	NOED = 9.62 µg product/bee NOEC = 62.8 mg product/kg food	Klix (2021f) KCP 10.3.1.3/01

Bold written values are used for the risk assessment.

zRMS comments:

Endpoints presented in Table 9.6.1-2 are in line with the EU agreed endpoints reported in Review Report (2004).

Studies on toxicity of HBZ10 to bees were evaluated by the zRMS and considered acceptable. For details of evaluation, please refer to Appendix 2. Endpoints reported in Table 9.6.1-3 are confirmed to be correct.

Mixture toxicity

According to EFSA Guidance (2013)⁶, the toxicity of formulated products with two active substances should be addressed using the concentration addition model based on EFSA/2009/1438. Endpoints for the formulated product as well as for both active substances are only available for acute oral and contact toxicity. The surrogate LD₅₀ for acute oral and contact toxicity will be calculated and used in the risk assessment following EFSA Guidance (2013).

The following equation was used to derive the respective surrogate endpoints:

$$1/EC_x \text{ (mix) or } 1/NOEC \text{ (mix)} = \left(\sum_i \frac{X(a.s._i)}{EC_x \text{ or } NOEC(a.s._i)} \right)$$

Where:

X(a.s.i) = fraction of active substance [i] in the mixture

ECx or NOEC(a.s.i) = toxicity value for active substance [i]

The estimation of the surrogate endpoints is presented below:

⁶ EFSA, 2013. EFSA Guidance Document on the risk assessment of plant protection products on bees (*Apis mellifera*, *Bombus* spp. and solitary bees). EFSA Journal 2013;11(7):3295

Table 9.6.1-4 Estimation of surrogate LD₅₀ for the mixture assuming dose additivity

Active substance	Concentration of each active substance in formulation [g a.s./L]	X (a.s.i) in the mixture	LD ₅₀ [µg a.s./bee]	tox per fraction [X (a.s.i)/LD ₅₀ (a.s.i)]	LD ₅₀ (mix) [Σ mg (a.s.i)/kg bw]
Acute oral toxicity					
Ethofumesate	125	0.5	106.3	212.60	27.81
Phenmedipham	125	0.5	> 16	32.00	
HBZ10	-	1.00	> 201.4*	-	-
Acute contact toxicity					
Ethofumesate	125	0.5	> 100	200	66.67
Phenmedipham	125	0.5	50	100	
HBZ10	-	1.00	81.1*	-	-

* Measured endpoint, as sum of both active substances; re-calculated based on the nominal content and density of active substance in the formulated product

The measured toxicity of the formulated product HBZ10 for acute oral and contact toxicity to bees is lower than the calculated surrogate mixture toxicity, therefore the calculated surrogate mixture toxicity is used in the acute oral and contact toxicity risk assessment following EFSA Guidance (2013).

zRMS comments:

The applicant proposed to use a surrogate mixture toxicity data. zRMS considered more appropriate and more consistent with current approach at EU level to use measured data.

9.6.1.1 Justification for new endpoints

The risk assessment is conducted with the available endpoints for the formulated product HBZ10. To address the risk for acute and chronic oral exposure to adult bees and honeybee larvae to contaminated water, the respective endpoints from the formulated product were re-calculated based on the nominal content of active substances.

Table 9.6.1.1-1 Re-calculation of endpoints from studies with HBZ10

	Endpoint	HBZ10	Σ Ethofumesate + Phenmedipham
Acute oral	LD ₅₀	> 787 µg product/bee	> 201.4 µg a.s./bee
Acute contact	LD ₅₀	317 µg product/bee	81.1 µg a.s./bee
Chronic oral	LDD ₅₀	29.6 µg product/bee per day	7.57 µg a.s./bee
Chronic oral	NOEDD	24.2 µg product/bee per day	6.19 µg a.s./bee/day
Larvae	NOED	9.62 µg product/larva	2.46 µg a.s./larva

Endpoints were re-calculated based on the nominal content of active substance in the formulated product

9.6.2 Risk assessment

The evaluation of the risk for bees was performed in accordance with the recommendations of EPPO Standard PP 3/10 (3) (2010)⁷ covering the current Terrestrial Guidance Document SANCO/10329/2002 rev.2 (final), and as proposed in the list of guidance documents relevant to the implementation of Regulation 1107/2009, published in the official EU Journal 2013/C 95/01 and 95/02.

For the risk assessment calculations according to EPPO (2010), the uses with identical single application rate are grouped and presented in one table (please refer to point 9.1.2).

9.6.2.1 Risk assessment according to EPPO (2010)/SANCO/10329/2002

The risk assessment according to EPPO (2010) covering SANCO/10329/2002 was conducted using the available endpoints for both active substances and the formulated product.

Risk assessment for acute contact and oral toxicity to adult bees

The hazard quotient for contact and oral toxicity (HQ) is calculated using the following equation:

⁷ OEPP/EPPO (2010). Bulletin OEPP/EPPO Bulletin 40, 323-331

$$HQ = \frac{AR}{\text{Acute LD}_{50}}$$

With:

AR = Application rate in g/ha

Acute LD₅₀ expressed in µg/bee

Use group no 2: 3 × 2.4 L product/ha, 6-day interval and use group no 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.6.2.1-1 First-tier assessment of the risk for bees due to the use of HBZ10 in **beet-crops groups 2 and 5**

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard		
Active substance	Ethofumesate		
Application rate [g/ha]	3 × 300		
Test design	LD ₅₀ (lab.) [µg a.s./bee]	Single application rate [g a.s./ha]	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 106.3	300	2.82
Contact toxicity	> 100		3.00
Active substance	Phenmedipham		
Application rate [g/ha]	3 × 300		
Test design	LD ₅₀ (lab.) [µg a.s./bee]	Single application rate [g a.s./ha]	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 16	300	18.75
Contact toxicity	50		6.00
Product	HBZ10		
Application rate [g/ha]	3 × 600*		
Test design	LD ₅₀ (lab.) [µg a.s./bee] *	Single application rate [g a.s./ha] *	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 201.4	600	2.98
Contact toxicity	81.1		7.40

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

* Sum of both active substances

The HQ values for the acute (oral and contact) toxicity for HBZ10 and both active substances Ethofumesate and Phenmedipham are below the trigger value of 50, respectively. Thus, an acceptable acute risk by oral and contact exposure can be concluded for honeybees following the application of HBZ10 in **beet-crops** at 3 × 2.4 L product/ha (6-day or 9-day interval).

Use group no 4: 3 × 1.8 L product/ha, 6-day interval

Table 9.6.2.1-2 First-tier assessment of the risk for bees due to the use of HBZ10 in **beet-crops group 4**

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard		
Active substance	Ethofumesate		
Application rate [g/ha]	3 × 225		
Test design	LD ₅₀ (lab.) [µg a.s./bee]	Single application rate [g a.s./ha]	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 106.3	225	2.12
Contact toxicity	> 100		2.25
Active substance	Phenmedipham		
Application rate [g/ha]	3 × 225		
Test design	LD ₅₀ (lab.) [µg a.s./bee]	Single application rate [g a.s./ha]	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 16	225	14.06
Contact toxicity	50		4.50
Product	HBZ10		
Application rate [g/ha]	3 × 450*		
Test design	LD ₅₀ (lab.) [µg a.s./bee] *	Single application rate [g a.s./ha] *	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 201.4	450	2.23
Contact toxicity	81.1		5.55

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

* Sum of both active substances

The HQ values for the acute (oral and contact) toxicity for HBZ10 and both active substances Ethofumesate and Phenmedipham are below the trigger value of 50, respectively. Thus, an acceptable acute risk by oral and contact exposure can be concluded for honeybees following the application of HBZ10 in beet crops at 3×1.8 L product/ha (6-day interval).

Use group no 1: 6×1.2 L product/ha, 5-day interval and use group no 3: 5×1.2 L product/ha, 7-day interval

Table 9.6.2.1-3 First-tier assessment of the risk for bees due to the use of HBZ10 in beet crops groups 1 and 3

Intended use	Beet crops Sugar beet, red beet, yellow beet, fodder beet and chard		
Active substance	Ethofumesate		
Application rate [g/ha]	6 × 150 or 5 × 150		
Test design	LD ₅₀ (lab.) [µg a.s./bee]	Single application rate [g a.s./ha]	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 106.3	150	1.41
Contact toxicity	> 100		1.50
Active substance	Phenmedipham		
Application rate [g/ha]	6 × 150 or 5 × 150		
Test design	LD ₅₀ (lab.) [µg a.s./bee]	Single application rate [g a.s./ha]	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 16	150	3.38
Contact toxicity	50		3.00
Product	HBZ10		
Application rate [g/ha]	6 × 300 or 5 × 300*		
Test design	LD ₅₀ (lab.) [µg a.s./bee] *	Single application rate [g a.s./ha] *	Q _{HO} , Q _{HC} criterion: Q _H ≤ 50
Oral toxicity	> 201.4	300	1.49
Contact toxicity	81.1		3.70

Q_{HO}, Q_{HC}: Hazard quotients for oral and contact exposure. Q_H values shown in bold breach the relevant trigger.

* Sum of both active substances

The HQ values for the acute (oral and contact) toxicity for HBZ10 and both active substances Ethofumesate and Phenmedipham are below the trigger value of 50, respectively. Thus, an acceptable acute risk by oral and contact exposure can be concluded for honeybees following the application of HBZ10 in beet crops at 6×1.2 L product/ha (5-day interval) and 5×1.2 L product/ha (7-day interval).

zRMS comments:

The acute risk assessment for bees presented in Tables 9.6.2-1 to 9.6.2.1-3 is agreed by the zRMS. Overall, acceptable risk to adult bees may be concluded from the intended uses of HBZ10. The chronic toxicity data are available for adult bees and larva according to requirement EU Reg.284/2009. Please note that the evaluation has been performed in line with SANCO/10329/2002 rev 2 final, as according to conclusions of the Central Zone Steering Committee (CZSC), recommendations of EFSA (2013) should not be considered for the zonal evaluations until the guidance is noted at the EU level. In addition, the EPPO 2010 scheme does not recommend a chronic assessment for adults for foliar spray applications. Therefore, further consideration of the chronic risk should be based on the MSs level, if relevant.

Following comments from concerned Member States, additional calculations for chronic toxicity to bees are provided below. In addition, risk assessment according to EFSA Guidance (2013) is provided below under point 9.6.2.2.

Risk assessment for chronic oral toxicity to adult bees

The EPPO 2010 scheme does not recommend a chronic assessment for adult bees for foliar spray applications. However, as an approach is proposed as an assessment refinement for seed coatings/soil treatments (point 7 on the scheme), this approach can be adapted to provide a worst-case assessment for foliar sprays.

A worst-case of potential exposure via residues in pollen / nectar can be estimated based on the default worst-case value of 1 mg a.s./kg proposed in the EPPO 2010 scheme (see Note 6), based on a database of measured values from aerial plant parts as a surrogate for nectar and pollen.

The default residues can then be combined with a measure of consumption in order to estimate the exposure of bees. Worst case data from Rortais et al., 2005 (*Agnès RORTAIS, Gérard ARNOLD, Marie-Pierre HALM, Frédérique TOUFFET-BRIENS (2005) Modes of honeybees exposure to systemic insecticides: estimated amounts of contaminated pollen and nectar consumed by different categories of bees. Apidologie 36 (2005) 71–83*) as proposed in the EPPO 2010 scheme have been used to estimate the consumption by bee foragers:

Worst case: forager consuming 898.8 mg sugar during 7 days (= 128 mg sugar /day).

Assuming 40% sugar content of nectar: $(898.8 * 2.5)/7 = 321$ mg nectar/day

Thus considering residues of 1 mg a.s./kg sugar x consumption of 321 mg nectar/bee/day

Total exposure ETE = 0.32 µg a.s./bee/day

This can be compared to the adult NOED of 6.19 µg sum of a.s./bee/day (Klix, 2021e, KCP 10.3.1.2/01).

TER = $6.19/0.32 = 19.34$ (EPPO 2010 trigger = 1)

Risk assessment for chronic oral toxicity to bee larvae

A worst-case risk assessment to honeybee larvae can be conducted through the calculation of a TER value as set out in the EPPO 2010 scheme (point 5 on the scheme). A worst-case potential exposure via residues in pollen / nectar can be estimated based on the default worst-case residue of 1 mg a.s./kg proposed in the EPPO 2010 scheme (see Note 6). The default residues can then be combined with a measure of consumption in order to estimate the exposure of bees. Worst case data from Rortais et al., 2005 as proposed in the EPPO scheme have been used to estimate the consumption by bee larvae:

Worst case: drone larvae consuming 98.2 mg sugar during 6.5 days (= 15.1 mg sugar /day).

Assuming a mean sugar content of 40% in nectar: $(98.2 * 2.5)/6.5 = 37.8$ mg nectar/larva/day

Thus considering residues of 1 mg a.s./kg x consumption of 37.8 mg nectar/larva/day:

Total exposure ETE = 0.0378 µg a.s./larva/day

This can be compared to the larval NOED of 2.46 µg sum of a.s./larva/day

TER = $2.46/0.0378 = 65$ (EPPO 2010 trigger = 1)

9.6.2.2 Risk assessment according to EFSA Guidance (2013)

Risk assessment for acute contact toxicity to adult bees

Screening step

Table 9.6.2.2-1 Screening assessment of the acute contact risk to honeybees due to the use of HBZ10 in beet crops - measured toxicity

Intended use		Beet crops				
Product		HBZ10				
Test design		Acute contact toxicity				
Use group no	Type of bee	LD ₅₀ (lab.) [µg/bee]	Single application rate [g/ha] *	Application technique	HQ _{contact}	Trigger value
2 and 5	Honeybee	317	2344.8	Downward spraying	7.4	42
	Bumblebee	> 781.6			< 3.0	7
4	Honeybee	317	1758.6	Downward spraying	5.5	42
	Bumblebee	> 781.6			< 2.25	7
1 and 3	Honeybee	317	1172.4	Downward spraying	3.7	42
	Bumblebee	> 781.6			< 1.5	7

HQ_{contact}: Hazard quotients for contact exposure. HQ value shown in bold breach the relevant trigger; HQ value < trigger value, indicate an acceptable risk for bees

* Calculated based on the intended application rate of in L product/ha and the product density of 0.977 g/mL

The screening HQ_{contact} values for HBZ10 are below the trigger values of 42 and 7 for honeybee and bumblebees for downward spraying, respectively, indicating an acceptable acute risk to honeybees and bumblebees by contact exposure following all intended uses of HBZ10.

Risk assessment for acute oral toxicity to adult bees

Screening step

Table 9.6.2.2-2 Screening assessment of the acute oral risk to honeybees due to the use of HBZ10 in beet crops - measured toxicity

Intended use		Beet crops				
Product		HBZ10				
Type of assessment		Acute oral exposure adult bees				
Use group no	Type of bee	LD ₅₀ (lab.) [µg/bee]	Single application rate [kg/ha] *	SV	ETR _{acute adult oral}	Trigger value
2 and 5	Honeybee	> 787	2.3448	7.6	< 0.02	0.2
	Bumblebee	> 1516.7		11.2	< 0.0173	0.036
4	Honeybee	> 787	1.7586	7.6	< 0.02	0.2
	Bumblebee	> 1516.7		11.2	< 0.0130	0.036
1 and 3	Honeybee	> 787	1.1724	7.6	< 0.01	0.2
	Bumblebee	> 1516.7		11.2	< 0.0087	0.036

ETR_{acute adult oral} value < trigger value indicates an acceptable risk for bees; SV: Short-cut value for the respective kind of application, application made via downward spraying

* Calculated based on the intended application rate in L product/ha and the product density of 0.977 g/mL

The screening ETR values for HBZ10 are below the trigger value of 0.2 and 0.036 for honeybee and bumblebee, respectively, indicating an acceptable acute risk to adult honeybees and bumblebees by oral exposure following the intended uses of HBZ10.

Risk assessment for chronic oral toxicity to adult bees

Screening step / first tier assessment

Table 9.6.2.2-3 Screening assessment of the chronic oral risk to honeybees due to the use of HBZ10 in beet crops - measured toxicity

Intended use		Beet crops				
Product		HBZ10				
Type of assessment		Chronic oral exposure adult bees				
Use group no	Type of bee	10-day LDD ₅₀ (lab.) [µg/bee/day]	Single application rate [kg/ha] *	SV	ETR _{chronic adult oral}	Trigger value
2 and 5	Honeybee	29.6	2.3448	7.6	0.602	0.03
4			1.7586		0.452	
1 and 3			1.1724		0.301	

ETR_{chronic adult oral} value < trigger value indicates an acceptable risk for bees; SV: Short-cut value for the respective kind of application, application made via downward spraying

* Calculated based on the intended application rate of 2.4 L product/ha and the product density of 0.977 g/mL

The screening ETR value for HBZ10 is above the trigger value of 0.03 indicating a possible chronic risk to adult honeybees by oral exposure following the intended uses of HBZ10. Therefore, a first-tier assessment of the chronic oral exposure of adult honeybees to the formulated product for the intended uses in beet crops is presented below.

Table 9.6.2.2-4 First-tier assessment of the chronic oral risk to honeybees due to the use of HBZ10 in beet crops - measured toxicity

beet crops - measured toxicity							
Scenario	Application rate	Exposure factor (Ef)	Short cut value (SV)	Endpoint	twa*	Honeybee	
						ETR	trigger
Chronic oral exposure adult bees							
Treated crop BBCH 10-39	Use groups 2 and 5: 2.3448 kg product/ha	1	5.8	29.6 µg product/bee per day	0.72	0.331	0.03
Weeds BBCH 10-39		1	2.9		0.72	0.165	0.03
Field margin BBCH 10-39		0.0092	2.9		0.72	0.002	0.03
Adjacent crop BBCH 10-39		0.0033	5.8		0.72	0.001	0.03
Next crop BBCH 10-39		1	0.54		0.72	0.031	0.03
Treated crop BBCH 10-39	Use group 4: 1.7586 kg product/ha	1	5.8	29.6 µg product/bee per day	0.72	0.248	0.03
Weeds BBCH 10-39		1	2.9		0.72	0.124	0.03
Field margin BBCH 10-39		0.0092	2.9		0.72	0.002	0.03
Adjacent crop BBCH 10-39		0.0033	5.8		0.72	0.001	0.03
Next crop BBCH 10-39		1	0.54		0.72	0.023	0.03

Scenario	Application rate	Exposure factor (Ef)	Short cut value (SV)	Endpoint	twa*	Honeybee	
						ETR	trigger
Treated crop BBCH 10-39	Use groups 1 and 3: 1.1724 kg product/ha	1	5.8	29.6 µg product/bee per day	0.72	0.165	0.03
Weeds BBCH 10-39		1	2.9		0.72	0.083	0.03
Field margin BBCH 10-39		0.0092	2.9		0.72	0.002	0.03
Adjacent crop BBCH 10-39		0.0033	5.8		0.72	0.001	0.03
Next crop BBCH 10-39		1	0.54		0.72	0.015	0.03

* The twa value of 0.72 is based on a default DT₅₀ of 10 days and a 10-day time window (see EFSA, 2009). The twa value of 0.85 is based on a default DT₅₀ of 10 days and a 5-day time window

The first tier ETR values for the chronic risk to adult honeybees are below the trigger value of 0.03 except for the treated crop, weed and next crop scenario at BBCH 10-39 indicating a possible risk following the intended uses of HBZ10 in beet crops.

According to the EFSA Guidance (2013, Appendix D), sugar beets are considered as of low attractiveness for bees considering the collection of pollen. However, collection of pollen cannot be excluded. In addition, nectar of sugar beets is considered of relevance. The risk for honeybees exposed to contaminated nectar and pollen is negligible as beet crops do not build flowers within the first year and beets are harvested by the end of the first-year vegetation period already. Therefore, an exposure to contaminated pollen and nectar is considered to be low taking into account the intended uses.

Since the treated weeds will die shortly after application of HBZ10, an exposure of bees to flowering weeds within the treated crop area cannot be excluded but is considered to be of short-term. Also, in practice, the chance of exposure for honeybees is low within weeds, since first applications are usually made early in the season (<BBCH 39) and any weeds present are treated and killed before they can reach flowering stages. As weeds' flowering occurs at BBCH 60, it is very unlikely bees are exposed to the formulation on flowering weeds, as they are controlled at an earlier growing stage according to recommended timing of application. Furthermore, the risk assessment following EPPO (2010) on chronic oral exposure indicates an acceptable risk to adult bees from chronic oral exposure to HBZ10 for the intended uses.

It should be noted EFSA guidance is currently under revision and even though it better addresses data requirements according to Reg (EU) No 284/2013, outcome of the risk assessment could be considered as provisional, while currently in force guidance leads to an acceptable risk for bees.

However, since no further data is available for refining the EFSA 2013 risk assessment, and in case Member States are considering the above risk assessment relevant for decision making, applicant proposes risk mitigation phrase SPe8 from Annex V of 1999/45/EC (still relevant under 1107/2009/EC according to Article 65.1). *“Do not apply when flowering weeds are present / Remove weeds before flowering.”*

Risk assessment for oral toxicity to bee larvae

Screening step / first tier assessment

Table 9.6.2.2-5 Screening assessment of the chronic oral risk to honeybee larvae due to the use of HBZ10 in beet crops - measured toxicity

Intended use		Beet crops				
Product		HBZ10				
Type of assessment		Chronic oral exposure larvae				
Use group no	Type of bee	NOED _{larvae} [µg/larvae/developmental period]	Single application rate [kg/ha] *	SV	ETR _{larvae}	Trigger value
2 and 5	Honeybee	9.62	2.3448	4.4	1.07	0.2
4			1.7586		0.80	
1 and 3			1.1724		0.54	

ETR_{larvae} value < trigger value indicates an acceptable risk for bees; SV: Short-cut value for the respective kind of application, application made via downward spraying; ETR values shown in bold breach the relevant trigger.

* Calculated based on the intended application rate of 2.4 L product/ha and the product density of 0.977 g/mL

The screening ETR value for HBZ10 is above the trigger value of 0.2 indicating possible chronic risk of honeybee larvae by oral exposure following the intended uses of HBZ10 in beet crops. Therefore, a first-tier risk assessment of the chronic oral exposure of honeybee larvae to the formulated product for the intended uses in beet crops is presented below.

Table 9.6.2.2-6 First-tier assessment of the chronic oral risk to honeybee larvae due to the use of HBZ10 in beet crops - measured toxicity

Scenario	Application rate	Exposure factor (Ef)	Short cut value (SV)	twa	Endpoint	Honeybee	
						ETR	trigger
Treated crop BBCH 10-39	Use groups 2 and 5: 2.3448 kg product/ha	1	4.4	1	9.62 µg product/larva	0.91	0.2
Weeds BBCH 10-39		1	2.2	1		0.46	0.2
Field margin BBCH 10-39		0.0092	2.2	1		0.00	0.2
Adjacent crop BBCH 10-39		0.0033	4.4	1		0.00	0.2
Next crop BBCH 10-39		1	0.4	1		0.08	0.2
Treated crop BBCH 10-39	Use group 4: 1.7586 kg product/ha	1	4.4	1	9.62 µg product/larva	0.68	0.2
Weeds BBCH 10-39		1	2.2	1		0.34	0.2
Field margin BBCH 10-39		0.0092	2.2	1		0.00	0.2
Adjacent crop BBCH 10-39		0.0033	4.4	1		0.00	0.2
Next crop BBCH 10-39		1	0.4	1		0.06	0.2

Scenario	Application rate	Exposure factor (Ef)	Short cut value (SV)	twa	Endpoint	Honeybee	
						ETR	trigger
Treated crop BBCH 10-39	Use groups 1 and 3: 1.1724 kg product/ha	1	4.4	1	9.62 µg product/larva	0.46	0.2
Weeds BBCH 10-39		1	2.2	1		0.23	0.2
Field margin BBCH 10-39		0.0092	2.2	1		0.00	0.2
Adjacent crop BBCH 10-39		0.0033	4.4	1		0.00	0.2
Next crop BBCH 10-39		1	0.4	1		0.04	0.2

ETR values shown in bold breach the relevant trigger.

For the formulated product HBZ10, the first tier ETR value for the chronic risk to honeybee larvae is below the trigger value of 0.2 except for treated crop and weed scenario at BBCH 10-39 indicating a possible risk following the intended uses of HBZ10 in beet crops.

The risk for honeybees exposed to contaminated nectar and pollen is negligible as beet crops do not build flowers within the first year and beets are harvested by the end of the first-year vegetation period already. Therefore, an exposure to contaminated pollen and nectar is considered to be low taking into account the intended uses. Since the treated weeds will die shortly after application of HBZ10, an exposure of bees to flowering weeds within the treated crop area cannot be excluded but is considered to be of short-term. Also, in practice, the chance of exposure for honeybees is low within weeds, since first applications are usually made early in the season (<BBCH 39) and any weeds present are treated and killed before they can reach flowering stages. As weeds' flowering occurs at BBCH 60, it is very unlikely bees are exposed to the formulation on flowering weeds, as they are controlled at an earlier growing stage according to recommended timing of application. Furthermore, the risk assessment following EPPO (2010) on chronic oral exposure indicates an acceptable risk to adult bees from chronic oral exposure to HBZ10 for the intended uses.

It should be noted EFSA guidance is currently under revision and even though it better addresses data requirements according to Reg (EU) No 284/2013, outcome of the risk assessment could be considered as provisional, while currently in force guidance leads to an acceptable risk for bees.

However, since no further data is available for refining the EFSA 2013 risk assessment, and in case Member States are considering the above risk assessment relevant for decision making, applicant proposes risk mitigation phrase SPe8 from Annex V of 1999/45/EC (still relevant under 1107/2009/EC according to Article 65.1). *“Do not apply when flowering weeds are present / Remove weeds before flowering.”*

Assessment of risk from exposure to contaminated water (EFSA Guidance, 2013)

Applicant is of opinion exposure to contaminated water and guttation water is not considered relevant since risk assessment via major routes of exposure (namely, contact and oral via consumption of pollen/nectar) can be considered as worst case.

For scenario ‘Guttation water’, the initial risk assessment recommended in the EFSA GD 2013 is based on the substance's solubility in water, it involves significant uncertainties and leads to an overestimation of exposure. Currently, the exposure of bees via guttation water cannot be quantified precisely. It is necessary to improve knowledge and to have elements enabling the identification of situations where guttation is a route of exposure that could be significant.

For scenario ‘Surface water’, bees can collect water from streams, lakes and ponds but it is not considered as a major source of exposure.

Therefore, based on worst case risk assessment via major routes of exposure as detailed above, applicant considers risk assessment for these scenarios as not necessary for the time being as they are not part of main exposure route.

Therefore, no risk assessment for “guttation water”, “contaminated water” in presented in this dossier.

zRMS comments:

The calculations of risk assessment for bees according to recommendations of EFSA (2013) are validated by zRMS. The first tier ETR values for the chronic risk to adult honeybees are below the trigger value of 0.03 except for the treated crop, weed and next crop scenario at BBCH 10-39 indicating a possible risk following the intended uses of HBZ10 in beet crops.

In reference to chronic risk for larvae it is noted that for the formulated product HBZ10, the first tier ETR value for the chronic risk to honeybee larvae is below the trigger value of 0.2 except for treated crop and weed scenario at BBCH 10-39 indicating a possible risk following the intended uses of HBZ10 in beet crops.

However, since no further data is available for refining the EFSA 2013 risk assessment, and in case Member States are considering the above risk assessment relevant for decision making, applicant proposes risk mitigation phrase SPe8 from Annex V of 1999/45/EC (still relevant under 1107/2009/EC according to Article 65.1). “Do not apply when flowering weeds are present / Remove weeds before flowering.”

This issue should be further resolved at the product authorisation in Member States considering indications of the not yet noted EFSA 2013 guidance in their national assessments.

9.6.2.2 Higher-tier risk assessment for bees (tunnel test, field studies)

Not relevant.

9.6.3 Effects on bumble bees

Two new studies addressing the acute oral and contact toxicity of HBZ10 to bumblebees (Klix, 2021b and Klix, 2021d) are listed in Appendix 1 and summarised in Appendix 2.

zRMS comments:

The acute risk assessment for bees presented in Table 9.6.2-1 and Table 9.6.2.1-3 covers the risk assessment for *Bombus terrestris*.

9.6.4 Effects on solitary bees

No data is currently available for solitary bees.

9.6.5 Overall conclusions

The evaluation of the risk for bees was performed in accordance with the recommendations of the EPPO Standard PP 3/10 (3) (2010) covering the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002).

There is no acute oral and contact risk to adult honeybees and bumblebees following application of HBZ10 in beet crops according to the intended use pattern. Following the EPPO (2010) risk assessment scheme, the chronic oral (adult bees) and honeybee larvae toxicity based on the predicted dose of HBZ10 consumed by adult and larval honeybees resulted in high margin of safety values, indicating a low chronic oral risk for adult honeybees and honeybee larvae.

According to EFSA Guidance (2013) there is an indication for a possible chronic oral risk to adult and larval honeybees in treated crop (BBCH 10-39), weeds (BBCH 10-39) and next crop scenario (BBCH 10-39, chronic oral expo-sure of adult bees only) following the application of HBZ10. The risk assessment based on the EFSA Guidance (2013) is not yet approved and certain parts are currently under revision. Therefore, the outcome of the risk assessment should not be evaluated based only on the EFSA Guidance (2013). Also, the results based on the decision scheme as described in EPPO (2010) should be taken into consideration.

As no further data is available for refining the EFSA 2013 risk assessment, and in case only the EFSA 2013

risk assessment is considered relevant for decision making, applicant proposes risk mitigation phrase SPe8 from Annex V of 1999/45/EC (still relevant under 1107/2009/EC according to Article 65.1). “*Do not apply when flowering weeds are present / Remove weeds before flowering.*”

9.7 Effects on arthropods other than bees (KCP 10.3.2)

9.7.1 Toxicity data

Studies on the toxicity to non-target arthropods have been carried out with formulations containing Ethofumesate and Phenmedipham. Full details of these studies are provided in the respective EU DAR (DAR Ethofumesate, 1998; DAR Phenmedipham, 1999) and related documents (DAR Addendum Ethofumesate, 2000; DAR Addendum Phenmedipham, 2001 and 2003).

Effects on non-target arthropods of HBZ10 were not evaluated as part of the EU assessment of Ethofumesate and Phenmedipham. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment deviates with the results of the EU review process. Since specific endpoints are available for HBZ10, these endpoints will be used in the risk assessment.

Nevertheless, a summary is given of the EU endpoints for Ethofumesate and Phenmedipham. These EU endpoints are all derived from formulated products and are therefore considered less appropriate to be used in the risk assessment for HBZ10 but listed here for completeness.

Table 9.7.1-1 Endpoints and effect values relevant for the risk assessment for non-target arthropods - Ethofumesate

Species	Substance	Exposure System	Results	Reference
<i>Aphidius rhopalosiphii</i> (adults)	Ethofumesate 500 SC	Laboratory test (2D)	LR ₅₀ > 1000 g a.s./ha ER ₅₀ > 1000 g a.s./ha	EFSA Conclusion (2016)
<i>Typhlodromus pyri</i> (protonymphs)	Ethofumesate 500 SC	Laboratory test (2D)	LR ₅₀ > 1000 g a.s./ha ER ₅₀ > 1000 g a.s./ha	EFSA Conclusion (2016)
<i>Aphidius rhopalosiphii</i> (adults)	Ethofol 500 SC	Laboratory test (2D)	LR ₅₀ > 1000 g a.s./ha ER ₅₀ > 1000 g a.s./ha	EFSA Conclusion (2016)
<i>Typhlodromus pyri</i> (protonymphs)	Ethofol 500 SC	Laboratory test (2D)	LR ₅₀ > 1000 g a.s./ha ER ₅₀ > 1000 g a.s./ha	EFSA Conclusion (2016)
Additional species				
<i>Aleochara bilineata</i>	Tramat 500	Laboratory test (2D)	LR ₅₀ > 1252.5 g a.s./ha ER ₅₀ > 1252.5 g a.s./ha	EFSA Conclusion (2016)
<i>Chrysoperla carnea</i> (larvae)	Tramat 500	Laboratory test (2D)	LR ₅₀ > 2000 g a.s./ha ER ₅₀ > 2000 g a.s./ha	EFSA Conclusion (2016)
<i>Poecilus cupreus</i> (adults)	Tramat 500	Laboratory test (2D)	LR ₅₀ > 2000 g a.s./ha	EFSA Conclusion (2016)
Field or semi-field tests				
-				

Table 9.7.1-2 Endpoints and effect values relevant for the risk assessment for non-target arthropods - Phenmedipham

Species	Substance	Exposure System	Results	Reference
<i>Aphidius rhopalosiphii</i> (adults)	Kemifam Flow (160 g PMP/L)	Laboratory test (2D)	Mortality 63% at 480 g a.s./ha 43% at 960 g a.s./ha	Review Report (2004)
<i>Aphidius rhopalosiphii</i> (adults)	Kemifam Flow (160 g PMP/L)	Extended lab (barley, 3D)	LR ₅₀ > 960 g a.s./ha ER ₅₀ > 960 g a.s./ha	Review Report (2004)
<i>Typhlodromus pyri</i> (protonymphs)	Kemifam Flow (160 g PMP/L)	Laboratory test (2D)	LR ₅₀ > 960 g a.s./ha ER ₅₀ > 960 g a.s./ha	Review Report (2004)
<i>Poecilus cupreus</i> (adults)	Kemifam Flow (160 g PMP/L)	Laboratory test (2D)	LR ₅₀ > 960 g a.s./ha	Review Report (2004)
<i>Chrysoperla carnea</i> (larvae)	Kemifam Flow (160 g PMP/L)	Laboratory test (2D)	LR ₅₀ > 960 g a.s./ha ER ₅₀ > 960 g a.s./ha	Review Report (2004)

PMP = Phenmedipham

zRMS comments:

Endpoints presented in Table 9.7.1-1 are in line with the EU agreed endpoints reported in EFSA Journal 2016;14(1):437 and endpoints presented in Table 9.7.1-2 are in line with the EU agreed endpoints reported in Review Report (2004).
The endpoints of both active substances from their respective EFSA journal initially presented by the applicant have been crossed out by zRMS. These endpoints are not needed as toxicity data with the formulation HBZ10 are available and thus, used for the risk assessment of HBZ10.

Table 9.7.1-3 Endpoints and effect values relevant for the risk assessment for non-target arthropods – HBZ10

Species	Substance	Exposure System	Results	Reference
<i>Aphidius rhopalosiphi</i> (adults)	HBZ10	Laboratory test (2D)	LR ₅₀ = 0.356 L product/ha	Klix, V. (2021g) KCP 10.3.2.1/01
<i>Typhlodromus pyri</i> (protonymphs)	HBZ10	Laboratory test (2D)	LR ₅₀ = 0.788 L product/ha	Klix, V. (2021h) KCP 10.3.2.1/02
<i>Aphidius rhopalosiphi</i>	HBZ10	Extended lab	LR ₅₀ > 5.52 L product/ha ER ₅₀ > 5.52 L product/ha	Maspohl, A-K. (2021a) KCP 10.3.2.2/01
<i>Typhlodromus pyri</i>	HBZ10	Extended lab	LR ₅₀ = 2.84 L product/ha ER ₅₀ > 1.84 L product/ha	Maspohl, A-K. (2021b) KCP 10.3.2.2/02
<i>Chrysoperla carnea</i>	HBZ10	Extended lab	NOER ≥ 7.20 L product/ha	Leopold, J. (2021) KCP 10.3.2.2/03
<i>Aleochara bilineata</i>	HBZ10	Extended lab	ER ₅₀ > 51.84 L product/ha	Knautz, T. (2021) KCP 10.3.2.2/04
<i>Typhlodromus pyri</i>	HBZ10	Extended lab aged residue test	≥ 5.52 L product/ha No effects on mortality and reduction in reproduction above 50 % of 0- and 14-d aged residues.	Wagenhoff, E. (2021) KCP 10.3.2.2/05

zRMS comments:

Studies on toxicity of HBZ10 to non-target arthropods were evaluated by the zRMS and considered acceptable. For details of evaluation, please refer to Appendix 2. Endpoints reported in Table 9.7.1-3 are confirmed to be correct.

9.7.1.1 Justification for new endpoints

The risk assessment is performed with the endpoints from the formulated product HBZ10. The results from the extended laboratory test with *Typhlodromus pyri* by Maspohl (2021b) are not considered in the higher-tier risk assessment of the in-field risk for non-target arthropods; the results at Day 0 from the aged residue test with *Typhlodromus pyri* by Wagenhoff (2021) are considered here instead, as this is a valid and higher tier study. This is further supported by the fact that three other test species show low sensitivity at the proposed rates at extended laboratory tests.

9.7.2 Risk assessment

The evaluation of the risk for non-target arthropods was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002), and in consideration of the recommendations of the guidance document ESCORT 2.

9.7.2.1 Risk assessment for in-field exposure

The risk assessment for in-field exposure of non-target arthropods is presented for all intended uses. Uses with identical number of applications and application rate are grouped and presented in one table (please refer to point 9.1.2).

Exposure

Non-target arthropods inhabiting the crop can be exposed to residues from HBZ10 by direct contact either as a result of overspray or through contact with residues on plants and soil or in food items. HBZ10 is applied up to 3 times at a maximum rate of 2.4 L product/ha.

The in-field exposure (Predicted Environmental Rate, PER) is calculated according to ESCORT 2 using the following equation:

$$PER_{in-field} = \text{application rate} \times \text{MAF}$$

Where:

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, DT₅₀ value and number of applications. Default foliar and soil MAF values following multiple applications are given in the ESCORT 2 Guidance Document.

Use group no 2: 3 × 2.4 L product/ha, 6-day interval and use group no 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.7.2.1-1 First- and higher-tier assessment of the in-field risk for non-target arthropods due to the use of HBZ10 in beet-crops groups 2 and 5

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard		
Active substance/product	Ethofumesate + Phenmedipham / HBZ10		
Application rate [L/ha]	3 × 2.4		
MAF	2.3 (foliar) / 2.7 (soil)		
Test species Tier I	LR₅₀ [L/ha] (lab.)	PER_{in-field} [L/ha]	HQ_{in-field} criterion: HQ ≤ 2
<i>Aphidius rhopalosiphi</i>	0.356	5.52 (foliar)	15.5
<i>Typhlodromus pyri</i>	0.788		7.0
<i>Aphidius rhopalosiphi</i>	0.356	6.48 (soil)	18.2
<i>Typhlodromus pyri</i>	0.788		8.2
Test species Higher-tier	Rate with ≤ 50% effect* [L/ha]	PER_{in-field} [L/ha]	PER_{in-field} below rate with ≤ 50% effect?
<i>Aphidius rhopalosiphi</i>	> 5.52	5.52 (foliar)	Yes
<i>Typhlodromus pyri</i>	5.52		Yes
<i>Chrysoperla carnea</i>	≥ 7.20		Yes
<i>Aleochara bilineata</i>	> 51.84	6.48 (soil)	Yes

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment.

Criteria values shown in bold breach the relevant trigger.

* If an LR₅₀ or ER₅₀ from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50% effect.

The in-field HQs at Tier I for the standard laboratory species *Aphidius rhopalosiphi* and *Typhlodromus pyri* are above the trigger value of 2, indicating that risk to non-target arthropods is high in in-field areas following the application of HBZ10 according to the proposed use pattern in beet-crops at 3 × 2.4 L product/ha (6-day or 9-day interval).

For the representative species *A. rhopalosiphi* and *Typhlodromus pyri*, as well as for the additional species *Chrysoperla carnea* and *Aleochara bilineata*, the in-field PER is below the Tier-2 endpoint indicating low in-field risk for the intended use.

Use group no 4: 3 × 1.8 L product/ha, 6-day interval

Table 9.7.2.1-1 First- and higher-tier assessment of the in-field risk for non-target arthropods due to the use of HBZ10 in *beet-crops* group 4

Intended use	<i>Beet-crops</i> Sugar beet, red beet, yellow beet, fodder beet and chard		
Active substance/product	Ethofumesate + Phenmedipham / HBZ10		
Application rate [L/ha]	3 × 1.8		
MAF	2.3 (foliar) / 2.7 (soil)		
Test species Tier I	LR ₅₀ [L/ha]	(lab.) PER _{in-field} [L/ha]	HQ _{in-field} criterion: HQ ≤ 2
<i>Aphidius rhopalosiphi</i>	0.356	4.14 (foliar)	11.6
<i>Typhlodromus pyri</i>	0.788		5.3
<i>Aphidius rhopalosiphi</i>	0.356	4.86 (soil)	13.7
<i>Typhlodromus pyri</i>	0.788		6.2
Test species Higher-tier	Rate with ≤ 50% effect*	PER _{in-field} [L/ha]	PER _{in-field} below rate with ≤ 50% effect?
<i>Aphidius rhopalosiphi</i>	> 5.52	4.14 (foliar)	Yes
<i>Typhlodromus pyri</i>	5.52		Yes
<i>Chrysoperla carnea</i>	≥ 7.20		Yes
<i>Aleochara bilineata</i>	> 51.84	4.86 (soil)	Yes

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment.

Criteria values shown in bold breach the relevant trigger.

* If an LR₅₀ or ER₅₀ from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50% effect.

The in-field HQs at Tier I for the standard laboratory species *Aphidius rhopalosiphi* and *Typhlodromus pyri* are above the trigger value of 2, indicating that risk to non-target arthropods is high in in-field areas following the application of HBZ10 according to the proposed use pattern *in-beet-crops* at 3 × 1.8 L product/ha (6-day interval).

For the representative species *A. rhopalosiphi* and *Typhlodromus pyri*, as well as for the additional species *Chrysoperla carnea* and *Aleochara bilineata*, the in-field PER is below the Tier-2 endpoint indicating low in-field risk for the intended use.

Use group no 1: 6 × 1.2 L product/ha, 5-day interval

Table 9.7.2.1-1 First- and higher-tier assessment of the in-field risk for non-target arthropods due to the use of HBZ10 in *beet-crops* group 1

Intended use	<i>Beet-crops</i> Sugar beet, red beet, yellow beet, fodder beet and chard		
Active substance/product	Ethofumesate + Phenmedipham / HBZ10		
Application rate [L/ha]	6 × 1.2		
MAF	3.2 (foliar) / 4.6 (soil)		
Test species Tier I	LR ₅₀ [L/ha]	(lab.) PER _{in-field} [L/ha]	HQ _{in-field} criterion: HQ ≤ 2
<i>Aphidius rhopalosiphi</i>	0.356	3.84 (foliar)	10.8
<i>Typhlodromus pyri</i>	0.788		4.9
<i>Aphidius rhopalosiphi</i>	0.356	5.52 (soil)	15.5
<i>Typhlodromus pyri</i>	0.788		7.0
Test species Higher-tier	Rate with ≤ 50% effect*	PER _{in-field} [L/ha]	PER _{in-field} below rate with ≤ 50% effect?
<i>Aphidius rhopalosiphi</i>	> 5.52	3.48 (foliar)	Yes
<i>Typhlodromus pyri</i>	5.52		Yes
<i>Chrysoperla carnea</i>	≥ 7.20		Yes
<i>Aleochara bilineata</i>	> 51.84	5.52 (soil)	Yes

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment.

Criteria values shown in bold breach the relevant trigger.

* If an LR₅₀ or ER₅₀ from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50% effect.

The in-field HQs at Tier I for the standard laboratory species *Aphidius rhopalosiphi* and *Typhlodromus pyri* are above the trigger value of 2, indicating that risk to non-target arthropods is high in in-field areas following the application of HBZ10 according to the proposed use pattern *in-beet-crops* at 6 × 1.2 L product/ha (5-day interval).

For the representative species *A. rhopalosiphi* and *Typhlodromus pyri*, as well as for the additional species *Chrysoperla carnea* and *Aleochara bilineata*, the in-field PER is below the Tier-2 endpoint indicating low in-field risk for the intended use.

Use group no 3: 5 × 1.2 L product/ha, 7-day interval

Table 9.7.2.1-1 First- and higher-tier assessment of the in-field risk for non-target arthropods due to the use of HBZ10 in beet-crops group 3

Intended use	Beet-crop: Sugar beet, red beet, yellow beet, fodder beet and chard		
Active substance/product	Ethofumesate + Phenmedipham / HBZ10		
Application rate [L/ha]	5 × 1.2		
MAF	3.0 (foliar) / 4.0 (soil)		
Test species	LR₅₀ (lab.) [L/ha]	PER_{in-field} [L/ha]	HQ_{in-field} criterion: HQ ≤ 2
Tier I			
<i>Aphidius rhopalosiphi</i>	0.356	3.60 (foliar)	10.1
<i>Typhlodromus pyri</i>	0.788		4.6
<i>Aphidius rhopalosiphi</i>	0.356	4.80 (soil)	13.5
<i>Typhlodromus pyri</i>	0.788		6.1
Test species	Rate with ≤ 50% effect*	PER_{in-field} [L/ha]	PER_{in-field} below rate with ≤ 50% effect?
Higher-tier			
<i>Aphidius rhopalosiphi</i>	> 5.52	3.60 (foliar)	Yes
<i>Typhlodromus pyri</i>	5.52		Yes
<i>Chrysoperla carnea</i>	≥ 7.20	4.80 (soil)	Yes
<i>Aleochara bilineata</i>	> 51.84		Yes

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; DALT: Days after last treatment.

Criteria values shown in bold breach the relevant trigger.

* If an LR₅₀ or ER₅₀ from a relevant extended laboratory test is available, it should be considered in place of the rate with ≤ 50% effect.

The in-field HQs at Tier I for the standard laboratory species *Aphidius rhopalosiphi* and *Typhlodromus pyri* are above the trigger value of 2, indicating that risk to non-target arthropods is high in in-field areas following the application of HBZ10 according to the proposed use pattern in beet-crops at 5 × 1.2 L product/ha (7-day interval).

For the representative species *A. rhopalosiphi* and *Typhlodromus pyri*, as well as for the additional species *Chrysoperla carnea* and *Aleochara bilineata*, the in-field PER is below the Tier-2 endpoint indicating low in-field risk for the intended use.

9.7.2.2 Risk assessment for off-field exposure

The risk assessment for off-field exposure of non-target arthropods is presented for all intended uses. Uses with identical number of applications and application rate are grouped and presented in one table (please refer to point 9.1.2).

The off-field exposure (Predicted Environmental Rate, PER) is calculated according to ESCORT 2 using the following equations:

$$\text{PER}_{\text{off-field}} = \text{application rate} \times \text{MAF} \times \left(\frac{\text{drift factor}}{\text{vegetation distribution factor}} \right)$$

Where:

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, DT₅₀ value and number of applications. Default foliar and soil MAF values following multiple applications are given in the ESCORT 2 Guidance Document.

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 distribution factor of 10 is recommended by ESCORT 2. However, in the EFSA Supporting publication 2019:EN-1673⁸, the experts recommended to use a VDF of 5 for all the tiers of the assessment.

⁸ EFSA, 2019. Technical report on the outcome of the Pesticides Peer Review Meeting on general occurring issues in ecotoxicology. EFSA supporting publication 2019:EN-1673

$$\text{correctedPER}_{\text{off-field}} = \text{PER}_{\text{off-field}} \times \text{correction factor}$$

Since a limited number of indicator species are tested when compared to the range of species which could be exposed in off field habitats, a 10 fold or 5 fold uncertainty (correction) factor is included to the calculation for laboratory (tier 1) and extended laboratory (higher tier) studies, respectively, to ensure a higher rate is tested which covers the inter species variability in sensitivity of off field non target arthropod species to plant protection products. However, by testing additional species, uncertainty can be reduced, and a safety factor less than 5 can be applied.

Use group no 2: 3 × 2.4 L product/ha, 6-day interval and use group no 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.7.2.2-1 First- and higher-tier assessment of the off-field risk for non-target arthropods due to the use of HBZ10 in beet-crops groups 2 and 5

Intended use		Beet-crops: Sugar beet, red beet, yellow beet, fodder beet and chard			
Active substance/product		Ethofumesate + Phenmedipham / HBZ10			
Application rate [L/ha]		3 × 2.4			
MAF		2.3 (foliar) / 2.7 (soil)			
vdf		5 (2D)			
Test species Tier I	LR ₅₀ (lab.) [L/ha]	Drift rate	PER _{off-field} [L/ha]	CF	HQ _{off-field} criterion: HQ ≤ 2
<i>Typhlodromus pyri</i>	0.356	0.0201	0.0222 (foliar)	10	0.623
<i>Aphidius rhopalosiphi</i>	0.788				0.282
<i>Typhlodromus pyri</i>	0.356		0.0261 (soil)		0.732
<i>Aphidius rhopalosiphi</i>	0.788				0.331

MAF: Multiple application factor; vdf: Vegetation distribution factor; (corr.) PER: (corrected) Predicted environmental rate; CF: Correction factor; HQ: Hazard quotient. Criteria values shown in bold breach the relevant trigger.

The off-field HQs at Tier I are below the trigger value of 2, indicating that risk to non-target arthropods is low in off-field areas following the application of HBZ10 according to the proposed use pattern in beet-crops at 3 × 2.4 L product/ha (6-day or 9-day interval).

Use group no 1: 6 × 1.2 L product/ha, 5-day interval

Table 9.7.2.2-2 First- and higher-tier assessment of the off-field risk for non-target arthropods due to the use of HBZ10 in beet-crops group 1

Intended use		Beet-crops: Sugar beet, red beet, yellow beet, fodder beet and chard				
Active substance/product		Ethofumesate + Phenmedipham / HBZ10				
Application rate [L/ha]		6 × 1.2				
MAF		3.2 (foliar) / 4.6 (soil)				
vdf		5 (2D)				
Test species Tier I	LR ₅₀ [L/ha]	(lab.)	Drift rate	PER _{off-field} [L/ha]	CF	HQ _{off-field} criterion: HQ ≤ 2
<i>Typhlodromus pyri</i>	0.356	0.0164	0.0126 (foliar)	10	0.354	
<i>Aphidius rhopalosiphi</i>	0.788				0.160	
<i>Typhlodromus pyri</i>	0.356		0.0181 (soil)		0.509	
<i>Aphidius rhopalosiphi</i>	0.788				0.230	

MAF: Multiple application factor; vdf: Vegetation distribution factor; (corr.) PER: (corrected) Predicted environmental rate; CF: Correction factor; HQ: Hazard quotient. Criteria values shown in bold breach the relevant trigger.

The off-field HQs at Tier I are below the trigger value of 2, indicating that risk to non-target arthropods is low in off-field areas following the application of HBZ10 according to the proposed use pattern in beet-crops at 6 × 1.2 L product/ha (5-day interval).

Use group no 3: 5 × 1.2 L product/ha, 7-day interval

Table 9.7.2.2-3 First- and higher-tier assessment of the off-field risk for non-target arthropods due to the use of HBZ10 in beet-crops group 3

Intended use		Beet-crops: Sugar beet, red beet, yellow beet, fodder beet and chard					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [L/ha]		5 × 1.2					
MAF		3.0 (foliar) / 4.0 (soil)					
vdf		5 (2D)					
Test Tier I	species	LR ₅₀ [L/ha]	(lab.)	Drift rate	PER _{off-field} [L/ha]	CF	HQ _{off-field} criterion: HQ ≤ 2
	<i>Typhlodromus pyri</i>	0.356		0.0175	0.0126 (foliar)	10	0.354
	<i>Aphidius rhopalosiphi</i>	0.788					0.160
	<i>Typhlodromus pyri</i>	0.356			0.0168 (soil)		0.472
	<i>Aphidius rhopalosiphi</i>	0.788					0.213

MAF: Multiple application factor; vdf: Vegetation distribution factor; (corr.) PER: (corrected) Predicted environmental rate; CF: Correction factor; HQ: Hazard quotient. Criteria values shown in bold breach the relevant trigger.

The off-field HQs at Tier I are below the trigger value of 2, indicating that risk to non-target arthropods is low in off-field areas following the application of HBZ10 according to the proposed use pattern in-beet steps at 5 × 1.2 L product/ha (7-day interval).

Use group no 4: 3 × 1.8 L product/ha, 6-day interval

Table 9.7.2.2-4 First- and higher-tier assessment of the off-field risk for non-target arthropods due to the use of HBZ10 in beet-crops group 4

Intended use		Beet-crops: Sugar beet, red beet, yellow beet, fodder beet and chard					
Active substance/product		Ethofumesate + Phenmedipham / HBZ10					
Application rate [L/ha]		3 × 1.8					
MAF		2.3 (foliar) / 2.7 (soil)					
vdf		5 (2D)					
Test Tier I	species	LR ₅₀ [L/ha]	(lab.)	Drift rate	PER _{off-field} [L/ha]	CF	HQ _{off-field} criterion: HQ ≤ 2
	<i>Typhlodromus pyri</i>	0.356		0.0201	0.0166 (foliar)	10	0.0467
	<i>Aphidius rhopalosiphi</i>	0.788					0.0211
	<i>Typhlodromus pyri</i>	0.356			0.0195 (soil)		0.0549
	<i>Aphidius rhopalosiphi</i>	0.788					0.0248

MAF: Multiple application factor; vdf: Vegetation distribution factor; (corr.) PER: (corrected) Predicted environmental rate; CF: Correction factor; HQ: Hazard quotient. Criteria values shown in bold breach the relevant trigger.

The off-field HQs at Tier I are below the trigger value of 2, indicating that risk to non-target arthropods is low in off-field areas following the application of HBZ10 according to the proposed use pattern in-beet steps at 3 × 1.8 L product/ha (6-day interval).

zRMS comments:

The in – field and off-field exposure to the formulated product is validated by the zRMS.

As a worst case the VDF of 5 has been considered, since available investigations indicate that VDF of 10 recommended by ESCORT 2 guidance document is not appropriate and may lead to underestimation of the exposure. It should be, however, noted that according to EFSA Supporting publication 2019:EN-1673, VDF of 5 should be considered as the interim solution that will be reflected in the SANCO/10329/2002 rev 2 final with its implementation considered further. Since use of VDF of 5 was not reflected in the current SANCO terrestrial guidance, its use is not yet mandatory. Nevertheless, the risk assessment performed with VDF of 5 is more protective and is thus agreed by the zRMS.

Based on calculations performed with consideration of the Tier I laboratory data acceptable off-field risk to non-target arthropods from the intended uses of may be concluded with no need for risk mitigation measures.

Overall, no unacceptable effects for NTA are expected following application of HBZ10.

9.7.2.3 Additional higher-tier risk assessment

The in-field Hazard Quotient value for *Aphidius rhopalosiphi* and *Typhlodromus pyri* are above the trigger value of 2; according to ESCORT 2 workshop (March 2000) further additional species in extended laboratory studies have been considered in the risk assessment. The results from these additional species indicate a low in-field risk for all intended uses, in addition, no risk to non-target arthropods was identified for the off-field exposure. Therefore, additional higher-tier risk assessment is not relevant.

9.7.2.4 Risk mitigation measures

No risk mitigation needed since no off-field risk to non-target arthropods is indicated.

9.7.3 Overall conclusions

The evaluation of the risk for non-target arthropods was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002), and in consideration of the recommendations of the guidance document ESCORT 2.

Effects of HBZ10 on non-target arthropods were not evaluated as part of the EU review of the active substances Ethofumesate and Phenmedipham. Two laboratory studies on glass plates were conducted with *Aphidius rhopalosiphi* and *Typhlodromus pyri*. Additional extended laboratory tests with *A. rhopalosiphi*, *T. pyri*, *Aleochara bilineata* and *Chrysoperla carnea* were performed.

For the representative species *A. rhopalosiphi* and *T. pyri*, the $HQ_{in-field}$ values at Tier 1 are above the trigger value of 2 indicating a possible risk after exposure to HBZ10 according to the proposed use pattern in beet crops.

For the representative species *A. rhopalosiphi* and *Typhlodromus pyri* as well as for the additional species *C. carnea* and *Aleochara bilineata*, the in-field PER is below the Tier-2 endpoint indicating low in-field risk for all intended uses.

The off-field HQs are below the trigger value of 2, indicating no risk to non-target arthropods is expected in off-field areas following the application of the product HBZ10 according to the proposed use pattern in beet-crops.

9.8 Effects on non-target soil meso- and macrofauna (KCP 10.4)

9.8.1 Toxicity data

Studies on the toxicity to earthworms and other non-target soil organisms (meso- and macrofauna) have been carried out with Ethofumesate, Phenmedipham and the relevant metabolites of Ethofumesate. Full details of these studies are provided in the respective EU DAR (DAR Ethofumesate, 1998; DAR Phenmedipham, 1999) and related documents (DAR Addendum Ethofumesate, 2000; DAR Addendum Phenmedipham, 2001 and 2003).

Effects on earthworms and other non-target soil organisms (meso- and macrofauna) of HBZ10 were not evaluated as part of the EU assessment of Ethofumesate and Phenmedipham. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment deviates from the results of the EU review process. Justifications are provided below.

Table 9.8.1-1 Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) – Ethofumesate and relevant metabolites

Species	Substance	Exposure System	Results	Reference
Earthworms				
<i>Eisenia fetida</i>	Ethofol 500 SC	Mixed into substrate / 56 d, chronic 5% peat content	NOEC _{corr} = 13.4 mg a.s./kg dw*	EFSA Conclusion (2016)
<i>Eisenia fetida</i>	Ethofumestae	Mixed into substrate / 56 d, chronic 5% peat content	NOEC _{corr} = 12.5 mg a.s./kg dw*	EFSA Conclusion (2016)
<i>Eisenia fetida</i>	NC 8493	Mixed into substrate / 56 d, chronic 10% peat content	NOEC = 16 mg/kg dw	EFSA Conclusion (2016)
<i>Eisenia fetida</i>	NC 8493	Mixed into substrate / 56 d, chronic 5% peat content	NOEC = 100 mg/kg dw	EFSA Conclusion (2016)
<i>Eisenia fetida</i>	NC 20645	Mixed into substrate / 56 d, chronic 5% peat content	NOEC = 100 mg/kg dw	EFSA Conclusion (2016)
Other soil macro-organisms				
<i>Folsomia candida</i>	Ethofol 500 SC	Mixed into substrate / 28 d, chronic 5% peat content	NOEC _{corr} = 13.35 mg a.s./kg dw*	EFSA Conclusion (2016)
<i>Folsomia candida</i>	NC 8493	Mixed into substrate / 28 d, chronic 5% peat content	NOEC = 100 mg/kg dw	EFSA Conclusion (2016)
<i>Folsomia candida</i>	NC 8493	Mixed into substrate / 28 d, chronic 5% peat content	NOEC = 556 mg/kg dw	EFSA Conclusion (2016)
<i>Folsomia candida</i>	NC 20645	Mixed into substrate / 28 d, chronic 5% peat content	NOEC = 100 mg/kg dw	EFSA Conclusion (2016)
<i>Hypoaspis aculeifer</i>	Ethofumesate 500 SC	Mixed into substrate 14 d, chronic 5% peat content	NOEC _{corr} = 22.1 mg a.s./kg dw*	EFSA Conclusion (2016)
<i>Hypoaspis aculeifer</i>	NC 8493	Mixed into substrate 14 d, chronic 5% peat content	NOEC = 309 mg/kg dw	EFSA Conclusion (2016)
Field studies				
-				

Species	Substance	Exposure System	Results	Reference
Litter bag test (EFSA Conclusion 2016)				
<p>Test item was the herbicide Ethofumesate SC45 (code: AE B049913 00 SC45 A203, analysed content of a.s. 43.8% w/w)</p> <p>An amount of 75 g a.s./ha (= 171 g prod./ha), corresponding to a plateau concentration of Ethofumesate of 0.05 mg a.s./kg soil, and an amount of 1000 g a.s./ha (= 2283 g prod./ha), the calculated annual application rate of ethofumesate, was applied to the treatment plots.</p> <p>The application of the estimated plateau concentration of ethofumesate resulted in soil residues of 42.9 µg a.s./kg dry soil, which is 85.8% of the nominal amount of 50 µg/kg. The application of the annual rate of Ethofumesate SC45 resulted in soil residues of 769 µg a.s./kg dry soil, corresponding to 107% of the nominal amount directly after the spray application.</p> <p>No statistically significant difference in proportion of straw degradation could be observed between untreated control plots and the plots treated with Ethofumesate SC45. The statistical power of the study was not assessed.</p>				

* Corrected value derived by dividing the endpoint by a factor of 2 in accordance with the EPPO earthworm scheme 2002.

zRMS comments:

Endpoints presented in Table 9.8.1-1 are in line with the EU agreed endpoints reported in EFSA Journal 2016;14(1):4374. For the active substance Ethofumesate the applicant did not use the same endpoint for *E. fetida* than the one retained in EFSA conclusion 2016. The NOEC of 13.4 mg as/kg soil was used while the NOEC of 12.5 mg as/kg soil was used in EFSA conclusion 2016.

Table 9.8.1-2 Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) – Phenmedipham

Species	Substance	Exposure System	Results	Reference
Earthworms				
<i>Eisenia fetida</i>	Phenmedipham	Mixed into substrate / 56 d, chronic	NOEC _{corr} = 10.35 mg a.s./kg dw*	Review Report (2004)
<i>Folsomia candida</i>	Phenmedipham	Mixed into substrate / 28 d, chronic	NOEC _{corr} ≥ 500 mg a.s./kg dw*	Frommholz, 2010 KCP 10.4.2.1/03

* Corrected value derived by dividing the endpoint by a factor of 2 in accordance with the EPPO earthworm scheme 2002; refined NOEC (actual application amount and actual soil bulk density)

zRMS comments:

The endpoint presented in Table 9.8.1-2 is in line with the EU agreed endpoint reported in Review Report (2004). The study for *Folsomia candida* was evaluated and agreed by the RMS in the course of the ongoing EU renewal process: with agreed endpoint NOEC_{corr}=500 mg a.s./kg dws, included in LIEP 2022, and EFSA Conclusion 2018). Although the renewal process is not finalized yet, no changes regarding the derived endpoints are expected. For this reason, the study was not re-evaluated by zRMS.

Table 9.8.1-3 Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) – HBZ10

Species	Substance	Exposure System	Results	Reference
Earthworms				
<i>Eisenia fetida</i>	HBZ10	Mixed into substrate / 56 d, chronic 10% peat content	EC ₁₀ = 138 mg product/kg dw	Winkelmann, G. (2021a) KCP 10.4.1/01
Other soil macro-organisms				
<i>Folsomia candida</i>	HBZ10	Mixed into substrate / 28 d, chronic 5% peat content	EC ₁₀ = 44.4 mg product/kg dw	Klix, V. (2021i) KCP 10.4.2.1/01
<i>Hypoaspis aculeifer</i>	HBZ10	Mixed into substrate / 14 d, chronic 5% peat content	NOEC = 244 mg product/kg dw	Klix, V. (2021j) KCP 10.4.2.1/02

zRMS comments:

Studies on toxicity of HBZ10 to non-target soil organisms were evaluated by the zRMS and considered acceptable. For details of evaluation, please refer to Appendix 2. Endpoints reported in Table 9.8.1-3 are confirmed to be correct.

9.8.1.1 Justification for new endpoints

The risk assessment is performed with EU agreed endpoints for the active substances Ethofumesate and Phenmedipham and their relevant metabolites, as well as with endpoints from studies with the formulated product HBZ10. Since no endpoint for the soil metabolite of Phenmedipham (MHPC) is stated in the Review Report (2004), a 10-times higher toxicity compared to the parent is assumed for the risk assessment.

9.8.2 Risk assessment

The evaluation of the risk for earthworms and other non-target soil organisms (meso- and macrofauna) was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

9.8.2.1 First-tier risk assessment

The relevant PEC_{soil} for risk assessments covering the proposed use pattern are taken from dRR, Part B, Section 8 (Environmental Fate), Point 8.7.2. According to the assessment of environmental-fate data, multi-annual accumulation in soil is considered for the active substances Ethofumesate and Phenmedipham. For the risk assessment of the active substances, the worst-case use group 2 (in-beet-crops (3×2.4 L product/ha, 6-day interval), use group 4 (3×1.8 L product/ha, 6-day interval) and use group 5 (3×2.4 L product/ha, 9-day interval) also covers the risk for non-target soil meso- and macrofauna from the intended use groups 1 & 3 (in-beet-crops (6×1.2 L product/ha, 5-day interval and 5×1.2 L product/ha, 7-day interval, respectively; please refer to point 9.1.2).

In addition to the risk assessment performed for the individual active substances, risk assessments for earthworms and other soil non-target soil organisms are presented for the formulated product. By using the measured toxicity endpoints on the chronic toxicity of HBZ10 to *Eisenia fetida*, *Folsomia candida* and *Hypoaspis aculeifer* (Table 9.8.1-3) and the PEC_{soil} value for the formulated product calculated for the worst-case application rate of 7.2 L product/ha (resulting in the highest total loading, considering 20% crop interception), the relevant TER_{LT} values are calculated in Table 9.8.2.1-4.

The maximum PEC_{soil} cumulative dose used for initial formulation risk assessment provided in Table 9.8.2.1-4 is considered as highest worst-case. Therefore, a more realistic approach is provided as refinement, considering the maximum single dose application rate per application of 2.4 L/ha, according to standard practice in risk assessment, since the formulation will break down to component parts after application and will not persist as formulated product. The PEC_{soil} presented below for the risk assessment was calculated with the highest maximum rate of 2.4 L/ha per application on beets, considering a 20% crop interception. The respective initial PEC_{soil} value for the formulated product was calculated considering a density of the product of 0.978 kg/dm^3 . New PEC_{soil} value used in risk assessment is of 2.504 mg/kg dw .

In addition, new study on *Folsomia candida* performed with Phenmedipham active substance is provided ($NOEC_{corr} = 500 \text{ mg/kg dry soil}$) to further assess the risk to *Folsomia candida* towards this active substance. Additional calculations are provided in Tables 9.8.2.1-1 to 9.8.2.1-3 below, and study summary is available in Appendix 2.

In order to address additional requests of Central zone Member States as raised during the commenting period, mixture risk assessments for earthworms and other non-target soil organisms are also performed based on (i) the combi-TER approach and (ii) the TER calculated as the ratio of the measured toxicity endpoint of the formulation expressed as the sum of the amount of individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

For the formulated product HBZ10, the PEC_{Soil} value was calculated based on the use in beets at 7.2 L product/ha which results in the highest total loading, considering 20% crop interception.

Use group no 2: 3 × 2.4 L product/ha, 6-day interval

Table 9.8.2.1-1 First-tier assessment of the acute and chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use of HBZ10 in beet crops group 2

Intended use		Beet crops: Sugar beet, red beet, yellow beet, fodder beet and chard	
Chronic effects on earthworms			
Active substance	NOEC/EC ₁₀ ^{corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	13.4 12.5	0.993	13.5 12.58
NC 8493	100	0.070	1428.6
Phenmedipham	10.35	0.874	11.8
MHPC	1.035	0.096	10.8
Chronic effects on other soil macro- and mesofauna – <i>Folsomia candida</i>			
Active substance	NOEC _{corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	13.35	0.993	13.4
NC 8493	556	0.070	7942.9
Phenmedipham	500	0.874	572.08
Chronic effects on other soil macro- and mesofauna – <i>Hypoaspis aculeifer</i>			
Active substance	NOEC _{corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	22.1	0.993	22.3
NC 8493	309	0.070	4414.3

TER values shown in bold fall below the relevant trigger.

Use group no 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.8.2.1-2 First-tier assessment of the acute and chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use of HBZ10 in beet crops group 5

Intended use		Beet crops: Sugar beet, red beet, yellow beet, fodder beet and chard	
Chronic effects on earthworms			
Active substance	NOEC/EC ₁₀ [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	13.4 12.5	0.981	13.7 12.74
NC 8493	100	0.070	1428.6
Phenmedipham	10.35	0.836	12.4
MHPC	1.035	0.096	10.8
Chronic effects on other soil macro- and mesofauna – <i>Folsomia candida</i>			
Active substance	NOEC _{corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	13.35	0.981	13.6
NC 8493	556	0.070	7942.9
Phenmedipham	500	0.836	598.1
Chronic effects on other soil macro- and mesofauna – <i>Hypoaspis aculeifer</i>			
Active substance	NOEC _{corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	22.1	0.981	22.5
NC 8493	309	0.070	4414.3

TER values shown in bold fall below the relevant trigger.

Use group no 4: 3 × 1.8 L product/ha, 6-day interval

Table 9.8.2.1-3 First-tier assessment of the acute and chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use of HBZ10 in beet crops group 4

Intended use		Beet crops: Sugar beet, red beet, yellow beet, fodder beet and chard
Chronic effects on earthworms		

Active substance	NOEC/EC ₁₀ corr [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	13.4 12.5	0.745	18.0 16.78
NC 8493	100	0.052	1923.1
Phenmedipham	10.35	0.656	15.8
MHPC	1.035	0.072	14.4
Chronic effects on other soil macro- and mesofauna – <i>Folsomia candida</i>			
Active substance	NOEC _{corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	13.35	0.745	17.9
NC 8493	556	0.052	10692.3
Phenmedipham	500	0.656	762.2
Chronic effects on other soil macro- and mesofauna – <i>Hypoaspis aculeifer</i>			
Active substance	NOEC _{corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
Ethofumesate	22.1	0.745	29.7
NC 8493	309	0.052	5942.3

TER values shown in bold fall below the relevant trigger.

The TER values for the active substances Ethofumesate and Phenmedipham are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 for all intended uses. **in beet crops.**

Formulated product HBZ10

Table 9.8.2.1-4

First-tier assessment of the ~~acute and~~ chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use of HBZ10 in ~~beet crops~~ all use groups (a)

Intended use	Beet crops Sugar beet, red beet, yellow beet, fodder beet and chard		
Chronic effects on earthworms			
Product	EC _{10corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
HBZ10	138-69.0	7.511 *	18.4-9.2
		2.504 **	27.6
Chronic effects on other soil macro- and mesofauna – <i>Folsomia candida</i>			
Product	EC _{10corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
HBZ10	11.4-22.2	7.511*	5.9-2.96
		2.504 **	8.9
Chronic effects on other soil macro- and mesofauna – <i>Hypoaspis aculeifer</i>			
Product	NOEC _{corr} [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
HBZ10	5.04-122	7.511 *	39.5-16.24
		2.504 **	48.7

TER values shown in bold fall below the relevant trigger.

* PEC_{Soil} value calculated using the maximum accumulated dose of 7.2 L/ha, considering 20% crop interception (unrealistic worst-case scenario)

** PEC_{Soil} value calculated using the maximum single application dose of 2.4 L/ha, considering 20% crop interception (realistic scenario considering the formulation breakdown and standard practice)

The TER values for the formulated product HBZ10 are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 according to the intended use pattern **for all intended uses in beet crops.**

In addition to the calculations presented in Table 9.8.2.1-4, TER_{LT} values for the formulated product are also calculated as the ratio of the measured toxicity endpoint of the formulation expressed as the sum of the amount of the individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

Table 9.8.2.1-5 First-tier assessment of the chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the use of HBZ10 in all use groups

Intended use		Sugar beet, red beet, yellow beet, fodder beet and chard	
Chronic effects on earthworms - <i>Eisenia fetida</i>			
Product	EC ₁₀ [Σ mg (a.s.i)/kg dw]	PEC _{Soil} [Σ mg (a.s.i)/kg dw]	TER _{LT} (criterion TER ≥ 5)
HBZ10	35.45 17.73 ^{a)}	1.75 (use group no 1) ^g	5.06
		1.867 (use group no 2) ^{b)}	10.0 9.5
		1.817 (use group no 5) ^{c)}	19.5 9.8
		1.401 (use group no 4) ^{d)}	25.3 12.7
Chronic effects on other soil macro- and mesofauna – <i>Folsomia candida</i>			
Product	EC ₁₀ [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
HBZ10	11.41 ^{e)}	1.75 (use group no 1) ^g	3.26
		1.867 (use group no 2) ^{b)}	6.4 3.1
		1.817 (use group no 5) ^{c)}	6.3 3.1
		1.401 (use group no 4) ^{d)}	8.1 4.1
Chronic effects on other soil macro- and mesofauna – <i>Hypoaspis aculeifer</i>			
Product	NOEC [mg/kg dw]	PEC _{Soil} [mg/kg dw]	TER _{LT} (criterion TER ≥ 5)
HBZ10	62.69 ^{f)}	1.75 (use group no 1) ^g	17.91
		1.867 (use group no 2) ^{b)}	33.6 16.8
		1.817 (use group no 5) ^{c)}	32.8 17.2
		1.401 (use group no 4) ^{d)}	44.7 22.4

TER values shown in bold fall below the relevant trigger.

- calculated based on the EC₁₀ of 438.69 mg product/kg dw, the certified product density (0.977 g/mL) and the certified content of the individual active substances Ethofumesate (0.125 kg/L) and Phenmedipham (0.126 kg/L) in the product
- sum of the PEC_{soil, accumulation} for Ethofumesate of 0.9934 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.874 mg/kg dw after multiple applications
- sum of the PEC_{soil, accumulation} for Ethofumesate of 0.981 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.836 mg/kg dw after multiple applications
- sum of the PEC_{soil, accumulation} for Ethofumesate of 0.745 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.656 mg/kg dw after multiple applications
- calculated based on the EC₁₀ of 22.4 mg product/kg dw, the certified product density (0.977 g/mL) and the certified content of the individual active substances Ethofumesate (0.125 kg/L) and Phenmedipham (0.126 kg/L) in the product
- calculated based on the NOEC of 122 mg product/kg dw, the certified product density (0.977 g/mL) and the certified content of the individual active substances Ethofumesate (0.125 kg/L) and Phenmedipham (0.126 kg/L) in the product
- sum of the PEC_{soil, accumulation} for Ethofumesate of 0.962 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.792 mg/kg dw after multiple applications

For *Eisenia fetida* and *Hypoaspis aculeifer*, the TER values for the formulated product HBZ10 expressed in a.s. are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 according to the intended use pattern.

For *Folsomia candida*, the TER values for the formulated product HBZ10 expressed as a.s. are below the trigger of 5, indicating a potential long-term risk to this organism after application of HBZ10 according to the intended use pattern. Therefore, further refinement is proposed below, by considering the following:

- For use groups No. 1 and 3, PEC_{soil} calculations have been performed by using Ethofumesate EU agreed DT₅₀ of 26.2 days (according to zRMS comment under point 8.4.1.1 of dRR section B8), instead of the worst-case DT₅₀ of 157 days used in calculations for other uses
- For use group No. 2, considered as worst-case use and thus covering use groups No. 4 and 5, PEC_{soil} calculations have been refined by splitting the overall BBCH range of application in early application (from BBCH 10 to 39, with consideration of a 20% crop interception in line with FOCUS groundwater interception values (EFSA, 2014)) and late application (from BBCH 20 to 39, with consideration of a 70% crop interception in line with FOCUS groundwater interception values (EFSA, 2014)). New PEC_{soil} calculations for use group No. 2 still consider a worst-case DT₅₀ of 157 days for the active substance Ethofumesate.

Additional TER calculations are provided in Table 9.8.2.1-6 below.

Table 9.8.2.1-6 First-tier assessment of the chronic risk for *Folsomia candida* due to the use of HBZ10 in all use groups with further refinements (c)

Intended use	Sugar beet, red beet, yellow beet, fodder beet and chard		
Chronic effects on other soil macro- and mesofauna – <i>Folsomia candida</i>			
Product	EC ₁₀ corr [Σ mg (a.s.i)/kg dw]	PEC _{Soil} [Σ mg (a.s.i)/kg dw]	TER _{LT} (criterion TER ≥ 5)
HBZ10	5.70 ^{a)}	1.076 (use group no 1) ^{b)}	5.3
		1.867 (use group no 2 for early application from BBCH 10) ^{c)}	3.1
		0.702 (use group no 2 for late application from BBCH 20) ^{d)}	8.1
		0.926 (use group no 3) ^{e)}	6.2

TER values shown in bold fall below the relevant trigger.

a) – calculated based on the EC₁₀ of 22.2 mg product/kg dw, the certified product density (0.977 g/mL) and the certified content of the individual active substances Ethofumesate (0.125 kg/L) and Phenmedipham (0.126 kg/L) in the product

b) – sum of the PEC_{soil, accumulation} for Ethofumesate of 0.284 mg/kg dw (refined value considering EU agreed DT₅₀ of 26.2 days) and the initial PEC_{soil} for Phenmedipham of 0.792 mg/kg dw

c) – sum of the PEC_{soil, accumulation} for Ethofumesate of 0.9934 mg/kg dw (considering early application from BBCH 10 onwards with 20% crop interception) and the initial PEC_{soil} for Phenmedipham of 0.874 mg/kg dw. Also covers risk assessment for used groups No. 4 and 5 and this use is considered as worst-case.

d) – sum of the PEC_{soil, accumulation} for Ethofumesate of 0.374 mg/kg dw (considering late application from BBCH 20 onwards with 70% crop interception) and the initial PEC_{soil} for Phenmedipham of 0.328 mg/kg dw. Also covers risk assessment for used groups No. 4 and 5 and this use is considered as worst-case.

e) – sum of the PEC_{soil, accumulation} for Ethofumesate of 0.279 mg/kg dw (refined value considering EU agreed DT₅₀ of 26.2 days) and the initial PEC_{soil} for Phenmedipham of 0.647 mg/kg dw –

Table 9.8.2.1-6 First-tier assessment of the chronic risk for *Folsomia candida* due to the use of HBZ10 in all use groups with further refinements (c)

Intended use	an use groups with further treatments (C) Sugar beet, red beet, yellow beet, fodder beet and chard		
Chronic effects on other soil macro- and mesofauna – <i>Folsomia candida</i>			
Product	EC _{10 corr} [Σ mg (a.s.i)/kg dw]	PEC _{Soil} [Σ mg (a.s.i)/kg dw], BBCH 10 and BBCH 20-39	TER _{LT} (criterion TER ≥ 5)
HBZ10	5.70 ^{a)}	1.75 (use group no 1, early application BBCH 10) ^c covers use no 3.	3.26
		0.659 (use group no 1, late application from BBCH 20) ^c covers use no 3.	8.65
		1.867 (use group no 2, early application , BBCH 10) ^b covers use no 4 and no 5.	3.10
		0.702 (use group no 2, late application from BBCH 20) ^b covers use no 4 and no 5.	8.11

TER values shown in bold fall below the relevant trigger.

a) – calculated based on the EC₁₀ of 22.2 mg product/kg dw, the certified product density (0.977 g/mL) and the certified content of the individual active substances Ethofumesate (0.125 kg/L) and Phenmedipham (0.126 kg/L) in the product

b) – sum of the PEC_{soil}, accumulation for Ethofumesate of 0.9934 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.874 mg/kg dw after multiple applications (use no 2)

c) – sum of the PEC_{soil}, accumulation for Ethofumesate of 0.962 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.792 mg/kg dw after multiple applications

As shown above, the TER values for the formulated product HBZ10 are above the trigger of 5 for use groups No. 1 and 3, indicating a low long-term risk to *Folsomia candida* after application of HBZ10 according to these intended use patterns.

With regards to use group No. 2 (covering both use groups No. 4 and 5), the TER values for the formulated product HBZ10 are below the trigger of 5. However, worst-case calculations based on PEC_{soil} values lead to marginal fail in risk assessment considering conservatism of this approach, whilst additional PEC_{soil} calculations provided for shorter BBCH stage 20-39 (instead of 10-39 initially) show an acceptable risk for *Folsomia candida*. According to these new PEC_{soil} estimates and TER results, it can be assumed the risk for *Folsomia candida* is only relevant at early stage of application (BBCH 10-19), which does not represent the full period of product application.

Moreover, the risk assessment based on endpoint for the formulation expressed as active substance, assumes that the entire toxicity of the formulation will be attributed to the substance under evaluation. Such approach results in a very conservative estimate of the risk for combination of the two a.i. and stays theoretical calculation based on conservative assumptions.

This gives further evidence that risk on *Folsomia candida* is expected to be low, by considering conservatism and margins of safety linked to the above assessment (formulation toxicity entirely attributed to the active substances, use of worst-case Ethofumesate DT₅₀, and short BBCH stage where this risk has been triggered).

According to calculations provided in table 9.8.2.1-4, for which no unacceptable risk following the use of HBZ10 is triggered, it can be considered formulation risk assessment has been performed in a comprehensive way, and low long-term risk to soil meso- and macrofauna is expected. Therefore, in accordance with Working document on Risk Assessment of Plant Protection Products in the Central Zone in ecotoxicology (May, 2021), the above risk assessment considering the endpoint for the formulation expressed as active substance should be considered as for information only.

For this purpose, new study on *Folsomia candida* performed with Phenmedipham active substance (NOECcorr = 500 mg/kg dry soil) will be used in the below combiTER assessment.

Even though no a.s. data on *Folsomia candida* exists for Ethofumesate, Ethofumesate toxicity endpoint for *Eisenia fetida* and Ethofumesate-based formulation toxicity endpoint for *Folsomia candida* show that Ethofol 500 SC has similar toxicity as Ethofumesate active substance (NOECcorr of 12.5 mg a.s./kg dw and NOECcorr of 13.35 mg a.s./kg dw, respectively). Therefore, the Ethofumesate EU agreed endpoint of 13.35 mg/kg dry soil is considered relevant for combiTER calculation as it properly reflects active substance toxicity.

As HBZ10 contains more than one active substance, In order to further support this assumption, the combination risk to earthworms *Eisenia fetida* and *Folsomia candida* is further assessed by combining the TERs for the individual active substances, also referred to as the combi-TER.

As the trigger values for each active substance (Ethofumesate and Phenmedipham) are equal, the combined TER value can be calculated according to:

$$TER_{combi} = 1/((1/TER_{substance\ 1})+(1/TER_{substance\ 2}))$$

Table 9.8.2.1-7 First-tier assessment of the chronic risk of HBZ10 to earthworms based on the combi-TER approach

Intended use	Ethofumesate TER _{LT}	Phenmedipham TER _{LT}	TER _{combi}
Use group 2, 3 × 2.4 L product/ha, 6-day interval	12.58	11.8	6.1
Use group 5, 3 × 2.4 L product/ha, 9-day interval	12.74	12.4	6.3
Use group 4, 3 × 1.8 L product/ha, 6-day interval	16.78	15.8	8.1

Table 9.8.2.1-8 First-tier assessment of the chronic risk of HBZ10 to *Folsomia candida* based on the combi-TER approach

Intended use	Ethofumesate TER _{LT}	Phenmedipham TER _{LT}	TER _{combi}
Use group 2, 3 × 2.4 L product/ha, 6-day interval	13.44	572.08	13.14
Use group 5, 3 × 2.4 L product/ha, 9-day interval	13.61	598.09	13.31
Use group 4, 3 × 1.8 L product/ha, 6-day interval	17.92	762.20	17.51

As the calculated TER_{combi} exceed the trigger of 5, an acceptable combination chronic risk of HBZ10 to earthworms and *Folsomia candida* is concluded.

zRMS comments:

Based on calculations in the Tables 9.8.2.1-1 to 9.8.2.1-3 above an acceptable risk to earthworms can be concluded, from active substances, its metabolites and product HBZ10.

No toxicity data ~~are~~ was available for *Hypoaspis aculeifer* and *Folsomia candida* for a.s. phenmedipham.

During commenting period process the new study for *Folsomia candida* for the a.s.- phenmedipham was performed by the Applicant. The study was evaluated and agreed by the RMS in the course of the ongoing EU renewal process: with agreed endpoint NOEC_{corr}=500 mg a.s./kg dws, included in EFSA Conclusion 2018). Although the renewal process is not finalized yet, no changes regarding the derived endpoints are expected. For this reason, the study was not re-evaluated by zRMS. The risk assessment for both active substance and its metabolites are considered acceptable as the trigger value above 5 was achieved.

~~However,~~ The studies for product for ~~these~~ soil organism were submitted and the risk assessment was provided in the Table 9.8.2.1-4 ~~is considered acceptable and sufficient for the product authorization.~~ for max. single application rate of 2.4 L/ha covering all proposed uses in the GAP table. Based on these calculations the risk from formulation is considered as acceptable.

In addition, TER_{LT} values for the formulated product were also calculated as the ratio of the measured toxicity endpoint of the formulation expressed as the sum of the amount of the individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

Based on this approach the TER_{LT} value for *Folsomia candida* for growth stage BBCH 10-19 did not achieved the trigger value of 5 but for later growth stage 20-39 BBCH an acceptable risk is concluded.

It should be indicated that the approach of assuming that the toxicity is entirely due to the substance under evaluation may result in a too conservative risk assessment. This is because the entire toxicity of the formulation will be attributed to the substance under evaluation. However, the approach agreed at the meeting in CZ is in line with Regulation (EU) 284/2013 and will only be used when an applicant does not provide a comprehensive formulation risk assessment. Therefore, in accordance with Working document on Risk Assessment of Plant Protection Products in the Central Zone in ecotoxicology (May, 2021), the above risk assessment considering the endpoint for the formulation expressed as active substance should be considered as for information only.

Mixture risk assessments for earthworms and other non-target soil organisms, including *Folsomia candida*, were also performed based on combi-TER_{mix} approach and acceptable risk assessment is concluded for all proposed uses. zRMS would like to stressed that final acceptance of the risk assessment for *Folsomia candida* from the product HBZ10 is left at MSs level.

Overall, in zRMS opinion no unacceptable effects for earthworm and soil macro-organism are expected following application of HBZ10.

9.8.2.2 Higher-tier risk assessment

Not relevant.

9.8.3 Overall conclusions

The evaluation of the risk for non-target soil meso- and macrofauna was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev.2 (final), October 17, 2002.

Effects of HBZ10 on non-target soil meso- and macrofauna were not evaluated as part of the EU review of the active substances Ethofumesate and Phenmedipham. Three laboratory studies assessing the effects of HBZ10 on *Eisenia fetida*, *Folsomia candida* and *Hypoaspis aculeifer* were conducted and are also considered in the risk assessment.

The TER values for the active substances Ethofumesate and Phenmedipham are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 for all intended uses ~~in beet crops~~.

When taking into account the more realistic PEC_{soil} value for the formulated product based on single application, the TER values for the formulated product HBZ10 are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 for all intended uses ~~in beet crops~~.

Mixture risk assessments for earthworms and other non-target soil organisms were also performed based on combi-TER approach and TER calculated as the ratio of the measured toxicity endpoint of the formulation expressed as the sum of the amount of individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

According to these additional calculations and weight of evidence, it can be considered a low long-term risk to soil meso- and macrofauna is expected from the combination of the two active ingredients after

application of HBZ10 according to the intended use pattern. However, the final acceptance of risk assessment from formulation is left at MSs level.

The TER values for the formulated product HBZ10 following mixture risk assessments for earthworms and other non-target soil organisms are above the trigger of 5, indicating a low long-term risk to soil meso- and macrofauna after application of HBZ10 according to the intended use pattern.

9.9 Effects on soil microbial activity (KCP 10.5)

9.9.1 Toxicity data

Studies on effects soil microorganisms have been carried out with Ethofumesate, Phenmedipham and the relevant metabolites of Ethofumesate. Full details of these studies are provided in the respective EU DAR (DAR Ethofumesate, 1998; DAR Phenmedipham, 1999) and related documents (DAR Addendum Ethofumesate, 2000; DAR Addendum Phenmedipham, 2001 and 2003).

Effects on soil microorganisms of HBZ10 were not evaluated as part of the EU assessment of Ethofumesate and Phenmedipham. New data submitted with this application are listed in Appendix 1 and summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment deviates from the results of the EU review process. Justifications are provided below.

Table 9.9.1-1 Endpoints and effect values relevant for the risk assessment for soil microorganisms - Ethofumesate and relevant metabolites

Endpoint	Substance	Exposure System	Results	Reference
N-mineralisation	Ethofol 500 SC	28 d, aerobic soil type	Nitrate formation rate 6.47 mg/kg soil dw -18.87% effect	EFSA Conclusion (2016)
N-mineralisation	NC 8493	28 d, aerobic soil type	Nitrate formation rate 12 mg/kg soil dw -15.2% effect	EFSA Conclusion (2016)
N-mineralisation	NC 20645	28 d, aerobic soil type	Nitrate formation rate 13.8 mg/kg soil dw +6.7% effect	EFSA Conclusion (2016)

zRMS comments:

Endpoints presented in Table 9.9.1-1 are in line with the EU agreed endpoints reported in EFSA Journal 2016;14(1):4374.

Table 9.9.1-2 Endpoints and effect values relevant for the risk assessment for soil microorganisms - Phenmedipham

Endpoint	Substance	Exposure System	Results	Reference
N-mineralisation	Not stated	Lab study with 2 soils	No effects at 1.3 and 13 mg a.s./kg dry soil	Review Report (2004)
Field study				
In a field study the nitrification rate was in one soil 43 to 30% lower in the treated soil compared to the unsprayed soil after 2 weeks and at harvesting when Phenmedipham formulation (1 kg Phenmedipham/ha) was sprayed as a tank mixture with Ethofumesate (0.75 kg/ha). In the other soil, the nitrification rate was 58% higher in the treated soil compared to the control. The use rate in this study corresponds to soil concentration of ca. 1.3 mg Phenmedipham/kg soil.				Review Report (2004)

zRMS comments:

Endpoints presented in Table 9.9.1-1 are in line with the EU agreed endpoints reported in Review Report (2004).

Table 9.9.1-3 Endpoints and effect values relevant for the risk assessment for soil microorganisms – HBZ10

Endpoint	Substance	Exposure System	Results	Reference
N-mineralisation	HBZ10	70 d, aerobic soil type	Nitrate formation rate 31.26 mg/kg soil dw $\leq \pm 25\%$ effect	Winkelmann, G. (2021b) KCP 10.5/01

zRMS comments:

The study on effects of HBZ10 on soil nitrogen transformation was evaluated by the zRMS and considered acceptable. For details of evaluation, please refer to Appendix 2. The endpoint reported in Table 9.9.1-3 is confirmed to be correct.

9.9.1.1 Justification for new endpoints

The risk assessment is performed with EU agreed endpoints for the active substances Ethofumesate and Phenmedipham and their relevant metabolites, as well as with endpoints from studies with the formulated product HBZ10. Since no endpoint for the soil metabolite of Phenmedipham (MHPC) is stated in the Review Report (2004), a 10-times higher toxicity compared to the parent is assumed for the risk assessment.

9.9.2 Risk assessment

The evaluation of the risk for soil microorganisms was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

The relevant PEC_{Soil} for risk assessments covering the proposed use pattern are taken from dRR, Part B, Section 8 (Environmental Fate), Point 8.7.2. According to the assessment of environmental-fate data, multi-annual accumulation in soil is considered for the active substances Ethofumesate and Phenmedipham. For the risk assessment of the active substances, the worst-case use group 2 (in-beet-crops (3 × 2.4 L product/ha, 6-day interval), use group 4 (3 × 1.8 L product/ha, 6-day interval) and use group 5 (3 × 2.4 L product/ha, 9-day interval) also covers the risk for soil microbial activity from the intended use groups 1 & 3 (in-beet-crops (6 × 1.2 L product/ha, 5-day interval and 5 × 1.2 L product/ha, 7-day interval, respectively; please refer to point 9.1.2).

In addition to the risk assessment performed for the individual active substances, risk assessments for soil microorganisms are presented for the formulated product. By using the maximum test concentration of HBZ10 with effects $\leq 25\%$ (Table 9.9.1-3) and the PEC_{Soil} value for the formulated product calculated for the worst-case application rate of 7.2 L product/ha (resulting in the highest total loading, considering 20% crop interception), risk acceptability for the formulated product is assessed in Table 9.9.2-4.

In order to address additional requests of Central zone Member States as raised during the commenting period, mixture risk assessments for soil microorganisms are also performed based on (i) the combination risk assessment in a way equivalent to the combi-TER approach and (ii) the ratio of the maximum test concentration of HBZ10 with effects $\leq 25\%$ expressed as the sum of the amount of individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

For the formulated product HBZ10, the PEC_{Soil} value was calculated based on the use in beets at 7.2 L product/ha which results in the highest total loading, considering 20% crop interception.

Use group no 2: 3 × 2.4 L product/ha, 6-day interval

Table 9.9.2-1 Assessment of the risk for effects on soil micro-organisms due to the use of HBZ10 in **beet crops group 2**

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard		
N-mineralisation			
Product/active substance	Max. conc. with effects ≤ 25% [mg/kg dw]	PEC _{Soil} [mg/kg dw]	Risk acceptable?
Ethofumesate	6.47 (at 28 d)	0.993	Yes
NC 8493	12 (at 28 d)	0.070	Yes
Phenmedipham	13	0.874	Yes
MHPC	1.3	0.096	Yes

Use group no 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.9.2-2 Assessment of the risk for effects on soil micro-organisms due to the use of HBZ10 in **beet crops group 5**

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard		
N-mineralisation			
Product/active substance	Max. conc. with effects ≤ 25% [mg/kg dw]	PEC _{Soil} [mg/kg dw]	Risk acceptable?
Ethofumesate	6.47 (at 28 d)	0.981	Yes
NC 8493	12 (at 28 d)	0.070	Yes
Phenmedipham	13	0.836	Yes
MHPC	1.3	0.096	Yes

Use group no 4: 3 × 1.8 L product/ha, 6-day interval

Table 9.9.2-3 Assessment of the risk for effects on soil micro-organisms due to the use of HBZ10 in **beet crops group 4**

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard		
N-mineralisation			
Product/active substance	Max. conc. with effects ≤ 25% [mg/kg dw]	PEC _{Soil} [mg/kg dw]	Risk acceptable?
Ethofumesate	6.47 (at 28 d)	0.745	Yes
NC 8493	12 (at 28 d)	0.052	Yes
Phenmedipham	13	0.656	Yes
MHPC	1.3	0.072	Yes

Formulated product HBZ10

Table 9.9.2-4 Assessment of the risk for effects on soil micro-organisms due to the use of HBZ10 in **beet crops all groups (a)**

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard		
N-mineralisation			
Product/active substance	Max. conc. with effects ≤ 25% [mg/kg dw]	PEC _{Soil} [mg/kg dw]	Risk acceptable?
HBZ10	31.26 (at 70 d)	7.511 2.5*	Yes Yes

*single application rate for product

In addition to the assessment presented in **Table 9.9.2-4**, the risk acceptability for the formulated product is also assessed as the ratio of the maximum test concentration of HBZ10 with effects ≤ 25% expressed as the sum of the amount of the individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

Table 9.9.2-5 Assessment of the risk for effects on soil micro-organisms due to the use of HBZ10 in all groups (b)

Intended use		Sugar beet, red beet, yellow beet, fodder beet and chard		
Product	Max. conc. with effects ≤ 25% [Σ mg (a.s.i)/kg dw]		PEC _{soil} [Σ mg (a.s.i)/kg dw]	Risk acceptable?
HBZ10	8.03 ^{a)}		1.867 (use group no 2) ^{b)}	Yes
			1.817 (use group no 5) ^{c)}	Yes
			1.401 (use group no 4) ^{d)}	Yes

- a) calculated based on the concentration of 31.26 mg product/kg dw, the certified product density (0.977 g/mL) and the certified content of the individual active substances Ethofumesate (0.125 kg/L) and Phenmedipham (0.126 kg/L) in the product
- b) sum of the PEC_{soil, accumulation} for Ethofumesate of 0.9934 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.874 mg/kg dw after multiple applications
- c) sum of the PEC_{soil, accumulation} for Ethofumesate of 0.981 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.836 mg/kg dw after multiple applications
- d) sum of the PEC_{soil, accumulation} for Ethofumesate of 0.745 mg/kg dw and the initial PEC_{soil} for Phenmedipham of 0.656 mg/kg dw after multiple applications

As HBZ10 contains more than one active substance, the combination risk to soil microorganisms is further assessed by combining the margins of safety (MoS) for the individual active substances in a way equivalent to the combi-TER approach. As the trigger values for each active substance (Ethofumesate and Phenmedipham) are equal, the combined MoS value can be calculated according to:

$$\text{MoS}_{\text{combi}} = 1 / ((1/\text{MoS}_{\text{substance 1}}) + (1/\text{MoS}_{\text{substance 2}}))$$

Table 9.9.2-6 Assessment of the risk of HBZ10 to soil microorganisms based on the combined MoS

Intended use	Ethofumesate MoS	Phenmedipham MoS	MoS _{combi}
Use group 2, 3 × 2.4 L product/ha, 6-day interval	6.5	14.9	4.5
Use group 5, 3 × 2.4 L product/ha, 9-day interval	6.6	15.6	4.6
Use group 4, 3 × 1.8 L product/ha, 6-day interval	8.7	19.8	6.0

As the calculated MoS_{combi} exceed the trigger of 1, an acceptable combination risk of HBZ10 to soil microorganisms is concluded.

zRMS comments:

The risk assessment presented in Tables 9.9.2-1 to 9.9-6 above is in general agreed by the zRMS.

Overall, no unacceptable effects on soil microbial activity are expected following application of HBZ10.

9.9.3 Overall conclusions

The evaluation of the risk for earthworms and other non-target soil organisms (meso- and macrofauna) was performed in accordance with the recommendations of the “Guidance Document on Terrestrial Ecotoxicology”, as provided by the Commission Services (SANCO/10329/2002 rev 2 (final), October 17, 2002).

Effects of HBZ10 on soil microbial activity were not evaluated as part of the EU assessment for the active substances Ethofumesate and Phenmedipham. A study on soil microbial activity has been carried out with the formulated product HBZ10.

The risk to soil micro-organisms following the application of HBZ10 was evaluated by comparing the PEC value in soil after application ~~to beet crops~~ according to the intended use pattern with the concentrations for the active substances Ethofumesate and Phenmedipham and their relevant metabolites, as well as for the formulated product HBZ10 at which the adverse effects on the soil microbial activity were below 25%. The results of the comparison expressed as Margin of Safety (MoS) for active substances Ethofumesate and Phenmedipham and their relevant metabolites, as well as for the formulated product HBZ10 indicate an acceptable risk following the application of HBZ10 ~~in beet crops~~ according to the intended use pattern.

Mixture risk assessment for soil microorganisms was also performed based on the combination risk assessment in a way equivalent to the combi-TER approach and the ratio of the maximum test concentration of HBZ10 with effects $\leq 25\%$ expressed as the sum of the amount of individual active substances to the PEC of the formulation expressed as the sum of the PECs of the individual active substances.

As a result, an acceptable combination risk of HBZ10 to soil microorganisms is concluded following the application of HBZ10 according to the intended use pattern.

9.10 Effects on non-target terrestrial plants (KCP 10.6)

9.10.1 Toxicity data

Studies on the toxicity to non-target terrestrial plants have been carried out with Ethofumesate. Full details of these studies are provided in the EU DAR (DAR Ethofumesate, 1998) and related documents (DAR Addendum Ethofumesate, 2000).

Effects on non-target terrestrial plants of HBZ10 were not evaluated as part of the EU assessment of Ethofumesate and Phenmedipham. New data submitted with this application are listed in Appendix 1 summarised in Appendix 2.

The selection of studies and endpoints for the risk assessment deviates from the results of the EU review process. Since specific endpoints are available for HBZ10, these endpoints will be used in the risk assessment.

Nevertheless, a summary is given of the EU endpoints for Ethofumesate. These EU endpoints are all derived from formulated products and are therefore considered less appropriate to be used in the risk assessment for HBZ10 but listed here for completeness.

Table 9.10.1-1 Endpoints and effect values relevant for the risk assessment for non-target terrestrial plants - Ethofumesate

Species	Substance	Exposure System	Results	Reference
<i>Avena sativa</i> _m (most sensitive species)	Ethofol 500 SC	21 d Seedling emergence	ER ₅₀ = 0.328 L product/ha	EFSA Conclusion (2016)
<i>Avena sativa</i> _m (most sensitive species)	Ethofol 500 SC	21 d Vegetative vigour	ER ₅₀ > 2 L product/ha	EFSA Conclusion (2016)
<i>Triticum aestivum</i> _m (most sensitive species)	Ethofumesate 500 SC	21 d Seedling emergence	ER ₅₀ = 0.101 L product/ha	EFSA Conclusion (2016)
<i>Triticum aestivum</i> _m (most sensitive species)	Ethofumesate 500 SC	21 d Vegetative vigour	ER ₅₀ = 1.24 L product/ha	EFSA Conclusion (2016)
-	-	21 d Seedling emergence	HC ₅ = 0.191 L product/ha	EFSA Conclusion (2016)

m: monocotyledonous; d: dicotyledonous

zRMS comments:

Endpoints presented in Table 9.10.1-1 are in line with the EU agreed endpoints reported in EFSA Journal 2016;14(1):4374.

Table 9.10.1-2 Endpoints and effect values relevant for the risk assessment for non-target terrestrial plants – HBZ10

Species	Substance	Exposure System	Results	Reference
<i>Avena sativa</i> _m (most sensitive species)	HBZ10	21 d Seedling emergence	ER ₅₀ = 1.25 L product/ha (shoot fresh weight)	Winkelmann, G. (2021c) KCP 10.6.2/01
<i>Lycopersicon esculentum</i> _d (most sensitive species)	HBZ10	21 Vegetative vigour	ER ₅₀ = 0.145 L product/ha (shoot fresh weight)	Winkelmann, G. (2021d) KCP 10.6.2/02

m: monocotyledonous; d: dicotyledonous

zRMS comments:

Studies on toxicity of HBZ10 to non-target terrestrial plants were evaluated by the zRMS and considered acceptable. For details of evaluation, please refer to Appendix 2. The endpoints reported in Table 9.10.1-2 were

confirmed to be correct since both studies have been evaluated and considered relevant for use in the risk assessment.

9.10.1.1 Justification for new endpoints

The risk assessment is performed with the endpoints for the formulated product HBZ10.

9.10.2 Risk assessment

9.10.2.1 Tier-1 risk assessment (based on screening data)

Not relevant.

9.10.2.2 Tier-2 risk assessment (based on dose-response data)

The risk assessment is based on the “Guidance Document on Terrestrial Ecotoxicology”, (SANCO/10329/2002 rev.2 final, 2002). It is restricted to off-field situations, as non-target plants are non-crop plants located outside the treated area.

The risk assessment is presented for all intended uses. Uses with identical number of applications and application rate are grouped and presented in one table (please refer to point 9.1.2).

To assess the risk to terrestrial plants following the use of HBZ10, the toxicity/exposure ratio (TER) for each scenario, which is the ratio between the effective concentration (in L/ha) and the exposure (in L/ha) was determined. The exposure was calculated by multiplying the application rate for a drift value as described in the BBA (2000)⁹.

PER_{off-field} values were calculated using the following equation:

$$\text{PER}_{\text{off-field}} = \text{Application rate} \times \text{MAF} \times \text{drift factor}$$

Use group no 2: 3 × 2.4 L product/ha, 6-day interval and use group no 5: 3 × 2.4 L product/ha, 9-day interval

Table 9.10.2.2-1 Assessment of the risk for non-target plants due to the use of HBZ10 in **beet-crops use groups 2 and 5**

Intended use	Beet-crops: Sugar beet, red beet, yellow beet, fodder beet and chard			
Active substance/product	Ethofumesate + Phenmedipham / HBZ10			
Application rate [L/ha]	3 × 2.4			
MAF	2.3 (leaf substrate) / 2.7 (soil) *			
Test species	ER ₅₀ [L/ha]	Drift rate	PER _{off-field} [L/ha]	TER criterion: TER ≥ 5
Seedling emergence (shoot fresh weight)	1.25	0.0201	0.130	11.2 9.6
Vegetative vigour (shoot fresh weight)	0.145		0.111	1.3

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio.

TER values shown in bold fall below the relevant trigger.

* the MAF for leaf substrate is used in the exposure assessment for vegetative vigour while the MAF for soil is used in the exposure assessment for seedling emergence

The TER value is above the trigger of 5 based on the effect rate for *Avena sativa* as most sensitive species in the seedling emergence test by Winkelmann, G. (2021c), indicating an acceptable risk for non-target terrestrial plants. However, The TER value is below the trigger of 5 based on the effect rate for *Lycopersicon esculentum* as most sensitive species in the vegetative vigour test by Winkelmann, G. (2021d), indicating a possible risk for non-target terrestrial plants following the application of HBZ10 in beet-crops at 3 × 2.4 L product/ha (6-day or 9-day interval).

⁹ Bundesanzeiger Jg. 52 (Official Gazette), Nr 100, S. 9879-9880 (25.05.2000) Bekanntmachung über die Abdriftwerte, die bei der Prüfung und Zulassung von Pflanzenschutzmitteln herangezogen werden

Use group no 4: 3 × 1.8 L product/ha, 6-day interval

Table 9.10.2.2-2 Assessment of the risk for non-target plants due to the use of HBZ10 in ~~beet-crops~~ use group 4

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard			
Active substance/product	Ethofumesate + Phenmedipham / HBZ10			
Application rate [L/ha]	3 × 1.8			
MAF	2.3 (leaf substrate) / 2.7 (soil) *			
Test species	ER₅₀ [L/ha]	Drift rate	PER_{off-field} [L/ha]	TER criterion: TER ≥ 5
Seedling emergence (shoot fresh weight)	1.25	0.0201	0.0977	15.0 12.8
Vegetative vigour (shoot fresh weight)	0.145		0.0832	1.7

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio.
TER values shown in bold fall below the relevant trigger.

* the MAF for leaf substrate is used in the exposure assessment for vegetative vigour while the MAF for soil is used in the exposure assessment for seedling emergence

The TER value is above the trigger of 5 based on the effect rate for *Avena sativa* as most sensitive species in the seedling emergence test by Winkelmann, G. (2021c), indicating an acceptable risk for non-target terrestrial plants. However, The TER value is below the trigger of 5 based on the effect rate for *Lycopersicon esculentum* as most sensitive species in the vegetative vigour test by Winkelmann, G. (2021d), indicating a possible risk for non-target terrestrial plants following the application of HBZ10 ~~in beet-crops~~ at 3 × 1.8 L product/ha (6-day interval).

Use group no 1: 6 × 1.2 L product/ha, 5-day interval

Table 9.10.2.2-3 Assessment of the risk for non-target plants due to the use of HBZ10 in ~~beet-crops~~ use group 1

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard			
Active substance/product	Ethofumesate + Phenmedipham / HBZ10			
Application rate [L/ha]	6 × 1.2			
MAF	3.2 (leaf substrate) / 4.6 (soil) *			
Test species	ER₅₀ [L/ha]	Drift rate	PER_{off-field} [L/ha]	TER criterion: TER ≥ 5
Seedling emergence (shoot fresh weight)	1.25	0.0164	0.0905	10.9 13.8
Vegetative vigour (shoot fresh weight)	0.145		0.0630	2.3

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio.
TER values shown in bold fall below the relevant trigger.

* the MAF for leaf substrate is used in the exposure assessment for vegetative vigour while the MAF for soil is used in the exposure assessment for seedling emergence

The TER value is above the trigger of 5 based on the effect rate for *Avena sativa* as most sensitive species in the seedling emergence test by Winkelmann, G. (2021c), indicating an acceptable risk for non-target terrestrial plants. However, The TER value is below the trigger of 5 based on the effect rate for *Lycopersicon esculentum* as most sensitive species in the vegetative vigour test by Winkelmann, G. (2021d), indicating a possible risk for non-target terrestrial plants following the application of HBZ10 ~~in beet-crops~~ at 6 × 1.2 L product/ha (5-day interval).

Use group no 3: 5 × 1.2 L product/ha, 7-day interval

Table 9.10.2.2-4 Assessment of the risk for non-target plants due to the use of HBZ10 in **beet-crops use group 3**

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard			
Active substance/product	Ethofumesate + Phenmedipham / HBZ10			
Application rate [L/ha]	5 × 1.2			
MAF	3.0 (leaf substrate) / 4.0 (soil) *			
Test species	ER₅₀ [L/ha]	Drift rate	PER_{off-field} [L/ha]	TER criterion: TER ≥ 5
Seedling emergence (shoot fresh weight)	1.25	0.0175	0.0840	19.8 14.9
Vegetative vigour (shoot fresh weight)	0.145		0.0630	2.3

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio.

TER values shown in bold fall below the relevant trigger.

* the MAF for leaf substrate is used in the exposure assessment for vegetative vigour while the MAF for soil is used in the exposure assessment for seedling emergence

The TER value is above the trigger of 5 based on the effect rate for *Avena sativa* as most sensitive species in the seedling emergence test by Winkelmann, G. (2021c), indicating an acceptable risk for non-target terrestrial plants. However, The TER value is below the trigger of 5 based on the effect rate for *Lycopersicon esculentum* as most sensitive species in the vegetative vigour test by Winkelmann, G. (2021d), indicating a possible risk for non-target terrestrial plants following the application of HBZ10 in beet-crops at 5 × 1.2 L product/ha (7-day interval).

According to the Terrestrial Guidance Document (SANCO/10329/2002 rev 2 final 17 October 2002), the risk to non-target plants should be considered acceptable if the lowest ER₅₀ endpoint is 5 times higher than the calculated maximum PER_{off-field} (TER = 5 or greater). The submitted studies indicate that the lowest ER₅₀ obtained from the biomass gain in the vegetative vigour study on tomato was 0.145 L product/ha (study by Winkelmann, G. 2021d).

The TER values for vegetative vigour and seedling emergence were calculated by comparing the most sensitive ER₅₀ values with the highest predicted exposure level (PER_{off-field}) using the 90th percentile estimates derived by BBA (2006)¹⁰ from the spray-drift predictions of Ganzelmeier & Rautmann (2000)¹¹. The results of the deterministic risk assessment for terrestrial plants on vegetative vigour show a TER based on the most sensitive ER₅₀ value below the trigger of 5. Thus, a refined risk assessment is required.

Probabilistic approach (SSD)

A probabilistic risk assessment was performed as a refinement option. TER values for vegetative vigour were calculated by comparing the HC₅ value with the highest predicted exposure level (PER_{off-field}).

In addition to the deterministic risk assessment, SANCO/10329/2002 rev. 2 recommends the use of the HC₅ (the concentrations below which less than 5% of the species will be harmed above the ER₅₀ level). The HC₅ can be calculated from the available data. The SANCO/10329/2002 rev. 2 states that if the ER₅₀ for less than 5% of the species is below the highest predicted level, the risk for terrestrial plants is assumed to be acceptable. Thus, the HC₅ itself (TER = 1) can be regarded to be protective.

Since data from a vegetative vigour study with 10 species are available, a probabilistic approach based on the species sensitivity distribution (SSD) is possible. Thus, a median HC₅ value with 90%-confidence limits for vegetative vigour is calculated with the program ETX 2.2 (Sep 2017)¹² based on available ER₅₀ values for the parameter shoot fresh weight.

Details on the data from the study by Winkelmann, G. (2021d; KCP 10.6.2/02) considered in the SSD is presented in the table below and the outcome is presented under results of the updated risk assessment.

¹⁰ Spray drift: according to BBA spray drift data from 27. March 2006 (www.jki.bund.de)

¹¹ Ganzelmeier H., Rautmann D. (2000). Drift, drift-reducing sprayers and sprayer testing. Aspects of Applied Biology 57, 2000, Pesticide Application. Public domain.

¹² Van Vlaardingen PLA, Traas TP, Wintersen AM, Aldenberg T. (2004). ETX 2.0. A program to calculate hazardous concentrations and fraction affected, based on normally distributed toxicity data. Bilthoven, the Netherlands: National Institute for Public Health and the Environment (RIVM). Report no. 601501028/2004, 68 pp.

Table 9.10.2.2-5 ER₅₀ values for shoot fresh weight (vegetative vigour)

Plant species	ER ₅₀ [L product/ha]
<i>Avena sativa</i>	2.29
<i>Tritium aestivum</i>	0.976
<i>Allium cepa</i>	1.38
<i>Brassica napus</i>	3.66
<i>Raphanus sativus</i>	0.676
<i>Linum usitatissimum</i>	0.972
<i>Helianthus annuus</i>	0.371
<i>Lactuca sativa</i>	0.592
<i>Lycopersicon esculentum</i>	0.145
<i>Glycine max</i>	2.07

The toxicity data of the definitive ER₅₀ values from the vegetative vigour study by Winkelmann, G. (2021d; KCP 10.6.2/02) were subjected to three different goodness of fit tests (Anderson-Darling, Kolmogorov-Smirnov, Cramer van Mises), where normality at all significance levels were accepted. The analysis of the ER₅₀ values show normal distribution of the data (see **Figure 9.10.2.2-1**). The results of the ETX calculation based on ER₅₀ values for vegetative vigour and the respective graphs of the species sensitivity distribution (SSD) are presented below.

Table 9.10.2.2-6 Parameters for the log-normal distribution for data set for terrestrial plants

Parameter	Value	Description
Mean	-0.03107076	Mean of the log of the toxicity values
s.d.	0.411839157	Sample standard deviation
n	10	Sample size

Table 9.10.2.2-7 Goodness of fit – Test for normality

Significance level	Anderson-Darling		Kolmogorov-Smirnov		Cramer von Mises	
	Critical	Normal?	Critical	Normal?	Critical	Normal?
0.1	0.631	Accepted	0.819	Accepted	0.104	Accepted
0.05	0.752	Accepted	0.895	Accepted	0.126	Accepted
0.025	0.873	Accepted	0.995	Accepted	0.148	Accepted
0.01	1.035	Accepted	1.035	Accepted	0.179	Accepted
Statistic	0.18879215		0.404179112		0.015624027	

SSD Histogram and PDF

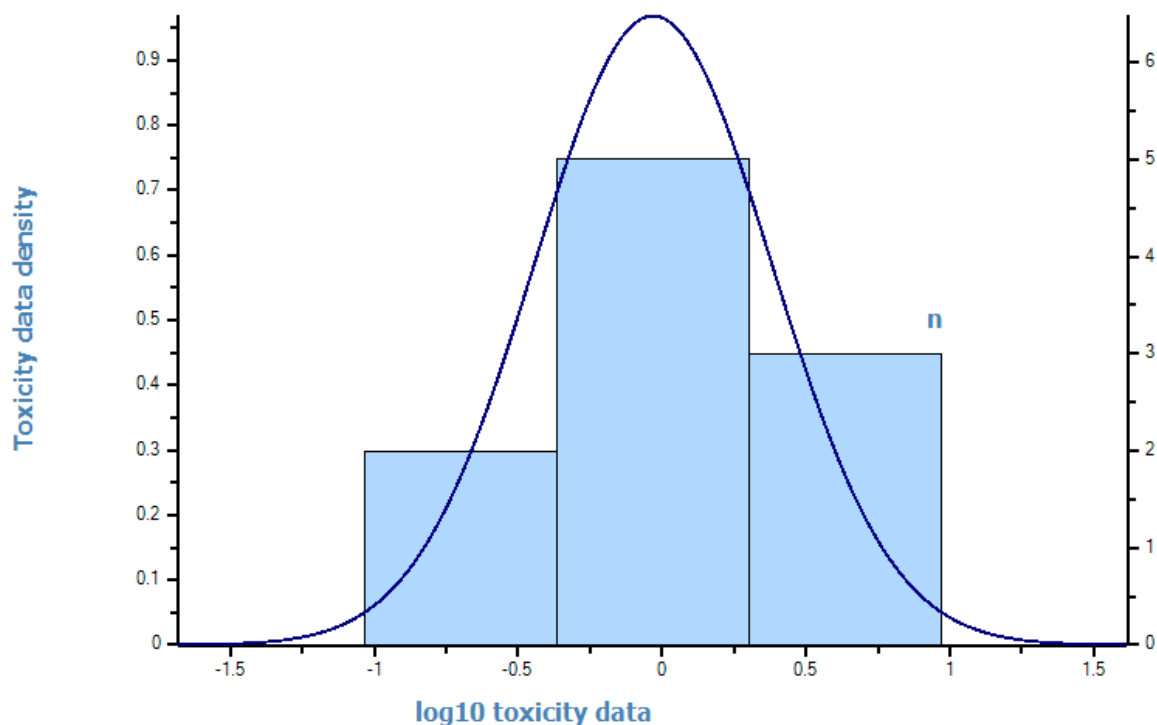


Figure 9.10.2.2-1 Species sensitivity distribution Histogram (vegetative vigour)

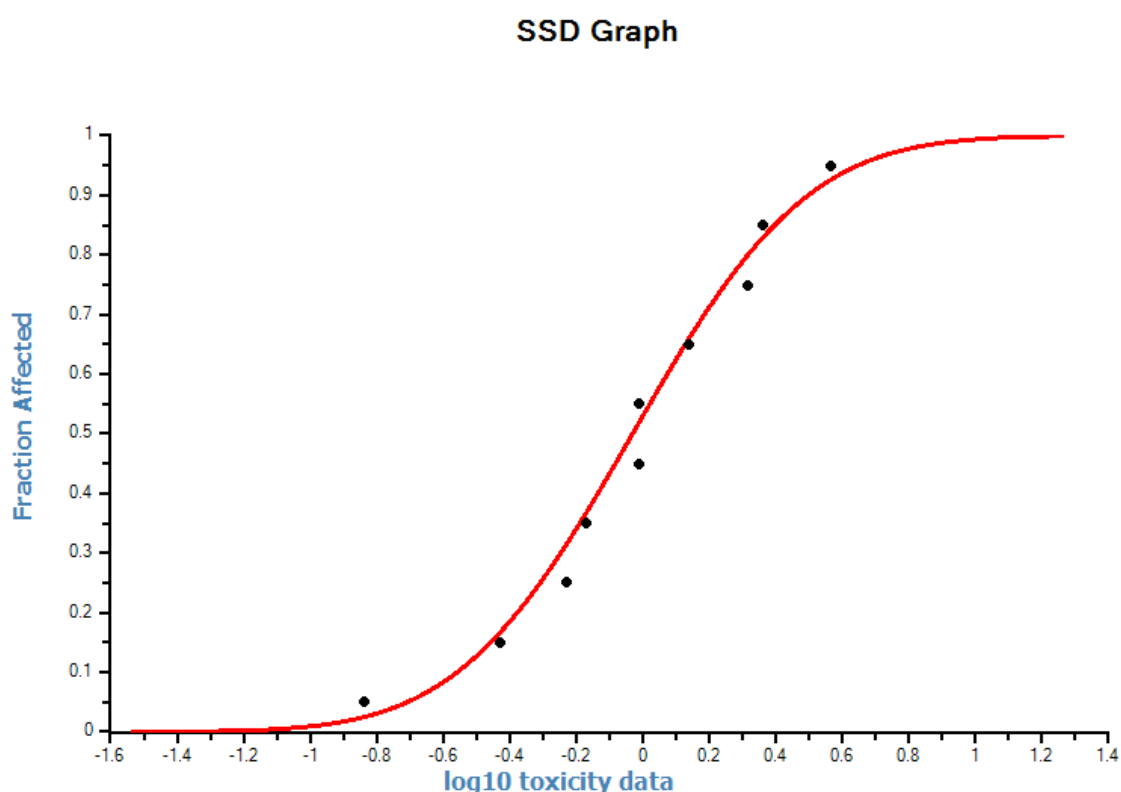


Figure 9.10.2.2-2 Species sensitivity distribution curve (vegetative vigour)

Table 9.10.2.2-8 Hazardous concentration of HC₅ calculations (vegetative vigour)

	Value [g a.s./ha]
Lower estimate of the HC ₅	0.0589 (90%-confidence limits)
Median estimate of the HC ₅	0.185
Upper estimate of the HC ₅	0.355 (90%-confidence limits)
Spread of the HC ₅	6.024

The TER values for vegetative vigour were calculated by comparing the median HC₅ value (0.185 L product/ha) with the highest predicted exposure level (PER_{off-field}) of 0.111 L product/ha (application rate of 2.4 L product/ha multiplied with the drift rate of 2.01%), at 1 m from the edge of the crop. The amount of spray drift reaching off-crop habitats is calculated using 90th percentile estimates derived by BBA (2006) from the spray drift predictions of Ganzelmeier & Rautmann (2000). The median HC₅ value is compared directly the respective with PER_{off-field} value considering a trigger of 1. The resulting TER values are presented in the table below.

Table 9.10.2.2-9 Assessment of the risk for non-target plants due to the use of HBZ10 in **beet-crops **all use groups****

Intended use	Beet-crops Sugar beet, red beet, yellow beet, fodder beet and chard					
Active substance/product	Ethofumesate + Phenmedipham / HBZ10					
HC₅ [L/ha]	0.185					
Vegetative vigour (shoot fresh weight)	Application [L/ha]	rate	MAF	Drift rate	PER_{off-field} [L/ha]	TER criterion: TER ≥ 1
Use group no 2 / 5	3 × 2.4		2.3	0.0201	0.111	1.67
Use group no 4	3 × 1.8		2.3	0.0201	0.832	2.2
Use group no 1	6 × 1.2		3.2	0.0164	0.06298	2.9
Use group no 3	5 × 1.2		3.0	0.0175	0.0630	2.9

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio.
TER values shown in bold fall below the relevant trigger.

Based on species sensitivity distribution (SSD) and the median HC₅ value for vegetative vigour, the TER value is above the trigger of 1 indicating an acceptable risk for non-target terrestrial plants after application of HBZ10 in **beet-crops** for all intended uses.

zRMS comments:

Probabilistic risk assessment conclusion:

The above probabilistic risk assessment has been checked and confirmed as correct by zRMS.

According to SANCO/10329/2002, no MAF value is recommended for the exposure calculation for non-target plants. As the applicant presented the calculations with the MAF value, it is a conservative approach and thus considered acceptable by zRMS.

Further, it is the position of the zRMS-PL that a trigger value of 1 should be used in the probabilistic risk assessment with a HR5 value of 0.185 L/ha; however, it is noted that this is not a Central Zone harmonised position and other member states may consider the use of a different trigger value at National Registration.

Based on the probabilistic risk assessment it is concluded that the use of the product HBZ10 will not produce unacceptable effects on terrestrial non-target plants growing near treated fields without risk mitigation measures.

In addition, zRMS provided the deterministic risk assessment in the Tables below:

Deterministic risk assessment:

Use group no 2: 3 × 2.4 L product/ha, 6-day interval and use group no 5: 3 × 2.4 L product/ha, 9-day interval.

Intended use		Beet crops			
Active substance/product		Ethofumesate + Phenmedipham / HBZ10			
Application rate (mL/ha)		3 × 2.4			
MAF		2.3			
Buffer strip (m)	Drift rate (%)	PER_{off-field} (mL/ha)	PER_{off-field} 50 % drift red. (mL/ha)	PER_{off-field} 75 % drift red. (mL/ha)	PER_{off-field} 90 % drift red. (mL/ha)
no buffer	0.0201	0.111	0.0555	0.02775	0.0111
5 m	0.0041	0.022	-	-	-
Toxicity value		TER			
ER ₅₀ = 0.145 L prod./ha (Vegetative vigour)		criterion: TER ≥ 5			
no buffer		1.3	2.6	5.2	13.1

5 m	6.6	-	-	-	
MAF: Multiple application factor; PER: Predicted environmental rates; TER: toxicity to exposure ratio. Criteria values shown in bold breach the relevant trigger.					
Use group no 4: 3 × 1.8 L product/ha, 6-day interval					
Intended use		Beet crops			
Active substance/product		Ethofumesate + Phenmedipham / HBZ10			
Application rate (mL/ha)		3 × 1.8			
MAF		2.3			
Buffer strip (m)	Drift rate (%)	PER_{off-field} (mL/ha)	PER_{off-field} 50 % drift red. (mL/ha)	PER_{off-field} 75 % drift red. (mL/ha)	PER_{off-field} 90 % drift red. (mL/ha)
no buffer	0.0201	0.0832	0.0416	0.0208	0.0208
5 m	0.0041	0.0169	-	-	-
Toxicity value		TER			
ER ₅₀ = 0.145 L prod./ha (vegetative vigour)		criterion: TER ≥ 5			
no buffer		1.7	3.5	7.0	7.0
5 m		8.6	-	-	-
MAF: Multiple application factor; PER: Predicted environmental rates; TER: toxicity to exposure ratio. Criteria values shown in bold breach the relevant trigger.					
Use group no 1: 6 × 1.2 L product/ha, 5-day interval					
Intended use		Beet crops			
Active substance/product		Ethofumesate + Phenmedipham / HBZ10			
Application rate (mL/ha)		3 × 1.2			
MAF		3.2			
Buffer strip (m)	Drift rate (%)	PER_{off-field} (mL/ha)	PER_{off-field} 50 % drift red. (mL/ha)	PER_{off-field} 75 % drift red. (mL/ha)	PER_{off-field} 90 % drift red. (mL/ha)
no buffer	0.0164	0.06298	0.03149	0.015745	0.006298
5 m	0.0034	0.0130	-	-	-
Toxicity value		TER			
ER ₅₀ = 0.145 L prod./ha (vegetative vigour)		criterion: TER ≥ 5			
no buffer		2.3	4.6	9.2	23.0
5 m		11.154	-	-	-
MAF: Multiple application factor; PER: Predicted environmental rates; TER: toxicity to exposure ratio. Criteria values shown in bold breach the relevant trigger.					
Use group no 3: 5 × 1.2 L product/ha, 7-day interval					
Intended use		Beet crops			
Active substance/product		Ethofumesate + Phenmedipham / HBZ10			
Application rate (mL/ha)		5 × 1.2			
MAF		3.0			
Buffer strip (m)	Drift rate (%)	PER_{off-field} (mL/ha)	PER_{off-field} 50 % drift red. (mL/ha)	PER_{off-field} 75 % drift red. (mL/ha)	PER_{off-field} 90 % drift red. (mL/ha)

no buffer	0.0175	0.0630	0.0315	0.01575	0.0063
5 m	0.0036	0.01296	-	-	-
Toxicity value ER ₅₀ = 0.145 L prod./ha (vegetative vigour)		TER criterion: TER ≥ 5			
no buffer		2.3	4.6	9.2	23.1
5 m		11.2	-	-	-

MAF: Multiple application factor; PER: Predicted environmental rates; TER: toxicity to exposure ratio. Criteria values shown in bold breach the relevant trigger.

Based on the deterministic risk assessment it is concluded that the use of the product will not produce unacceptable effects on terrestrial non-target plants growing near treated fields, when considering the following mitigation measures:

- 5 m buffer zone, or alternatively 75% drift reducing spray nozzles for all proposed uses.

Final risk mitigation measures should be decided at MSs level.

9.10.2.3 Higher-tier risk assessment

Based on the outcome of the first-tier risk assessment, no higher tier risk assessment is required.

9.10.2.4 Risk mitigation measures

No risk mitigation needed.

9.10.3 Overall conclusions

The risk assessment is based on the Guidance Document on Terrestrial Ecotoxicology, (SANCO/10329/2002 rev.2 final, 2002).

After refinement of the risk assessment using a probabilistic approach, the TER value is above the trigger of 1 at the drift rate following the application of HBZ10 according to the proposed use pattern. Thus, the risk to non-target plants after the application of HBZ10 is considered acceptable.

9.11 Effects on other terrestrial organisms (flora and fauna) (KCP 10.7)

The spectrum of the biological activity of HBZ10 is well represented by the results and the risk assessments in this Section. Therefore, further data from biological primary screening or other preliminary tests are not considered relevant, as they would not change the ecotoxicological assessment.

9.12 Monitoring data (KCP 10.8)

The spectrum of the biological activity of HBZ10 is well represented by the results and the risk assessments in this Section. Therefore, further monitoring data is not considered relevant, as it would not change the ecotoxicological assessment.

9.13 Classification and Labelling

Table 9.13-1 Proposals of classification for the active substances and the product HBZ10

Compounds	Toxicity	Classification (CLP) 8 th ATP to the Regulation (EC) No 1272/2008	
		Hazard category	Code H
Ethofumesate (NRD)	Acute LC ₅₀ = 10.92 mg a.s./L (<i>C. carpio</i>) EC ₅₀ = 1.7 mg a.s./L (<i>C. virginica</i>) ErC ₅₀ = 16.3 mg a.s./L (<i>P. subcapitata</i>)	-	-
	Chronic NOEC = 0.156 mg a.s./L (<i>D. rerio</i>) NOEC = 0.25 mg a.s./L (<i>D. magna</i>)	Aquatic chronic 2 ^b	H411: Toxic to aquatic life with long lasting effects
Phenmedipham (NRD)	Acute LC ₅₀ = 1.1 mg a.s./L (<i>O. mykiss</i>) EC ₅₀ = 0.41 mg a.s./L (<i>D. magna</i>) ErC ₅₀ = 0.192 mg a.s./L (<i>S. capricornutum</i>)	Aquatic acute 1 ^a	H400: Very toxic to aquatic life
	Chronic NOEC = 0.32 mg a.s./L (<i>O. mykiss</i>) NOEC = 0.025 mg a.s./L (<i>D. magna</i>) ErC ₅₀ = 3.9 mg a.s./L (<i>L. minor</i>)	Aquatic chronic 1 ^b	H410: Very toxic to aquatic life with long lasting effects
HBZ10	Acute EC ₅₀ = 3.96 mg f.p./L (<i>D. magna</i>) ErC ₅₀ = 0.827 mg/L (<i>P. subcapitata</i>)	Aquatic acute 1 ^a	H400: Very toxic to aquatic life
	Chronic ErC ₅₀ = 0.167 mg/L (<i>L. gibba</i>)	Aquatic chronic 2 ^b	H411: Toxic to aquatic life with long lasting effects

a.s. active substance; f.p. formulated product; NRD not readily biodegradable

^a Refer to Table 4.1.0 (a) of 8th ATP to the Regulation (EC) No 1272/2008

^b Refer to Table 4.1.0 (b, i) of 8th ATP to the Regulation (EC) No 1272/2008

Justification of the proposal of classification of HBZ10 based on the 8th ATP to the Regulation (EC) No 1272/2008:

Acute classification for HBZ10 is required based on the lowest ErC₅₀ value of 0.827 mg product/L in *Pseudokirchneriella subcapitata* (single acute endpoint ≤ 1 mg/L).

The chronic classification for HBZ10 is based on the lowest ErC₅₀ of 0.167 mg/L in *Lemna gibba*, no further chronic data for other taxonomic groups (e.g., *Daphnia magna*) are available. Based on the lowest endpoint, a M-factor of 1 is applied. The formulation HBZ10 can therefore be classified as Aquatic Chronic 2 (please refer to Table 4.1.0 of 8th ATP and Table 4.1.2 to the Regulation (EC) No 1272/2008).

Implications for labelling resulting from ecotoxicological assessment according to Regulation (EC) No 1272/2008:

Hazard pictograms



Signal word

None.

Hazard statement

H411: Toxic to aquatic life with long lasting effects

zRMS comment:

Acute classification for HBZ10 is required as E_rC_{50} value are below 1 mg/L and for this reason H400 is applied. Chronic classification for HBZ10 cannot be based only on measured data.

Based on chronic data for a.s., the most sensitive for phenmedipham is aquatic invertebrates and according to Regulation (EC) No 1272/2008, M-factor 10 should be used for chronic classification.

The relevant calculations are provided by zRMS below :

Step 1: Classify as Chronic 1 if:

$$\sum(\text{Chronic 1} \times M) \geq 25 \%$$

$$= 12.5 \times 10 > 25$$

The product HBZ10 should thus be classified as chronic 1 (H410).

Hazard pictograms



Signal word

None.

Hazard statement

H410: Very toxic to aquatic life with long lasting effects

P391: Collect spillage

P501: Dispose of contents/container to hazardous or special waste collection point, in accordance with local, regional, national and/or international regulation

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.2.1/01	Scheerbaum, D.	2021a	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): ACUTE IMMOBILIZATION TEST TO DAPHNIA MAGNA, SEMI-STATIC, 48 HOURS Report No. SO20127 / DAI18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.2.1/02	Scheerbaum, D.	2021b	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): ALGA, GROWTH INHIBITION TEST WITH PSEUDOKIRCHNERIELLA SUBCAPITATA, 72 HOURS Report No. SO20126 / SPO18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.2.1/03	Scheerbaum, D.	2021c	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): AQUATIC PLANT TOXICITY TEST, LEMNA GIBBA, SEMI-STATIC, 7 DAYS Report No. SO20128 / SLG18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.2.1/04	Scheerbaum, D.	2021d	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): WATER-SEDIMENT MYRIOPHYLLUM SPICATUM TOXICITY TEST SEMI-STATIC, 14 D Report No. SO20129 / SMS18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.2.2/01	Scheerbaum, D.	2021e	MHPC: DAPHNIA MAGNA REPRODUCTION TEST, SEMI-STATIC, 21 DAYS Report No. SO20407 / DRE19098 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.1.1.1/01	Klix, V.	2021a	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): ACUTE ORAL TOXICITY TO THE HONEYBEE APIS MELLIFERA (HYMENOPTERA, APIDAE)	N	UPL

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			Report No. SO20043 / IBO 18743 Noack Laboratorien GmbH, Germany GLP Unpublished		
KCP 10.3.1.1.1/02	Klix, V.	2021b	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): ACUTE ORAL TOXICITY TEST ON THE BUMBLEBEE BOMBUS TERRESTRIS Report No. SO20046 / IUO18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.1.1.2/01	Klix, V.	2021c	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): ACUTE CONTACT TOXICITY TO THE HONEYBEE APIS MELLIFERA (HYMENOPTERA, APIDAE) Report No. SO20044 / IBT 18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.1.1.2/02	Klix, V.	2021d	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): ACUTE CONTACT TOXICITY ON THE BUMBLEBEE BOMBUS TERRESTRIS Report No. SO20045 / IUT18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.1.2/01	Klix, V.	2021e	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): CHRONIC ORAL TOXICITY TEST ON THE HONEYBEE APIS MELLIFERA (HYMENOPTERA, APIDAE) Report No. SO20047 / IBC18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.1.3/01	Klix, V.	2021f	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): HONEYBEE (APIS MELLIFERA) LARVAL TOXICITY TEST, REPEATED EXPOSURE Report No. SO20048 / IBL18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.3.2.1/01	Klix, V.	2021g	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): EFFECTS ON THE PARASITIC WASP APHIDIUS RHOPALOSIPHI (HYMENOPTERA: BRACONIDAE) IN A GLASS PLATE LABORATORY TEST Report No. SO20131 / IWA18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.2.1/02	Klix, V.	2021h	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): A GLASS PLATE LABORATORY STUDY WITH THE PREDATORY MITE TYPHLODROMUS PYRI (ACARI: PHYTOSEIIDAE) Report No. SO20132 / IRL18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.2.2/01	Maspohl, A.-K.	2021a	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): EXTENDED LABORATORY TEST ON THE PARASITIC WASP APHIDIUS RHOPALOSIPHI, EXPOSED TO BARLEY PLANTS (HYMENOPTERA: BRACONIDAE) Report No. SO20512 / IWE18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.2.2/02	Maspohl, A.-K.	2021b	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): EXTENDED LABORATORY STUDY WITH THE PREDATORY MITE TYPHLODROMUS PYRI (ACARI: PHYTOSEIIDAE) Report No. SO20513 / IRE18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.3.2.2/03	Leopold, J.	2021	ETHOFUMESATE + PHENMEDIPHAM 125/125 G/L EC: EFFECTS ON THE LACEWING CHRYSOPERLA CARNEA (NEUROPTERA: CHRYSOPIDAE), EXTENDED LABORATORY STUDY - DOSE RESPONSE TEST - Report No. 159181047 IBACON GmbH, Rossdorf, Germany GLP Unpublished	N	UPL

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.3.2.2/04	Knautz, T.	2021	HBZ10: EFFECTS ON THE REPRODUCTION OF ROVE BEETLES ALEOCHARA BILINEATA - EXTENDED LABORATORY STUDY - DOSE-RESPONSE TEST - Report No. 159181071 IBACON GmbH, Rossdorf, Germany GLP Unpublished	N	UPL
KCP 10.3.2.2/05	Wagenhoff, E.	2021	ETHOFUMESATE + PHENMEDIPHAM 125 + 125 G/L: TOXICITY TO THE PREDATORY MITE, TYPHLODROMUS PYRI SCHEUTEN (ACARI, PHYTOSEIIDAE) AFTER EXPOSURE TO FRESHLY APPLIED AND AGED SPRAY DEPOSITS ON APPLE LEAVES Report No. S21-05449 Eurofins Agrosience Services Ecotox GmbH, Niefern-Öschelbronn, Germany GLP Unpublished	N	UPL
KCP 10.4.1/01	Winkelmann, G.	2021a	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): EARTHWORM (EISENIA FETIDA), EFFECTS ON REPRODUCTION Report No. SO20133 / RBN18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.4.2.1/01	Klix, V.	2021i	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): COLLEMBOLAN (FOLSOMIA CANDIDA) REPRODUCTION TEST IN SOIL Report No. SO20135 / ICR18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.4.2.1/02	Klix, V.	2021j	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): PREDATORY MITE REPRODUCTION TEST IN SOIL (HYPOASPIS ACULEIFER) Report No. SO20134 / IHL18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.4.2.1/03	Frommholz, U.	2010	Phenmedipham A.S.: Influence On The Reproduction Of The Collembolan Species <i>Folsomia candida</i> Tested In Artificial Soil Report No. FRM-COLL-83/10 Bayer CropScience AG Development Environmental Safety, Ecotoxicology, Germany GLP Unpublished	N	TFP
KCP 10.4.2.1/03	Frommholz, U.	2010	PHENMEDIPHAM A.S.: INFLUENCE ON THE REPRODUCTION OF THE COLLEMBOLAN SPECIES FOLSOMIA CANDIDA TESTED IN ARTIFICIAL SOIL REPORT NO. FRM-COLL-83/10 BAYER CROPSCIENCE AG DEVELOPMENT ENVIRONMENTAL SAFETY, ECOTOXICOLOGY, GERMANY GLP UNPUBLISHED	N	TFP
KCP 10.5/01	Winkelmann, G.	2021b	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): SOIL MICRO-ORGANISMS: NITROGEN TRANSFORMATION TEST Report No. SO20136 / TBN18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.6.2/01	Winkelmann, G.	2021c	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): TERRESTRIAL PLANT TEST: SEEDLING EMERGENCE AND SEEDLING GROWTH TEST Report No. SO20031 / TNK18743 Noack Laboratorien GmbH, Germany GLP Unpublished	N	UPL
KCP 10.6.2/02	Winkelmann, G.	2021d	ETHOFUMESATE/PHENMEDIPHAM 125/125 G/L EC (HBZ10): TERRESTRIAL PLANT TEST: VEGETATIVE VIGOUR TEST Report No. SO20032 / TNW18743 Noack Laboratorien GmbH, Germany	N	UPL

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

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

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.1.2.2	Diesing, L.	2014	PHENMEDIPHAM. TOXICITY ENDPOINT FOR THE WILD MAMMAL LONG-TERM & REPRODUCTIVE RISK ASSESSMENT Report No. M-486883-01-1 Bayer CropScience AG, Monheim, Germany Not GLP Unpublished	N	TFP
KCP 10.4.2.1/03	Frommholz, U.	2010	PHENMEDIPHAM A.S.: INFLUENCE ON THE REPRODUCTION OF THE COLLEMBOLAN SPECIES FOLSOMIA CANDIDA TESTED IN ARTIFICIAL SOIL REPORT NO. FRM-COLL-83/10 BAYER CROPSCIENCE AG DEVELOPMENT ENVIRONMENTAL SAFETY, ECOTOXICOLOGY, GERMANY GLP UNPUBLISHED	N	TFP

TFP: Task Force on Phenmedipham (to which UPL is being part with Bayer CropScience)

List of data submitted by the applicant and not relied on

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

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

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

Appendix 2 Detailed evaluation of the new studies

A 2.1 KCP 10.1 Effects on birds and other terrestrial vertebrates

A 2.1.1 KCP 10.1.1 Effects on birds

A 2.1.1.1 KCP 10.1.1.1 Acute oral toxicity

No new study is submitted.

A 2.1.1.2 KCP 10.1.1.2 Higher tier data on birds

Based on the outcome of the first-tier risk assessments, no higher-tier data on birds are required.

A 2.1.2 KCP 10.1.2 Effects on terrestrial vertebrates other than birds

A 2.1.2.1 KCP 10.1.2.1 Acute oral toxicity to mammals

Mammalian toxicity tests with the formulation were not performed, since it is possible to extrapolate from data obtained with the active substances.

A 2.1.2.2 KCP 10.1.2.2 Higher tier data on mammals

No higher-tier data on mammals have been submitted.

A 2.1.3 KCP 10.1.3 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)

No data submitted. There was no indication of effects on other terrestrial vertebrate wildlife (reptiles and amphibians) of active substance in the evaluation for the Annex I inclusion or re-inclusion. Further, due to the acceptable risk demonstrated for birds and mammals, it is not anticipated that the intended use of formulation would cause adverse effects to other terrestrial vertebrate wildlife.

A 2.2 KCP 10.2 Effects on aquatic organisms

A 2.2.1 KCP 10.2.1 Acute toxicity to fish, aquatic invertebrates, or effects on aquatic algae and macrophytes

A 2.2.1.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 202 with minor deviations.</p> <p>It was noted that the deviation of the final pH-values (old media, 48 hours) from the initial values (fresh media, 24 hours) exceeded 1.5 units (1.62 to 2.02 units) and the hardness was slightly above 250 mg CaCO₃/L (255 and 260 mg/L). However, these deviations are considered to have no impact on the outcome of the study as all the validity criteria were met.</p> <p>The test concentrations of both active substances were verified in the fresh media at the start of the exposure and at the renewal of the test solutions, and in the 24-hours old media at the renewal and at the end of the test in all concentration levels. The measured concentrations of Phenmedipham were in the range of 100 to 107% of the nominal values at the start of the exposure intervals and at the renewal of the test solutions (0 and 24 hours) and 26 to 59 % in the old media at the renewal and at the end of the test exposure. The measured concentrations of Ethofumesate were in the range of 88 to 109% of the nominal values at the start of the exposure intervals and at the renewal of the test solutions (0 and 24 hours) and 96 to 111% in the old media at the renewal and at the end of the test (24 hours and 48 hours). Therefore, the endpoint is reported based on geometric mean measured concentrations of Phenmedipham and Ethofumesate.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>EC₅₀ = 3.96 mg product/L (based on geometric mean measured concentration)</p>
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Reference:	KCP 10.2.1/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Acute immobilization test to <i>Daphnia magna</i> , semi-static, 48 hours, Scheerbaum, D., 2021a, report No, SO20127/DAI18743
Guideline(s):	OECD 202 (2004)
Deviations:	Minor (see the commenting box above) No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The acute toxicity of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to *Daphnia magna* was investigated in a 48-hour semi-static test with the nominal concentrations 0 (control), 0.300, 0.660, 1.45, 3.19, 7.03 mg product/L (corresponding to the geometric mean measured concentrations of (control), 0.244, 0.522, 1.18, 2.56, 5.62 mg product/L).

The 48-h EC₅₀ of HBZ10 to *Daphnia magna* was determined to be 3.96 mg product/L based on geometric mean measured concentrations. After 48 hours, no mortality was observed in the control group and up to 2.56 mg product/L, at 5.62 mg product/L, a mean mortality of 90% was observed.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.05.2022
Vehicle / control(s)	Control: Dilution water

Test System

Species	<i>Daphnia magna</i> Straus
Age	Less than 24 h old
Culture medium	Elendt M4
Acclimatisation	At least 2 hours in ISO Test Water
Supplier	Laboratory breeding; origin: Institut für Wasser-, Boden- und Lufthygiene (WaBoLu), 14195 Berlin, Germany
Food	Mix of unicellular green algae, e.g., <i>Pseudokirchneriella subcapitata</i> and <i>Desmodesmus subspicatus</i> , <i>ad libitum</i> 5 times per week

Test Conditions

Temperature	19 - 20°C
pH value	6.57 - 6.59 ⁴ (at test start/renewal); 6.62 – 8.42 (in 24-hours old media and at the end of exposure)
Dissolved concentration	O ₂ 8.09 - 9.13 mg/L (at test start/renewal); 7.49 – 8.47 mg/L (in 24-hours old media and at the end of exposure)
Hardness	255 - 260 mg CaCO ₃ /L
Photoperiod	Light/dark cycle of 16/8 hours
Light intensity	Max 1500 lx
Loading	5 Daphnids per replicate (in 20 mL ISO Test Water according to OECD 202)

Study Design and Methods

In-life dates	18.08.2020 – 20.08.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	48 h
Test design	Semi-static
Test concentrations	0 (control), 0.300, 0.660, 1.45, 3.19, 7.03 mg product/L (nominal)
Test groups / Replicates	4 replicates for each test item group and control
Treatment	The daphnids were exposed to a range of test item concentrations and a control for 48 hours. The test concentrations were chosen based on a non-GLP range-finding test. A reference test with potassium dichromate was conducted as an acute immobilization test in a separate study. 30 mg product/L were freshly prepared with dilution water for the start of the exposure (day 0) and the renewal (day 1). The dispersion was agitated until the solution was visually clear. Out of the stock solution 5 concentrations were tested in a geometric series with a dilution factor of 2.2: 0.300, 0.660, 1.45, 3.19, 7.03 mg/L (nominal).

Observations	<p>Dilution water without test item incubated under the same conditions as the test groups was used as control.</p> <p>The test solutions were renewed after 24 hours. For this purpose, a second set of test vessels was filled with the freshly prepared test solutions and the daphnids were transferred by pipette</p> <p>Immobilization was determined in all groups after 24 and 48 hours. A daphnid was considered immobile, if it was not able to swim in the water phase within 15 seconds after gentle agitation of the test vessel. Observation of other adverse, sub-lethal effects (e.g., discoloration, abnormal behavior etc.) was done, but none occurred during the course of the study.</p> <p>Prior to the start of the exposure (0 hours) and the renewal of the test solutions (24 hours), the water quality parameters (i.e., pH value, dissolved oxygen concentration, temperature, conductivity and total hardness) of the dilution water were measured.</p> <p>At the start of the exposure and at the renewal (0 and 24 hours), the water quality parameters of the fresh media (i.e., pH value, dissolved oxygen concentration) were measured in one additional replicate (without daphnids) per concentration level and control.</p>
Analytical verification	<p>At the renewal and at the end of the exposure (24 and 48 hours), the water quality parameters of the old media were measured in one appropriate replicate (containing daphnids) per concentration level and control. The replicate with the highest immobilization rate per concentration level and the control were measured.</p> <p>All concentration levels and the control were analytically verified via LC-MS/MS in the fresh media at the start of exposure and at the renewal of the test solutions (0 and 24 hours) as well as in the 24-hours old media at the renewal and at the end of the exposure (24 and 48 hours). The analytical method was validated based on SANCO/3029/99 rev. 4.</p>
Statistics	<p>The $EC_{10/50}$-values after 24 and 48 hours of exposure were calculated by straight line regression with the software GraphPad Prism. The respective 95% confidence limits were calculated from the standard error and the t distribution wherever possible. In the case that the confidence limits could not be calculated by the software, the respective confidence limits were empirically derived from the observation data. All calculations were carried out from the best-fit values with the software GraphPad Prism.</p>

RESULTS AND DISCUSSIONS

Validity criteria

Mortality in the control should not exceed 10% (actual: 0%) at the end of the test. The dissolved oxygen concentration must have at least 3 mg O₂/L (actual: ≥ 7.49 mg/L) in the 24-hours old media at the renewal of the test solutions and at the end of the exposure in all concentration levels and in the control.

Analytical results

The concentrations of the active ingredients Phenmedipham and Ethofumesate, as well as the metabolites MHPC and m-Toluidine (Phenmedipham) of the test item Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) were analytically verified via LC-MS/MS in the fresh media at the start of the exposure and at the renewal of the test solutions (0 and 24 hours) and in the 24-hours old media at the renewal and at the end of the test (24 and 48 hours) in all concentration levels and the control.

The measured concentrations of Phenmedipham were in the range of 100% to 107% of the nominal values at the start of the exposure intervals and at the renewal of the test solutions (0 and 24 hours) demonstrating the correct preparation of the test item concentrations. Phenmedipham is known to hydrolyse and form the metabolites MHPC and m-Toluidine. Phenmedipham concentrations were decreased in the old media in all test item concentrations, whereas MHPC and m-Toluidine concentrations were increased. The sum of the active ingredient and its derivatives MHPC and m-Toluidine (calculation based on molar relationships) were calculated as Phenmedipham equivalents in the 24-hours old media at the renewal and at the end of the test (24 and 48 hours). All effect values given were based on geometric mean measured concentrations of Phenmedipham and Ethofumesate, active substances of the test item.

The measured concentrations of Ethofumesate were in the range of 88% to 109% of the nominal values at the start of the exposure intervals and at the renewal of the test solutions (0 and 24 hours) and 96% to 111% in the old media at the renewal and at the end of the test (24 hours and 48 hours). The measured concentrations of the active ingredient Ethofumesate remained stable within $\pm 20\%$ of the nominal concentrations throughout the exposure period.

Table A 2.2.1.1-1 Geometric mean measured concentrations

Nominal concentration [mg product/L]	Geometric mean measured concentration			
	Phenmedipham [mg a.s./L]	Ethofumesate [mg a.s./L]	HBZ10 [mg product/L]	[%]
7.03	0.566	0.878	5.62	80
3.19	0.257	0.401	2.56	80
1.45	0.118	0.185	1.18	81
0.660	0.0502	0.0840	0.522	79
0.300	0.0233	0.0393	0.244	81

a.s. = active substance

% = percent of the nominal concentration of the product

Biological results

Following 48 hours of exposure, immobility of 0%, 0%, 0%, 0% and 90% was recorded among daphnids exposed to 0.300, 0.660, 1.45, 3.19, 7.03 mg product/L nominal treatment levels (corresponding to 0.244, 0.522, 1.18, 2.56, 5.62 mg product/L geometric mean measured treatment levels, respectively). No immobility was observed among daphnids exposed to the control. Biological results are presented in the following table.

Table A 2.2.1.1-2 Immobility of *Daphnia magna* exposed to HBZ10 for 48 hours

Concentration [mg product/L]		Immobility [%]	
Nominal	Geometric mean measured	24 hours	48 hours
Control	0	0	0
0.300	0.244	0	0
0.660	0.522	0	0
1.45	1.18	0	0
3.19	2.56	0	0
7.03	5.62	55	90

CONCLUSION

The 48-hour EC₅₀ of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to *Daphnia magna* was determined as 3.96 mg product/L with 95% confidence limits of 3.73 – 4.22 mg/L, based on geometric mean measured concentrations.

A 2.2.1.2 Study 2

Comments of zRMS:	The study was conducted in line with OECD 201 with no deviations.
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	<p>The test concentrations of both active substances were verified in the fresh media (0 hours) and old media (72 hours) of all tested concentration levels. The measured concentrations of Phenmedipham were in the range of 101 to 108% of the nominal values at the start of the exposure intervals (0 hours) and < LOQ to 3 % at the end of the exposure (72 hours). The measured concentrations of Ethofumesate were in the range of 88 to 94% of the nominal values at the start of the exposure intervals (0 hours) and 94 to 109% at the end of the exposure (72 hours). Therefore, the endpoints are based on geometric mean measured concentrations of Phenmedipham and Ethofumesate.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p> E_rC_{50} = 0.827 mg product/L (geometric mean measured concentration) E_rC_{10} = 0.148 mg product/L (geometric mean measured concentration) E_rC_{20} = 0.279 mg product/L (geometric mean measured concentration) NOE_rC = 0.0326 mg product/L (geometric mean measured concentration) </p> <p> E_yC_{50} = 0.175 mg product/L (geometric mean measured concentration) E_yC_{10} = 0.0534 mg product/L (geometric mean measured concentration) E_yC_{20} = 0.0744 mg product/L (geometric mean measured concentration) NOE_yC = 0.0326 mg product/L (geometric mean measured concentration) </p>
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Reference:	KCP 10.2.1/02
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Alga, Growth Inhibition Test with <i>Pseudokirchneriella subcapitata</i> , 72 hours, Scheerbaum, D., 2021b, report No SO20126 / SPO18743
Guideline(s):	OECD 201 (2011)
Deviations:	None No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The toxicity (effects on growth rate and yield) of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to the unicellular freshwater green alga *Pseudokirchneriella subcapitata* was determined over a period of 72 hours.

The study was conducted under static conditions with an initial cell density of 5375 cells/mL with the nominal concentrations 0 (control), 0.0500, 0.158, 0.500, 1.58, 5.00 mg product/L (corresponding to the geometric mean measured concentrations of (control), 0.0326, 0.0928, 0.268, 0.881, 2.72 mg product/L).

All concentration levels and the control were analysed via LC-MS/MS at the beginning and at the end of the exposure. Freshly prepared and old media were analysed.

The 72-h E_rC_{50} of HBZ10 to *P. subcapitata* was determined to be 0.827 mg product/L based on geometric mean measured concentrations.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)

Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Dilution water
Test System	
Species	<i>Pseudokirchneriella subcapitata</i> Hindák (Sphaeropleales: Selenastraceae) Strain: CCAP 278/4 (axenic)
Source	Laboratory stock on Z-agar; origin: Culture Collection of Algae and Protozoa (CCAP), SAMS Research Services Ltd, Dunstaffnage Marine Laboratory, Dunbeg, OBAN; Argyll PA37 1QA; Scotland, UK
Culture medium	Nutrient medium Z according to LÜTTGE et al. (1994)
Acclimatisation period	A four-days old preculture, prepared in dilution water was used as inoculum
Initial cell density	0.5375×10^4 cells/mL (actual)
Test Conditions	
Temperature	21.0 - 22.5°C
pH value	6.63 - 6.99 (test start) / 8.00 - 8.50 (test end)
Photoperiod	Continuous illumination
Light intensity	5984 lux (mean)
Study Design and Methods	
In-life dates	18.08.2020 – 21.08.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	72 hours
Test design	Static
Test concentrations	0 (control), 0.0500, 0.158, 0.500, 1.58, 5.00 mg product/L (nominal)
Test groups / Replicates	Six replicates for the control, three replicates per concentration level
Treatment	<p><i>P. subcapitata</i> was exposed to a range of test item concentrations and a control for 72 hours. The test concentrations were chosen based on a non-GLP range-finding test. A reference test with potassium dichromate was conducted in a separate study.</p> <p>A test with nominal concentrations of 0.0500, 0.158, 0.500, 1.58, 5.00 mg/L and control was performed. Six replicates were performed for the control and three for each test item concentration. The test was performed in 250 mL Erlenmeyer flasks under continuous illumination. The final volume in each test vessel was approx. 100 mL.</p> <p>After 72 hours algae were transferred from the two highest concentration levels (1.58 and 5.00 mg/L) and the control into fresh medium. 10.0 mL and 3.125 mL algae suspension from the two highest concentrations (1.58 and 5.00 mg/L) and 0.5 mL from the control were filled up with dilution water to 100 mL and allowed for growth for a period up to 9 (in this study 3 days) days to determine whether the effect of the item is reversible (algicidal or algistatic effects).</p>
Observations	The cell density was measured daily via Chlorophyll a-fluorescence, excitation at 436 nm, emission at 685 nm. Dilution water was used as a background signal.

	<p>The algae cells were evaluated microscopically at the start and the end of the incubation period. The cells were checked for unusual cell shapes, colour differences, differences in chloroplast morphology, flocculation, adherence of algae to test containers and agglutination of algae cells.</p> <p>The pH-value at the start of the exposure was measured in one additional replicate of each test item concentration and the control. At the end of the exposure, it was measured in a pooled sample of the test item concentrations and the control. The room temperature was measured continuously. Light intensity was measured prior to the start of the test.</p>
Analytical verification	<p>All concentration levels and the control were analytically verified via LC-MS at the start (0 hours) of the exposure (72 hours). The analytical method was validated based on SANCO/3029/99 rev. 4.</p>
Statistics	<p>EC₁₀-, EC₂₀- and EC₅₀- values with confidence intervals of growth rate inhibition and yield inhibition after 72 hours were calculated by sigmoidal dose-response regression with the GraphPad Prism Software.</p> <p>The NOEC / LOEC was determined by calculation of statistically significant differences of growth rate and yield using Dunnett's Method. A Shapiro-Wilk's Normality test and a Brown-Forsythe's Equal Variance test were done first. P-values for both Normality and Equal Variance tests are 0.05. The α-value (acceptable probability of incorrectly concluding that there is a difference) is $\alpha = 0.01$.</p> <p>Calculations were carried out using software Excel, MICROSOFT CORPORATION, SigmaPlot, SPSS INC., GraphPad Prism, GRAPHPAD SOFTWARE, INC.</p>

RESULTS AND DISCUSSIONS

Validity criteria

The biomass in the control(s) should have increased exponentially by a factor of at least 16 (actual: 186) within the 72-hour test period, corresponding to a specific growth rate of 0.92 per day (actual: 1.74 per day).

The mean coefficient of variation for section-by-section specific growth rates in the control(s) must not exceed 35% (actual: 10.3%).

The coefficient of variation of average specific growth rates during the whole test period in replicate control cultures must not exceed 7% (actual: 1.73%).

Analytical results

The concentrations of the active ingredients Phenmedipham and Ethofumesate, as well as the metabolites MHPC and m-Toluidine (Phenmedipham) of the test item Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) and the control were determined in fresh media (0 hours) and old media (72 hours) of all tested concentration levels and the control via LC-MS/MS.

The measured concentrations of Phenmedipham were in the range of 101% to 108% of the nominal values at the start of the exposure intervals (0 hours) demonstrating the correct preparation of the test item concentrations. Phenmedipham is known to hydrolyse and form the derivatives MHPC and m-Toluidine. Phenmedipham concentrations were decreased in the old media in all test item concentrations, whereas MHPC and m-Toluidine concentrations were increased. The sum of the active ingredient and its metabolites MHPC and m-Toluidine (calculation based on molar relationships) were calculated as Phenmedipham equivalents at the end of the exposure intervals (72 hours).

The measured concentrations of Ethofumesate were in the range of 88% to 94% of the nominal values at the start of the exposure intervals (0 hours) and 94% to 109% at the end of the exposure (72 hours). The measured concentrations of the active ingredient Ethofumesate remained stable within $\pm 20\%$ of the nominal concentrations throughout the exposure period.

Table A 2.2.1.2-1 Geometric mean measured concentrations

Nominal concentration of the test item [mg product/L]	Geometric mean measured concentrations			
	Phenmedipham [mg a.s./L]	Ethofumesate [mg a.s./L]	HBZ10 [mg product/L]	[%]
5.00	0.118	0.582	2.72	54
1.58	0.0309	0.195	0.881	56
0.500	0.00655	0.0622	0.268	54
0.158	0.00377	0.0201	0.0928	59
0.0500	0.00205	0.00634	0.0326	65

a.s. = active substance

% = percent of the nominal concentration of the active ingredient

Biological results

Inhibitory effects of HBZ10 to *P. subcapitata* were observed at geometric mean measured concentrations of 0.0928, 0.268, 0.881, 2.72 mg product/L after 3 days of exposure for growth rate and yield. Microscopic evaluation of the cells at the start and the end of exposure revealed no morphological abnormalities. All effect values given are based on the geometric mean measured test item concentration of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10).

Table A 2.2.1.2-2 Summary of effects on cell density

Concentration [mg product/L]	Mean cell density [$\times 10^4$ cells/mL]			
Geometric mean measured	0 hour	24 hours	48 hours	72 hours
Control	0.5375	2.6191	15.2192	100.2177
0.0326	0.5375	2.4877	14.2737	102.5378
0.0928	0.5375	1.7221	9.7112	71.6104
0.268	0.5375	1.2555	5.6827	38.0946
0.881	0.5375	0.5411	1.4210	6.4898
2.72	0.5375	0.4336	0.5272	0.7428

Table A 2.2.1.2-3 Evaluation of effects on growth inhibition of HBZ10 to *P. subcapitata* after 72 hours

Geometric mean test item concentration [mg/L]	Growth rate [d ⁻¹]		Inhibition of growth rate [%]	Yield [cells/mL]		Inhibition of yield [%]
Control		1.74			996802	
0.0326	(-)	1.75	0	(-)	1020003	-2
0.0928	(+)	1.63	6	(+)	710729	29
0.268	(+)	1.42	19	(+)	375571	62
0.881	(+)	0.828	52	(+)	59523	94
2.72	(+)	0.107	94	(+)	2053	100

Statistically significant differences of growth rates and yield compared to control values are marked (+), not significant differences are marked (-)

Recovery of algae cells

After 72 hours algae were transferred from the two highest concentration levels (0.881 and 2.72 mg/L) and the control into fresh medium. 10.0 mL and 3.125 mL algae suspension from the two highest concentrations (0.881 and 2.72 mg/L) and 0.5 mL from the control were filled up with dilution water to 100 mL and allowed for growth for a period up to 9 (in this study 3 days) days to determine whether the effect of the item is reversible (algicidal or algistatic effects).

Table A 2.2.1.2-4 Evaluation of effects on growth inhibition of HBZ10 to *P. subcapitata* after 72 hours

Geometric mean test item concentration	Incubation time	Cell density [cells/mL]		Growth rate after incubation time
[mg/L]	[d]	Initial*	Final	[d ⁻¹]
2.72	3	232	10699	1.28
			49839	1.79
			56173	1.83
0.881		6490	231770	1.19
			276706	1.25
			215496	1.17
Control		5011	317537	1.38
			236706	1.29

*) cell density was calculated from the cell density of the definitive test replicates after 72 hours

CONCLUSION

Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) was found to inhibit the growth of the freshwater green alga *Pseudokirchneriella subcapitata* after 72 hours with the following effect values (based on geometric mean measured test item concentrations): The EC₅₀-values for inhibition of growth rate (E_rC₅₀) and yield (E_yC₅₀) after 72 hours were 0.827 mg product/L (95% confidence limits: 0.774 – 0.886 mg product/L) and 0.175 mg product/L (95% confidence limits: 0.154 – 0.198 mg product/L), respectively. The NOEC-values for both inhibition of growth rate and yield after 72 hours were 0.0326 mg product/L.

A 2.2.1.3 Study 3

Comments of zRMS:	<p>The study was conducted in line with OECD 221 with no deviations.</p> <p>The test concentrations of both active substances were verified at the beginning and at the end of the exposure and on every renewal day of all tested concentration levels. The measured concentrations of Phenmedipham were in the range of 104% to 117% of the nominal values in freshly prepared medium (Day 0, 2 and 5) and < LOQ to 115% of the nominal values in old medium (Day 2, 5 and 7). The measured concentrations of Ethofumesate were in the range of 99% to 119% of the nominal values in freshly prepared medium (Day 0, 2 and 5) and 88% to 118% of the nominal values in old medium (Day 2, 5 and 7). Therefore, the endpoints are based on the geometric mean measured test item concentrations calculated from the geometric mean measured concentration of the active ingredients Ethofumesate and Phenmedipham.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>Growth rate based on frond number: E_rC₅₀ = 0.286 mg product/L (based on geometric mean measured concentration) E_rC₂₀ = 0.122 mg product/L (based on geometric mean measured concentration) E_rC₁₀ = 0.0783 mg product/L (based on geometric mean measured concentration) NOE_rC = 0.0184 mg product/L (based on geometric mean measured concentration)</p> <p>Yield based on frond number: E_yC₅₀ = 0.119 mg product/L (based on geometric mean measured concentration) E_yC₂₀ = 0.0580 mg product/L (based on geometric mean measured concentration) E_yC₁₀ = 0.0429 mg product/L (based on geometric mean measured concentration) NOE_yC = 0.0184 mg product/L (based on geometric mean measured concentration)</p> <p>Growth rate based on dry weight: E_rC₅₀ = 0.167 mg product/L (based on geometric mean measured concentration) E_rC₂₀ = 0.0676 mg product/L (based on geometric mean measured concentration)</p>
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	$E_rC_{10} = 0.0423$ mg product/L (based on geometric mean measured concentration) $NOE_rC = 0.0184$ mg product/L (based on geometric mean measured concentration) Yield based on dry weight: $E_yC_{50} = 0.0619$ mg product/L (based on geometric mean measured concentration) $E_yC_{20} = 0.0324$ mg product/L (based on geometric mean measured concentration) $E_yC_{10} = 0.0246$ mg product/L (based on geometric mean measured concentration) $NOE_yC = 0.0184$ mg product/L (based on geometric mean measured concentration)
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Reference:	KCP 10.2.1/03
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Aquatic Plant Toxicity Test, <i>Lemna gibba</i> , semi-static, 7 days, Scheerbaum, D., 2021c, report No SO20128 / SLG18743
Guideline(s):	OECD 221 (2006)
Deviations:	None No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The impact of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to the aquatic plant *Lemna gibba* was determined in 7-day semi-static test with the nominal concentrations 0 (control), 0.0200, 0.0632, 0.200, 0.632, 2.00 mg product/L (corresponding to the geometric mean measured concentrations (control), 0.0221, 0.0630, 0.208, 0.653, 2.09 mg product/L).

All concentration levels and the control were analysed via LC-MS/MS at the beginning and at the end of the exposure and on every renewal day. Freshly prepared and old media were analysed.

Based on frond number, the 7-day EC_{50} for yield (E_yC_{50}) and growth rate (E_rC_{50}) of HBZ10 to *Lemna gibba* was determined to be 0.119 mg product/L and 0.286 mg product/L, respectively, based on geometric mean measured concentrations. Based on dry weight, the 7-day EC_{50} for yield (E_yC_{50}) and growth rate (E_rC_{50}) of HBZ10 to *Lemna gibba* was determined to be 0.0619 mg product/L and 0.167 mg product/L, respectively, based on geometric mean measured concentrations. The 7-day NOEC (yield and growth rate) was determined to be 0.0184 mg product/L based on frond number and dry weight.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.05.2022
Vehicle / control(s)	Control: Dilution water

Test System

Species	<i>Lemna gibba</i> (clone: G3), Lemnaceae, Arales, Arecidae, Monocotyledonae
Source	Cultured in the test facility, origin: EUROFINS-GAB GmbH, Eutingen Str. 24, 75223 Niefern-Öschelbronn, Germany

Culture medium	Steinberg medium, pH-value 5.5 ± 0.2
Test vessel	Crystallization dishes with a volume of 500 mL, covered with glass tops and filled with 200 mL test solution, were used in the test.
Initial cell density	3 uniform, healthy plants (colonies of 4 fronds each)
Test Conditions	
Temperature	22.6 – 23.2°C
pH value	5.41 – 7.05
Hardness	170 mg CaCO ₃ /L
Photoperiod	Continuous illumination
Light intensity	6595 – 6788 lux
Study Design and Methods	
In-life dates	19.08.2020 – 26.08.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	7 days
Test design	Semi-static
Test concentrations	0 (control), 0.0200, 0.0632, 0.200, 0.632, 2.00 mg product/L (nominal)
Test groups / Replicates	3 replicates per concentration level, 6 for the control
Treatment	<i>Lemna gibba</i> was exposed to a range of test item concentrations and a control for 7 days. The test concentrations were chosen based on a non-GLP range-finding test. A reference test with 3,5-dichlorophenol was conducted in a separate study. The main test was performed with nominal concentrations of 0.0200, 0.0632, 0.200, 0.632, 2.00 mg product/L and a control under defined conditions in a growth medium. The controls were prepared in six replicates and the test item concentrations were prepared in three replicates, each. The test flasks were inoculated with three plant of four fronds, with an initial frond number of 12. Semi-static test design, with renewal of the test solutions on day 2 and 5 (i.e., exposure to freshly prepared test and control solutions on two occasions during the test).
Observations	The numbers of plants and fronds were determined at the start and the end of the exposure. The number of fronds was determined every 2 - 3 days from each replicate of the control and the test concentrations. Every frond that visibly projected beyond the edge of a parent frond was counted as a separate frond. Fronds that lost their pigmentation were not counted. Observations of frond size, appearance, indication of necrosis, chlorosis or gibbosity, colony break-up or loss of buoyancy, of root length and appearance, as well as of change in colour and destruction of roots, were made on every determination day and at the end of the exposure. After 7 days, the determination of dry weight was carried out from 3 replicates per test concentration and 6 control replicates. Colonies from each test vessel were collected, rinsed with deionized water and then dried at 60°C to a constant weight. Any root fragments were included. The dry weight was expressed to an accuracy of 0.1 mg. The dry weight of the starting biomass was determined based on a sample of fronds (same number of fronds as in the test vessels) taken from the same batch used to inoculate the test vessels.

Analytical verification	<p>The pH-values were measured in the fresh solutions before the renewal and in the aged solutions. The pH-values of the fresh solutions were measured before distribution into the replicates. The pH-values of the aged solution were measured from pooled replicates per concentration and control. The temperature of the medium in a surrogate vessel held under the same conditions in the growth room was recorded at least daily. The light intensity was measured prior to the start of the exposure at points which had the same distance from the light source as the <i>Lemna</i> fronds.</p> <p>All test item concentrations and the control were analytically verified via LC-MS at the start (0 day) and at the end of the exposure (7 days) and on every renewal day. Freshly prepared and aged media were analysed. The analytical method was validated based on SANCO/3029/99 rev. 4.</p>
Statistics	<p>The NOEC and LOEC were determined by calculation of statistically significant differences of growth rates and yield (based on frond number and dry weight).</p> <p>EC₁₀-, EC₂₀- and EC₅₀- values (0 - 7 d) of the growth rate and yield (frond number and dry weight) inhibition were calculated by sigmoidal dose-response regression. Calculations of the confidence intervals of EC₁₀-, EC₂₀- and EC₅₀- values were carried out from the best fit values, the standard error and the t-distribution with the software GraphPad Prism.</p> <p>Calculations were carried out using software SigmaPlot, SPSS INC., GraphPad Prism, GRAPHPAD SOFTWARE, INC and ToxRat Version 3.3.0, ToxRat Solutions GmbH.</p>

RESULTS AND DISCUSSIONS

Validity criteria

The doubling time of frond number in the control must be < 2.5 days (actual: 1.60 days), corresponding to approximately 7-fold increase in seven days (actual: 21-fold) and an average specific growth rate of 0.275 per day (actual: 0.434 per day).

Analytical results

The measured concentrations of Phenmedipham were in the range of 104% to 117% of the nominal values in freshly prepared medium (Day 0, 2 and 5) and < LOQ to 115% of the nominal values in old medium (Day 2, 5 and 7). Phenmedipham is known to hydrolyse and form the metabolites MHPC and m-Toluidine. The sum of the active ingredient and its metabolites MHPC and m-Toluidine (calculation based on molar relationships) were calculated as Phenmedipham equivalents in the old media (Day 2, 5 and 7).

The measured concentrations of Ethofumesate were in the range of 99% to 119% of the nominal values in freshly prepared medium (Day 0, 2 and 5) and 88% to 118% of the nominal values in old medium (Day 2, 5 and 7), demonstrating the correct preparation of the test concentrations. The measured concentrations of the active ingredient Ethofumesate remained stable within ± 20% of the nominal concentrations throughout the exposure period.

Table A 2.2.1.3-1 Geometric mean measured concentrations

Nominal concentration [mg product/L]	Geometric mean measured concentrations			
	Phenmedipham [mg a.s./L]	Ethofumesate [mg a.s./L]	HBZ10 [mg product/L]	[%]
2.00	0.266	0.272	2.09	105
0.632	0.0830	0.0847	0.653	103
0.200	0.0263	0.0272	0.208	104
0.0632	0.00769	0.00850	0.0630	100
0.0200	0.0203	0.00271	0.0184	92

a.s. = active substance

% = percent of the nominal concentration of the active ingredient

Biological results

At day 7, statistically significant effects on growth rate and yield compared to the control were observed at 0.0630, 0.208, 0.635 and 2.09 mg product/L (geometric mean measured). The dry weight of exposed plants was significantly affected at 0.0630, 0.208, 0.635 and 2.09 mg product/L (geometric mean measured) by test termination.

Signs of chlorosis and necrosis were observed at concentrations 0.0630, 0.208, 0.635 and 2.09 mg product/L (geometric mean measured).

Mean frond numbers and dry weights are presented in the tables below along with the growth rate, yield and respective inhibition values.

Table A 2.2.1.3-2 Summary of effects on growth rate and yield of *Lemna gibba* based on frond number

Concentration [mg product/L]		Based on frond number (0-7 days)				
Nominal	Geometric Mean measured	Mean Growth rate (per day)	Mean Inhibition of growth rate [%]	Mean Yield [No. of fronds]	Mean Inhibition of yield [%]	Mean Doubling time [d]
2.00	2.09	0.0380 (+)	91	4 (+)	98	19.1
0.632	0.653	0.0960 (+)	78	12 (+)	95	7.32
0.200	0.208	0.275 (+)	37	70 (+)	71	2.53
0.0632	0.0630	0.399 (+)	8	184 (+)	23	1.74
0.0200	0.0184	0.443 (-)	-2	257 (-)	-7	1.57
Control	0	0.434	-	240	-	1.60

Statistically significant differences of growth rates and yield compared to control values are marked (+), not significant differences are marked (-)

Table A 2.2.1.3-3 Summary of effects on growth rate and yield of *Lemna* based on dry weight

Concentration [mg product/L]		Mean dry weight (day 7) [mg]	Based on dry weight (0-7 days)			
Nominal	Geometric mean measured		Mean Growth rate (per day)	Mean Inhibition of growth rate [%]	Mean Yield [mg]	Mean Inhibition of yield [%]
2.00	2.09	1.3	-0.0080 (+)	102	-0.100 (+)	100
0.632	0.653	2.1	0.0540 (+)	90	0.7 (+)	99
0.200	0.208	6.6	0.220 (+)	58	5.2 (+)	90
0.0632	0.0630	26.8	0.422 (+)	19	25.4 (+)	51
0.0200	0.0184	52.0	0.515 (-)	1	50.6 (-)	2
Control	0	53.1	0.518	-	51.7	-

Statistically significant differences of growth rates and yield compared to control values are marked (+), not significant differences are marked (-)

Table A 2.2.1.3-4 Evaluation of phytotoxicity of HBZ10 to *Lemna gibba*

Geometric mean test item concentration [mg/L]	Observations on day		
	2	5	7
2.09	3.1 + 3.2 +	2.2 ++ 2.5 +++ 3.1 +++ 3.2 +++ 4.1 ++	2.2 ++ 2.5 +++ 3.1 +++ 3.2 +++ 4.1 ++
0.653	3.1 + 3.2 +	2.2 ++ 2.5 +++ 3.1 +++ 3.2 +++	2.2 ++ 2.5 +++ 3.1 +++ 3.2 +++
0.208	3.1 + 3.2 +	2.1 + 2.5 ++ 3.1 +++ 3.2 ++ 3.4 +++	2.1 + 2.5 ++ 3.1 +++ 3.2 +++ 3.4 +++
0.0630	1	2.5 + 3.1 ++ 3.4 +	2.5 + 3.1 ++ 3.4 +
0.0184	1	1	1
Control	1	1	1

1 = no observed effects

2.1 = chlorosis / 2.2 = necrosis of fronds / 2.5 = fronds are smaller, compared to the control

3.1 = roots shortened / 3.2 = loss of roots / 3.4 = necrosis of roots

4.1 = Break up of plants

+ = slight effects / ++ = medium effects / +++ = strong effects

The effect endpoints of HBZ10 to *Lemna gibba* based on geometric mean measured concentrations are presented in the following table.

Table A 2.2.1.3-5 Effect concentrations of HBZ10 to *Lemna gibba* based on mean measured concentrations

Effect concentration [mg product/L]	Based on frond number		Based on dry weight	
	Growth rate	Yield	Growth rate	Yield
7-day EC ₅₀ (95% confidence interval)	0.286 (0.257 – 0.321)	0.119 (0.0940 – 0.153)	0.167 (0.149 – 0.187)	0.0619 (0.0493 – 0.0739)
7-day EC ₂₀ (95% confidence interval)	0.122 (0.103 – 0.143)	0.0580 (0.0429 – 0.0763)	0.0676 (0.0568 – 0.0799)	0.0324 (0.0249 – 0.0426)
7-day EC ₁₀ (95% confidence interval)	0.0783 (0.0622 – 0.0972)	0.0429 (0.0300 – 0.0594)	0.0423 (0.0333 – 0.0524)	0.0246 (< 0.0184 – 0.0341)
7-day NOEC	0.0184	0.0184	0.0184	0.0184

CONCLUSION

Based on frond number, the 7-day EC₅₀ for yield (E_yC₅₀) and growth rate (E_rC₅₀) of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to *Lemna gibba* was determined to be 0.119 mg product/L and 0.286 mg product/L, respectively, based on geometric mean measured concentrations. Based on dry weight, the 7-day EC₅₀ for yield (E_yC₅₀) and growth rate (E_rC₅₀) of HBZ10 to *Lemna gibba* was determined to be 0.0619 mg/L and 0.167 mg/L, respectively, based on geometric mean measured concentrations.

A 2.2.1.4 Study 4

Comments of zRMS:	The study was conducted in line with OECD 239 with no deviations.
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	<p>The test concentrations of both active substances were verified at the beginning and at the end of the exposure in all tested concentration levels. The measured concentrations in the fresh media for the aqueous layer were in the range of 105 to 117% of Ethofumesate, 88 to 118% of Phenmedipham. In the day 14 media the measured concentrations in the aqueous layer were 94 to 107% of Ethofumesate and up to 1 % of Phenmedipham. Therefore, the endpoints are based on the geometric mean measured test item concentrations calculated from the geometric mean measured concentration of the active ingredients Ethofumesate and Phenmedipham.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>Growth rate based on total shoot length: $E_rC_{50} = 1.21 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_rC_{20} = 0.418 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_rC_{10} = 0.210 \text{ mg product/L}$ (based on geometric mean measured concentration) $NOE_rC = 0.131 \text{ mg product/L}$ (based on geometric mean measured concentration)</p> <p>Yield based on total shoot length: $E_yC_{50} = 0.673 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_yC_{20} = 0.198 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_yC_{10} = 0.0900 \text{ mg product/L}$ (based on geometric mean measured concentration) $NOE_yC = 0.0498 \text{ mg product/L}$ (based on geometric mean measured concentration)</p> <p>Growth rate based on fresh weight: $E_rC_{50} = 0.852 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_rC_{20} = 0.235 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_rC_{10} = 0.123 \text{ mg product/L}$ (based on geometric mean measured concentration) $NOE_rC = 0.131 \text{ mg product/L}$ (based on geometric mean measured concentration)</p> <p>Yield based on fresh weight: $E_yC_{50} = 0.470 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_yC_{20} = 0.169 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_yC_{10} = 0.0919 \text{ mg product/L}$ (based on geometric mean measured concentration) $NOE_yC = 0.131 \text{ mg product/L}$ (based on geometric mean measured concentration)</p> <p>Growth rate based on dry weight: $E_rC_{50} = 1.20 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_rC_{20} = 0.192 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_rC_{10} = 0.0834 \text{ mg product/L}$ (based on geometric mean measured concentration) $NOE_rC = 0.131 \text{ mg product/L}$ (based on geometric mean measured concentration)</p> <p>Yield based on dry weight: $E_yC_{50} = 0.746 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_yC_{20} = 0.133 \text{ mg product/L}$ (based on geometric mean measured concentration) $E_yC_{10} = 0.0704 \text{ mg product/L}$ (based on geometric mean measured concentration) $NOE_yC = 0.131 \text{ mg product/L}$ (based on geometric mean measured concentration)</p>
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Reference:	KCP 10.2.1/04
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Water-Sediment <i>Myriophyllum spicatum</i> Toxicity Test semi-static, 14 d, Scheerbaum, D., 2021d, report No SO20129 / SMS18743
Guideline(s):	OECD 239 (2014)
Deviations:	None No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The impact of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the submerge growth of the rooted, aquatic plant species *Myriophyllum spicatum*, was determined in a 14-day semi-static test using the nominal concentrations 0 (control), 0.0700, 0.221, 0.700, 2.21, 7.00 mg product/L (corresponding to the geometric mean measured concentrations of X1 (control), 0.0498, 0.131, 0.404, 1.25, 4.42 mg product/L). Plants were grown in a water-sediment system and exposed to the test chemical through applications made via the water column.

The concentrations of Ethofumesate and Phenmedipham, and the metabolites of Phenmedipham (MHPC and m-Toluidine) were analysed in all concentration levels and the control via LC-MS/MS. Fresh aqueous media were analysed on day 0, 4, 7 and 11, the corresponding aged media were analysed on day 4, 7, 11 and 14. Sediment and pore water were determined on day 0 and day 14.

Based on shoot length, the 14-day EC₅₀ for yield (E_yC₅₀) and growth rate (E_rC₅₀) of HBZ10 to *Myriophyllum spicatum* was determined to be 0.673 mg product/L and 1.21 mg product/L, respectively, based on geometric mean measured concentrations. Based on fresh weight, the 14-day EC₅₀ for yield (E_yC₅₀) and growth rate (E_rC₅₀) of HBZ10 to *Myriophyllum spicatum* was determined to be 0.470 mg product/L and 0.852 mg product/L, respectively, based on geometric mean measured concentrations. Based on dry weight, the 14-day EC₅₀ for yield (E_yC₅₀) and growth rate (E_rC₅₀) of HBZ10 to *Myriophyllum spicatum* was determined to be 0.746 mg product/L and 1.20 mg product/L, respectively, based on geometric mean measured concentrations.

The 14-day NOE_yC was determined to be 0.0498, 0.131 and 0.131 mg product/L based on shoot length, fresh weight and dry weight, respectively, while the 14-day NOE_rC was determined to be 0.131, 0.131 and 0.131 mg product/L based on shoot length, fresh weight and dry weight, respectively.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.05.2022
Vehicle / control(s)	Control: Dilution water (Smart & Barko medium)

Test System

Species	<i>Myriophyllum spicatum</i> L., Haloragaceae, Haloragales, Dicotyledoneae
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Source	Cultured in the test facility, origin: Institut für Gewässerschutz MESOCOSM GmbH, Neu-Ulrichstein 5; 35315 Homberg (Ohm), Germany
Culture medium	Modified Andrews' medium according to OECD guideline 238
Sediment composition	Artificial sediment used in OECD 239: 4% peat (< 1 mm), 20% kaolin clay (kaolinite content above 30%), 76% quartz sand (grain size 0.05 - 0.2 mm), pH 6.86
Acclimatisation period	Preliminary submerge rooting phase of 7 days
Test vessel	2-L glass beakers (24 cm high and 11 cm in diameter)
Test Conditions	
Temperature	20.0 – 21.7 ³ °C
pH value	Control: 7.24 – 9.62, treatment groups: 7.18 – 9.60 7.60
Dissolved concentration	O ₂ Control: mean 97 – 100%, treatment groups: mean 52 96 - 100%
Hardness	Not stated
Photoperiod	Continuous illumination
Light intensity	6659 – 8651 lux
Study Design and Methods	
In-life dates	02.10.2020 – 16.10.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	14 days
Test design	Semi-static
Test concentrations	0 (control), 0.0700, 0.221, 0.700, 2.21, 7.00 mg product/L (nominal)
Test groups / Replicates	3 plants/replicate; 6 replicates/control, 4 replicates/treatment
Treatment	Seven days prior to the start of the test, an adaptation/rooting phase was started. Apical shoots of <i>Myriophyllum spicatum</i> were transferred into sediment moistened with culture medium, topped up with Smart & Barko medium. Five uniform (size, appearance) shoot tips were planted into each pot containing the sediment (as described above) such that the lower 2 - 3 cm were beneath the sediment surface. The additional plants were removed at the end of the rooting phase / start of the definitive test from each planting pot to leave three uniform individuals. Care was taken to use uniform plants with regard to size and appearance. During the rooting phase, the pots were maintained in vessels and the plants were fully covered with medium. The rooting phase was conducted under the same environmental conditions as the definite exposure phase. For application, the planting pots with three plants were placed into the test vessels (one pot per vessel). The readily prepared test solutions were added very carefully via a flexible tube to each glass beaker in order to avoid disturbance of the sediment. The glass beakers were covered loosely with a lid. A reference test with 3,5-dichlorophenol was conducted in a separate study.
Observations	The shoot length of plants (above sediment), number and length of side shoots were determined at test start and end from each plant per test replicate using a ruler. Visual observations of plant health were recorded on day 0, 4, 7 and 14 of exposure. Parameters to be included on every determination day: necrosis, chlorosis or other discolouration; development of bacterial or algal contamination; growth abnormalities (e.g. stunting, altered intermodal length,

	<p>distorted shoots/leaves, proliferation of side shoots, leaf loss, loss of turgor and stem fragmentation).</p> <p>Visual assessments of root health were done at test end by carefully washing sediment from the roots and assessing the following parameters: roots absent; few roots; moderate root development; very good root development.</p> <p>At test end, the fresh weight and dry weight of shoots (cut at sediment level) was determined. Plants from each test vessel were collected, rinsed with tap water, dried up on a paper towel and weighed.</p> <p>After determination of the fresh weight, each shoot was placed individually in a drying cabinet at 60°C and dried to a constant weight.</p> <p>pH-value, temperature and oxygen concentration were measured in the fresh media at test start and at every renewal (days 4, 7, 11) of the test solutions (from one replicate per test concentration and control) as well as in the old media on days 4, 7, 11 and at test end (from each test replicate).</p>
Analytical verification	<p>All concentration levels and the control were analytically verified via LC-MS at the start (0 day) and at the end of the exposure (14 days) and on every renewal day. Freshly prepared and aged media were analysed. Sediment and pore water of all test item concentrations and the control were analysed at test start and test end of the exposure. The analytical method was validated based on SANCO/3029/99 rev. 4.</p>
Statistics	<p>The NOEC and LOEC were determined by calculation of statistically significant differences of growth rates and yield. EC₁₀-, EC₂₀- and EC₅₀- values of the shoot length, fresh and dry weight inhibition and corresponding confidence intervals after 14 days were calculated by sigmoidal dose-response regression.</p> <p>Calculations were carried out using software SigmaPlot, SPSS INC., GraphPad Prism, GRAPHPAD SOFTWARE, INC and ToxRat Version 3.3.0, ToxRat Solutions GmbH.</p>

RESULTS AND DISCUSSIONS

Validity criteria

The mean total shoot length and mean total shoot fresh weight in control plants should at least double (actual: 5.12-fold for total shoot length, 3.38-fold for shoot fresh weight) during the exposure phase. Control plants did not show any visual symptoms of chlorosis and were visibly free from contamination. The mean coefficient of variation for yield based on shoot fresh weight in the control cultures must not exceed 35% (actual: 20.4%) between replicates.

Analytical results

The measured concentrations in the fresh media for the aqueous layer were in the range of 105% to 117% of Ethofumesate, 88% to 118% of Phenmedipham. In the 14 days old media the measured concentrations in the aqueous layer were 94% to 107% of Ethofumesate and up to 1% of Phenmedipham. In the sediment, only < LOQ or 0% were measured at test start. At test end the measured concentrations in the sediment were up to 16% of Ethofumesate and up to 12% of Phenmedipham. In the pore water, only minor concentrations were measured at test start and test end. Therefore, MHPC and m-Toluidine as the metabolites of Phenmedipham were analysed in the aged media.

Table A 2.2.1.4-1 Geometric mean measured concentrations of the Active Ingredients Ethofumesate and Phenmedipham and the Geometric Mean Measured Concentration of the Test Item in the Aqueous Layer

Nominal concentration of the test item [mg product/L]	Geometric mean measured concentrations			
	Phenmedipham [mg a.s./L]	Ethofumesate [mg a.s./L]	HBZ10 [mg product/L]	[%]
7.00	0.178	0.958	4.42	63
2.21	0.0210	0.299	1.25	56
0.700	0.00855	0.0953	0.404	58
0.221	0.00503	0.0286	0.131	59
0.0700	0.00302 ⁽¹⁾	0.00976	0.0498	71

a.s. = active substance

% = percent of the nominal concentration of the active ingredient

⁽¹⁾ = values < LOQ were included in the calculation with ½ LOQ

Biological results

Following exposure to HBZ10, inhibition based on fresh weight was found to be more sensitive than based on dry weight and total shoot length. Shoot length, fresh and dry weight measurements are presented in the tables below along with their response variables (i.e., growth rate, yield) and respective inhibition values.

Table A 2.2.1.4-2 Summary of effects on growth rate and yield of *Myriophyllum spicatum* based on total shoot length

Concentration [mg product/L]		Mean total shoot length [cm]		Based on total shoot length (0-14 days)			
Nominal	Geometric mean measured	0 day	14 day	Mean Growth rate (per day)	Mean Inhibition of growth rate [%]	Mean Yield [mm]	Mean Inhibition of yield [%]
Control	0	7.1	36.5	0.117	-	293.7	-
0.0700	0.0498	7.2	34.7	0.113 (-)	4	275.2 (-)	6
0.221	0.131	7.1	32.4	0.110 (-)	6	253.7 (+)	14
0.700	0.404	6.9	25.8	0.094 (+)	19	188.7 (+)	36
2.21	1.25	7.7	17.1	0.057 (+)	51	94.5 (+)	68
7.00	4.42	8.1	10.3	0.017 (+)	85	21.6 (+)	93

Statistically significant differences of growth rates and yield compared to control values are marked (+), not significant differences are marked (-)

Table A 2.2.1.5-3 Summary of effects on growth rate and yield of *Myriophyllum spicatum* based on fresh weight

Concentration [mg product/L]		Mean Fresh weight (day 14) [mg]	Based on fresh weight (0-14 days)			
Nominal	Geometric mean measured		Mean Growth rate (per day)	Mean Inhibition of growth rate [%]	Mean Yield [mg]	Mean Inhibition of yield [%]
Control	Control	1127.7	0.087	-	794	-
0.0700	0.0498	1064.6	0.082 (-)	5	731 (-)	8
0.221	0.131	1046.1	0.082 (-)	6	713 (-)	10
0.700	0.404	737.3	0.056 (+)	35	404 (+)	49
2.21	1.25	572.3	0.038 (+)	56	239 (+)	70
7.00	4.42	437.0	0.020 (+)	78	104 (+)	87

Statistically significant differences of growth rates and yield compared to control values are marked (+), not significant differences are marked (-)

Table A 2.2.1.5-4 Summary of effects on growth rate and yield of *Myriophyllum spicatum* based on dry weight

Concentration [mg product/L]		Mean Dry weight (day 14) [mg]	Based on dry weight (0-14 days)			
Nominal	Geometric mean measured		Mean Growth rate (per day)	Mean Inhibition of growth rate [%]	Mean Yield [mg]	Mean Inhibition of yield [%]
Control	Control	65.2	0.059	-	36.6	-
0.0700	0.0498	63.0	0.056 (-)	6	34.4 (-)	6
0.221	0.131	59.8	0.053 (-)	11	31.3 (-)	15
0.700	0.404	47.7	0.036 (+)	39	19.2 (+)	48
2.21	1.25	45.6	0.033 (+)	45	17.0 (+)	54
7.00	4.42	33.3	0.011 (+)	82	4.70 (+)	87

Statistically significant differences of growth rates and yield compared to control values are marked (+), not significant differences are marked (-)

The effect endpoints of HBZ10 to *Myriophyllum spicatum* based on geometric mean measured concentrations are presented in the following table.

Table A 2.2.1.5-5 Effect concentrations of HBZ10 to *Myriophyllum spicatum* based on geometric mean measured concentrations

Effect concentration [mg product/L]	Based on shoot length		Based on fresh weight		Based on dry weight	
	Growth rate	Yield	Growth rate	Yield	Growth rate	Yield
14-day EC ₅₀ (95% CL)	1.21 (1.02-1.48)	0.673 (0.545-0.481)	0.852 (0.616-1.28)	0.470 (0.343-0.675)	1.20 (0.614-2.65)	0.746 (0.313-2.02)
14-day EC ₂₀ (95% CL)	0.418 (0.305-0.545)	0.198 (0.138-0.280)	0.235 (0.148-0.350)	0.169 (0.105-0.259)	0.192 (< 0.0498- 0.458)	0.133 (< 0.0498- 0.331)
14-day EC ₁₀ (95% CL)	0.210 (0.118-0.328)	0.0900 (< 0.0498- 0.149)	0.123 (< 0.0498- 0.217)	0.0919 (< 0.0498- 0.175)	0.0834 (< 0.0498- 0.263)	0.0704 (< 0.0498- 0.205)
14-day LOEC	0.404	0.131	0.404	0.404	0.404	0.404
14-day NOEC	0.131	0.0498	0.131	0.131	0.131	0.131

CL = confidence limits

CONCLUSION

Based on shoot length, the 14-day EC₅₀ for yield (E_yC₅₀) and growth rate (E_rC₅₀) of HBZ10 to *Myriophyllum spicatum* was determined to be 0.673 mg product/L and 1.21 mg product/L, respectively, based on geometric mean measured concentrations. Based on fresh weight, the 14-day EC₅₀ for yield (E_yC₅₀) and growth rate (E_rC₅₀) of HBZ10 to *Myriophyllum spicatum* was determined to be 0.470 mg product/L and 0.852 mg product/L, respectively, based on geometric mean measured concentrations. Based on dry weight, the 14-day EC₅₀ for yield (E_yC₅₀) and growth rate (E_rC₅₀) of HBZ10 to *Myriophyllum spicatum* was determined to be 0.746 mg product/L and 1.20 mg product/L, respectively, based on geometric mean measured concentrations.

A 2.2.2 KCP 10.2.2 Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms

A 2.2.2.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 211 with no deviations.</p> <p>The analytical measurements of the test item (metabolite of Phenmedipham) showed that the measured concentrations were maintained at 80 – 120% of the nominal during the study. Therefore, the endpoints are expressed as nominal concentrations.</p> <p>It was noted that, although it is not a validity criterion, according to the respective guideline, in a well-run test the coefficient of variation around the mean number of living offspring produced per parental animal in the controls should be ≤ 25% but in the present study the CV was 36.1%.</p>
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	<p>All the validity criteria were met and the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>EC₅₀ (reproduction) = 8.78 mg test item/L (based on nominal concentration) EC₁₀ (reproduction) = 5.25 mg test item/L (based on nominal concentration) NOEC (reproduction) = 5.00 mg test item/L (based on nominal concentration)</p>
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Reference:	KCP 10.2.2/01
Report	MHPC: <i>Daphnia magna</i> Reproduction Test, Semi-static, 21 days, Scheerbaum, D., 2021e, report No SO20407 / DRE19098
Guideline(s):	OECD 211 (2012)
Deviations:	None No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The long-term and reproductive toxicity of MHPC to *Daphnia magna* was investigated in a 21-day semi-static test with the nominal concentrations 0 (control), 0.50, 1.58, 5.00, 15.8, 50.0 mg/L. Ten daphnids, held individually, were used per concentration level and control.

The test item concentrations of MHPC were analytically verified via LC-MS/MS in the fresh media at the start of the exposure-renewal intervals on days 0, 7, 16 (0 hours) and in the old media at the end of the exposure intervals on days 2, 9, 19 (48 or 72 hours, respectively) in all concentration levels (with surviving daphnids) and in the control. Since the measured test item concentrations were within $\pm 20\%$ of the nominal concentrations, the nominal test item concentrations were used for the evaluation of the effect-concentrations.

The EC₅₀ for reproduction was calculated to be 8.78 mg/L (nominal). The NOEC for reproduction was determined to be 5.00 mg/L (nominal).

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	MHPC (methyl N-(3-hydroxyphenyl)carbamate)
Batch no.	R485857
Purity	95%
Characteristics	Grey, solid, powder and chunks
Density	Not required
Storage conditions	Room temperature.
Stability (expiry date)	05.11.2022
Vehicle / control(s)	Control: Dilution water

Test System

Species	<i>Daphnia magna</i> Straus
Age	< 24 hours old (first instar)
Culture medium	Elendt M4
Source	Laboratory breeding; origin: Institut für Wasser-, Boden- und Lufthygiene (WaBoLu), 14195 Berlin, Germany
Acclimatisation period	
Food	At least 5 times per week <i>ad libitum</i> with a mix of unicellular green algae, e.g., <i>Pseudokirchneriella subcapitata</i> and <i>Desmodesmus subspicatus</i>

Test Conditions

Temperature	19.9 - 20.8°C
pH value	7.21 - 8.00 (fresh media); 7.27 – 7.71 (old media)
Dissolved O ₂ concentration	8.77 - 8.87 mg/L (fresh media); 5.29 – 8.17 (old media)
Hardness	258 - 290 mg/L CaCO ₃ (fresh media); 237 – 287 mg/L CaCO ₃ (old media)
Photoperiod	16 hours light / 8 hours darkness
Light intensity	Max. 1500 lux
Aeration of the test water	No aeration during the test

Study Design and Methods

In-life dates	07.10.2020 – 28.10.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	21 days, semi-static
Test concentrations	0 (control), 0.50, 1.58, 5.00, 15.8, 50.0 mg/L
Test groups / Replicates	10 replicates/treatment (and control); 1 animal per replicate
Treatment	The study was conducted as a semi-static dose-response test with medium renewal 3 times per week. The test concentrations were chosen based on the results of an acute toxicity test of MHPC with <i>Daphnia magna</i> . For each exposure level and the control, ten first instar <i>Daphnia</i> housed in separate vessels were adopted. Less than 24 hours old daphnids from a healthy stock were used for the study. The juveniles born within the following period were used for the test. No first brood progeny was used for the test. The cultures were fed algae on a daily basis corresponding to max. 0.2 mg C per <i>Daphnia</i> and day.
Observations	The number of parental daphnids, which were immobilized or dying during the test and the dates of death were observed and recorded once a day at least at the same time as the offspring was counted. Dead daphnids were removed as soon as they were detected. First appearance of juveniles was checked daily. The number of neonates (alive and dead progeny) was counted, and dates of release were recorded once a day from the first day of appearance of neonates until the end of the exposure. The neonates (alive and dead) were removed after counting and before addition of algae to prevent them from consuming food intended for the adults. The number of aborted eggs or dead offspring and dates of observation were recorded. Test temperature was recorded daily in each test vessel. Dissolved oxygen, pH and temperature were measured before and after each test media renewal in all treatment levels and the control.
Analytical verification	All concentration levels and the control were analysed via LC-MS/MS at least 3 times during the test (e.g., once within a period of 7 days) in the fresh media at the start of an exposure-renewal interval (0 hours) as well as in the old media at the end of an exposure-renewal interval (48 or 72 hours). The analytical method was validated based on SANCO/3029/99 rev. 4.

Statistics

The NOEC and LOEC for the reproduction and the adult mortality were determined with the software ToxRat Professional. Significant differences of reproduction were determined in comparison to the control using statistical standard procedures as normality test (Shapiro-Wilk's test), variance homogeneity test (Levene's test), Multiple Sequentially-rejective Welsh-t-test (Bonferroni-Holm) for reproduction and Step-Down Cochran-Armitage test for adult mortality.

The EC_{10/50}-values for the reproductive output with 95% confidence limits were calculated by point estimates from the 3 parametric normal CDF with the software ToxRat Professional.

RESULTS AND DISCUSSIONS

Validity criteria

The mortality of the parent female *Daphnia* in the control should not $\geq 20\%$ (actual: 10%) at the end of the test.

The mean number of living offspring produced per parent animal surviving at the end of the test should be ≥ 60 (actual: 100).

Analytical results

The test item concentrations of MHPC were analytically verified via LC-MS/MS in the fresh media at the start of the exposure-renewal intervals on days 0, 7, 16 (0 hours) and in the old media at the end of the exposure intervals on days 2, 9, 19 (48 hours or 72 hours, respectively) in all concentration levels (with surviving daphnids) and in the control. The measured concentrations of the test item in fresh media at the start of the respective exposure-renewal intervals (0 hours) were in the range of 86% to 113% of the nominal concentrations. At the end of the respective exposure-renewal intervals (48 hours or 72 hours, respectively), the measured test item concentrations in the old media were in the range of 95% to 107% of the nominal concentrations.

Table A 2.2.2.1-1 Measured concentrations of MHPC during the test

Nominal concentration		Day 0 Fresh medium 0 hours		Day 2 Old medium 48 hours		Day 7 Fresh medium 0 hours		Day 9 Old medium 48 hours		Day 16 Fresh medium 0 hours		Day 19 Old medium 72 hours	
test item [mg/L]	active substance [mg a.s./L]	Meas. [mg a.s./L]	[%]	Meas. [mg a.s./L]	[%]	Meas. [mg a.s./L]	[%]	Meas. [mg a.s./L]	[%]	Meas. [mg a.s./L]	[%]	Meas. [mg a.s./L]	[%]
50.0	47.5	47.9	101	48.6	102	n.d.		n.d.		n.d.		n.d.	
15.8	15.0	14.9	99	16.1	107	16.2	108	14.7	98	n.d.		n.d.	
5.00	4.75	4.76	100	4.96	104	5.38	113	4.50	95	4.98	105	4.51	95
1.58	1.50	1.45	97	1.56	104	1.59	106	1.44	96	1.61	107	1.43	95
0.500	0.475	0.410	86	0.497	105	0.483	102	0.450	95	0.524	110	0.465	98
Control		< LOQ		< LOQ		< LOQ		< LOQ		< LOQ		< LOQ	

Meas. = measured concentration of the test item, dilution factors taken into account

% = percent of the nominal concentration of the test item

a.s. = active substance

LOQ = limit of quantification (0.0100 mg/L of the test item)

n.d. = not determined, due to 100% mortality

Biological results

Since the Cochran-Armitage test procedure revealed a significant increasing trend ($p \leq 0.05$) in adult mortality, the evaluation was done based on the cumulative offspring per introduced parent. A statistically significant reduction of the reproductive output in comparison to the reproductive output in the control was determined at the concentration level 15.8 mg/L (Welsh-t-test after Bonferroni-Holm, $\alpha = 0.05$). The determination of the EC₁₀-, EC₂₀- and the EC₅₀-value and their 95% confidence limits were carried out by point estimates from the 3 parametric normal CDF.

The intrinsic rates of natural increase (IR) of the survived parental daphnids accounting for generation time and number of offspring were used for calculation of population growth and maintenance. In the control as well as in the concentration levels 0.50 to 50.0 mg/L no stillborn juveniles or aborted eggs were observed during the exposure period of 21 days. The mean values of the body length (excluding the anal spine) of the survived parental daphnids in the tested concentration levels 0.50 to 50.0 mg/L were in the range of 4.75 to 4.90 mm per daphnid and 5.00 mm per daphnid in the control group. The mean dry weight of the survived parental daphnids was in the range of 0.43 to 0.54 mg per daphnid in the concentration levels 0.50 to 50.0 mg/L and 0.36 mg per daphnid in the control.

By 21 days of exposure, survival of organisms exposed to control was 90%. Mean number of offspring released per female organism in control was 90.3 offspring per female. 100% mortality was observed at exposure to the highest treatment levels (15.8 and 50.0 mg test item/L) which were significantly reduced as compared to control after 21 days. Survival of 100, 90 and 100% was observed among daphnids exposed to the 0.50, 1.58, 5.00 mg test item/L treatment groups. After 21 days of exposure, no offspring per female were released by daphnids in the 15.8 and 50.0 mg test item/L treatment groups.

Table A 2.2.2.1-2 Summary of effects on adult survival and reproduction of *Daphnia magna* during the 21-day exposure to MHPC

Test item [mg/L]	Mortality of adult daphnids (day 21) [%]	Mean number of offspring per introduced parent	Mean intrinsic rate	First appearance of juveniles [day]
Control	10	90.3 ± 32.6	0.387 ± 0.0490	7.3
0.50	0	111 ± 8.63	0.400 ± 0.0325	7.5
1.58	10	103 ± 18.3	0.404 ± 0.0240	7.4
5.00	0	120 ± 10.3	0.404 ± 0.0336	7.2
15.8	100*	0.4 ± 1.26	n.d.	11
50.0	100*	0	n.d.	-

SD Standard deviation

* Significant difference (Step down Cochran-Armitage Test Procedure, $\alpha = 0.05$)

n.d.= not determined, due to 100% mortality

CONCLUSION

The 21-day LC₅₀ for immobilization (mortality) was determined to be 7.29 mg/L (95% confidence limits: 5.00 - 15.8 mg/L) based on nominal concentrations.

The 21-day EC₅₀ for reproduction was determined to be 8.78 mg/L (95% confidence limits: 7.60 - 10.2 mg/L) based on nominal concentrations. The 21-day NOEC for reproduction was determined to be 5.00 mg/L based on nominal and mean measured concentration s, respectively.

A 2.2.3 KCP 10.2.3 Further testing on aquatic organisms

Based on the results of the risk assessment (refer to Point 9.5.2), no further testing on aquatic organisms with HBZ10 is required.

A 2.3 KCP 10.3 Effects on arthropods

A 2.3.1 KCP 10.3.1 Effects on bees

A 2.3.1.1 KCP 10.3.1.1 Acute toxicity to bees

A 2.3.1.1.1 KCP 10.3.1.1.1 Acute oral toxicity to bees

A 2.3.1.1.1.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 213 with no deviations.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>oral LD₅₀ >787 µg product/bee (corresponding to > 101 µg Ethofumesate/bee and > 102 µg Phenmedipham/bee; based on actual food uptake)</p>
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Reference:	KCP 10.3.1.1.1/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Acute Oral Toxicity to the Honeybee <i>Apis mellifera</i> (Hymenoptera, Apidae), Klix, V., 2021a, report No SO20043 / IBO 18743
Guideline(s):	OECD 213 (1998)
Deviations:	None No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The aim of the study is to determine the acute oral of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to honeybees under laboratory conditions. The oral test was performed at concentrations of 48.9, 97.7, 195, 391, 782 µg product/bee. 50% aqueous sucrose solution was used as control. Danadim Progress (38.2% dimethoate) was used as a reference item with nominal doses of 0.046, 0.10, 0.22, 0.46 µg dimethoate/bee.

The duration of the test was 48 hours with three replicates for the test concentrations and the toxic reference, and five replicates for the control group, each replicate consisting of 10 bees. The assessment of mortality was performed after 4, 24 and 48 hours.

HBZ10 did not cause adverse effects on *Apis mellifera* L. after oral exposure. The oral LD₅₀ value (48 h) was estimated to be > 787 µg product/bee (based on actual consumed dose).

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place

Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: 50% aqueous sucrose solution Toxic reference item: Danadim progress (38.2% dimethoate)
Test System	
Species	<i>Apis mellifera</i> L. (Hymenoptera, Apidae), subspecies <i>A. m. carnica</i> Pollm.
Age	Adult worker bees
Source	Queen-right, healthy, untreated colony at test facility. The used hive was not treated with chemical substances such as treatments against Varroa mites for at least 4 weeks.
Acclimatisation period	Young worker bees were collected from honey frames in the morning of the application day. The bees were adapted to test conditions for about 1 hour. After adaption, the bees were inserted in the test cages and starved for approximately 1 hour prior to oral application under test conditions.
Food	The bees were transferred to the laboratory immediately after collection. They were allowed to feed on 50% sucrose solution <i>ad libitum</i> .
Test Conditions	
Temperature	24.6 – 25.2°C
Relative Humidity	51.5 – 57.0%
Photoperiod	Darkness, except during observation
Study Design and Methods	
In-life dates	24.06.2020 – 26.06.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	48 hours
Test concentrations	48.9, 97.7, 195, 391, 782 µg product/bee
Test vessels	Test cages made of a stainless-steel frame (10.2 × 5.6 × 8.6 cm)
Treatment	The final study used 48.9, 97.7, 195, 391, 782 µg product/bee. The test comprised 5 dose level of test item, 4 treatments of the toxic reference and one control, each test item and toxic reference treatment was replicated three times, the control consisted of 5 replicates. Each replicate consisted of 10 honeybees. The individual dosing was carried out using the test item in 50% sucrose solution. As bees share their food among themselves due to their reciprocal social feeding behaviour, the test item and toxic reference item per replicate (10 bees) contained 200 µL of a 50% sucrose solution. Danadim Progress (38.2% dimethoate) was used as a reference item with nominal doses of 0.046, 0.10, 0.22, 0.46 µg dimethoate/bee. A control was maintained with 50% sucrose solution. The test item uptake was determined after about 4 hours by weighing the feeding tubes. Afterwards the bees were fed <i>ad libitum</i> with 50% sucrose solution.
Observations	Each group of bees were observed for moribund, mortality, lethargy and impaired coordination at 4-, 24- and 48-hours post-treatment. All moribund were counted as mortalities. Bees showing lethargy or impaired coordination were counted as affected.

Statistics

A normality test (Shapiro-Wilk) and a Kruskal-Wallis One Way Analysis of Variance on Ranks were performed to determine statistically significant difference compared to the control for mortality.

The LD₅₀ value for the reference item was calculated by sigmoidal dose-response regression. Calculation of the 95% confidence intervals for the LD₅₀ value was carried out using standard procedures. The LD values were based on the actual consumed test and reference item doses.

All calculations, especially food uptake, were done based on the concentrations µg Ethofumesate/bee. Concentrations of test item and Phenmedipham regarding effect values were calculated from the Ethofumesate concentrations.

RESULTS AND DISCUSSIONS

Validity criteria

The average mortality for the total number of controls must not exceed 10% (actual: 0%) at the end of the test. The LD₅₀ of the toxic reference item is within 0.10 - 0.35 µg dimethoate/bee (actual: 0.13 µg dimethoate/bee).

Biological results

The control fed with 50% sucrose solution showed no bee mortality after 48 hours. In the test item treatment group, no mortality occurred after oral consumption of 49.5, 99.6, 193 µg product/bee, after 48 hours. In the test item groups at 399 and 787 µg product/bee, a mean mortality of 20% and 16.7% was observed after 48 hours, respectively. No statistically significant mortality up to the highest test concentration was observed. The LD₅₀ (48 h) was estimated to be > 787 µg product/bee (based on actual consumed dose).

An overview of the results is presented in the table below.

Table A 2.3.1.1.1-1 Mortality of bees exposed to HBZ10 for 48 hours

Treatment group	Test doses		Testing period		
			4 hours	24 hours	48 hours
	(nominal)	(consumed)	Mean mortality [%]	Mean mortality [%]	Mean mortality [%]
Control	Sucrose solution		0.0	0.0	0.0
HBZ10 [µg product/bee]	48.9	49.5	0.0	0.0	0.0
	97.7	99.6	0.0	0.0	0.0
	195	193	0.0	0.0	0.0
	391	399	0.0	20.0	20.0
	782	787	0.0	13.3	16.7
Reference item [µg a.s./bee]	0.046	0.047	0.0	0.0	-
	0.10	0.10	0.0	6.67	-
	0.22	0.22	0.0	100	-
	0.46	0.46	0.0	100	-

CONCLUSION

The acute oral toxicity of HBZ10 was tested on honeybees under laboratory conditions over 48 hours. The oral LD₅₀ after 48 hours was estimated to be > 787 µg product/bee (based on actual consumed dose; corresponding to > 101 µg Ethofumesate/bee and > 102 µg Phenmedipham/bee).

A 2.3.1.1.1.2 Study 2

Comments of zRMS:	<p>The study was conducted in line with OECD 247 with a minor deviation.</p> <p>It was noted that according to the guideline the bumblebees should be collected from at least three colonies but bumblebees from only two colonies were used in the study. However, this deviation should not invalidate the study.</p>
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	<p>All the validity criteria were met and the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>oral LD₅₀ > 1.5167 mg product/bumblebee (based on food consumed), corresponding to > 194 µg Ethofumesate/ bumblebee and > 196 µg Phenmedipham/ bumblebee</p>
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Reference:	KCP 10.3.1.1.1/02
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Acute Oral Toxicity to the Bumblebee <i>Bombus terrestris</i> , Klix, V., 2021b, report No SO20046 / IUO18743
Guideline(s):	OECD 247 (2017)
Deviations:	Minor (see the commenting box above) No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The aim of the study is to determine the acute oral toxicity of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to bumblebees under laboratory conditions. The oral test was performed as an extended limit test at concentrations of 0.7816, 1.5632 mg product/bumblebee (corresponding to 100, 200 µg Ethofumesate/bumblebee and 101, 202 µg Phenmedipham/bumblebee). 50% aqueous sucrose solution was used as control. Danadim Progress (38.2% dimethoate) was used as a reference item with a nominal dose of 4 µg dimethoate/bumblebee.

The duration of the test was 48 hours with 50 replicates for the test concentrations and control, 30 replicates for the toxic reference, each replicate consisting of 1 bumblebee. The assessment of mortality was performed after 4, 24 and 48 hours.

The concentrations of the test item Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) were determined by analysis of the test item stock solution (dissolved in dechlorinated tap water), feeding solution (test item in 50% sucrose solution) and control solutions (50% sucrose solution and dechlorinated tap water) via LC-MS/MS.

HBZ10 did not cause adverse effects on *Bombus terrestris* after oral exposure. The oral LD₅₀ value (48 h) was estimated to be > 1.5167 mg product/bbee (based on actual consumed dose).

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: 50% aqueous sucrose solution Toxic reference item: Danadim progress (38.2% dimethoate)

Test System

Species	<i>Bombus terrestris</i>
Age	Adult worker bumblebees

Source	Biobest Group N.V. (Belgium); delivered by Katz Biotech AG, An der Birkenpfuhlheide 10, 15837 Baruth, Germany.
Acclimatisation period	The colonies were kept under controlled climatic conditions (20 to 35°C, relative humidity 40 to 60%) for 6 days in the laboratory. The bumblebees were adapted to test conditions for approximately 24 hours. Adaption to single housing was done for approximately 24 hours, while adaption to temperature and relative humidity was done for approximately 8 hours.
Food	During keeping and adaption the bumblebees were fed <i>ad libitum</i> with 50% sucrose solution.
Test Conditions	
Temperature	25 - 26°C
Relative Humidity	48 - 56%
Photoperiod	Darkness, except during observation
Study Design and Methods	
In-life dates	02.12.2020 – 04.12.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	48 hours
Test concentrations	0.7816, 1.5632 mg product/bumblebee
Test vessels	NICOT [®] queen breeding cages
Treatment	Bumblebees with homogenous body size were used for the study. Each bumblebee was weighed before the start of exposure (day -1) and randomly allocated to the treatments. Each treatment included bumblebees from both colonies. The final study used 0.7816, 1.5632 mg product/bumblebee. The test comprised 2 dose level of test item, 1 treatment of the toxic reference and one control, each test item and control were replicated 50 times, the toxic reference consisted of 30 replicates. Each replicate consisted of 1 bumblebee. The individual dosing was carried out using the test item in 50% sucrose solution. The bumblebees were starved for approximately 2 to 3 hours (but not more than 4 hours) prior to application. After the starvation period each bumblebee was provided with 40 µL application solution. Danadim Progress (38.2% dimethoate) was used as a reference item with nominal dose of 4 µg dimethoate/bee. A control was maintained with 50% sucrose solution. The test item uptake was determined after about 4 hours by weighing the feeding tubes. Afterwards the bees were fed <i>ad libitum</i> with 50% sucrose solution.
Observations	Mortality and sublethal effects (affected, moribund) were determined after 4, 24 and 48 h.
Analytical verification	The concentrations of the test item HBZ10 were determined by analysis of the test item stock solution (dissolved in dechlorinated tap water), feeding solution (test item in 50% sucrose solution) and control solutions (50% sucrose solution and dechlorinated tap water) via LC-MS/MS. The analytical method was validated based on SANCO/3029/99 rev. 4.

Statistics

The mean food consumption of control, test and reference item, the percentage of food consumption and the real consumed test and reference item (active substance) was calculated.

Non-feeders are bumblebees, which consume < 80% of the mean food consumption of the respective treatment group. No non-feeders were found in the control, test item replicates or reference item replicates.

No statistical analysis was performed, since mortality in the control and limit test item treatments was identical.

RESULTS AND DISCUSSIONS

Validity criteria

The average mortality for the total number of controls must not exceed 10% (actual: 0%) at the end of the test. The mean mortality in the toxic reference treatment must exceed 50% (actual: 100%) at the end of the test.

Analytical verification

The concentrations of the test item Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) were determined by analysis of the test item stock solution (dissolved in dechlorinated tap water), feeding solution (test item in 50% sucrose solution) and control solutions (50% sucrose solution and dechlorinated tap water) via LC-MS/MS.

The recoveries of the test item in the feeding solutions were 82% to 99% of Ethofumesate and 81% to 98% of Phenmedipham of the nominal concentrations. The recoveries of the test item in the stock solutions were 91% to 92% of Ethofumesate and 83% to 89% of Phenmedipham of the nominal concentration. The recoveries indicate the correct preparation of the feeding solution for both tests. Biological results are based on nominal test item concentrations.

Biological results

Control mortality and mortality in both limit test item treatments was 0.0% at test end. No sublethal effects in the test item treatment compared to the control were observed. Therefore, the study demonstrates that the LD₅₀ and the NOED is greater than the consumed concentration of 194 µg Ethofumesate/bumblebee, corresponding to 196 µg Phenmedipham/bumblebee and 1.5167 mg product/bumblebee. The LD₅₀ (48 h) was estimated to be > 1.5167 mg product/bumblebee (based on actual consumed dose).

Table A 2.3.1.1.2-1 Mortality of bumblebees exposed to HBZ10 for 48 hours

Treatment group	Test doses		Testing period		
			4 hours	24 hours	48 hours
	(nominal)	(consumed)	Mean mortality [%]	Mean mortality [%]	Mean mortality [%]
Control	Sucrose solution		0.0	0.0	0.0
HBZ10	0.7816	0.7867	0.0	0.0	0.0
[mg product/bee]	1.5632	1.5167	0.0	0.0	0.0
Reference item	4	4.2	0.0	100	100
[µg a.s./bee]					

CONCLUSION

The acute oral toxicity of HBZ10 was tested on bumblebees under laboratory conditions over 48 hours. The oral LD₅₀ after 48 hours was estimated to be > 1.5167 µg product/bumblebee (based on actual consumed dose; corresponding to > 194 µg Ethofumesate/bumblebee and > 196 µg Phenmedipham/bumblebee).

A 2.3.1.1.2 KCP 10.3.1.1.2 Acute contact toxicity to bees

A 2.3.1.1.2.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 214 with no deviations.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoint relevant for the risk assessment:</p>
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	contact LD ₅₀ = 317 µg product/bee (corresponding to 40.6 µg Ethofumesate/bee and 40.9 µg Phenmedipham/bee)
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Reference:	KCP 10.3.1.1.2/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10). Acute Contact Toxicity to the Honeybee <i>Apis mellifera</i> (Hymenoptera, Apidae), Klix, V., 2021c, report No SO20044 / IBT 18743
Guideline(s):	OECD 214 (1998)
Deviations:	None No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The aim of the study is to determine the acute contact toxicity of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to honeybees under laboratory conditions. The contact test was performed at concentrations of 48.9, 97.7, 195, 391, 782 µg product/bee. Water and Tween 85 (1%) were used as control. Danadim Progress (38.2% dimethoate) was used as a reference item with nominal doses of 0.046, 0.10, 0.22, 0.46 µg dimethoate/bee.

The duration of the test was 48 hours with three replicates for the test concentrations and the toxic reference, and five replicates for the control groups, each replicate consisting of 10 bees. The assessment of mortality was performed after 4, 24 and 48 hours. Also, it was recorded any sign of intoxication and abnormal behaviour.

HBZ10 does not cause adverse effects on *Apis mellifera* L. after contact exposure up to 195 µg product/bee. At 391 and 782 µg product/bee, statistically significant mortality was observed compared to the control. The respective contact LD₅₀ value (48 h) was determined to be 317 µg product/bee.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: water / Tween 85 (1%) Toxic reference item: Danadim progress (38.2% dimethoate)

Test System

Species	<i>Apis mellifera</i> L. (Hymenoptera, Apidae), subspecies <i>A. m. carnica</i> Pollm.
Age	Adult worker bees
Source	Queen-right, healthy, untreated colony at test facility. The used hive was not treated with chemical substances such as treatments against Varroa mites for at least 4 weeks.
Acclimatisation period	Young worker bees were collected from honey frames in the morning of the application day. The bees were adapted to test conditions for about 1 hour.

Food	The bees were transferred to the laboratory immediately after collection. They were allowed to feed on 50% sucrose solution <i>ad libitum</i> .
Test Conditions	
Temperature	24.6 – 25.2°C
Relative Humidity	51.5 – 57.0%
Photoperiod	Darkness, except during observation
Study Design and Methods	
In-life dates	23.06.2020 – 25.06.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	48 hours
Test concentrations	48.9, 97.7, 195, 391, 782 µg product/bee
Test vessels	Test cages made of a stainless-steel frame (10.2 × 5.6 × 8.6 cm)
Treatment	The final study used 48.9, 97.7, 195, 391, 782 µg product/bee. The test comprised 5 dose level of test item, 4 treatments of the toxic reference and two controls (water / 1% Tween 85), each test item and toxic reference treatment was replicated three times, the controls consisted of 5 replicates. Each replicate consisted of 10 honeybees. Test item, controls and toxic reference were applied onto the thorax of each bee. The bees were briefly anaesthetized with CO ₂ for the duration of the application. The application volume was 1 µL for the controls, and each test item and toxic reference treatment. Danadim Progress (38.2% dimethoate) was used as a reference item with nominal doses of 0.046, 0.10, 0.22, 0.46 µg dimethoate/bee.
Observations	Each group of bees were observed for moribund, mortality, lethargy and impaired coordination at 4-, 24- and 48-hours post-treatment. All moribund were counted as mortalities. Bees showing lethargy or impaired coordination were counted as affected.
Statistics	Dunn's method (multiple comparisons vs control group) was carried out to determine statistically significant differences compared to the control for mortality. A normality test (Shapiro-Wilk) and Kruskal-Wallis One Way Analysis of Variance on Ranks were performed first. The LD ₅₀ value for the test and reference item was calculated by sigmoidal dose-response regression. Calculation of the 95% confidence intervals for the LD ₅₀ value was carried out using standard procedures. Test concentrations, doses and effect levels were calculated based on the certified concentration of the active ingredient Ethofumesate. The corresponding values of effect levels for the a.i. Phenmedipham and test item were calculated based on the evaluation for Ethofumesate. All calculations were based on the certified amount.

RESULTS AND DISCUSSIONS

Validity criteria

The average mortality for the total number of controls must not exceed 10% (actual: 0%) at the end of the test.

The LD₅₀ of the toxic reference item (dimethoate) is within 0.10 - 0.30 µg a.s./bee (actual: 0.12 µg a.s./bee).

Biological results

In the control groups either treated with deionised water or 1% tween solution, no mortality was observed after 48 hours. In the test item treatment groups, ~~no mortality was observed~~ after application of 48.9, 97.7, 195 µg product/bee to the thorax mean mortalities of 3.33, 13.3 and 13.3%, respectively, were observed. In the test item groups 391 and 782 µg product/bee, a mean mortalities of 73.3 and 100% were observed after 48 hours, resulting in a statistically significantly increased mortality compared to the control. The LD₅₀ (48 h) was determined to be 317 µg product/bee.

Table A 2.3.1.1.2.1-1 Mortality of bees exposed to HBZ10 for 48 hours

Treatment group	Test dose	Testing period		
		4 hours	24 hours	48 hours
		Mean mortality [%]	Mean mortality [%]	Mean mortality [%]
Control	Deionised water	0.0	0.0	0.0
	1% Tween 85	0.0	0.0	0.0
HBZ10 [µg product/bee]	48.9	0.0	3.33	3.33
	97.7	0.0	10.0	13.3
	195	0.0	10.0	13.3
	391	0.0	73.3	73.3*
	782	0.0	100	100*
Reference item [µg a.s./bee]	0.046	0.0	0.0	-
	0.10	0.0	10.0	-
	0.22	0.0	100	-
	0.46	0.0	100	-

* Significant difference compared to control (Dunn's test; $\alpha = 0.05$)

CONCLUSION

The acute contact toxicity of HBZ10 was tested on honeybees under laboratory conditions over 48 hours. The contact LD₅₀ after 48 hours was determined to be 317 µg product/bee (corresponding to 40.6 µg Ethofumesate/bee and 40.9 µg Phenmedipham/bee).

A 2.3.1.1.2.2 Study 2

Comments of zRMS:	<p>The study was conducted in line with OECD 246 with no deviations.</p> <p>The analytical measurements showed that the concentrations of both active substances were within 80 – 120 % of nominal. Therefore, the endpoint is expressed as nominal concentration.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>contact LD₅₀ > 0.7816 mg product/bumblebee (based on nominal concentration), corresponding to > 100 µg Ethofumesate/bumblebee and > 101 µg Phenmedipham/bumblebee</p>
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Reference:	KCP 10.3.1.1.2/02
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Acute Contact Toxicity on the Bumblebee <i>Bombus terrestris</i> , Klix, V., 2021d, report No SO20045 / IUT18743
Guideline(s):	OECD 246 (2017)
Deviations:	None No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The aim of the study is to determine the acute contact toxicity of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) to bumblebees under laboratory conditions. The contact test was performed as limit test at 0.7816 mg product/bumblebee (corresponding to 100 µg Ethofumesate/bumblebee and 101 µg

Phenmedipham/bumblebee). Water and Triton X-100 (0.1%) were used as controls. Danadim Progress (38.2% dimethoate) was used as a reference item with a nominal dose of 10 µg dimethoate/bumblebee. The duration of the test was 48 hours with 50 replicates for the test concentrations and controls, 30 replicates for the toxic reference, each replicate consisting of 1 bumblebee. The assessment of mortality was performed after 4, 24 and 48 hours.

After start of exposure the test item stock solution (application solution) as well as the control solutions were analytically verified via LC-MS/MS.

HBZ10 does not cause adverse effects on *Bombus terrestris* after contact exposure. The contact LD₅₀ value (48 h) was estimated to be > 0.7816 mg product/bumblebee.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: water / Triton X-100 (0.1%) Toxic reference item: Danadim progress (38.2% dimethoate)

Test System

Species	<i>Bombus terrestris</i>
Age	Adult worker bumblebees
Source	Biobest Group N.V. (Belgium); delivered by Katz Biotech AG, An der Birkenpfuhlheide 10, 15837 Baruth, Germany. The colonies were kept under controlled climatic conditions (22 to 31°C, relative humidity 50 to 77%) for 7 days in the laboratory.
Acclimatisation period	Young worker bees were collected from honey frames in the morning of the application day. The bees were adapted to test conditions for ≥ 8 hours.
Food	The bumblebees were fed with 50% sucrose solution <i>ad libitum</i> .

Test Conditions

Temperature	23 - 27°C
Relative Humidity	55 – 65%
Photoperiod	Darkness, except during observation

Study Design and Methods

In-life dates	28.10.2020 – 30.10.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	48 hours
Test concentrations	0.7816 mg product/bbee
Test vessels	NICOT® queen breeding cages

Treatment	<p>Bumblebees with homogenous body size were used for the study. Each bumblebee was weighed before the start of exposure (day -2) and randomly allocated to the treatments. Each treatment included bumblebees from all 3 colonies.</p> <p>The final study used 0.7816 mg product/bumblebee. The test comprised 1 dose level of test item, 1 treatment of the toxic reference and two controls, each test item and controls were replicated 50 times, the toxic reference consisted of 30 replicates. Each replicate consisted of 1 bumblebee.</p> <p>Test item, controls and reference item were applied onto the thorax of each bumblebee. A drop of 2 µL was applied with a micro piston pipette after paralysation of the bumblebee with CO₂ (approximately 5 sec.).</p> <p>Danadim Progress (38.2% dimethoate) was used as a reference item with nominal dose of 10 µg dimethoate/bee. Water and Triton X-100 (0.1%) were used as controls</p>
Observations	Mortality and sublethal effects (affected, moribund) were determined after 4, 24 and 48 h.
Analytical verification	The concentrations of the test item HBZ10 were determined by analysis of the test item stock solution (application solution) and control solutions via LC MS/MS. The analytical method was validated based on SANCO/3029/99 rev. 4.
Statistics	No statistical analysis was performed, since mortality in the controls and limit test item treatment was identical.

RESULTS AND DISCUSSIONS

Validity criteria

The average mortality for the total number of controls must not exceed 10% (actual: 0% for water and solvent control) at the end of the test. The mean mortality in the toxic reference treatment must exceed 50% (actual: 100%) at the end of the test.

Analytical verification

The concentrations of the test item Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) were determined by analysis of the test item stock solution (application solution) and control solutions (water and 0.1% Triton X-100) via LC MS/MS.

The measured concentration was 120% (Phenmedipham) and 96% (Ethofumesate), active substances of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10), indicating the correct preparation of the test item solution. Biological results are based on nominal test item concentrations.

Biological results

In the control groups either treated with deionised water or 0.1% Triton X-100 solution, no mortality was observed after 48 hours. In the test item treatment group, no mortality was observed after application of 0.7816 mg product/bumblebee to the thorax. The LD₅₀ (48 h) was estimated to be > 0.7816 mg product/bumblebee.

Table A 2.3.1.1.2.2-1 Mortality of bumblebees exposed to HBZ10 for 48 hours

Treatment group	Test dose	Testing period		
		4 hours	24 hours	48 hours
		Mean mortality [%]	Mean mortality [%]	Mean mortality [%]
Control	Deionised water	0.0	0.0	0.0
	0.1% Triton X-100	0.0	0.0	0.0
HBZ10 [mg product/bee]	0.7816	0.0	0.0	0.0
Reference item [µg a.s./bee]	10	0.0	100	-

* Significant difference compared to control (Dunn's test; $\alpha = 0.05$)

CONCLUSION

The acute contact toxicity of HBZ10 was tested on bumblebees under laboratory conditions over 48 hours. The contact LD₅₀ after 48 hours was estimated to be > 0.7816 mg product/bumblebee (corresponding to 100 µg Ethofumesate/bumblebee and 101 µg Phenmedipham/bumblebee).

A 2.3.1.2 KCP 10.3.1.2 Chronic toxicity to bees

A 2.3.1.2.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 245 with a minor deviation.</p> <p>It was noted that the analytical measurements were done only on the lowest concentration of the feeding solution and the stock solution; no measurements were done on the highest concentration of the feeding solution. However, the stock solution and the feeding solutions were prepared fresh every day and the analytical measurements carried out twice during the study indicated that the concentrations of both active substances were maintained at 80-120 % of the nominal concentration. Therefore, this deviation is considered to be acceptable.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>LDD₅₀ = 29.6 µg product/bee/day NOEDD = 24.2 µg product/bee/day</p> <p>LC₅₀ = 1.64 g product/kg food NOEC = 1.12 g product/kg food</p>
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Reference:	KCP 10.3.1.2/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Chronic oral toxicity test on the Honeybee <i>Apis mellifera</i> (Hymenoptera, Apidae), Klix, V., 2021e, report No SO20047 / IBC18743
Guideline(s):	OECD 245 (2017)
Deviations:	Minor (see the commenting box above) No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

In a 10-day chronic toxicity feeding test, 2 days old worker honeybees (*Apis mellifera* L. subspecies *carnica*) were exposed to a daily application of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) diluted in the bee food (50% w/v aqueous sucrose solution). The chronic toxicity of the test item was determined at nominal doses of 1.12, 2.57, 5.91, 13.6 and 31.3 g product/kg food. Effective doses were 24.2, 39.2, 48.9, 120 and 185 µg consumed product/bee/day.

Additionally, honeybees were treated with Danadim Progress as toxic standard at a nominal dose of 0.8 mg a.s./kg food. Untreated 50% (w/v) aqueous sucrose solution served as control.

The LDD₅₀ value was determined to be 29.6 µg consumed product/bee/day and the LC₅₀ to be 1.64 g product/kg food, respectively. The NOEDD was determined to be 24.2 µg consumed product/bee/day and the NOEC to be 1.12 g product/kg food, respectively.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: 50% aqueous sucrose solution Toxic reference item: Danadim progress (38.2% dimethoate)

Test System

Species	<i>Apis mellifera</i> L. (Hymenoptera, Apidae), subspecies <i>A. m. carnica</i> Pollm.
Age	Young worker bees (max. 2 days old)
Source	Queen-right, healthy colony of the test facility.
Pre-treatment culturing conditions	4 days before the start of exposure, two brood combs with sealed brood and without bees were taken out from a hive and kept under controlled climatic conditions (about 33°C and 50 - 65 relative humidity) in a glass box (40 × 22.5 × 27.5 cm). The hatching was observed daily to obtain young worker bees which were maximum 2 days old at test start.
Food	50% (w/v) sucrose solution <i>ad libitum</i> .

Test Conditions

Temperature	30.8 - 33.3°C*
Relative Humidity	39.8 - 73.7%*
	* During observation and maintenance periods temperature and especially humidity differed for ≤ 2 hours.
Photoperiod	Darkness, except during observation

Study Design and Methods

In-life dates	25.08.2020 – 04.09.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	10 days
Test concentrations	1.12, 2.57, 5.91, 13.6, 31.3 g product/kg food, equivalent to 0.287, 0.658, 1.51, 3.48, 8.01 g a.s./kg food (as sum of both active substances based on the respective nominal content of a.s. in the formulated product); 0.143 – 0.329 – 0.756 – 1.74 – 4.0 g Ethofumesate/kg food; 0.144 – 0.332 – 0.762 – 1.75 – 4.03 g Phenmedipham/kg food
Test vessels	Stainless steel cages, size 102 mm × 56 mm × 86 mm with holes punched into the bottom plate and a glass plate at front.

Treatment	<p>The application of the respective item dose took place daily for a period of successional 10 days. Test solutions were freshly prepared every day right before administration of food.</p> <p><u>Test item:</u> 1.12, 2.57, 5.91, 13.6 and 31.3 g product/kg food (applied) 24.2, 39.2, 48.9, 120 and 185 µg product/bee/day (consumed)</p> <p><u>Control:</u> 50% (w/v) aqueous sucrose solution</p> <p><u>Reference:</u> 0.8 mg dimethoate/kg food (applied) 12.9 µg dimethoate/bee/day (consumed)</p> <p>Five replicates for the control and three replicates for the test item concentrations and the reference item concentration, each containing 10 bees, were tested.</p>
Observations	<p>Test item uptake was determined every day (1-10) by weighing the feeding syringes. Mortality and abnormal behaviour were determined every day, too (1-10). Additionally, 3 replicates without bees were tested under the same test conditions to determine the evaporation of the 50 % feeding solution.</p> <p>The room temperature and humidity were continuously recorded with a hygro-thermograph (day 0 to day 10) and every hour with a datalogger (day 0 to day 10).</p>
Analytical verification	<p>During the experimental phase, the concentration of the test item (both a.s.) was confirmed twice by analysis of the test item stock solution (freshly prepared, on day 0 and 6). At the same time, the concentration of the test item was verified in the freshly prepared lowest test item solution and the control. The samples were analysed with a LC-MS/MS method.</p> <p>The analytical method was validated based on SANCO/3029/99 rev. 4.</p>
Statistics	<p>Significant analysis of mortality data in comparison with the control group was conducted with a Step-Down Cochran-Armitage Test Procedure.</p> <p>Significant analysis of daily food consumption data in comparison with the control group was conducted with a Williams Multiple Sequential t-test Procedure.</p> <p>The LDDx and LCx values were calculated by Probit analysis using linear maximum likelihood regression.</p> <p>All evaluations were done based on the concentrations g Ethofumesate/kg food or µg Ethofumesate/bee/day. Effect levels based on g test item/kg food and µg test item/bee/day were calculated from the Ethofumesate levels.</p>

RESULTS AND DISCUSSIONS

Validity criteria

The average mortality in the untreated controls is $\leq 15\%$ (actual: 12%) at the end of the test.

The mortality in the toxic reference item group is $\geq 50\%$ (actual: 100%) at the end of the test.

Analytical results

The stock solution and the lowest dilution from day 0 and day 6 were analytically verified. The measured concentrations of Phenmedipham and Ethofumesate in the stock solutions were between 97% to 107%. In the lowest test item dilution, the measured concentrations of Phenmedipham and Ethofumesate ranged from 64% to 112%. Since the mean measured concentration in the lowest test item concentration (88%) is inside the nominal range (80 - 120%), the preparation is considered correct for the respective application day.

Biological results

After 10 days a mean mortality of 12.0% was observed in control group. Taking into account the actual food uptake and the evaporated amount of feeding solution, the bees effectively consumed doses of 24.2, 39.2, 48.9, 120 and 185 µg product/bee/day which caused mortalities of 23.3, 80.0, 100, 100 and 100%,

respectively after 10 days. Mortalities in the treatment groups at 39.2, 48.9, 120 and 185 µg consumed product/bee/day were statistically significantly increased compared to the control group. The reference item tested in the study was 0.8 mg a.s./kg food (actual consumption on average per day: 12.9 µg a.s./bee), which caused a mean mortality of 100.0%.

Table A 2.3.1.2.1-1 Mean mortality and food consumption of bees in the chronic toxicity feeding test after 10 days

Treatment group	Concentration	Mean Daily food consumption per bee	Mean Test item uptake per bee	After 10 days Mean mortality ± SD	
	[g product/kg food]	[mg product/bee/day] ± SD	[µg product/bee/day] ± SD	Absolute [%] ± SD	Corrected [%]
Control	-	24.3 ± 5.98	-	12.0 ± 8.37	-
HBZ10	1.12	21.6 ± 11.2	24.2 ± 12.4	23.3 ± 15.3	12.9
	2.57	15.2 ± 9.64	39.2* ± 24.8	80.0* ± 10.0	77.3
	5.91	8.27 ± 2.27	48.9* ± 13.4	100*	100
	13.6	8.82 ± 6.94	120* ± 94.7	100*	100
	31.3	5.91 ± 5.87	185* ± 184	100*	100
	[mg a.s./kg food]		[ng a.s./bee/day]		
Reference item	0.8	16.2 ± 8.38	12.9 ± 6.71	100	100

* Significant difference compared to control (mortality: Step-Down Cochran-Armitage Test Procedure, $\alpha = 0.05$; food consumption: Williams Multiple Sequential t-test Procedure)

Table A 2.3.1.2.1-2 Endpoints determined after 10 days in a chronic toxicity feeding test with HBZ10

	Endpoints	10 d
Test item doses	LDD ₅₀ [µg consumed product/bee/day] ¹	29.6 (25.8 - 31.3)
	NOEDD [µg consumed product/bee/day] ²	24.2
Test item concentrations	LC ₅₀ [g product/kg food] ¹	1.64 (1.33 - 1.96)
	NOEC [g product/kg food] ²	1.12

¹ Median lethal dietary dose/concentration (95% cl lower-upper) were calculated by Probit analysis using linear maximum likelihood regression

² No observed effect dietary dose/concentration were calculated using Step-down Cochran-Armitage Test Procedure

CONCLUSION

The chronic oral toxicity of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on young adult honeybees (*Apis mellifera* L.) was investigated in a 10-day chronic feeding study under laboratory conditions.

The LDD₅₀ value was determined to be 29.6 µg consumed product/bee/day (corresponding to 7.57 µg consumed a.s./bee/day as sum of both active substances) and the LC₅₀ to be 1.64 g product/kg food (corresponding to 0.420 g a.s./kg food as sum of both active substances).

The NOEDD was determined to be 24.2 µg consumed product/bee/day (corresponding to 6.19 µg consumed a.s./bee/day as sum of both active substances).

A 2.3.1.3 KCP 10.3.1.3 Effects on honeybee development and other honey bee life stages

A 2.3.1.3.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 239 with minor deviations.</p> <p>It was stated in the report that the study was modified from the guidance due to new research results (as described in Pollinator Research Task Force, LLC and Schmehl et. al, section 14). The following modifications increased the survival of the larva:</p> <ul style="list-style-type: none"> • No dental rolls and no sterilising solution were filled into the wells underneath the grafting cells in the 48-well plate. • The water content of diet A and B was increased. • Between day 7 to 8 the larvae were transferred to the pupal plates. • The adult emergence was determined daily from day 18 to 20. The adult bees were removed from the plates. <p>It was determined that these deviations had no impact on quality and integrity of the study.</p>
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	<p>It was also noted that the study was finished after 20 days, because all bees had hatched or had died. Temperature on days 1-8 was 33.8°C which was slightly lower than the recommended 34°C. Relative humidity observed below the recommendations according to guideline was caused by obligatory measurements and observations of the test organisms (≤ 2 hours) and hence was not preventable. These deviations are also considered to have had no impact on the outcome of the study.</p> <p>The analytical measurements confirmed that the concentrations of both active substances were within 80 – 120 % of nominal, therefore the endpoints can be expressed as nominal concentrations.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>EC₅₀ = 133 mg test item/kg food (corresponding to 17.0 mg Ethofumesate/kg food and 17.1 mg Phenmedipham/kg)</p> <p>NOEC = 62.8 mg test item/kg food (corresponding to 8.02 mg Ethofumesate/kg food and Phenmedipham/kg food)</p> <p>ED₅₀ = 20.4 µg test item/larva (corresponding to 2.61 µg Ethofumesate/larva and 2.63 µg Phenmedipham/larva)</p> <p>NOED = 9.62 µg test item/larva (corresponding to 1.23 µg Ethofumesate/larva and 1.24 µg Phenmedipham/larva)</p>
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Reference:	KCP 10.3.1.3/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Honeybee (Apis mellifera) larval toxicity test, repeated exposure, Klix, V., 2021f, report no SO20048 / IBL18743
Guideline(s):	OECD GD 239 (2016) (ENV/JM/MONO(2016)34)
Deviations:	<p>Minor (see the commenting box above) Yes (The study was modified from the guidance as follows, due to new research results (see Pollinator Research Task Force, LLC and Schmehl et. al, section 14). These modifications increased the survival of the larva:</p> <ul style="list-style-type: none"> • No dental rolls and no sterilising solution were filled into the wells underneath the grafting cells in the 48 well plate. • The water content of diet A and B was increased. • Between day 7 to 8 the larvae were transferred to the pupal plates. • The adult emergence was determined daily from day 18 to 20. The adult bees were removed from the plates.) <p>These deviations had no impact on quality and integrity of the study.</p>
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

In a feeding toxicity test with repeated exposure, honeybee larvae were exposed to Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) diluted in the larval food. The toxicity of the test item was determined at total doses of 9.62, 29.0, 86.9, 261, 783 µg product/larva (~~corresponding to 2.46, 7.42, 22.2, 66.8, 200 µg a.s./larva as sum of both active substances,~~ equivalent to 1.23, 3.70, 11.1, 33.3, 100 µg Ethofumesate/larva and 1.25, 3.74, 11.2, 33.7, 101 µg Phenmedipham/larva). The concentrations of test item in the diet were 62.8, 189, 565, 1700, 5090 mg product/kg diet, corresponding to 8.02, 24.1, 72.2, 217, 650 mg Ethofumesate/kg diet and 8.08, 24.3, 72.8, 219, 655 mg Phenmedipham/kg diet. Dechlorinated water (10% in the diet) was used as control and Dimethoate was used as reference item (7.39 µg a.s./larva corresponding to 48 mg a.s./kg diet).

36 larvae, divided into 3 replicates from 3 different colonies, were used for all treatments. Daily, between day 4 to day 8, the mortality of the larvae was recorded, and the uneaten food was documented qualitatively. On day 15 the number of pupae were determined and from day 18 to day 20 the hatched adult bees were counted.

In the test item groups, larval mortalities at day 8 ranged between 2.78% and 100%. Pupal mortalities on day 20 ranged between 39.7% and 100% in the test item treatment groups. The emergence rate on day 20 ranged between 0.0% and 61.1%.

The ED₅₀ (successful adult emergence up to day 20) was calculated to be 20.4 µg product/larva (corresponding to 5.22 µg a.s./larva as sum of both active substances, 2.61 µg Ethofumesate/larva and 2.63 µg Phenmedipham/larva).

The EC₅₀ for emergence rate was calculated to be 133 mg product/kg food (corresponding to 34.0 mg a.s./larva as sum of both active substances, 17.0 mg Ethofumesate/kg food and 17.1 mg Phenmedipham/kg food).

The respective NOED for emergence rate was determined to be 9.62 µg product/larva (corresponding to 2.46 µg a.s./larva as sum of both active substances, 1.23 µg Ethofumesate/larva and 1.24 µg Phenmedipham/larva) and the corresponding NOEC for emergence rate was determined to be 62.8 mg product/kg food (8.02 mg Ethofumesate/kg food and 8.08 mg Phenmedipham/kg food).

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Reference toxicant	Control: untreated larval diet Toxic reference item: Dimethoate tech.

Test System

Species	<i>Apis mellifera</i> L. (Hymenoptera, Apidae), subspecies <i>A. m. carnica</i> Pollm.
Age	One days old, first instar larvae
Origin	Queen-right, healthy and untreated colonies of the test facility. First instar synchronised larvae were collected from a comb and reared in the laboratory. The used beehives are not treated with chemical substances (such as against Varroa mites) for at least 4 weeks.
Methods for producing the larvae	The larvae were taken from 3 different colonies. The queens of the bee colonies to be used were confined in exclusion cages containing an empty comb within their own colony for about 24 hours on day -3. After release of the queen from the cage, the comb was checked for presence of eggs. Then the breeding combs remained in the hive close to the brood nest until grafting.
Food and water	A sufficient amount of food was present in the beehives. The diets were prepared freshly directly before the test start and stored in the fridge by 6 ± 2°C (not frozen). The sugar solutions were mixed with royal jelly every day before each feeding occasion. Each larva was fed separately using a sterile pipette. The food drop was placed next to the larvae to avoid drowning. Before feeding, the final diets were warmed up to 34.5°C. During the process the culture plate in operation was placed on a warming plate.

Test Conditions

Temperature	D1 - D7: 33.8 - 34.8°C D7 - D15: 34.1 - 34.4°C D15 - D20: 34.0 - 34.4°C
Relative humidity	D1 - D7: 45.9* - 99.9% D7 - D15: 47.7* - 77.0% D15 - D20: 61.9 – 76.3% * Relative humidity observed below the recommendations according to OECD GD 239 is caused by obligatory measurements and observations of the test organisms (≤ 2 hours) and hence are not preventable. This has no impact on the outcome of the study.
Illumination:	constant darkness throughout the test
Study Design and Methods	
In-life dates	19.08.2020 – 05.09.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	20 days
Treatment concentrations	9.62, 29.0, 86.9, 261, 783 µg product/larva, equivalent to 2.46, 7.42, 22.2, 66.8, 200 µg a.s./larva as sum of both active substances (based on nominal content in the formulated product) 62.8, 189, 565, 1700, 5090 mg product/kg diet, equivalent to 16.1, 48.4, 144.6, 435.0, 1302.5 µg a.s./larva as sum of both active substances (based on nominal content in the formulated product)
Test design	On day 1 the comb with first instar larvae were taken to a climate chamber. The combs were kept covered to protect them from ventilation and drying. A grafting tool was used to collect the larvae from the comb. Each larva was placed carefully on the surface of the food (Diet A) in 48 well plates. The plates with the food were warmed in the incubator before grafting. An excess of larvae was grafted. After grafting, the plates were placed into a desiccator inside an incubator to provide stable climatic conditions. On day 3 the surviving larvae were randomized before application. Uniform larvae were selected from the acclimatisation plates to the larval plates for control, reference item and each test item treatment. On 4 successive days (day 3 to day 6) the larvae were chronically exposed to HBZ10 diluted in the larvae's food (aqueous sugar solution mixed with royal jelly). After the applications, no additional feedings of the larvae took place.
Replicates	3 per treatment group, control and reference item with 12 larvae/replicate
Observations	The mortality of the larvae was assessed daily from day 3 to 8, dead larvae were removed. On day 4 to 8, uneaten food was documented qualitatively. The larvae were transferred to the pupal plate between day 7 to 9 if the bees consumed the diet completely. On day 15 the number of pupae were determined. Dead pupae/larva were removed. From day 18 to 20 the number of hatched adult bees was counted. Abnormal behaviour or deformations were documented in the raw data and given in the report. During feeding and observation, the larvae were placed on a warming plate maintained at 34 - 35°C. The study was finished after 20 days, because all bees had hatched. The test ended on day 20 (final assessment) and the bees which emerged successfully were counted. Lifeless pupae and bees or those, which were unable to leave the breeding cups on their own accord, were marked as dead.

Analysis of test item solutions	The highest and lowest test item stock solutions and the control were analytically verified via LC-MS/MS on each feeding day (day 3 to 6). The analytical method was validated based on SANCO/3029/99 rev. 4.
Statistics	For larval mortality and emergence rate a Step-Down Cochran-Armitage Test Procedure was carried out. A Qualitative Trend Analysis by Contrasts and a Tarone's Test Procedure were run before. For pupal mortality a Chi2 2x2 Table Test with Bonferroni Correction was carried out. A Qualitative Trend Analysis by Contrasts was run before. ECx and EDx values were calculated using a probit analysis using maximum linear likelihood regression for larval mortality, pupal mortality and emergence rate. Confidence intervals could not be determined. All evaluations were done based on the values for mg Ethofumesate/g diet or µg Ethofumesate/larva. Other units (i.e. mg test item/g diet) were obtained by calculation from the Ethofumesate values.

RESULTS AND DISCUSSIONS

Validity criteria

The cumulative larval mortality in the control from day 3 to day 8 should be $\leq 15\%$ (actual: 2.78%) across all replicates.

The adult emergence rate in the control on day 20 should be $\geq 70\%$ (actual: 72.2%) across all replicates.

The larval mortality in the toxic reference item should be $\geq 50\%$ (actual: 100%) on day 8 across all replicates.

Analytical results

The concentrations of the test item Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) were determined by analysis of the highest and lowest test item stock solution and control on each feeding day (days 3 -6) via LC-MS/MS. The recoveries of Ethofumesate in the stock solutions ranged between 89% and 110% of the nominal concentration. The recoveries of Phenmedipham in the stock solutions ranged between 91% and 112% of the nominal concentration. Thus, the concentration of both a.s. were in the nominal range of 80 – 120 %. The recoveries indicate the correct preparation of the feeding solutions.

Biological results

Cumulative mortality

On day 8, larval mortality of 2.78% was observed in the control. Pupal mortality (between day 8 and day 20) was 28.8% in the control. The control group showed a mean emergence rate of 72.2% on D20.

In the test item groups, larval mortalities at day 8 ranged between 2.78% and 100%. Pupal mortalities (between day 8 and day 20) ranged between 39.7% and 100% in the test item treatment groups. The mean emergence rate on day 20 ranged between 0.0 and 61.1%.

On day 8, a statistically significant mortality compared to the control was observed in the test item treatments of 86.9, 261, 783 µg product/larva (corresponding to 22.2, 66.8, 200 µg a.s./larva as sum of both active substances; Step-Down Cochran-Armitage Test Procedure).

On day 15 the pupal mortality was determined. The number of pupa and the number of dead larvae were observed. In the control the pupal mortality on day 20 was 28.8%. In the test item treatments, the pupal mortality ranged between 39.7 to 93.5% (treatments where no larvae were alive on day 8 were not taken into account for determination of pupal mortality). A statistically significant effect was observed in the test item treatment 86.9 783 µg product/larva (corresponding to 22.2 µg a.s./larva as sum of both active substances; Chi2 2x2 Table Test with Bonferroni Correction).

Adult emergence success:

Between day 18 and day 20 the adult bees hatched. In the control 72.2% of the introduced larvae hatched to adult bees. In the test item treatments, the emergence rate ranged between 16.7% - 61.1%. A statistically significantly effect was observed in the test item treatments 29.0, 86.9, 261, 783 µg product/larva (corresponding to 7.42, 22.2, 66.8, 200 µg a.s./larva as sum of both active substances; Step-Down Cochran-Armitage Test Procedure).

Other observations

No sublethal effects were observed during larval stage. No sublethal effects were observed during pupation and emergence stage.

Table A 2.3.1.3.1-1 Cumulated mortality and emergence rate of larvae in the chronic toxicity test

Treatment group	Dose	Concentration	On day 8	On day 20	
			Mean larval mortality	Pupal mortality Day 8 – day 20	Adult emergence
	[µg product/larva]	[mg product/kg food]	[%]	[%]	[%]
Control	-	-	2.78	28.8	72.2
Test item	9.62	62.8	2.78	39.7	61.1
	29.0	189	8.33	52.1	52.8*
	86.9	565	11.1	93.5	16.7*
	261	1700	100	100#	0*
	783	5090	100	100#	0*
	[µg a.s./larva]	[mg a.s./kg food]			
Reference	7.39	48	100	-	-

Results are averages based on 3 replicates, containing 12 larvae each; all bees were emerged after 20 days

* Statistically significant if compared to the control (Step-down Cochran-Armitage Test)

No living larvae were found on day 8. Pupal mortality is considered to be 100 % and emergence rate is 0 %.

Table A 2.3.1.3.1-2 Calculated endpoints of the repeated exposure larvae toxicity test

Treatment	Endpoint: Successful adult emergence	20 d*
Test item doses	ED ₅₀ [µg product/larva] ²	20.4
	NOED [µg product/larva] ¹	9.62
Test item concentrations	EC ₅₀ [mg product/kg food] ²	133
	NOEC [mg product/kg food] ¹	62.8

¹ Step-down Cochran-Armitage Test

² Probit analysis using linear max. likelihood regression

*All bees were emerged after 20 days

CONCLUSION

In a repeated exposure larval toxicity study with HBZ10, the ED₅₀ (successful adult emergence up to day 20) was calculated to be 20.4 µg product/larva (corresponding to 5.22 µg a.s./larva as sum of both active substances).

The EC₅₀ was calculated to be 133 mg product/kg food (corresponding to 34.0 mg a.s./larva as sum of both active substances).

The respective NOED was determined to be 9.62 µg product/larva (corresponding to 2.46 µg a.s./larva as sum of both active substances).

A 2.3.1.4 KCP 10.3.1.4 Sub-lethal effects

No new study is submitted.

A 2.3.1.5 KCP 10.3.1.5 Cage and tunnel tests

No new study is submitted.

A 2.3.1.6 KCP 10.3.1.6 Field tests with honeybees

No new study is submitted.

A 2.3.2 KCP 10.3.2 Effects on arthropods other than bees

A 2.3.2.1 KCP 10.3.2.1 Standard laboratory testing for non-target arthropods

A 2.3.2.1.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with the respective guideline with minor deviations.</p> <p>It was noted that the wasps were fed with a mixture of honey and water in a ratio of 1:6 v/v instead of 1:3 v/v in order to ensure a good development of the wasps. This deviation is considered to have no impact on the outcome of the study since all the validity criteria were met.</p> <p>Reproduction assessment was not carried out in this study.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>LR₅₀ = 0.356 L product/ha</p>
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Reference:	KCP 10.3.2.1/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Effects on the parasitic wasp <i>Aphidius rhopalosiphi</i> (Hymenoptera: Braconidae) in a glass plate laboratory test, Klix, V., 2021g, report No SO20131 / IWA18743
Guideline(s):	Mead-Briggs et al (2000)
Deviations:	<p>Minor (see the commenting box above) The study was conducted with the following deviations from the guideline:</p> <ul style="list-style-type: none"> The wasps were fed with a honey solution in a ratio of 1:6 v/v, instead of 1:3 v/v. This should ensure a good development of the wasps. No reproduction phase for the surviving wasps after 48 hours was carried out. The study is used to determine the LR₅₀ for consecutive extended laboratory studies. <p>These deviations had no impact on quality and integrity of the study.</p>
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the survival of *Aphidius rhopalosiphi* exposed to the test item were determined. All treatments were applied at an application rate of 200 L/ha to glass plates. Nominal treatment rates were 0.0707, 0.177, 0.442, 1.10, 2.76 L product/ha, corresponding to 8.83, 22.1, 55.2, 138, 345 g Ethofumesate/ha and 8.90, 22.3, 55.6, 139, 348 g Phenmedipham/ha. A toxic reference and an untreated control were included in the test. Survival of the wasps was determined after 2, 24 and 48 hours.

Under worst case laboratory test conditions, the 48-h LR₅₀ of HBZ10 to the parasitic wasp, *Aphidius rhopalosiphi*, was determined as 0.356 L product/ha.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A

Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Danadim progress (38.2% dimethoate)
Test System	
Species	<i>Aphidius rhopalosiphi</i> (Hymenoptera: Braconidae)
Age	Adults (not older than 48 hours)
Source	Katz Biotech Ag, An der Birkenpfehlheide 10, D-15837 Baruth, Germany
Acclimatisation period	Approximately 2 hours under test conditions
Food	The hatched wasps were fed with a mixture of honey and dechlorinated water (1:6 v/v).
Test Conditions	
Temperature	18.3 - 21.9°C
Humidity	60.0 - 76.7%
Photoperiod	16 h light/8 h dark
Light intensity	1304 ± 333 lux
Study Design and Methods	
In-life dates	14.07.2020 – 16.07.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	48 h
Test concentrations	0.0707, 0.177, 0.442, 1.10, 2.76 L product/ha
Test vessels / Exposure unit	Glass plates
Treatment	<i>Aphidius rhopalosiphi</i> were exposed to dried residues of HBZ10 on glass plates for 48 hours. 0.0707, 0.177, 0.442, 1.10, 2.76 L product/ha were diluted in demineralised water to give a final application volume of 200 L/ha. Danadim progress at 0.3 mL product/ha in 200 L water was used as toxic reference and deionised water as control. 5 replicates per control and 4 replicates per test and reference item rate were used in the test. 10 adult wasps (5 females and 5 males) were used for each replicate of the control, test item and reference item. A total of 50 adults per control and a total of 40 adults for each test and reference item treatment were tested.
Observations	Observations of mortality were recorded approximately 2, 24 and 48 hours after test initiation. The number of wasps alive, affected, moribund and dead was recorded.
Statistics	Mortality was defined as the sum of the number of moribund, not found and dead wasps. Mortality was corrected according to Abbott and improvements by Schneider-Orelli. The Multiple Comparisons versus Control Group (Dunn's Method, $\alpha=0.05$) was carried out to determine statistically significant differences compared to the control. A Normality Test following Kolmogorov-Smirnov and a Kruskal-Wallis One Way Analysis of Variance on Ranks were run before. The LR ₅₀ was calculated by sigmoidal dose-response (variable slope).

RESULTS AND DISCUSSIONS

Validity criteria

Control mortality during the first 48 hours should not exceed 13% (actual mortality of 4.0%), mortality in the reference treatment after 24 hours should be more than 75% (actual mortality 100.0%).

Biological results

After application of the test item, the treated glass plates showed concentration dependent clear residues. In the lowest test item rate of 0.0707 L product/ha no residues were observed.

After 48 h there was 4.0% mortality in the control and 2.50% - 100% mortality in all test item treatment groups. The highest test item treatment of 2.76 L product/ha was excluded from the final statistical evaluation but was found to be significantly different from the control in a preliminary evaluation (documented in the raw data, not given in the report).

In the toxic reference treatment, 100.0% mortality was observed at 48 h. The 48 h LR₅₀ for HBZ10 was determined to be 0.356 L product/ha.

Table A 2.3.2.1.1-1 Effects of HBZ10 on mortality of *Aphidius rhopalosiphi*

Treatment [L product/ha]	Number of wasps introduced	Number of wasps alive after 48 h	Mortality after 48 h [%]	Mortality corr. ¹ [%]
Control	50	48	4.0	--
0.0707	40	39	2.50	-1.56
0.177	40	36	10.5	6.25
0.442	40	4*	90.0*	89.6
1.10	40	40*	100*	100
2.76	40	40*	100*	100
Toxic reference	40	40	100	100

¹ Mortality corrected according to Abbott (Abbott, 1925)

* Statistically significant compared to the control (Dunn's Method)

CONCLUSION

Under worst case laboratory conditions, the LR₅₀ for HBZ10 was determined to be 0.356 L product/ha (95% confidence limits: 0.319 - 0.395 L product/ha) in 200 L water/ha.

A 2.3.2.1.2 Study 2

Comments of zRMS:	<p>The study was conducted in line with the respective guideline with minor deviations.</p> <p>It was noted that the relative humidity exceeded the recommended maximum value of 90 % for almost the whole duration of the exposure with the exception of 13 consecutive hours. However, since all the validity criteria were met, this deviation is considered to have no impact on the outcome of the study.</p> <p>Reproduction assessment was not carried out in this study.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>LR₅₀ = 0.788 L product/ha (corresponding to 98.4 g Ethofumesate/ha and 99.5 g Phenmedipham/ha)</p>
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Reference:	KCP 10.3.2.1/02
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): A glass plate laboratory study with the predatory mite <i>Typhlodromus pyri</i> (Acari: Phytoseiidae), Klix, V., 2021h, report No SO20132 / IRL18743
Guideline(s):	Blümel et al (2000)
Deviations:	Minor (see the commenting box above) The study was conducted with the following deviations from the guideline: – No reproduction phase for the surviving wasps after 7 days was carried out. The study is used to determine the LR₅₀ for consecutive extended laboratory studies. – The humidity during the exposure phase was > 90% during almost the whole duration, except 13 non-consecutive hours. These deviations had no impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the survival of *Typhlodromus pyri* exposed to the test item were determined. All treatments were applied at an application rate of 200 L/ha to glass plates. Nominal treatment rates were 0.141, 0.353, 0.883, 2.21, 5.52 L product/ha, corresponding to 17.6, 44.1, 110, 276, 690 g Ethofumesate/ha and 17.8, 44.5, 111, 278, 696 g Phenmedipham/ha. A toxic reference and an untreated control were included in the test.

Under worst case laboratory test conditions, the 7-day LR₅₀ of HBZ10 to the predatory mite, *Typhlodromus pyri* was determined as 0.788 L product/ha.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Danadim progress (38.2% dimethoate)

Test System

Species	<i>Typhlodromus pyri</i> (Acari: Phytoseiidae)
Age	Protonymphs (0 - 24 hours old)
Source	Katz Biotech Ag, An der Birkenpfuhlheide 10, D-15837 Baruth, Germany
Acclimatisation period	The test organisms were received as eggs 3 days prior to test start and kept at the test facility at temperature of 19 to 25°C and a relative humidity of about 80%. The mean light intensity during those days was 644 ± 98.0 lux. The hatched mites were held under test conditions until the start of exposure.
Food	Apple pollen

Test Conditions

Temperature 24 - 25°C
Humidity 66% - 96% *

* The humidity during the exposure phase was > 90 % during almost the whole duration, except 13 non-consecutive hours. Relative humidity observed below the recommendations according to OECD GD-239 is caused by obligatory measurements and observations of the test organisms (≤ 2 hours) and hence are not preventable. This has no impact on the outcome of the study.

Photoperiod 16 h light/8 h dark
Light intensity 1158 \pm 171 lux

Study Design and Methods

In-life dates 02.11.2020 – 09.11.2020
Conducted at Noack Labororien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany

Test duration 7 days
Test concentrations 0.141, 0.353, 0.883, 2.21, 5.52 L product/ha

Test vessels / Exposure unit Glass plates

Treatment *Typhlodromus pyri* were exposed to dry residues of HBZ10 on glass plates for 7 days. 0.141, 0.353, 0.883, 2.21, 5.52 L product/ha were diluted in demineralised water to give a final application volume of 200 L/ha.

Danadim progress at 15 mL product/ha in 200 L water was used as toxic reference and deionised water as control.

Observations 100 protonymphs, divided in 5 replicates of 20 mites each, were used for the control and reference item treatments. 60 protonymphs divided in 3 replicates of 20 mites each were used for the test item treatments. Mortality and the number of escaped mites (trapped in the insect glue barrier, drowned in the water split or not found) were recorded on days 3 and 7. On day 7, the sex of surviving mites was determined.

Statistics Mortality was calculated by adding the number of escapees to the number of dead mites. Mortality was corrected according to Abbott and improvements by Schneider-Orelli. A Step-Down Cochran-Armitage Test Procedure ($\alpha=0.05$) was carried out to determine statistically significant differences compared to the control. A Qualitative Trend Analysis by Contrasts (Monotonicity of Rate/Response) and a Tarone's Test Procedure were run before.

The LR₅₀ was calculated by Probit analysis using linear max. likelihood regression. The confidence limits were determined according to Fieller's theorem.

RESULTS AND DISCUSSIONS

Validity criteria

The mortality in the control over the initial 7 days should be $\leq 20\%$ (actual mortality 3.0%), corrected mortality in the toxic reference group should be between 50 and 100% (actual corrected mortality 91.8%).

Biological results

After 7 days of exposure, observed mortality reached 3.0% in the control and 5.50 8.33 to 100% corrected mortality in the test item treatment groups. The LR₅₀ of HBZ10 was determined to be 0.788 L product/ha. There was 91.8% corrected mortality in the reference item group.

Table A 2.3.2.1.2-1 Effects of HBZ10 on mortality of *Typhlodromus pyri*

Treatment [L product/ha]	Mortality after 7 d (including escapees) [%]	Mortality corr. ¹ [%]	Escapees after 7 days [%]
Control	3.00	-	2.00
0.141	8.33	5.50	5.00
0.353	28.3	26.1*	25.0*
0.883	55.0	53.6*	51.7*
2.21	76.7	76.0*	53.3*
5.25	100	100*	73.3*
Reference substance	92.0	91.8	70.0

¹ Mortality corrected according to Abbott (Abbott, 1925); negative values indicate better survivorship compared to control

* Significantly different compared to control (Step-Down Cochran-Armitage Test Procedure, $\alpha = 0.05$)

CONCLUSION

Under worst case laboratory conditions, the LR₅₀ of HBZ10 was determined to be 0.788 L product/ha (95% confidence limits: 0.647 - 0.958 L product/ha) in 200 L water/ha.

A 2.3.2.2 KCP 10.3.2.2 Extended laboratory testing, aged residue studies with non-target arthropods

A 2.3.2.2.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with the respective guideline with minor deviations.</p> <p>It was noted that at the test start the barley plants were on average 9.3 cm, instead of 10 - 12 cm as recommended by the guideline. During phase 1 (mortality) the relative humidity was outside the specified range for about 3 h in total and the light intensity was too high, however, a high proportion of the wasps stayed on the plants in all treatments. All the validity criteria were met; therefore, it is considered that these deviations had no impact on the outcome of the study.</p> <p>Overall, the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>LR₅₀ > 5.52 L product/ha ER₅₀ > 5.52 L product/ha</p>
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Reference:	KCP 10.3.2.2/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Extended Laboratory Test on the parasitic wasp <i>Aphidius rhopalosiphi</i> , Exposed to Barley Plants (Hymenoptera: Braconidae), Maspohl, A.-K., 2021a, report No SO20512 / IWE18743
Guideline(s):	Mead-Briggs et al. (2009)
Deviations:	Minor (see the commenting box above) No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the mortality (phase 1) survival and reproduction (phase 2) of *Aphidius rhopalosiphi* exposed to the test item on barley plants were determined in an extended laboratory study. All treatments were applied at an application rate of 400 L/ha to detached bean leaves. Nominal treatment rates were 0.0681, 0.204, 0.613, 1.84, 5.52 L product/ha,

corresponding to 8.51, 25.5, 76.6, 230, 690 g Ethofumesate/ha and 8.58, 25.7, 77.2, 232, 696 g Phenmedipham/ha. A toxic reference (8 g a.i./ha) and an untreated control were included in the test. After exposure to dried residues of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) treatments for 48 hours, no mortalities were observed in the control. The mortality in test item treatments ranged between 0 to 10%. No statistically significant effect compared to the control could be observed. Therefore, the NOER was determined to be ≥ 5.52 L product/ha. The LR₅₀ value was determined to be > 5.52 L product/ha because no mortalities $> 50\%$ were observed in any of the test item rates. No abnormal behaviour (e.g. coordination problems) were observed in any test item treatments. No statistically significant effects on the reproduction rate of the parasitic wasp *Aphidius rhopalosiphi* were observed in all test item treatments. Therefore, the NOEC for reproduction was determined to be ≥ 5.52 L product/ha. The ER₅₀ value was determined to be > 5.52 L product/ha because no reduction of reproduction $> 50\%$ were observed in any test item treatments. All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Danadim progress (37.6% dimethoate)

Test System

Species	<i>Aphidius rhopalosiphi</i> (DeStefani-Perez) (Hymenoptera: Braconidae)
Age	Adults (not older than 48 hours)
Source	Katz Biotech Ag, An der Birkenpfuhlheide 10, D-15837 Baruth, Germany
Acclimatisation period	The test organisms were received as mummies and kept under controlled climatic conditions (18 - 19°C and 66 - 99% relative humidity, 754 \pm 72 lux) for 4 days.
Food	The hatched wasps were fed with a mixture of honey and dechlorinated water (1 :6 v/v)

Test Conditions

Temperature	19 – 21°C (phase 1); 18 – 22°C (phase 2)
Humidity	Acclimatisation , exposure period (phase 1): 65 – 94% * * The relative humidity was outside the specified range for about 3 h in total, respectively (not in series). According to the guideline deviations < 2 hours are not relevant.
Photoperiod	16 h light/8 h dark
Light intensity	Acclimatisation , exposure (phase 1), parasitisation period : 4800 \pm 980 lux* Post-parasitisation period (reproduction – phase 2): 2904 - 5751 lux * The light intensity was too high for the total phase 1. As a high proportion of the wasps stayed on the plants in all treatments, it is considered that the deviation has no impact on quality and integrity of the study.

Study Design and Methods

In-life dates	20.04.2021 – 04.05.2021
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany

Test duration	14 days
Test concentrations	0.0681, 0.204, 0.613, 1.84, 5.52 L product/ha
Test vessels / Exposure unit	Barley seedlings
Treatment	<p>Barley seedlings (8-10 plants, approx. 9.3 cm tall, at the 2nd leaf growth stage, BBCH 11-12) were sprayed about 120 min before application with 10% fructose solution (w/w) and were left to dry. The sugar solution provides foraging for the wasps being released to the plants. The soil in the plant pots was covered with dry quartz sand to create a uniform surface. Afterwards, the plants were sprayed with either control, test item or reference item solutions. After drying of the spray (approximately 1 h) the plants were enclosed with cylinders of clear acetate sheeting (9 cm diameter, 25 cm tall) and the wasps were introduced. The cylinders were closed at their top with fine-mesh nylon netting to prevent a build-up of pesticide vapour in the test units. Danadim Progress was used as toxic reference and deionised water as control. Six replicates were set up per treatment for the test item, control and toxic reference, each with 5 female parasitoids. <i>A. rhopalosiphi</i> were exposed to these dried residues on barley seedlings for 48 hours.</p> <p>Reproduction phase: 20 replicates were tested per control and test item treatment. One surviving female = one replicate. No reproduction test was carried out for the reference item treatment. Single surviving females were transferred to pots (\varnothing = 9cm) with seedling barley (ca. 10-15 plants, 8-15 cm tall). The plants were previously infested with > 100 aphids of <i>Rhopalosiphum padi</i> (adults and nymphs) and enclosed within cylinders of clear acetate sheeting (\varnothing = 9 cm, h = 25 cm), closed at its top with fine-mesh nylon netting. The females were removed after 24 hours and the aphid-infested plants left for further 13 - 14 days before the numbers of aphid mummies that had developed were assessed.</p>
Observations	<p>Observations of mortality were recorded approximately 2, 24 and 48 hours after test initiation. The number of parasitoids alive, affected, moribund and dead was recorded.</p> <p>To determine whether residues of the test item were repellent to the wasps, observations on the position of the individual insects were made during the initial 3 h after their release. Five separate observations were made at approximately 30-minute intervals starting approximately 30 minutes after the introduction of all wasps. Each wasp was recorded as being on the treated plants, on the walls of the test arena, and on the sand below the plants.</p> <p>Fecundity was determined by counting the number of aphid mummies 11-12 days after the 24 hours parasitisation period in all replicates where the females were alive.</p>

Statistics

Mortality: Multiple Sequentially-rejective Fisher Test after Bonferroni-Holm ($\alpha=0.05$) was carried out to determine statistically significant differences compared to the control. A Qualitative Trend Analysis by Contrasts (Monotonicity of Rate/Response) and a Tarone's Test Procedure were run before.

Repellency assessment (SigmaPlot): A Multiple Sequentially-rejective Welch-t-test after Bonferroni-Holm ($\alpha=0.05$) was carried out to determine statistically significant differences compared to the control. A Shapiro-Wilk's Test on Normal Distribution and an Levene's Test on Variance Homogeneity (with Residuals) were run at first.

Reproduction: A Dunnett's Multiple t-test Procedure ($\alpha=0.05$) was carried out to determine statistically significant differences compared to the control. A Shapiro-Wilk's Test on Normal Distribution and a Levene's Test on Variance Homogeneity (with Residuals) were run at first.

The software used to perform the statistical analysis was Toxrat, Professional, Version 3.3.0, Toxrat©Solutions GmbH.

RESULTS AND DISCUSSIONS

Validity criteria

The mean mortality (phase 1) in the control group after 48 h should be $\leq 10\%$ (actual mortality 0%), corrected mortality in the toxic reference group should be $> 50\%$ (actual mortality 100%). The mean number of mummies per female in the control group should be ≥ 5 mummies per female (actual: 29.3 mummies per female) and ≤ 2 females with no mummies (actual: 0 females with 0 mummies).

Biological results

Phase 1: Mortality, Behaviour and Repellency assessment

The mortality was determined after 2, 24 and 48 hours. After 48 hours, the mortality was 0% in the control. The mortality in the test item treatments ranged between 0% and 10.0%. No statistically significant effects compare to the control could be observed, therefore the NOEC for mortality was determined to be ≥ 5.52 L product/ha and the LOEC > 5.52 L product/ha. The LR₅₀ value was determined to be > 5.52 L product/ha because no mortality $> 50\%$ were observed in any test item rate.

No abnormal behaviour (e.g. coordination problems) was observed in any treatment group.

In the first 3 hours after insert of the wasps, on average of 50.8% (5.52 L product/ha) to 78.0% (0.204 L product/ha) of the wasps were settled on the plants. In the control treatment, 80.7% of the wasps settled on the plants. The effect was statistically significant compared to the control in the test item treatment 5.52 L product/ha. Only in the last observation period (2.5 hours after insert of the wasps in the test cylinder) a high proportion of the wasps avoided the plants and stayed on the cylinder in this test item treatment.

Phase 2: Reproduction

The reproduction rate (number of mummies) of the surviving females of phase 1 was determined on day 13 to 14.

The mean reproduction rate of the control was 29.0 mummies per female. The mean number of mummies in the test item treatments ranged between 21.9 - 35.6 mummies per female (for details see Table 17). No statistically significant effect compared to the control could be observed. Therefore, the NOEC for reproduction was determined to be ≥ 5.52 L product/ha, the LOEC > 5.52 L product/ha and the ER₅₀ value > 5.52 L product/ha.

Table A 2.3.2.2.1-1 Effects of HBZ10 on mortality and reproduction of *Aphidius rhopalosiphi*

Treatment [L product/ha]	Mortality [%] ± SD	Corrected mortality* [%]	Reproduction [mummies/females] ± SD	Inhibition of reproduction [%]
Control	0 ± 0	-	29.3 ± 13.6	-
0.0681	3.33 ± 8.16	3.33	31.2 ± 11.8	-6.67
0.204	3.33 ± 8.16	3.33	35.6 ± 20.0	-21.7
0.613	0 ± 0	0	35.0 ± 18.3	-19.5
1.84	0 ± 0	0	21.9 ± 13.4	25.1
5.52	10.0 ± 16.7	10.0	27.8 ± 12.4	5.13
Reference substance	100 ± 0	100	---	---
NOER	≥ 5.52		≥ 5.52	
LOER	> 5.52		> 5.52	
LR ₅₀ /ER ₅₀	> 5.52		> 5.52	

--- = no reproduction test was carried out

- = not determined

* According to SCHNEIDER-ORELLI 1947

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the survival and reproduction of *Aphidius rhopalosiphi* exposed to the test item on barley plants were determined in an extended laboratory study.

The LR₅₀ value was determined to be > 5.52 L product/ha, the NOER for reproduction was determined to be ≥ 5.52 L product/ha.

A 2.3.2.2.2 Study 2

Comments of zRMS:	<p>The study was conducted in line with the respective guideline with minor deviations.</p> <p>It was noted that short-term deviations (< 1 hour) in the relative humidity during the reproduction phase of the study occurred. However, since all the validity criteria were met, this deviation is considered to have no impact on the outcome of the study.</p> <p>Overall, the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>LR₅₀ = 2.84 L product/ha EC₅₀ > 1.84 L product/ha</p>
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Reference:	KCP 10.3.2.2/02
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Extended Laboratory Study with the predatory mite <i>Typhlodromus pyri</i> (Acari: Phytoseiidae), Maspohl, A.-K., 2021, report No SO20513 / IRE18743
Guideline(s):	Blümel et al. (2000)
Deviations:	Minor (see the commenting box above) No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the survival and reproduction of *Typhlodromus pyri* exposed to the test item were determined. All treatments were applied at an application rate of 200 L/ha to detached bean leaves. Nominal treatment rates were 0.0681, 0.204, 0.613, 1.84, 5.52 L product/ha, corresponding to 8.51, 25.5, 76.6, 230, 690 g Ethofumesate/ha and 8.58, 25.7, 77.2, 232, 696 g Phenmedipham/ha. A toxic reference and an untreated control were included in the test.

Mortality was evaluated as the combination of dead and escaped and/or missing mites. A statistically significant increase in mortality compared to the control was observed in the test item treatments 0.204, 0.613, 1.84 and 5.52 L product/ha. Therefore, the NOER was determined to be 0.0681 L product/ha. The LR₅₀ value was determined to be 2.84 L product/ha (95% confidence limits: 2.05 - 4.32 L product/ha).

The mites of the test item treatments 0.0681, 0.204, 0.613 and 1.84 L product/ha and the control were tested for their fecundity. No statistically significant effects of the reproduction rate compared to the control were observed in these test item treatments. Therefore, the NOER for reproduction was determined to be ≥ 1.84 L product/ha.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Danadim progress (37.6% dimethoate)

Test System

Species	<i>Typhlodromus pyri</i> (Acari: Phytoseiidae)
Age	Protonymphs (0 - 24 hours old)
Source	Katz Biotech Ag, An der Birkenpfuhlheide 10, D-15837 Baruth, Germany
Acclimatisation period	The test organisms were received as eggs 2 days prior to test start and kept at the test facility under controlled test conditions (about 20 - 25°C and 48 - 78% relative humidity, 638 \pm 15.0 lux). The hatched mites were acclimatised to test conditions one day before the start of exposure.
Food	Apple pollen

Test Conditions

Temperature
Humidity

Mortality: 23 - 25°C; reproduction: 24 - 25°C
Mortality: 50* - 78%; reproduction: 74 - 79%

* The relative humidity was outside the range for < 1 hour. This is caused by obligatory measurements and observations and hence are not preventable. This has no impact on the outcome of the study.

Photoperiod
Light intensity

16 h light/8 h dark
Mortality and reproduction: 672 ± 43.6 lux

Study Design and Methods

In-life dates
Conducted at

09.04.2021 – 23.04.2021
Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany

Test duration

14 days

Test concentrations

0.0681, 0.204, 0.613, 1.84, 5.52 L product/ha

Test vessels / Exposure unit

detached leaves (leaf-discs) of bean

Treatment

Typhlodromus pyri were exposed to dry residues of HBZ10 on detached bean leaves for 7 days. The treated leaves were put on a cotton wool pad lying in a petri dish filled with dechlorinated tap water. A band of insect trap coating was applied on the leaves to form a barrier that prevents the mites from escaping. This barrier was touched up using an insect needle, so that corners were rounded off and the walls were smooth and without niches. A water supply was ensured by placing a small strip of filter paper on the leaf with one end lying on the wet cotton wool pad (strip was fixed in the glue barrier). Danadim Progress at 70 mL/ha was used as toxic reference and deionised water as control.

The control and reference items were tested with 5 replicates and each test item treatment was tested with 3 replicates. 20 protonymphs were used for each replicate.

The mortality phase was followed by a reproduction period of 7 days where the sub-lethal effects of the test item on reproductive capacity (fertility and fecundity) were assessed. The reproduction phase was carried out, with alive and apparently unaffected female found before the oviposition period after hatching and after the adults were sexed.

The sex ratio (n females / (n females + n males)) was ≤ 0.83 (5 females: 1 male) in all replicates.

No reproduction evaluation was carried out for the test item treatment group 5.52 L product/ha (corrected mortality > 50%) and for the reference item.

Observations

Mortality and the number of escaped mites (trapped in the insect glue barrier, drowned in the water split or not found) were recorded on days 3 and 7. On day 7, the sex of surviving mites was determined. Eggs laid until day 7 were removed from the test arena and were not taken into account.

On days 10, 12 and 14, laid eggs, juvenile mites, females and males were counted.

Statistics

Mortality / Escapees: A Qualitative Trend Analysis by Contrasts (Monotonicity of Rate/Response) and a Tarone's Test Procedure were run before the Step-down Rao-Scott-Cochran-Armitage Test Procedure (Mortality) and Step-down Cochran-Armitage Test Procedure (Escapees) respectively, was carried out to determine statistically significant differences compared to the control.

Reproduction: A Williams Multiple Sequential t-test Procedure ($\alpha=0.05$) was carried out to determine statistically significant differences compared to the control. A Shapiro-Wilk's Test on Normal Distribution, a Levene's Test on Variance Homogeneity and a Trend analysis by Contrasts were run at first.

The LRx values for the test item were calculated by Probit analysis using linear max. likelihood regression. No ERx values were calculated because no statistically significant effects during the reproduction phase were observed.

RESULTS AND DISCUSSIONS

Validity criteria

The mean mortality (dead and escaped mites) in the control group on day 7 should be $\leq 20\%$ (actual mortality 2.0%), corrected mortality in the toxic reference group should be between 50 and 100% (actual corrected mortality 69.4%). The cumulative number of eggs per female in the control group (day 7-14) should be ≥ 4 eggs per female (actual: 7.52 eggs per female).

Biological results

After 7 days the control mortality was 2.0%. In the test item treatments, the corrected mortality after 7 days ranged between 1.36 and 69.4%. A statistically significant increased mortality (counting escapees and actually dead mites) compared to the control was observed at the test item treatments of 0.204, 0.613, 1.84 and 5.52 L product/ha (Step-down Rao-Scott-Cochran-Armitage Test Procedure, $\alpha=0.05$).

In the control and in the test item treatments 0.0681, 0.204 and 0.613 L product/ha the mortality and the number of escaped mites were identical or similar to one another. In the test item treatments 0.204, 0.613, 1.84 and 5.52 L product/ha (Step-down Cochran-Armitage Test Procedure, $\alpha=0.05$), the percentage of escaped mites was statistically significantly increased compared to the control. The test item thus seems to be repellent to *Typhlodromus pyri*.

In the lower treatment rates up to 0.613 L product/ha, mortality only (without escapees) was not observed to a significant amount. Only the highest application rates (1.84 and 5.52 L product/ha) lead to a significant mortality rate compared to the control.

The mites of the application rates 0.0681, 0.204, 0.613 and 1.84 L product/ha and the control were tested for their fecundity. No reproduction evaluation was carried out for the test item treatment group 5.52 L product/ha, because the corrected mortality was $> 50\%$.

In the control the mean cumulative number of eggs per female was 7.52. In the test item treatments, the cumulative number of eggs per female ranged between 4.73 and 9.81. There was no statistically significant reduction of the reproduction at the test item treatments compared to the control (Williams Multiple Sequential t-test Procedure, $\alpha = 0.05$).

Table A 2.3.2.2.2-1 Effects of HBZ10 on mortality and reproduction of *Typhlodromus pyri*

Treatment [L product/ha]	Mortality after 7 d (including escapees) [%]	Mortality corr. ₁ [%]	Escapees after 7 days [%]	Reproduction rate [eggs per female]	Reduction of reproduction [%]
Control	2.00	-	2.00	7.52	-
0.0681	3.33	1.36	3.33	7.88	-4.79
0.204	11.7*	9.86	11.7*	9.81	-30.4
0.613	16.7*	15.0	13.3*	6.66	11.5
1.84	36.7*	35.4	26.7*	4.73	37.1
5.52	70.0*	69.4	50.0*	-	-
Reference substance	70.0*	69.4	48.0*	-	-

¹ Mortality corrected according to Abbott (Abbott, 1925); negative values indicate better survivorship compared to control

* Significantly different compared to control (mortality: Step-Down Rao-Scott-Cochran-Armitage Test Procedure, $\alpha = 0.05$; escapees: Step-down Cochran-Armitage Test Procedure, $\alpha=0.05$)

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the predatory mite *Typhlodromus pyri* were observed under extended laboratory conditions, with exposure to dried spray residues applied to the surface of detached bean leaves.

The LR₅₀ value was determined to be 2.84 L product/ha (95% confidence limits: 2.05 - 4.32 L product/ha), the NOER for reproduction was determined to be ≥ 1.84 L product/ha.

A 2.3.2.2.3 Study 3

Comments of zRMS:	<p>The study was conducted in line with the respective guideline with minor deviations.</p> <p>It was noted that the temperature temporarily dropped below the recommended minimum of 23 °C down to 21.2 °C for 7.5 hours at the end of the exposure period due to the heating failure in the laboratory. Since it was a slight deviation of a relatively short duration (1.4 – 2.4 % of the exposure time) and its small amplitude shortly before the end of the exposure period and the fact that the test organisms were in a good condition during exposure and post-exposure, this deviation is considered to have no impact on the outcome of the study.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>LR₅₀ > 7.2 L product/ha EC₅₀ > 7.2 L product/ha</p>
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Reference:	KCP 10.3.2.2/03
Report	Ethofumesate/Phenmedipham 125/125 g/L EC: Effects on the lacewing <i>Chrysoperla carnea</i> (Neuroptera: Chrysopidae), Extended Laboratory Study – Dose Response Test -, Leopold, J., 2021, report No 159181047
Guideline(s):	Vogt <i>et al.</i> (2000), this guideline was modified for exposure of <i>C. carnea</i> on natural substrate
Deviations:	Minor (see the commenting box above) No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the survival and reproduction of *Chrysoperla carnea* exposed to the test item were determined. All treatments were applied at an application rate of 200 L/ha to treated blackberry leaves. Nominal treatment rates were 2.52, 3.27, 4.25, 5.52, 7.20 L product/ha. A toxic reference and an untreated control were included in the test.

The mean mortality of *Chrysoperla carnea* was 15.0% in the control treatment and was between 17.5% and 25.0% in the test item treatments. Mortality was not statistically significantly increased compared to the control up to and including the highest application rate of 7.20 L product/ha (Chi2 2x2 Table Test with Bonferroni Correction, one-sided greater, $\alpha = 0.05$).

Reproduction of *C. carnea* was assessed in the control and at all test item application rates. The mean number of eggs per female and day was 15.7 in the control treatment. In the test item treatments, it ranged from 12.4 eggs per female and day (2.52 L product/ha) to 20.4 eggs per female and day (4.25 L product/ha) and was > 15 eggs per female and day with exception of the test item application rates of 2.52 L product/ha (12.4 eggs per female and day) and 7.20 L product/ha (14.0 eggs per female and day).

The mean hatching was higher than 70% in the control and at all test item application rates and ranged from 95.4% to 96.7%.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-4D
Active ingredient content	Ethofumesate (127 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.9771 g/mL
Storage conditions	At 20 ± 5°C, in the dark
Stability (expiry date)	27.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Danadim progress (38.5% dimethoate)

Test System

Species	<i>Chrysoperla carnea</i> (Neuroptera: Chrysopidae)
Age	2 - 3-day old larvae
Source	Katz Biotech Ag, An der Birkenpfuhlheide 10, D-15837 Baruth, Germany
Acclimatisation period	2 - 3 days under test conditions
Food	Larvae: UV-sterilised <i>Sitotroga cerealella</i> Oliv. eggs, ad libitum Adults: artificial diet: 1 egg, 1 egg yolk, 15 mL condensed milk, 20 g fructose, 30 g honey, 30 g brewer's yeast, 50 g wheat germ and deionised water (approximately 45 mL) mixed homogeneously, ad libitum

Test Conditions

Temperature	21 - 27°C
Humidity	60 - 72%
Photoperiod	16 h light/8 h dark
Light intensity	1010 - 1250 lux

Study Design and Methods

In-life dates	25.02.2021 – 07.06.2021
Conducted at	Ibacon GmbH, Arheilger Weg 17, 64380 Rossdorf, Germany
Test duration	22 days
Test concentrations	2.52, 3.27, 4.25, 5.52, 7.20 L product/ha
Test vessels / Exposure unit	Blackberry leaves

Treatment

This study encompassed 7 treatment groups (5 dose rates of the test item, control, reference item) with 40 replicates each containing 1 larva. The larvae were exposed to dried residues on treated leaf surfaces (blackberry leaves). Exposure lasted until pupae were transferred to the reproduction units for development of adults. Mortality checks were carried out regularly until hatching of adult lacewings. In addition, for the control and the test item treatment groups where the corrected mortality was $\leq 50\%$, the reproduction performance, i.e. egg deposition and larval hatching rate, was determined (2 checks/week, 24 hours period each check).

Exposure units: Detached leaves of blackberry plants (*Rubus fruticosus* L.) were cut to discs of about 55 mm in diameter. These leaf cuts were treated on their upper surface.

The leaf discs were placed with their treated side upwards on a wet cotton wool pad in a petri dish (60 mm in diameter). The petri dish had a hole for a wick. A Fluon treated cylinder was fixed on each leaf by two elastic bands to guarantee a close position on the leaves. The height of the cylinder was 30 mm, and the diameter was 46 mm. The lower part of the cylinder was not treated with Fluon to avoid contamination of the larvae. Escaping of the larvae was prevented by the close position of the cylinder to the leaf and the Fluon on the walls of the cylinder. The exposure units of one treatment group were placed in a bowl. A wick was connected with the cotton wool pad in the exposure units and was wetted regularly.

Post-exposure units: An acrylic cylinder (15 cm high and 10 cm in diameter) with a cotton net on the top for egg-laying and a hole (diameter approximately 2 cm) on the bottom to provide water through a cotton plug.

Observations

For assessment of fecundity the number of eggs was counted by two egg samples (checks) within one week. Each check covered an egg laying period of 24 h. For this the acrylic cylinder was covered with a new gauze. Eggs of each sample were incubated in separate plastic boxes. For assessment of fertility hatched larvae were removed daily; *Sitotroga* eggs were added to avoid cannibalism. When no further hatching of larvae was observed (after 6 - 7 days), the remaining eggs where no alive larva had hatched were determined as unhatched. All eggs on the gauze were counted and the percentage of hatched eggs was determined.

The number of living and dead larvae and number of pupae developed was determined at least 3 times a week after test start and number of adults hatched was checked regularly.

The number of eggs was counted after 24-hour egg-laying periods (checks) and 2 checks were done within one week. The number of larvae was determined after hatching of all larvae and the hatching rate was calculated.

Reproduction was performed where the corrected mortality (M_{corr}) was $\leq 50\%$.

No reproduction testing was performed with the reference item.

Statistics

The LR₅₀ was not calculated as no mortality above 50% was noted. Mortality data obtained from the control and test item treatments were analysed for significance using the Chi2 2x2 Table Test with Bonferroni Correction (one-sided greater, $\alpha = 0.05$), which is a distribution-free test and does not require testing for normality or homogeneity prior to analysis. However, a qualitative trend analysis by contrasts ($\alpha = 0.05$) had to be carried out previously to check for the presence of linear or quadratic trends. The two-sample comparison between the reference item and control was analysed using the Fisher's Exact Binomial Test (one-sided greater, $\alpha = 0.05$). The reproductive performance is evaluated only qualitatively due to the high species-inherent variability in egg-laying performance in accordance with Vogt *et al.* 2000. The software used to perform the statistical analysis was ToxRat Professional, Version 3.3.0, © ToxRat Solutions GmbH.

RESULTS AND DISCUSSIONS

Validity criteria

The pre-imaginal mortality in the control group should be $\leq 20\%$ (actual mortality 15.0%), the pre-imaginal mortality in the toxic reference group should be at least 50% (actual corrected mortality 79.4%). The mean fecundity in the control group should be at least 15 eggs per female (actual: 15.7 eggs per female). Fertility (mean larval hatching rate) in the control group should be higher than 70% (actual: 96.5% larval hatching rate).

Biological results

The mortality of *Chrysoperla carnea* was 15.0% in the control treatment and was between 17.5 and 25.0% in the test item treatments. It was not statistically significantly increased compared to the control up to and including the highest application rate of 7.20 L product/ha (Chi2 2x2 Table Test with Bonferroni Correction, one-sided greater, $\alpha = 0.05$).

Reproduction of *C. carnea* was assessed in the control and at all test item application rates. The mean number of eggs per female and day was 15.7 in the control treatment. In the test item treatments, it ranged from 12.4 eggs per female and day (2.52 L product/ha) to 20.4 eggs per female and day (4.25 L product/ha) and was > 15 eggs per female and day with exception of the test item application rates of 2.52 L product/ha (12.4 eggs per female and day) and 7.20 L product/ha (14.0 eggs per female and day).

The mean hatching was higher than 70% in the control and at all test item application rates and ranged from 95.4% to 96.7%.

Table A 2.3.2.2.3-1 Effects of HBZ10 on mortality and reproduction of *Chrysoperla carnea*

Treatment [L product/ha]	Mortality [%]	Mortality corr. ¹ [%]	Reproduction [Eggs per female per day]	Effect on reproduction [%] ²	Larval hatching rate [%]
Control	15.0	-	15.7 ± 1.4	-	96.5 ± 0.6
2.52	20.0	5.9	12.4 ± 0.4	21.4	95.7 ± 0.2
3.27	17.5	2.9	15.0 ± 3.0	5.0	96.7 ± 0.4
4.25	17.5	2.9	20.4 ± 3.9	-29.4	95.9 ± 1.2
5.52	17.5	2.9	16.3 ± 0.9	-3.3	95.8 ± 0.0
7.20	25.0	11.8	14.0 ± 1.3	11.0	95.4 ± 0.1
Reference substance	82.5*	79.4	-	-	-

¹ Mortality corrected according to Abbott (Abbott, 1925); negative values indicate better survivorship compared to control

* Significantly different compared to control (Fisher's Exact Binomial Test; one-sided greater; $\alpha = 0.05$)

² Calculated on the exact raw data; negative values indicate better performance compared to the control

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on *Chrysoperla carnea* were observed under extended laboratory conditions, with exposure to dried spray residues applied to the surface of detached blackberry leaves.

The NOER (no observed effect rate) for mortality effects were equal or greater than 7.20 L product/ha, there was no negative effect of the test item on reproductive performance of *C. carnea* up to and including 7.20 L product/ha.

A 2.3.2.2.4 Study 4

Comments of zRMS:	<p>The study was conducted in line with the respective guideline with no deviations.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>ER₅₀ > 51.84 L product/ha</p>
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Reference:	KCP 10.3.2.2/04
Report	HBZ10: Effects on the reproduction of rove beetles <i>Aleochara bilineata</i> – Extended Laboratory Study – Dose Response Test -, Knautz, T., 2021, report No 159181071
Guideline(s):	Grimm et al. (2000)
Deviations:	None No deviations to the study plan occurred.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the reproduction efficiency of *Aleochara bilineata* exposed to natural soil treated with the test item ~~were~~ **will be** determined. Nominal treatment rates were 3.24, 6.48, 12.96, 25.96, 51.84 L product/ha. A toxic reference and an untreated control ~~were~~ **are** included in the test.

Each treatment group ~~will~~ **included** 4 replicates with 10 female and 10 male beetles, respectively. The larvae hatched from eggs laid in the soil by the female beetles ~~will~~ **parasitised** the fly pupae. To assess the reproductive efficiency the number of beetles emerging from the successfully parasitised fly pupae ~~were~~ **will be** counted.

~~The study is currently ongoing, and the study summary will be completed after the final report of the study is available.~~

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-4D
Active ingredient content	Ethofumesate (127 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.9771 g/mL
Storage conditions	At 20 ± 5°C, in the dark
Stability (expiry date)	27.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Danadim progress (38.5% dimethoate)

Test System

Species	<i>Aleochara bilineata</i> Gyll. (Coleoptera: Staphylinidae)
Age	2-5 1–7 -day old adults
Source	De Groene Vlieg, Duivenwaardsedijk 1, 3244 LG-Nieuwe Tonge, The Netherlands

Acclimatisation period	Under test conditions
Host organism	<i>Delia antiqua</i> ; approx. 500 <i>Delia antiqua</i> pupae per container were will be added on day 7, 14, and 21. The pupae were will be carefully mixed into the soil (depth approx. 2-3 cm) and homogenously distributed within the test unit
Food	Frozen midge larvae (commercial food for aquarium fish; <i>Chironomus</i> sp.), every 1-3 days <i>ad libitum</i> , first feeding was will be done after application
Test Conditions	
Temperature	19-21 20 ± 2 °C
Humidity	66-80 60–90 %
Photoperiod	16 h light/8 h dark
Light intensity	650-930 <2000 lux
Study Design and Methods	
In-life dates	16.06.2021-30.08.2021
Conducted at	Ibacon GmbH, Arheilger Weg 17, 64380 Rossdorf, Germany
Test duration	28 days of exposure
Test concentrations	3.24, 6.48, 12.96, 25.96, 51.84 L product/ha
Exposure unit	Plastic boxes (18.3 cm × 13.6 cm × 6 cm), covered with perforated plastic lid, filled with 900 g dry soil
Emergence container	The parasitised fly pupae were will be placed in a funnel (placed on a glass beaker), the bottom of the funnel is perforated with holes (diameter approx. 2 mm) through which the hatched beetles fell will fall into the glass beaker below. The fly pupae will remained in the funnel.
Soil characteristics	Natural soil (LUFA 2.1, Speyer, Germany) details of soil characteristics will be given Soil Type: silty sand (according to DIN) Content of Carbon [%]: 0.67 pH: 4.7 Density [g/1000 mL]: 1416 Analysis of Grain Size (DIN) [%]: < 0.002 mm: 3.9 0.002 - 0.006 mm: 1.5 0.006 - 0.02 mm: 3.3 0.02 - 0.063 mm: 6.6 0.063 - 0.2 mm: 28.9 0.2 - 0.63 mm: 53.4 0.63 - 2.0 mm: 2.4 Max. Water Holding Capacity: 32.0% The LUFA 2.1 soil met the guideline recommendations of an organic C content of < 1 %.
Treatment	This study will encompassed 7 treatment groups (5 dose rates of the test item, control, reference item) with 4 replicates each containing 10 female and 10 male adult beetles. A single application with a laboratory spraying equipment (with 400 L spray liquid/ha) was will be performed. The adult test organisms were will be exposed to the test item for 28 days. After 28 days all surviving adult beetles were will be removed and the number was will be recorded. The substrate and the parasitised fly pupae were will be returned to the test vessels and returned for one further week to allow the substrate to dry. 35 days after start of each bioassay, the pupae were will be washed or sieved out of the soil and the pupae of each replicate were will be transferred into a separate emergence container.

Observations	Emerging beetles were will be counted and removed from the emergence container at least 3 times per week. Emergence of the F1-generation was will be monitored until the control treatment falls below a rate of two beetles per replicate per day. The reproduction efficiency was will be assessed by counting the total number of beetles emerged from the offered fly pupae until the emergence of the F1-generation has finished.
Statistics	Test Item: Williams Multiple Sequential t-test; Reference Item: Student t-test for homogeneous variances, both tests one-sided smaller, $\alpha = 0.05$.

RESULTS AND DISCUSSIONS

Validity criteria

The mean number of emerged beetles in the control group should be > 400 (actual: 803 ± 38 beetles), the effect on reproduction in the toxic reference group should be at least 50% (actual mortality 97.4 %).

Biological results

Table A 2.3.2.2.4-1 Effects of HBZ10 on reproduction of *Aleochara bilineata*

Treatment [L product/ha]	Reproduction efficiency [Number of emerged beetles \pm Standard Deviation]	Effect on reproduction [%] ¹
Control	803 ± 38	-
3.24	736 ± 73	+ 8.4
6.48	$695 \pm 102^*$	+ 13.5
12.96	$639 \pm 98^*$	+ 20.4
25.92	$543 \pm 78^*$	+ 32.4
51.84	$529 \pm 79^*$	+ 34.2
Reference substance 2.0	$21 \pm 7^*$	+ 97.4

¹ Effect on reproduction according to the following formula: $(1-R_t/R_c) \cdot 100\%$ calculated on the exact raw data (positive values represent a decreased reproduction compared to the control)

* = statistically significant difference compared to the control; Test Item: Williams multiple sequential t-test procedure; Reference Item: Student t-test, one-sided smaller, $\alpha = 0.05$.

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on *Aleochara bilineata* were observed under extended laboratory conditions, with exposure to treated natural soil.

The reduction of the reproduction capacity at rates of 3.24, 6.48, 12.96, 25.92 and 51.84 L product/ha compared to the control group (=100 %) was 8.4, 13.5, 20.4, 32.4 and 34.2 %, respectively. Positive values represent a decreased reproduction compared to the control. The reference item (2.00 L product/ha) led to a significantly reduced reproduction by 97.4 %.

The ER50 (effect rate for 50 % of the individuals) for the reproduction was estimated to be > 51.84 L product/ha, the ER20 12.23 L product/ha and the ER10 3.48 L product/ha, respectively. The NOER (no observed effect rate) for the reproduction was determined to be 3.24 L product/ha.

A 2.3.2.2.4 Study 5

Comments of zRMS:	<p>The study was conducted in line with the respective guideline with minor deviations.</p> <p>It was noted that there were 10 replicates with 10 protonymphs each while the guideline recommends 5 replicates with 20 protonymphs. This deviation is considered to have no impact on the test results, since a relevant number of individuals was tested.</p> <p>In Trial L1 the control, test item and reference item were applied with a higher spray volume of 1000 L/ha instead of the recommended 200 L/ha. Nevertheless, the application rates of the test item group and the reference item group were not affected.</p> <p>In replicate number 7 of the control group of trial L1, test organisms escaped because the replicate has dried out during the first 7 days of exposure. This replicate was excluded from</p>
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	<p>evaluation and statistical analysis. Since there were still 9 replicates left, the exclusion of replicate number 7 did not have any negative impact on the outcome and the integrity of the study.</p> <p>All these deviations are considered to have no impact on the outcome of the study since all the validity criteria were met.</p> <p>Overall, the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>LR₅₀ > 5.52 L product/ha ER₅₀ > 5.52 L product/ha</p>
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Reference:	KCP 10.3.2.2/05
Report	Ethofumesate + Phenmedipham 125 + 125 G/L: Toxicity To The Predatory Mite, Typhlodromus Pyri Scheuten (Acari, Phytoseiidae) After Exposure To Freshly Applied And Aged Spray Deposits On Apple Leaves. Wagenhoff, E., 2021, Report No S21-05449
Guideline(s):	<p>No Guideline available but based on IOBC (BLÜMEL <i>et al.</i>, 2000), 'Laboratory residual contact test with the predatory mite <i>Typhlodromus pyri</i> Scheuten (Acari: Phytoseiidae) for regulatory testing of plant protection products' and in accordance with the ESCORT 2 guidance document (CANDOLFI <i>et al.</i>, 2001).</p> <p>Guideline was modified for an exposure on freshly applied and aged spray deposits on natural substrate.</p>
Deviations:	Minor (see the commenting box above) None
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the survival and reproduction of *Typhlodromus pyri* exposed to freshly applied and aged spray deposits of the test item were determined. The test item was applied at an application rate of 1000 L/ha to apple leaves. Nominal treatment rate was 5.52 L product/ha, corresponding to 696 g Ethofumesate/ha and 701 g Phenmedipham/ha. A toxic reference and an untreated control were included in the test.

The test item and the reference item were applied once in trial 01 to potted apple trees under semi-field conditions (i.e. rain protected). During ageing the treated plants were kept rain protected under an UV-permeable roof.

A total of two biological trials were carried out in the laboratory: The first trial (L1) was conducted with freshly treated foliage. In the second trial (L2) test item treated foliage aged for 14 days was used whereas the reference item was freshly sprayed on detached apple leaves with a track sprayer in the laboratory.

Mortality was evaluated as the combination of dead and escaped and/or missing mites.

Ethofumesate + Phenmedipham 125 + 125 g/L EC, applied once at a single application rate of 5.52 L/ha to potted apple trees under semi-field conditions caused no statistically significant increase in the mortality and escaping rate of *Typhlodromus pyri* in both trials L1 (freshly applied spray deposits) and L2 (14 day-aged spray residues) compared to the control group. Furthermore, mortality rates of *Typhlodromus pyri* were clearly below 50 % at the end of both trials.

Reproduction of *Typhlodromus pyri* was not reduced compared to the control group at the test item rate of 5.52 L Ethofumesate + Phenmedipham 125 + 125 g/L EC/ha in both trials L1 (freshly applied spray deposits) and L2 (aged spray residues for 14 days). Furthermore, reduction in reproduction was clearly below 50 % in both trials.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-4F
Active ingredient content	Ethofumesate (126 g/L, analysed) Phenmedipham (127 g/L, analysed)
Characteristics	Light yellow, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	15.04.2022
Vehicle / control(s)	Control: tap water Toxic reference item: BAS 152 65 I (38.8% dimethoate)

Test System

Species	<i>Typhlodromus pyri</i> (Acari: Phytoseiidae)
Age	Protonymphs (≤ 25 hours 0 – 24 hours old)
Source	Laboratory culture at the test facility (stock keeping according to OVERMEER, 1985)
Acclimatisation period	The test organisms were received as eggs 4 days prior to test start and kept at the test facility under controlled test conditions (24.6-25.6°C and 68.1 – 78.3% relative humidity, 3000-3500 lux).
Food	Pollen of bean and birch

Test Conditions

Temperature	Trial L1: 24.8 24.2 – 25.5°C Trial L2: 24.2 – 25.4°C
Humidity	Trial L1: 69.4 – 75.6 % Trial L2: 51.7* – 78.9% (*short term deviations (< 2 hours))
Photoperiod	16 h light/8 h dark
Light intensity	Mortality and reproduction: Trial L1: 2500 – 4700 lux; Trial L2: 2550 – 4800 lux

Study Design and Methods

In-life dates	10.09.2021 – 08.10.2021
Conducted at	Eurofins Agroscience Services Ecotox GmbH, Eutinger Str. 24, D-75223 Niefern-Öschelbronn, Germany
Test duration	28 days (14 days for each trial)
Test concentrations	5.52 L product/ha
Test vessels / Exposure unit	Application A 1, semi-field application to potted apple trees with a knapsack sprayer (test item and reference item); spray volume: 1000 L/ha (test item and reference item) Application A 2, laboratory application on untreated, detached apple leaves with a laboratory track sprayer for the reference item; spray volume: 200 L/ha

Treatment	<p><i>Typhlodromus pyri</i> were exposed to dry residues of HBZ10 on detached apple leaves in an open test unit for 14 days. Two trials (bioassays) were carried out with foliage, collected on the day of application (freshly applied spray deposits – Trial L1) and 14 days after application (aged spray deposits – Trial L2). The ageing of the spray deposits was conducted under semi-field conditions (rain protected, under a roofed area).</p> <p>BAS 152 65 I at application rates of 0.2 L/ha in A1 and 0.03 L/ha in A2 70 mL/ha was used as toxic reference and tap water as control.</p> <p>The control and reference items and test item treatment were tested with 10 replicates per treatment group. 10 protonymphs were used for each replicate.</p> <p>Mortality and any change in behavior with respect to the control was assessed 3 and 7 days after start of the trial. Reproduction was assessed from day 7 to day 14 with a maximum interval of 3 days.</p>
Observations	<p>Mortality and the number of escaped mites (trapped in the insect glue barrier, drowned in the water split or not found) were recorded on days 3 and 7. On day 7, the sex of surviving mites was determined. Eggs laid until day 7 were removed from the test arena and were not taken into account.</p> <p>On days 10, 12 and 14, laid eggs, juvenile mites, females and males were counted.</p>
Statistics	<p>Mortality and Escape Rate: Chi2-test (one-sided greater, $\alpha = 0.05$) was performed for mortality and escape rate.</p> <p>Reproduction: Since the number of juveniles in the control group was lower than in the test item group in both trials, no statistical analysis was performed.</p>

RESULTS AND DISCUSSIONS

Validity criteria

The mean mortality (dead and escaped mites) in the control group on day 7 should be $\leq 20\%$ (actual mortality trial L1: 3.3 %, trial L2: 2.0 %), corrected mortality in the toxic reference group should be between 50 and 100% (actual corrected mortality trial L1: 100 %, trial L2: 99.0 %). The cumulative number of eggs per female in the control group (day 7-14) should be ≥ 4 eggs per female (actual trial L1: 8.3, trial L2: 7.1).

Biological results

Trial L1 (application of control, test item and reference item under semi-field conditions [A1]; exposure on leaves containing freshly applied dry spray deposits):

Treatment group	Application rates	Cumulative juvenile mortality ^b	Corrected mortality	Cumulative reproduction (mean \pm SD)	Reduction in reproduction rate ^c
	[L product/ha]	[%]	[%]	[eggs/female]	[%]
Control	0	3.3	-	8.3 \pm 3.2	-
Ethofumesate + Phenmedipham 125 + 125 g/L EC	5.52	4.0	0.7	10.5 \pm 3.9	-26.5
Reference item ^a	0.200	100.0	100.0	n.d.	n.d.

SD: Standard deviation; n.d.: not determined

^a BAS 152 65 I, active ingredient: dimethoate at 400 g/L, nominal

^b Based on the sum of dead and escaped mites

^c Negative values indicate higher reproduction compared to the control

Trial L2 (application of reference item in the laboratory [A2]; exposure on leaves containing aged spray deposits for the test item and the control and on detached leaves containing freshly applied dry spray deposits for the reference item):

Treatment group	Application rates	Cumulative juvenile mortality ^b	Corrected mortality	Cumulative reproduction (mean ± SD)	Reduction in reproduction rate ^c
	[L product/ha]	[%]	[%]	[eggs/female]	[%]
Control	0 ^a	2.0	-	7.1 ± 2.8	-
Ethofumesate + Phenmedipham 125 + 125 g/L EC	5.52	4.0	2.0	8.0 ± 2.6	-12.7
Reference item ^a	0.030	99.0	99.0	n.d.	n.d.

SD: Standard deviation; n.d.: not determined

^a BAS 152 65 I, active ingredient: dimethoate at 400 g/L nominal

^b Based on the sum of dead and escaped mites

^c Negative values indicate higher reproduction compared to the control

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the predatory mite *Typhlodromus pyri* were observed under extended laboratory conditions, with exposure to freshly applied and aged dried spray residues applied to the surface of apple leaves.

Ethofumesate + Phenmedipham 125 + 125 g/L EC, applied once at a single application rate of 5.52 L/ha to potted apple trees under semi-field conditions caused no statistically significant increase in the mortality and escaping rate of *Typhlodromus pyri* in both trials L1 (freshly applied spray deposits) and L2 (14 day-aged spray residues) compared to the control group. Furthermore, mortality rates of *Typhlodromus pyri* were clearly below 50 % at the end of both trials.

Reproduction of *Typhlodromus pyri* was not reduced compared to the control group at the test item rate of 5.52 L Ethofumesate + Phenmedipham 125 + 125 g/L EC/ha in both trials L1 (freshly applied spray deposits) and L2 (aged spray residues for 14 days). Furthermore, reduction in reproduction was clearly below 50 % in both trials.

A 2.3.2.3 KCP 10.3.2.3 Semi-field studies with non-target arthropods

No new study is submitted.

A 2.3.2.4 KCP 10.2.3.4 Field studies with non-target arthropods

No new study is submitted.

A 2.3.2.5 KCP 10.2.3.5 Other routes of exposure for non-target arthropods

No new study is submitted.

A 2.4 KCP 10.4 Effects on non-target soil meso- and macrofauna

A 2.4.1 KCP 10.4.1 Earthworms

A 2.4.1.1 KCP 10.4.1 Earthworms – sub-lethal effects

A 2.4.1.1.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 222 with minor deviations.</p> <p>It was noted that the study was conducted with the following deviations:</p> <ul style="list-style-type: none"> - Food was provided on day 0 (test start) instead of day 1 due to good experience with this procedure. - At test end, the soil moisture deviated by more than 10% from the initial value in all treatments. - The room temperature temporarily increased to a maximum of 24°C and decreased to a minimum of 17°C. In total the room temperature exceeded the recommended 18 to 22 °C for about 56 hours which was 4.24% of the overall test duration. However, its impact on the soil temperature is judged to be negligible as shown by the fulfilment of all the validity criteria. <p>In zRMS opinion these deviations are considered to have no impact on the outcome of the study since all the validity criteria were met.</p> <p>The test design was relevant to derive both NOEC and ECx values (8 concentrations, 8 replicates for control, 4 replicates per treatment group).</p> <p>The reliability of the EC₁₀ value was evaluated in line with the recommendations of EFSA Supporting publication 2019:EN-1673:</p> <ul style="list-style-type: none"> - NW (normalised width) of 0.014 was calculated, which results with rating “excellent” in line with Table E9 in EFSA Supporting publication 2019:EN-1673, - median EC₁₀ (138 mg product/kg soil dw) is lower than EC_{20,low} (178 mg product/kg soil dw), - the dose-response curve is medium with steepness of 0.47 (i.e. <0.66 and >0.33). <p>Based on above indications the calculated EC₁₀ is considered to be sufficiently reliable.</p> <p>Overall, the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>56d NOEC = 152 mg product/kg soil dw 56d EC₁₀ = 138 mg product/kg soil dw</p>
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Reference:	KCP 10.4.1/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Earthworm (<i>Eisenia fetida</i>), Effects on Reproduction, Winkelmann, G., 2021a, report No SO20133 / RBN18743
Guideline(s):	OECD 222 (2016)
Deviations:	Minor (see the commenting box above) The study was conducted with the following deviations: Food was provided on day 0 (test start) instead of day 1 due to good experience with this procedure. At test end, the soil moisture deviated by more than 10% from the initial value in all treatments. The room temperature temporarily increased to a maximum of 24°C and decreased to a minimum of 17°C. In total the room temperature exceeded the recommended 18 to 22 °C for about 56 hours which is 4.24% of the overall test duration. However, its impact on the soil temperature is judged to be negligible as shown by the fulfilment of all validity criteria. These deviations are considered to have no impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effect of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on *Eisenia fetida* was examined over a test period of 56 days. The test item was mixed into artificial soil at nominal concentrations of 37, 59, 95, 152, 244, 390, 625, 1000 mg product/kg dry soil. 8 replicates were used for the control and 4 replicates for the test item treatment groups, each replicate consisted of 10 adult earthworms.

After 28 days of exposure in soil, neither evident earthworm mortalities (< 10%) nor pathological symptoms or changes in the behaviour of adult earthworms were observed in the control and the test item concentrations 37 to 625 mg product/kg dry soil. However, at the test item concentration 1000 mg product/kg dry soil 45% mortality occurred.

After a further four weeks, the reproduction rate (average number of juveniles produced) was 67 in the control and ranged from 0 to 64 in the test item treatment rates. There were no statistically significant differences in earthworm reproduction in the treatment rates 37 to 152 mg product/kg dry soil compared to the control. However, at the test item concentrations 244 to 1000 mg product/kg dry soil the earthworm reproduction was statistically significantly reduced.

Taking into account mortality and reproductive capacity, the NOEC for HBZ10 was determined as 625 mg product/kg dry soil and 152 mg product/kg dry soil, respectively.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Carbendazim

Test System

Species	<i>Eisenia fetida</i> (Annelida, Lumbricidae)
Age	adult worms (approximately 2 - 12 months old with clitellum)

Weight	0.38 to 0.55 g
Source	Breeding stock culture in the test facility
Acclimatisation period	2 days in artificial soil under test conditions
Food	During breeding, the earthworms are fed with a litter of dried stinging nettle leaves and porridge oats.
Test Conditions	
Temperature	17 – 24°C* * The room temperature temporarily increased to maximum 24°C and decreased to minimum 17°C. In total the room temperature exceeded the recommended 18 to 22°C for about 56 hours which is 4.24% of the overall test duration. However, its impact on the soil temperature is judged to be negligible as shown by the fulfilment of all validity criteria. This deviation is considered to have no impact on quality and integrity of the study.
Photoperiod	16 h light/ 8 h dark
Light intensity	519 ± 91 lux
pH	6.52 – 6.78
Test soil	Artificial soil with 10% peat, 20% kaolin clay, 0.5% calcium carbonate and 69% quartz sand with the pH of 6.0 ± 0.5. Two days before test start the artificial soil (28000 g) was pre-moistened with 2501 g demineralised water to achieve moisture content corresponding to 27% of the WHCmax of the artificial soil. The moistened soil was kept covered to prevent evaporative water losses prior to the start of exposure. Moisture of dry weight: 23.8 – 32.7 %, WHCmax of artificial soil 45.5 g/100g dry weight.
Study Design and Methods	
In-life dates	10.06.2020 – 04.08.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	56 days
Test concentrations	37, 59, 95, 152, 244, 390, 625, 1000 mg product/kg dry soil
Test vessels / Exposure unit	Test units containing about 600 g dry soil were round plastic boxes with an inner diameter of 15.0 cm corresponding to a bottom surface area of 177 cm ² and a height of 14 cm. Transparent and perforated lids enable sufficient gas exchange, light input and prevent the test substrate from drying.
Treatment	The study was conducted over 8 weeks with 8 different concentrations mixed into the artificial soil containing 10% peat. For each test item treatment group 40 test organisms were divided into 4 replicate groups, each containing 10 test organisms. The untreated control group comprised 8 replicates with 10 test organisms each. The earthworms were fed with 5 g of air-dried cattle manure (moistened with 10 g demineralised water) per replicate on a weekly basis during the first 4 weeks of the test. At test start and at day 28 the food was mixed carefully into the soil on the other days the food was placed onto the soil surface. No further feeding took place during the remaining 4 weeks of the test. The toxic reference test is conducted once within twelve months. The most recent test was carried out from 30.01.2020 to 26.03.2020 using artificial soil containing 5% peat.

Observations

At start and end of the test, pH-value and moisture content of the test medium were determined. The body weight of the adult earthworms was individually determined at day 0 and at day 28. After the first four weeks the adult earthworms were removed. Mortality and behavioural abnormalities of the adult earthworms were recorded. After further four weeks, the number of offspring hatched from the cocoons was counted.

Statistics

The arithmetic mean values and the standard deviation per treatment and per control for reproduction, mortality and biomass were calculated. For identifying the NOEC values, Qualitative Trend Analysis by Contrasts (Monotonicity of Concentration/Response), Tarone's Test Procedure, Step-down Cochran-Armitage Test Procedure for mortality and Shapiro-Wilk's Test on Normal Distribution, Levene's Test on Variance Homogeneity (with Residuals), Trend Analysis on Contrasts (Monotonicity of Concentration/Response) and Williams's Multiple Sequential t-test Procedure for reproduction / biomass were used. The EC_{10,20,50} - values for reproduction and biomass were calculated using 3-param. normal CDF.

The statistical analysis was performed with the software ToxRat Professional 3.3.0.

RESULTS AND DISCUSSIONS

Validity criteria

The mean mortality of the control should be less than 10% at the end of the test (actual: 0.0%). The mean number of juveniles per vessel on the control should be ≥ 30 at the end of the test (actual: 67). For the control, the coefficient of variation calculated for the number of juveniles between replicates should be $\leq 30\%$ at the end of the definitive test (actual: 23.5%).

Biological results

Adult mean mortality in the control was 0.0% at the end of the test (28 DAA). In the case of the test item HBZ10, mean mortality of adult earthworms ranged between 0.0% and 45% for all rates tested respectively at the end of the test (28 DAA).

Adult mean body weight change in the control increased 21.9% at the end of the test (28 DAA). In the case of the test item HBZ10, mean body weight change of adult earthworms ranged between -1.63% and 24.1%. Mean reproduction in the control was 67 juveniles per replicate at the end of the test (56 DAA). In the case of the test item HBZ10, mean reproduction of earthworms ranged between 0.0 juveniles for the eighth rate tested (1000.0 mg product/kg dry soil) and 64 juveniles at the second rate tested (59 mg product/kg dry soil).

Table A 2.4.1.1.1-1 Effect of HBZ10 on *Eisenia fetida* in a 56-day reproduction test

Application rate [mg product/kg d.s.]	Mortality [%]	Weight change [%] [‡]	Mean reproduction (No. juveniles)	CV [%]	Reduction in reproduction [%]
Control	0.0	21.9 ± 6.71	67 ± 15.4	23.5	--
37	2.5	13.0 ± 10.9	60 ± 9.71	16.2	10.4
59	2.5	23.1 ± 3.98	64 ± 11.4	17.8	4.5
95	5.0	24.1 ± 8.09	60 ± 29.7	49.4	10.4
152	0.0	16.3 ± 5.74	57 ± 23.1	40.5	14.9
244	0.0	17.5 ± 6.90	40 ± 16.1*	40.3	40.3
390	0.0	13.4 ± 7.88	19 ± 6.40*	33.7	71.6
625	5.0	8.53 ± 9.65*	9 ± 3.87*	43.0	86.6
1000.0	45.0*	-1.63 ± 7.24*	0.0*	-	100

* Statistically significantly different compared to control (mortality: Step-down Cochran-Armitage Test Procedure, $\alpha = 0.05$; reproduction/weight change: Williams Multiple Sequential t-test Procedure, $\alpha = 0.05$)

Table A 2.4.1.1.1-2 Endpoints of HBZ10 on *Eisenia fetida* in a 56-day reproduction test

Endpoint [mg product/kg dry soil]	Mortality	Biomass	Reproduction
NOEC	625	390	152
EC ₁₀ (95% confidence limits)	401 (n.d.)	632 (532 - 749)	138 (137 - 139)
EC ₂₀ (95% confidence limits)	823 (n.d.)	729 (633 - 842)	179 (178 - 180)
EC ₅₀ (95% confidence limits)	> 1000 (n.d.)	961 (796 - >1000)	295 (292 - 297)

n.d. = not determined

CONCLUSION

In a 56-day reproduction test, the effects of HBZ10 on earthworms (*Eisenia fetida*) were observed. Taking into account mortality and reproductive capacity, the NOEC for HBZ10 was determined as 625 mg product/kg dry soil and 152 mg product/kg dry soil, respectively. The EC₁₀ value for reproduction was determined as 138 mg product/kg dry soil (95% confidence limits: 137-139 mg product/kg dry soil).

A 2.4.1.2 KCP 10.4.1.2 Earthworms - field studies

A 2.4.2 KCP 10.4.2 Effects on non-target soil meso- and macrofauna (other than earthworms)

A 2.4.2.1 KCP 10.4.2.1 Species level testing

A 2.4.2.1.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 232 with no deviations.</p> <p>The test design was relevant to derive both NOEC and EC_x values (8 concentrations, 8 replicates for control, 4 replicates per treatment group).</p> <p>The reliability of the EC₁₀ value was evaluated in line with recommendations of EFSA Supporting publication 2019:EN-1673:</p> <ul style="list-style-type: none"> - NW (normalised width) of 0.52 was calculated, which results in rating “fair” in line with Table E9 in EFSA Supporting publication 2019:EN-1673, - median EC₁₀ (44.4 mg/kg soil dw) is lower than EC_{20,low} (46.6 mg/kg dw), - the dose-response curve is medium with steepness of 0.42 (i.e. <0.66 and >0.33). <p>Taking the above results into account, the calculated EC₁₀ is considered to be sufficiently reliable.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoints relevant for the risk assessment:</p> <p>NOEC = 52.9 mg product/kg soil dw EC₁₀ = 44.4 mg product/kg soil dw</p>
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Reference:	KCP 10.4.2.1/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Collembolan (<i>Folsomia candida</i>) reproduction test in soil, Klix, V., 2021i, report No SO20135 / ICR18743
Guideline(s):	OECD 232 (2016)
Deviations:	None No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

Folsomia candida were exposed to Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) for a period of 28 days. The test item was mixed thoroughly with artificial soil (5% peat content) which was filled in glass vessels before the Collembola were introduced to the vessels. Concentrations of 16.3, 29.4, 52.9, 95.3, 171, 309, 556 and 1000 mg product/kg dry soil (corresponding to 128, 71.1, 39.5, 21.9, 12.2, 6.78, 3.76, 2.08 mg Ethofumesate/kg soil dw and 129, 71.6, 39.8, 22.1, 12.3, 6.83, 3.79, 2.11 mg Phenmedipham/kg soil dw) and one control were tested. Four replicates per treated rate (test item and reference item) and eight replicates for the control, with ten Collembola each were tested. Assessment of adult mortality and reproduction was performed after 28 days.

For mortality, a statistically significant effect was observed at 171, 309, 556 and 1000 mg product/kg dry soil. Thus, the NOEC for mortality was determined as 95.3 mg product/kg dry soil and the LC₅₀ was estimated to be 116 mg product/kg dry soil.

For reproduction, a statistically significant reduction in the number of juveniles was observed at 95.3, 171, 309, 556, 1000 mg product/kg dry soil. Thus, the NOEC was determined as 52.9 mg product/kg dry soil and the EC_{10/50} values for reproduction as 44.4 and 105 mg product/kg dry soil, respectively.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Boric acid

Test System

Species	<i>Folsomia candida</i> Willem (Mandibulata, Antennata, Apterygota, Collembola)
Age	Juveniles (9 - 10 days old at test start)
Source	Laboratory breeding
Acclimatisation period	None
Food	Granulated dry yeast

Test Conditions

Temperature	19 - 20°C
Photoperiod	16 h light / 8 h dark

Light intensity	506 ± 30 – 577 ± 60.5 lux* * Due to technical reasons, the incubation chamber was changed on day 13 of the exposure phase. Therefore, the light intensity is given for both climatic chambers.
pH	6.03 – 7.01
Test soil	Artificial soil with 5% peat, 20% kaolin clay, 74% quartz sand and 0.3% calcium carbonate to adjust the pH of 6.0 ± 0.5. The pH of the artificial soil was determined to be 6.20. The maximum water holding capacity (45.3 %) and the moisture of the soil (2 %) were determined. At test's start, appropriate volumes of deionised water were mixed with the soil using a laboratory mixer to adjust the soil to about 60% of the water holding capacity at the start of the study. During the test soil moisture as % of WHC _{max} was 23.9 – 24.4.
Study Design and Methods	
In-life dates	16.03.2021 - 19.04.2021
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	28 days
Test concentrations	16.3, 29.4, 52.9, 95.3, 171, 309, 556 and 1000 mg product/kg dry soil
Test vessels / Exposure unit	Glass beakers with a volume of 100 mL were used and covered with Parafilm.
Treatment	Collembola were exposed to concentrations of 16.3, 29.4, 52.9, 95.3, 171, 309, 556 and 1000 mg/kg artificial soil for a period of 28 days. Collembola of the control group were exposed to artificial soil only (moistened with deionised water). A total amount of 55 g of the application solutions were added to 403 g soil (360 g DW) adjusted to 30% WHC _{max} to obtain the required test item rates and a soil moisture of about 60% WHC _{max} . Control: 73 mL demineralised water was added to 538 g soil (480 g DW) adjusted to about 30% WHC _{max} to obtain a soil moisture of about 60% WHC _{max} . After application, the test medium was thoroughly mixed with a blender to ensure a homogenous distribution of the test item and the water. 30 g soil dry weight (38.2 g wet soil) was filled without compression into each replicate vessel (depth in the test vessel was 2 - 4 cm). Per test concentration, 4 replicates, and 8 replicates for the control were prepared, 40 collembola per group (80 for the control), and 10 organisms per replicate. Boric acid was used as toxic reference in a separate test conducted once within 12 months.
Observations	After 28 days of exposure, the numbers of both surviving adults (i.e. the originally introduced springtails) and juvenile springtails in each test area were recorded. The soil moisture and maximum water holding capacity was determined prior to experimental starting. At test start and test end, pH-value and moisture content of the test medium were determined in the additional container for the test item concentrations and control. After 14 days, the arenas were reweighed, but as the change in the mean weight (through water loss from the soil) was < 2% of the soil's original water content, no further water was added.

Statistics

Mortality: Step-Down Rao-Scott-Armitage Test Procedure ($\alpha = 0.05$) was carried out to determine statistically significant differences compared to the control. A Qualitative Trend Analysis and a Tarone's Test Procedure were run before.

Reproduction: Multiple Sequentially-rejective Welsh-t-test Procedure ($\alpha = 0.05$) was carried out to determine statistically significant differences compared to the control. A Shapiro Wilk's Test on Normal Distribution, a Levene's Test on Variance Homogeneity were run at first.

The LC_x / EC_x values were calculated by probit analysis.

ToxRat Professional 3, ToxRat® Solutions GmbH was used to perform the statistical analysis.

RESULTS AND DISCUSSIONS

Validity criteria

The mean mortality of the control should be $\leq 20\%$ at the end of the test (actual: 12.5%). The mean number of juveniles per vessel on the control should be > 100 at the end of the test (actual: 634). For the control, the coefficient of variation calculated for the number of juveniles between replicates was less than 30% at the end of the definitive test (actual: 12.0%).

Biological results

Adult mean mortality in the control was 12.5% at the end of the test. In the case of the test item HBZ10, mean mortality of adult collembolans ranged between 5.0% and 100%.

Mean reproduction in the control was 634 juveniles per vessel at the end of the test. In the case of the test item HBZ10, mean reproduction of collembolans ranged between 625 juveniles and 0 juveniles.

Table A 2.4.2.1.1-1 Effect of HBZ10 on Collembola (*Folsomia candida*) in a 28-day reproduction study

Application rate [mg product/kg soil dw]	Mortality [%]	Mean reproduction (No. juveniles)	CV [%]	Reduction in reproduction [%]
Control	12.5 ± 8.86	634 ± 75.7	12.0	--
16.3	5.0 ± 5.77	625 ± 79.1	12.7	1.34
29.4	5.0 ± 10.0	563 ± 102	18.2	11.1
52.9	5.0 ± 5.77	532 ± 74.8	14.1	16.0
95.3	27.5 ± 48.6	375 ± 128*	34.1	40.8
171	67.5 ± 20.6*	147 ± 132*	89.8	76.8
309	100*	0*	-	100
556	100*	0*	-	100
1000	100*	0*	-	100

* Statistically significant effect compared to the control (mortality: Step-Down Rao-Scott-Armitage Test Procedure, $\alpha = 0.05$; reproduction: Multiple Sequentially-rejective Welsh-t-test Procedure, $\alpha = 0.05$).

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on *Folsomia candida* was examined under laboratory conditions over 28 days.

For reproduction, a statistically significant reduction in the number of juveniles was observed at 95.3, 171, 309, 556, 1000 mg product/kg dry soil. Thus, the NOEC was determined as 52.9 mg product/kg dry soil and the $EC_{10/50}$ values for reproduction as 44.4 and 105 mg product/kg dry soil, respectively.

A 2.4.2.1.2 Study 2

Comments of zRMS:	The study was conducted in line with OECD 226 with minor deviations.
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	<p>It was noted that the temperature in the soil during phase 3 of the extraction process was below the nominal temperature. To check for reasons of this deviation, a second datalogger was installed to measure the ambient air temperature inside the extractor. Since the internal thermometer of the extractor and the temperature of the ambient were within the nominal range, the values from the datalogger measuring the soil temperature are considered not reliable and caused by a malfunction of the datalogger. However, this deviation is considered to have no impact on integrity or validity of the study.</p> <p>The test design was relevant to derive both NOEC and EC_x values (8 concentrations, 8 replicates for control, 4 replicates per treatment group). EC₁₀ value could not be evaluated for its reliability because the 95% confidence intervals of EC_x values could not be determined either due to mathematical reasons or the value was beyond the tested concentrations by more than a factor of 1000.</p> <p>All the validity criteria were met and the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>NOEC (reproduction) = 244 mg product/kg soil dw</p>
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Reference:	KCP 10.4.2.1/02
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Predatory mite reproduction test in soil (<i>Hypoaspis aculeifer</i>), Klix, V., 2021j, report No SO20134 / IHL18743
Guideline(s):	OECD 226 (2016)
Deviations:	<p>Minor (see the commenting box above)</p> <p>The temperature in the soil during phase 3 of the extraction process was outside the nominal range. Since the air temperature inside the extractor was inside the nominal, this is considered as a malfunction of the respective datalogger, measuring the soil. This deviation is considered to have no impact on integrity or validity of the study.</p>
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

Hypoaspis aculeifer were exposed to Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) for a period of 14 days. The test item was mixed thoroughly with artificial soil which was filled in glass vessels before the adult mites were introduced to the vessels. Concentrations of 37.3, 59.6, 95.4, 153, 244, 391, 625, 1000 mg product/kg dry soil and one control were tested. Four vessels per treated rate (test item) and eight vessels for the reference item and for the control groups, with ten adult female mites each, were tested. Assessment of adult mortality and reproduction was performed after 14 days.

For mortality, a statistically significant effect was observed at 1000 mg product/kg dry soil. Thus, the NOEC for mortality was determined as 625 mg product/kg dry soil and the LC₅₀ was estimated to be > 1000 mg product/kg dry soil.

For reproduction, a statistically significant reduction in the number of juveniles was observed at 391, 625, 1000 mg product/kg dry soil. Thus, the NOEC was determined as 244 mg product/kg dry soil and the EC_{10/50} values for reproduction as 388 and 659 mg product/kg dry soil, respectively.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A

Active ingredient content	Ethofumesate (125 g/L, analysed)
Characteristics	Phenmedipham (126 g/L, analysed)
Density	Yellowish orange, clear, liquid
Storage conditions	0.977 g/mL
Stability (expiry date)	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Vehicle / control(s)	25.02.2022
	Control: Deionised water
	Toxic reference item: Boric acid
Test System	
Species	<i>Hypoaspis (Geolaelaps) aculeifer</i> Canestrini (Acari: Laelapidae)
Age	Adult females, 30 - 33 days old after start of egg laying period
Source	Katz Biotech AG, An der Birkenpfehlheide 10, D-15837 Baruth, Germany
Acclimatisation period	4 days before test start, synchronized females were delivered by Katz Biotech AG. The mites were kept in covered polyethylene flasks (h = 4 cm, Ø = 8.8 cm) on artificial soil, containing 8 parts by weight calcium sulfate dehydrate (dw) (plaster) and 1 part by weight powdered activated charcoal (dw), at the test facility at test conditions
Food	The mites were fed <i>ad libitum</i> with cheese mites, species <i>Tyrophagus putrescentiae</i> . The mites were delivered by Katz Biotech AG
Test Conditions	
Temperature	19.3 - 19.9°C
Photoperiod	16 h light / 8 h dark
Light intensity	534 ± 44.1 lux
Test soil	Artificial soil with 5% peat, 20% kaolin clay, 74 % quartz sand and 0.18% calcium carbonate to adjust the pH of 6.0 ± 0.5. At test's start, appropriate volumes of deionised water were mixed with the soil using a laboratory mixer to adjust the soil to about 60% of the water holding capacity at the start of the study.
Study Design and Methods	
In-life dates	11.01.2021 – 28.01.2021
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	14 days
Test concentrations	37.3, 59.6, 95.4, 153, 244, 391, 625, 1000 mg product/kg dry soil
Test vessels / Exposure unit	Glass beakers with a volume of 100 mL were used and covered with Parafilm.
Treatment	The mites were exposed to concentrations of 37.3, 59.6, 95.4, 153, 244, 391, 625, 1000 mg product/kg artificial soil for a period of 14 days. The mites of the control group were exposed to artificial soil only (moistened with deionised water). Boric acid (300 mg/kg dry soil) was used as toxic reference. After application the test medium was thoroughly mixed with a blender to ensure a homogenous distribution of the test item. 20 g soil dry weight were filled without compression into each replicate vessel. For each test item group and the toxic reference, 40 test organisms were divided into 4 replicate groups, each containing 10 test organisms. The untreated control comprised 8 replicates with 10 test organisms each.

Observations	<p>The soil moisture and maximum water holding capacity was determined prior to experimental starting. At test start and test end, pH-value and moisture content of the test medium was determined in additional container for the test item concentrations and control. Three times per week, the soil moisture was determined by weighing the test vessels and the soil was re-moistened, if necessary.</p> <p>Number of living adult female mites and number of juvenile mites at day 14 after application, counted after extraction on day 16 after application.</p>
Statistics	<p>The mean number of dead adult female mites and of juvenile mites for each treatment and NOEC and LOEC values were determined. Mortality data were statistically analysed by Step-down Cochran-Armitage Test Procedure ($\alpha = 0.05$) to determine statistically significant differences between the test item treatments and the control. Reproduction data were tested for normal distribution and homogeneity of variance using Shapiro-Wilk's test and Levene's test. Further statistical evaluation was performed using Williams Multiple Sequential t-test Procedure ($\alpha = 0.05$).</p> <p>The ECx values for mortality and reproduction were determined by probit analysis and 3-parametrical normal CDF analysis, respectively.</p>

RESULTS AND DISCUSSIONS

Validity criteria

Mean adult female mortality should be $\leq 20\%$ at the end of the test in the untreated control group (actual: 6.25%). The mean number of juveniles per replicate should be least 50 at the end of the test in the untreated control group (actual: 210). The coefficient of variation calculated for the number of juvenile mites per replicate should be $\leq 30\%$ at the end of the definitive test in the untreated control group (actual: 8.80%). The reduction in reproduction of the toxic reference item group met the guideline specified value of more than 50% at the end of the test (actual: 77.4%).

Biological results

Adult mean mortality in the untreated control was 6.25% at the end of the trial (14 DAA). In the case of the test item HBZ10, mean mortality of adult mites ranged between 5.0% and 77.5%. Mean mortality of the adult mites treated with the reference item was 7.50% at the end of the test.

Mean reproduction in the untreated control was 210 juveniles per vessel at the end of the test (14 DAA). In the case of the test item HBZ10, mean reproduction of mites ranged between 12.87 and 219 juveniles per vessel. Mean reproduction of the mites treated with the reference item was 47.58 juveniles per vessel at the end of the test.

Table A 2.4.2.1.2-1 Effect of HBZ10 on the predatory mite *Hypoaspis aculeifer* in a 14-day reproduction test

Application rate [mg product/kg dry soil]	Mean mortality [%] ¹	Mean reproduction (No. juveniles)	CV [%]	Reduction in reproduction [%]
Control	6.25 ± 9.16	210 ± 18.5	8.80	--
37.3	5.00 ± 5.77	219 ± 38.0	17.4	-4.17
59.6	10.0 ± 11.6	211 ± 25.0	11.9	-0.24
95.4	7.50 ± 9.57	211 ± 23.2	11.0	-0.24
153	17.5 ± 12.6	186 ± 12.4	6.68	11.7
244	5.00 ± 5.77	214 ± 21.7	10.1	-1.79
391	12.5 ± 9.57	158* ± 21.7	13.7	24.9
625	12.5 ± 12.6	139* ± 20.1	14.5	34.1
1000.0	77.5* ± 9.57	12.8* ± 8.92	70.0	93.9
Reference item: Boric acid				
300	7.50 ± 7.07	47.5 ± 11.5	24.2	77.4

¹ Based on the number of dead organisms

* Statistically significant effect compared to the control (mortality: Step-down Cochran-Armitage Test Procedure, $\alpha = 0.05$; reproduction: Williams Multiple Sequential t-test Procedure, $\alpha = 0.05$)

Table A 2.4.2.1.2-2 Endpoints of HBZ10 on *Hypoaspis aculeifer* in a 14-day reproduction test

Endpoint [mg product/kg dry soil]	Mortality	Reproduction
NOEC	625	244
EC ₁₀ (95% confidence limits)	124 (n.d.)	388 (n.d.)
EC ₂₀ (95% confidence limits)	279 (n.d.)	465 (n.d.)
EC ₅₀ (95% confidence limits)	> 1000 (n.d.)	659 (n.d.)

n.d. = not determined

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on *Hypoaspis aculeifer* was examined under laboratory conditions over 14 days.

For reproduction, a statistically significant reduction in the number of juveniles was observed at 391, 625, 1000 mg product/kg dry soil. Thus, the NOEC was determined as 244 mg product/kg dry soil and the EC_{10/50} values for reproduction as 388 and 659 mg product/kg dry soil, respectively.

A 2.4.2.1.3 Study 3

Comments of zRMS:	<p>The study for <i>Folsomia candida</i> was evaluated and agreed by the RMS in the course of the ongoing EU renewal process: with agreed endpoint NOEC_{corr}=500 mg a.s./kg dws, included in LIEP 2022, and EFSA Conclusion 2018). Although the renewal process is not finalized yet, no changes regarding the derived endpoints are expected.</p> <p>For this reason, the study was not re-evaluated by zRMS.</p> <p>Agreed endpoint: NOEC_{corr}= 500 mg a.s./kg dws</p>
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Reference:	KCP-10.4.2.1/03
Report:	Phenmedipham a.s.: Influence on the reproduction of the collembolan species <i>Folsomia candida</i> tested in artificial soil. Frommholz, U., 2010, report No FRM-COLL-83/10
Guideline(s):	OECD 232 (2009)
Deviations:	None
GLP:	Yes
Acceptability:	Yes
Duplication (if vertebrate study):	No

Material and methods:

Test material:	Phenmedipham a.s.
Lot/Batch No.:	EDHB010864; Specification No.: 102000011516
Purity:	99.1% w/w
Test species:	<i>Folsomia candida</i> (9-12 days old)
Test system/test conditions:	<p>- Ten collembolans (10-12 days old) per replicate (8 replicates for the control group and 4 replicates for each treatment group) were exposed to control (water treated), 100, 177, 316, 562 and 1000 mg a.s./kg artificial soil dry weight. The test item was applied as a test-item-quartz-sand-mixture which was thoroughly mixed into 500 g artificial dry weight artificial soil.</p> <p>- During the study, Collembolans were fed with granulated dry yeast. Mortality and reproduction were determined after 28 days. Numbers of collembola were counted from each vessel by a digital image.</p> <p>- Test conditions: temperature 20 ± 2°C, intensity 400 – 800 lux with 16h light:8h dark, pH at the test start of the test 5.51 and 5.57-5.62.</p>
Data analysis:	<p>Normal distribution: Kolmogorov-Smirnov test ($\alpha = 0.05$)</p> <p>Homogeneity of variances: Cochran's test ($\alpha = 0.05$)</p> <p>Mortality: Could not be calculated; EC₅₀ value was greater than value</p> <p>Reproduction: William's-t test, one-sided smaller, $\alpha = 0.05$</p>

Results:

Table A.2.4.2.1.3-1: Validity criteria of the study

Validity criteria (for the control group)	Required	Obtained
Mortality of the adults	< 20%	12.5%
Mean number of juveniles per vessel at the end of the test	> 100	1110
Coefficient of variance of reproduction	< 30%	18.7%

The most recent non-GLP-test (FRM-Coll-Ref-14/10, U. Frommholz, March 03, 2010) with the reference item Boric acid showed an EC₅₀ of 96 mg test item/kg artificial soil dry weight (95 % CI: 87 -105 mg Boric acid/kg soil dry weight). The results showed that the test organisms were sufficiently sensitive according to the guideline. The result is in the recommended range of the guideline (about 100 mg Boric acid/kg artificial soil dry weight).

Biological results:

Mortality

In the control group 12.5 % of the adult *Folsomia candida* died which is below the allowed maximum of ≤ 20 % mortality. A LC50 could not be calculated and is considered to be > 1000 mg a.s./kg artificial soil dry weight (Table B.9.4.2-3).

Reproduction

Concerning the number of juvenile's statistical analysis revealed no significant difference between control and any treatment group. Therefore, the NOEC for reproduction is ≥ 1000 mg a.s./kg soil dry weight. The LOEC for reproduction is > 1000 mg a.s./kg soil dry weight. An EC50 could not be calculated and is considered to be > 1000 mg test item/kg soil dry weight (Table A.2.4.2.1.3-2).

Table A.2.4.2.1.3-2: Effects of phenmedipham on *Collembola (Folsomia candida)* in a 28-day reproduction study.

Test item Test object Exposure	Phenmedipham a.s. <i>Folsomia candida</i> Artificial soil		
mg test item/kg soil dry weight nominal concentration	Adult mortality (%)	Mean number of juveniles \pm SD	Reproduction (% of control)
Control	12.5	1110 \pm 208	1
100	10.0	1109 \pm 227	100 ^{n.s.}
177	7.5	931 \pm 231	84 ^{n.s.}
316	5.0	1156 \pm 321	104 ^{n.s.}
562	17.5	875 \pm 306	79 ^{n.s.}
1000	7.5	1098 \pm 241	99 ^{n.s.}

The calculations were performed with unrounded values

n.s. = statistically not significant (William's T-test one-sided-smaller, $\alpha = 0.05$)

The NOEC_{reproduction} was ≥ 1000 mg a.s./kg soil dry weight and LOEC_{reproduction} was > 1000 mg a.s./kg soil dry weight.

Due to the lack of a concentration-response relationship it was not possible to perform a valid EC₁₀ or EC₂₀ calculation.

A 2.4.2.2 KCP 10.4.2.2 Higher tier testing

No new study is submitted.

A 2.5 KCP 10.5 Effects on soil nitrogen transformation

A 2.5.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 216 with minor deviations.</p> <p>It was noted in the study report that due to unusually high temperatures during the summer months the room temperature exceeded 22°C (up to a maximum of 23.9 °C). The room temperature fell below 18°C (minimum 16.4 °C, for approximately 16 hours) because the air condition was forgotten to switch off. Since the test item is liquid, the amount was pipetted instead of weighing it out. The cleaned extracts were diluted 1:4 (day 42, 56, 70) and 1:8 (day 80) instead of 1:2 because the expected extinctions were above the calibration range. These deviations were considered to have no impact quality and integrity of the study since all the validity criteria were met.</p> <p>Overall, the study is considered acceptable.</p> <p>It may be concluded that the effects of the test item on soil nitrogen formation rates were < 25 % at the end of the study period (70 days) up to 31.26 mg product/kg soil dw</p>
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Reference:	KCP 10.5/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Soil Micro-Organisms: Nitrogen Transformation Test, Winkelmann, G., 2021b, report No SO20136 / TBN18743
Guideline(s):	OECD 216 (2000)
Deviations:	<p>Minor (see the commenting box above)</p> <p>Due to unusual high temperatures during the summer months the room temperature exceeded 22°C (by maximum 23.9 °C). The room temperature fell below 18°C because the air condition was forgotten to switch off.</p> <p>These deviations were considered to have no impact quality and integrity of the study.</p>
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

In a soil microbial activity study, the effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the nitrogen transformation (NO₃-nitrogen-production) in soil by comparison of nitrogen transformation in test item treated soil with a non-treated soil. The test was terminated after 70 days. Three treatment groups (control and test item at two concentrations: 2.4 and 24 L product/ha, corresponding to 3.126 and 31.26 mg product/kg dry soil) with three replicates each were incubated in the dark.

In order to stimulate nitrogen transformation, the soil was mixed with lucerne meal (concentration in soil: 0.5%). On day 7, 14, 28, 42, 56 and 70, the mineral nitrogen content was determined.

The nitrate formation rates for the whole study period intervals (*e.g.*, day 0 - 28) deviated less than 25% from the control group for the lower test item rate continuously from day 28 on, however, the deviation from the control were > 25% for the higher test item rate from day 28-56. On day 70, the nitrate formation rates deviated less than 25% from the control for both test item rates. HBZ10 caused no long-term effects (difference to control < 25%, OECD 216) on the soil nitrogen transformation (measured as NO₃-N production) at a test concentration of 31.26 mg product/kg dry soil, 70 days after application (time interval 0 - 70 days after application).

The study was performed in a field soil (silty sand) at concentrations up to 31.26 mg product/kg dry soil. All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water Toxic reference item: Cyanoguanidine

Test System

Soil	One single, common, agricultural soil type was used for the study
Source	LUFA Speyer, Obere Langgasse 40, 67346 Speyer, Germany
Soil parameter	Silty sand / pH 6.1 / CEC 6.8 meq/100g / total organic carbon (0.5-1.5%) / 0.496% organic carbon / microbial biomass (3.20% of TOC) / WHCmax 35.2 g/100g dry soil/ 57.6% sand, 35.2% silt, 7.3% clay

Test Conditions

Temperature	16.4 – 23.9°C
Photoperiod	Constant dark

Study Design and Methods

In-life dates	24.06.2020 – 02.09.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	70 days
Test concentrations	2.4 and 24.0 L product/ha, corresponding to 3.126 and 31.26 mg product/kg dry soil
Test vessels / Exposure unit	Plastic boxes (volume 1.0 L, food grade) with perforated tops to enable gas exchange
Treatment	Prior to the initiation of the study, the moisture content of the soil and the amount of water needed to bring the soil moisture content to 42% WHCmax were determined. For the nitrogen turnover, the soil was thoroughly mixed with ground lucerne meal before application. The final concentration of the dried lucerne meal was 0.5% of the soil dry weight. HBZ10 was applied at 2.4 and 24.0 L product/ha. The toxic reference test is conducted once within twelve months. The most recent test was carried out from 29.01.2020 to 02.03.2020
Observations	Measurements of inorganic nitrate were carried out after 0, 7, 14, 28, 42, 56 and 70 days. The pH values and water contents were determined on day 0, 28, 42, 56 and 70. Over the 70-day period the pH values ranged between 5.67 and 6.46, WHC ranged between 40.2 and 43.5 %.
Statistics	Nitrate was extracted from soil samples with a mineral salt solution. For the elimination of coloured organic matter in the extraction solution a cleaning step with SPE (Solid Phase Extraction) cartridges was carried out. Thereafter, photometric determination took place. Mean nitrate-N values, standard deviations and coefficients of variation were calculated for each assessment date and treatment group. No statistical evaluation was performed.

RESULTS AND DISCUSSIONS

Validity criteria

The variation between replicate control samples was less than $\pm 15\%$ for each sampling date. In this study variations of nitrate-N contents between control replicates were 6% at day 0, 4% at day 7 and day 70, 5% at day 14 and day 56, 1% at day 28 and 6% at day 42.

Biological results

No adverse effects of the test item on nitrogen transformation in soil were observed at the test concentrations (3.126 mg product/kg dry soil and 31.26 mg product/kg dry soil) after 70 days (time interval 0 - 70).

Table A 2.5.1-1 Effects on nitrogen transformation rate in soil after treatment with HBZ10

Time Interval (days)	Control	3.126 mg product/kg dry soil		31.26 mg product/kg dry soil	
	NO ₃ -N/day [mg/kg dry soil]	NO ₃ -N/day [mg/kg dry soil]	Deviation from control [%] ¹⁾	NO ₃ -N/day [mg/kg dry soil]	Deviation from control [%] ¹⁾
0 - 7	0.713	0.976	-37.0	1.48	-108
0 - 14	0.497	0.554	-11	0.961	-93
0 - 28	0.520	0.610	-17	0.820	-58
0 - 42	0.511	0.493	4	0.668	-31
0 - 56	0.630	0.611	3	0.802	-27
0 - 70	0.424	0.432	-2	0.511	-21

The calculations were performed with non-rounded values

¹⁾ negative value = promotion of nitrate-N content / formation rate; positive value = inhibition of nitrate-N content / formation rate

CONCLUSION

HBZ10 caused no long-term effects (difference to control < 25%, OECD 216) on the soil nitrogen transformation (measured as NO₃-N production) at a test concentration of 31.26 mg product/kg dry soil, 70 days after application (time interval 0 - 70 days after application).

A 2.6 KCP 10.6 Effects on terrestrial non-target higher plants

A 2.6.1 KCP 10.6.1 Summary of screening data

No new study is submitted.

A 2.6.2 KCP 10.6.2 Testing on non-target plants

A 2.6.2.1 Study 1

Comments of zRMS:	<p>The study was conducted in line with OECD 208 with a minor deviation in environmental conditions.</p> <p>It was noted that there was a short-term decrease of the relative humidity to 31.5 % (below the recommended minimum of 45 %) during daylight periods but it had no negative impact on plant growth since all the validity criteria were met.</p> <p>The analytical measurements showed that the concentrations of both active substances were within 80 – 120 % of nominal; therefore, the endpoint can be expressed as nominal concentration.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>ER_{50,shoot fresh weight} = 1.25 L product/ha (the most sensitive species was wheat <i>Triticum aestivum</i>)</p>
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Reference:	KCP 10.6.2/01
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Terrestrial Plant Test: Seedling Emergence and Seedling Growth, Winkelmann, G., 2021c, report No SO20031 / TNK18743
Guideline(s):	OECD 208 (2006)
Deviations:	Minor (see the commenting box above) No deviation with impact on quality and integrity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the seedling emergence of 10 plant species (3 monocotyledons: *Avena sativa*, *Triticum aestivum*, *Allium cepa* and 7 dicotyledons: *Brassica napus*, *Raphanus sativus*, *Linum usitatissimum*, *Helianthus annuus*, *Lactuca sativa*, *Lycopersicon esculentum*, *Glycine max*) was examined in comparison with a water control under greenhouse conditions over 21 days. HBZ10 at test concentrations of 0.197, 0.454, 1.04, 2.40, 5.52 L product/ha (*Avena*, *Triticum*, *Lactuca*) and 0.454, 1.04, 2.40, 5.52, 12.7 L product/ha (*Allium*, *Brassica*, *Raphanus*, *Linum*, *Helianthus*, *Lycopersicon*, *Glycine*) was applied at test start on the soil surface after the seeds were sown.

Potential toxic effects of the test item were assessed on day 7, 14 and 21 by visual observations (phytotoxic effects, number of dead plants and number of emerged seedling) and at test end by shoot height and shoot fresh weight determination.

The spray solutions (highest application rates and control) were sampled prior to application and subsequently analytically verified. The measured concentrations of Ethofumesate were 90% to 101% and 88% to 107% of Phenmedipham, indicating the correct preparation of the spray solutions.

Triticum aestivum was identified as most sensitive species. For shoot fresh weight, a statistically significant inhibition was observed at 1.04, 2.40, 5.52 L product/ha, resulting in a NOEL of 0.454 L product/ha, the ER₅₀ was determined to be 1.25 L product/ha.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water

Test System

Species	<i>Avena sativa</i> , <i>Triticum aestivum</i> , <i>Allium cepa</i> , <i>Brassica napus</i> , <i>Raphanus sativus</i> , <i>Linum usitatissimum</i> , <i>Helianthus annuus</i> , <i>Lactuca sativa</i> , <i>Lycopersicon esculentum</i> , <i>Glycine max</i>
Growth stage	Not stated
Acclimatization	Not stated
Irrigation	Bottom-watered

Test Conditions

Temperature	16.3 – 25.8°C
Humidity	31.5 – 87.2%
Photoperiod	16 h light / 8 h dark
Light intensity	4997 ± 692 lux
Soil	A 2:1 mixture of natural soil LUFA 2.2 (batch number: Sp2.21320, loamy sand (DIN classification)) and quartz sand (12a) was used.

Study Design and Methods

In-life dates	05.05.2020 – 05.06.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	21 days
Test concentrations	0.197, 0.454, 1.04, 2.40, 5.52 L product/ha (<i>Avena</i> , <i>Triticum</i> , <i>Lactuca</i>) 0.454, 1.04, 2.40, 5.52, 12.7 L product/ha (<i>Allium</i> , <i>Brassica</i> , <i>Raphanus</i> , <i>Linum</i> , <i>Helianthus</i> , <i>Lycopersicon</i> , <i>Glycine</i>)
Test vessels / Exposure unit	Plastic container (standard flower pots) with a diameter of ca. 12 cm and a surface area of approximately 113 cm ² were used.
Treatment	The seeds were sown in the test containers prior to application. Test containers were filled with soil and the seeds were placed on the soil surface. Afterwards, the seeds were covered with a thin soil layer. Oats, winter wheat, onion, rape, radish, flax, lettuce, tomato: 5 seeds per 113 cm ² ; Sunflower, soybean: 3 seeds per 113 cm ² . The test item was sprayed in 200 L water/ha at test concentrations of 0.197, 0.454, 1.04, 2.40, 5.52 L product/ha (<i>Avena</i> , <i>Triticum</i> , <i>Lactuca</i>) and 0.454, 1.04, 2.40, 5.52, 12.7 L product/ha (<i>Allium</i> , <i>Brassica</i> , <i>Raphanus</i> , <i>Linum</i> , <i>Helianthus</i> , <i>Lycopersicon</i> , <i>Glycine</i>). 8 replicates per application rate and control were tested

Observations	<p>During the observation period the plants were observed for number of emerged seedlings, visual phytotoxic effects and number of dead plants on day 7, 14 and 21. The rating of the treated plants was done in relation to the untreated control plants.</p> <p>Observations included all variations, either inhibitory or stimulatory, between the treated test replicates and the untreated control replicates. Such variations were phytotoxic symptoms (e.g. chlorosis, necrosis, wilting), formative effects and growth and development rates.</p> <p>At the end of the study, shoot height (in cm), measured after cutting the plants, and shoot fresh weight of the shoots (in mg) were measured additionally.</p> <p>The room temperature and relative humidity were recorded continuously throughout the test.</p>
Analytical verification	<p>The spray solutions (highest application rates and control) were sampled prior to application and subsequently analytically verified. Analytical evaluation of Ethofumesate and Phenmedipham, active ingredients of the test item, was carried out via UPLC-MS/MS on a reversed phase column. The analytical method was validated based on SANCO/3029/99 rev. 4.</p>
Statistics	<p>One Way Analysis of Variance (ANOVA) and Dunnett's test were carried out for the determination of statistically significant differences compared to control replicates. When running a One-Way Analysis of Variance, a Normality test (Shapiro-Wilk) and an Equal Variance test (Brown-Forsythe) were done first. P-values for both, Normality and Equal Variance test, are 0.05. The α-value for ANOVA and Dunnett's test (acceptable probability of incorrectly concluding that there is a difference) is $\alpha = 0.05$.</p> <p>Failure of the normality test and / or the equal variance test can be caused by extremely homogeneous emergence and growth patterns as opposed to higher variances in other treatments. Due to the high and even number of replicates in the control and treatment groups, the failure had no influence on the robustness of the calculations.</p> <p>ER_{25/50}-values were calculated by sigmoidal dose-response regression using GraphPadPrism. Four parameter were used for dose-response fitting. Calculation of the confidence intervals for ED-values was carried out using standard procedures provided by GraphPadPrism.</p>

RESULTS AND DISCUSSIONS

Validity criteria

The germination rate of control seed was at least 70%. The mean survival of emerged control seedlings was at least 90%. The control seedlings did not exhibit visible phytotoxic effects and the plants exhibited only normal variation in growth and morphology for the particular species.

Analytical results

The spray solutions (highest application rates and control) were sampled prior to application and subsequently analytically verified. The measured concentrations of Ethofumesate were 90% to 101% and 88% to 107% of Phenmedipham, indicating the correct preparation of the spray solutions.

Biological results

Application rates with treatment related visual phytotoxic effects at the study end are given in **Table A 2.6.2.1-1**. The statistically calculated NOEL values as well as the ED₂₅ and ED₅₀ values for shoot height and shoot fresh weight are given in **Table A 2.6.2.1-2** and **Table A 2.6.2.1-3**. The calculated NOEL, ED₂₅ and ED₅₀ values for number of emerged seedlings are given in **Table A 2.6.2.1-4**.

Table A 2.6.2.1-1 Treatment related visual phytotoxic effects of HBZ10 at study termination

Species	Main observed visual effects*	Appearance at application rates [L product/ha]
<i>Avena sativa</i>	Deformation of leaves Stunted growth Necrosis	≥ 2.40 0.197, ≥ 2.40 5.52
<i>Tritium aestivum</i>	Deformation of leaves Stunted growth Necrosis	≥ 0.454 ≥ 0.454 5.52
<i>Allium cepa</i>	None	-
<i>Brassica napus</i>	Deformation of leaves Stunted growth	≥ 5.52 ≥ 5.52
<i>Raphanus sativus</i>	Deformation of leaves Stunted growth	≥ 1.04 ≥ 1.04
<i>Linum usitatissimum</i>	Deformation of leaves Stunted growth Necrosis	≥ 2.40 ≥ 2.40 2.40 and 5.52
<i>Helianthus annuus</i>	None	-
<i>Lactuca sativa</i>	Deformation of leaves Stunted growth	≥ 1.04 ≥ 1.04
<i>Lycopersicon esculentum</i>	Deformation of leaves Stunted growth Lighter green	≥ 5.52 ≥ 2.40 ≥ 2.40
<i>Glycine max</i>	Deformation of leaves Stunted growth Necrosis	≥ 5.52 ≥ 5.52 12.7

* Effects were considered treatment related when > 2 replicates were influenced

Table A 2.6.2.1-2 Shoot height: NOEL, ED₂₅ and ED₅₀ values with confidence range (p)

Species	NOEL [L product/ha]	ED ₂₅ [L product/ha]	p = 95% [L/ha]	ED ₅₀ [L product/ha]	p = 95% [L/ha]
<i>Avena sativa</i>	1.04	2.58	2.03 - 3.18	4.40	2.03 - > 5.52
<i>Tritium aestivum</i>	0.454	0.751	0.610 - 0.897	1.39	1.20 - 1.64
<i>Allium cepa</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-
<i>Brassica napus</i>	0.454	8.29	5.97 - 11.7	≥ 12.7	-
<i>Raphanus sativus</i>	2.40	10.9	6.19 - > 12.7	≥ 12.7	-
<i>Linum usitatissimum</i>	1.04	2.20	1.65 - 2.78	4.82	3.74 - 6.45
<i>Helianthus annuus</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-
<i>Lactuca sativa</i>	1.04	2.19	1.99 - 2.40	3.92	3.41 - 4.47
<i>Lycopersicon esculentum</i>	5.52	10.1	8.24 - 12.2	≥ 12.7	-
<i>Glycine max</i>	2.40	7.50	6.33 - 8.63	≥ 12.7	-

Table A 2.6.2.1-3 Shoot fresh weight: NOEL, ED₂₅ and ED₅₀ values with confidence range (p)

Species	NOEL [L product/ha]	ED ₂₅ [L product/ha]	p = 95% [L/ha]	ED ₅₀ [L product/ha]	p = 95% [L/ha]
<i>Avena sativa</i>	1.04	1.51	0.826 - 2.26	3.08	2.29 - 3.98
<i>Tritium aestivum</i>	0.454	0.703	0.511 - 0.913	1.25	1.03 - 1.52
<i>Allium cepa</i>	≥ 12.7	12.0	7.42 - > 12.7	≥ 12.7	-
<i>Brassica napus</i>	0.454	2.42	1.15 - 4.13	9.60	6.96 - > 12.7
<i>Raphanus sativus</i>	2.40	4.98	2.10 - 9.21	≥ 12.7	-
<i>Linum usitatissimum</i>	1.04	1.96	1.30 - 2.70	3.97	2.98 - 5.62
<i>Helianthus annuus</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-
<i>Lactuca sativa</i>	2.40	2.48	2.01 - 3.25	3.98	2.90 - > 5.52
<i>Lycopersicon esculentum</i>	2.40	5.03	3.29 - 6.99	11.4	8.93 - > 12.7
<i>Glycine max</i>	2.40	7.66	4.61 - 12.0	≥ 12.7	-

- not determinable

Table A 2.6.2.1-4 Number of Emerged Seedlings: NOEL, ED₂₅ and ED₅₀ values with confidence range (p)

Species	NOEL [L product/ha]	ED ₂₅ [L product/ha]	p = 95% [L/ha]	ED ₅₀ [L product/ha]	p = 95% [L/ha]
<i>Avena sativa</i>	≥ 5.52	≥ 5.52	-	≥ 5.52	-
<i>Triticum aestivum</i>	≥ 5.52	≥ 5.52	-	≥ 5.52	-
<i>Allium cepa</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-
<i>Brassica napus</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-
<i>Raphanus sativus</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-
<i>Linum usitatissimum</i>	≥ 12.7	12.7	9.21 - > 12.7	≥ 12.7	-
<i>Helianthus annuus</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-
<i>Lactuca sativa</i>	≥ 5.52	≥ 5.52	-	≥ 5.52	-
<i>Lycopersicon esculentum</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-
<i>Glycine max</i>	≥ 12.7	≥ 12.7	-	≥ 12.7	-

- not determinable

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the seedling emergence of 10 plant species (3 monocotyledons and 7 dicotyledons) was examined in comparison with a water control under greenhouse conditions over 21 days.

Triticum aestivum was identified as most sensitive species. For the shoot fresh weight, a statistically significant inhibition was observed at 1.04, 2.40, 5.52 L product/ha, resulting in a NOEL of 0.454 L product/ha, the ER₅₀ was determined to be 1.25 L product/ha.

A 2.6.2.2 Study 2

Comments of zRMS:	<p>The study was conducted in line with OECD 227 with minor deviations.</p> <p>It was noted that the minimum relative humidity was 44.5 % which was slightly below the recommended minimum of 45 % but it had no negative impact on plants growth since all the validity criteria were met.</p> <p>The environmental conditions from 2020-07-06 to 2020-07-14 (9 days) were deleted before saving. Therefore, no data are available for this period.</p> <p>For rape (<i>Brassica napus</i>) at 0.141 L/ha one replicate was identified as outlier (determined by Grubb's test) and only 7 replicates were used for further calculations.</p> <p>These deviations were considered to have no impact on the integrity or the validity of the study.</p> <p>The analytical measurements showed that the concentrations of both active substances were within 80 – 120 % of nominal; therefore, the endpoint can be expressed as nominal concentration.</p> <p>Overall, the study is considered acceptable with the following endpoint relevant for the risk assessment:</p> <p>ER_{50,shoot fresh weight} = 0.146 L product/ha (the most sensitive species was tomato <i>Lycopersicon esculentum</i>)</p>
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Reference:	KCP 10.6.2/02
Report	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10): Terrestrial Plant Test: Vegetative Vigour Test, Winkelmann, G., 2021d, report No SO20032 / TNW18743
Guideline(s):	OECD 227 (2006)
Deviations:	Minor (see the commenting box above) Inadvertently, the environmental conditions from 2020-07-06 to 2020-07-14 were deleted before saving. Therefore, no data are available for this period. For <i>Brassica napus</i>, at 17.7 g a.i./ha: One replicate was identified as outlier, determined by Grubb's test, only 7 replicates were used for calculations. These deviations were considered to have no impact on integrity or validity of the study.
GLP:	Yes
Acceptability:	Acceptable Yes
Duplication (if vertebrate study)	No

Executive Summary

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the vegetative vigour of 10 plant species (3 monocotyledons: *Avena sativa*, *Triticum aestivum*, *Allium cepa* and 7 dicotyledons: *Brassica napus*, *Raphanus sativus*, *Linum usitatissimum*, *Helianthus annuus*, *Lactuca sativa*, *Lycopersicon esculentum*, *Glycine max*) was examined in comparison with a water control under greenhouse conditions over 21 days. HBZ10 was applied onto the foliage of plants in the 2 to 4 leaf stage at application rates of 0.141, 0.353, 0.883, 2.21, 5.52 L product/ha (*Avena*, *Triticum*, *Brassica*, *Glycine*), 0.0296, 0.0889, 0.267, 0.800, 2.40 L product/ha (*Allium*, *Raphanus*, *Linum*, *Helianthus*, *Lactuca*, *Lycopersicon*), and additionally for *Allium*, *Raphanus*, *Lactuca* of 7.20 L product/ha with a spray volume corresponding to 200 L water/ha. In the test, 8 replicates with 3 plants per replicate were used for *Avena sativa*, *Triticum aestivum*, *Allium cepa*, *Brassica napus*, *Raphanus sativus*, *Linum usitatissimum*, *Helianthus annuus*, *Lycopersicon esculentum*, *Glycine max* and 7 replicates with 3 plants per replicate for *Lactuca sativa*. Potential toxic effects of the test item were assessed on day 7, 14 and 21 by visual observations (phytotoxic effects and number of dead plants) and on day 21 by shoot height and shoot fresh weight determination.

The spray solutions (highest application rates and control) were sampled prior to application and subsequently analytically verified. Analytical recovery in the stock solutions were between 84% and 103% of Ethofumesate and between 93% and 97% of Phenmedipham, indicating the correct preparation of the spray solutions.

Lycopersicon esculentum was identified as most sensitive species. For shoot fresh weight, a statistically significant inhibition was observed at 0.0889, 0.267, 0.800, 2.40 L product/ha, resulting in a NOEL of 0.0296 L product/ha, the ER₅₀ was determined to be 0.146 L product/ha.

All validity criteria of the respective test guideline were met.

MATERIALS AND METHODS

Test Item

Designation	Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10)
Lot / Batch no.	FL20-024-2A
Active ingredient content	Ethofumesate (125 g/L, analysed) Phenmedipham (126 g/L, analysed)
Characteristics	Yellowish orange, clear, liquid
Density	0.977 g/mL
Storage conditions	Room temperature. Keep container tightly closed in a dry and well-ventilated place
Stability (expiry date)	25.02.2022
Vehicle / control(s)	Control: Deionised water

Test System

Species	<i>Avena sativa</i> , <i>Triticum aestivum</i> , <i>Allium cepa</i> , <i>Brassica napus</i> , <i>Raphanus sativus</i> , <i>Linum usitatissimum</i> , <i>Helianthus annuus</i> , <i>Lactuca sativa</i> , <i>Lycopersicon esculentum</i> , <i>Glycine max</i>
Growth stage	BBCH 12 - 14
Acclimatisation	Not stated
Irrigation	Bottom-watered

Test Conditions

Temperature	17.5 - 25.2°C
Humidity	44.5 - 97.0%
Photoperiod	16 h light / 8 h dark
Light intensity	7295 ± 1011 lux
Soil	A 2:1 mixture of natural soil LUFA 2.2 (batch number: Sp2.21320, loamy sand (DIN classification)) and quartz sand (12a) was used

Study Design and Methods

In-life dates	18.06.2020 - 17.07.2020
Conducted at	Noack Laboratorien GmbH, Käthe-Paulus-Str.1, 31157 Sarstedt, Germany
Test duration	21 days
Test concentrations	0.141, 0.353, 0.883, 2.21, 5.52 L product/ha (<i>Avena</i> , <i>Triticum</i> , <i>Brassica</i> , <i>Glycine</i>) 0.0296, 0.0889, 0.267, 0.800, 2.40 L product/ha (<i>Allium</i> , <i>Raphanus</i> , <i>Linum</i> , <i>Helianthus</i> , <i>Lactuca</i> , <i>Lycopersicon</i>) 7.20 L product/ha (additionally for <i>Allium</i> , <i>Raphanus</i> , <i>Lactuca</i>)
Test vessels / Exposure unit	Plastic container (standard flower pots) with a diameter of ca. 12 cm and a surface area of approximately 113 cm ² were used.
Treatment	<p>Prior to experimental starting the seeds were sown in sowing container. After homogeneous and sufficient emergence ($\geq 70\%$, assessed by visual observation) and complete opening of the cotyledons the plants were transplanted into the test containers. During cultivation the plants were bottom watered and fertilized as necessary. The climatic conditions were the same as in the test. The cultivation period depended on the rate of growth. The test was started when the plants had reached a 2-4 true leaf stage.</p> <p>The test item was sprayed in 200 L water/ha at test concentrations of 0.141, 0.353, 0.883, 2.21, 5.52 L product/ha (<i>Avena</i>, <i>Triticum</i>, <i>Brassica</i>, <i>Glycine</i>) and 0.0296, 0.0889, 0.267, 0.800, 2.40 L product/ha (<i>Allium</i>, <i>Raphanus</i>, <i>Linum</i>, <i>Helianthus</i>, <i>Lactuca</i>, <i>Lycopersicon</i>). Additionally, 7.20 L product/ha were tested for <i>Allium</i>, <i>Raphanus</i>, <i>Lactuca</i>.</p> <p>In the test, 8 replicates with 3 plants per replicate were used for <i>Avena</i>, <i>Triticum</i>, <i>Allium</i>, <i>Brassica</i>, <i>Raphanus</i>, <i>Linum</i>, <i>Helianthus</i>, <i>Lycopersicon</i>, <i>Glycine</i> and 7 replicates with 3 plants per replicate for <i>Lactuca</i>.</p>

Observations	<p>At test start the growth stage of the plants was documented according to BBCH code. During the observation period the plants were observed on day 7, 14 and 21 for visual phytotoxic effects and number of dead plants.</p> <p>The rating of the treated plants was done in relation to the untreated control plants. Observations included all variations, either inhibitory or stimulatory, between the treated replicates and the untreated controls. Such variations were phytotoxic symptoms (e.g. chlorosis, necrosis, wilting), formative effects of growth and development rates. At the end of the study, the shoot height (in cm), measured after cutting the plants, and the fresh weights of the shoots (in g) were measured additionally.</p> <p>The room temperature and relative humidity were recorded continuously throughout the test.</p>
Analytical verification	<p>The spray solutions (highest application rates and control) were sampled prior to application and subsequently analytically verified. Analytical evaluation of Ethofumesate and Phenmedipham, active ingredients of the test item, was carried out via UPLC-MS/MS on a reversed phase column. The analytical method was validated based on SANCO/3029/99 rev. 4.</p>
Statistics	<p>The percentage of inhibition of biomass growth (shoot height, shoot fresh weight) for each plant species was calculated in relation to the control. All dead plants were observed and weighed and included in the calculation as possible. No shoot height determination was carried out for dead plants.</p> <p>One Way Analysis of Variance (ANOVA) and Dunnett's test were carried out for the determination of statistically significant differences compared to control replicates. When running a One-Way Analysis of Variance, a Normality test (Shapiro-Wilk) and an Equal Variance test (Brown-Forsythe) were done first. P-values for both, Normality and Equal Variance test, are 0.05. The α-value for ANOVA and Dunnett's test (acceptable probability of incorrectly concluding that there is a difference) is $\alpha = 0.05$.</p> <p>ED_{25/50}-values were calculated by sigmoidal dose-response regression using GraphPadPrism. Four parameter were used for dose-response fitting. Calculation of the confidence intervals for ED-values was carried out using standard procedures provided by GraphPadPrism.</p>

RESULTS AND DISCUSSIONS

Validity criteria

The seedling emergence rate for all species were $\geq 70\%$. For the control group the mean plant survival for the duration of the study was at least 90% at the end of the test. The mean growth and morphology in the control group were within the normal variation for the particular plant species. Plants in the control group exhibited no visible phytotoxic effects.

Analytical results

The spray solutions (highest application rates and control) were sampled prior to application and subsequently analytically verified. The measured concentrations of Ethofumesate were 84% to 103% and 93% to 97% of Phenmedipham, indicating the correct preparation of the spray solutions.

Biological results

Application rates with treatment related visual phytotoxic effects at the study end are given in **Table A 2.6.2.2-1**. The statistically calculated NOEL values as well as the ED₂₅ and ED₅₀ values for shoot height and shoot fresh weight are given in **Table A 2.6.2.1-2** and **Table A 2.6.2.1-3**. The calculated NOEL, ED₂₅ and ED₅₀ values for number of emerged seedlings are given in **Table A 2.6.2.1-4**.

Table A 2.6.2.2-1 Treatment related visual phytotoxic effects and mortality of HBZ10 at study termination

Species	Main observed visual effects*	Appearance at application rates [L product/ha]
<i>Avena sativa</i>	Stunted growth Necrosis Lighter green Mortality	≥ 2.21 ≥ 2.21 ≥ 2.21 5.52
<i>Tritium aestivum</i>	Deformation of leaves Stunted growth Necrosis Mortality	0.883 ≥ 0.883 ≥ 2.21 5.52
<i>Allium cepa</i>	Necrosis Mortality	0.800 and 2.40 7.20
<i>Brassica napus</i>	Deformation of leaves Stunted growth Necrosis Mortality	≥ 0.141 5.52 ≥ 0.883 5.52
<i>Raphanus sativus</i>	Deformation of leaves Necrosis Lighter green Mortality	0.267 and 0.800 0.267 to 2.40 0.0889 to 0.800 2.40
<i>Linum usitatissimum</i>	Stunted growth Necrosis Mortality	≥ 0.800 ≥ 0.800 2.40
<i>Helianthus annuus</i>	Stunted growth Necrosis Lighter green Mortality	≥ 0.800 ≥ 0.800 0.800 2.40
<i>Lactuca sativa</i>	Stunted growth Necrosis Lighter green Mortality	2.40 0.800 and 2.40 0.800 and 2.40 ≥ 2.40
<i>Lycopersicon esculentum</i>	Stunted growth Necrosis Lighter green Mortality	0.267 and 0.800 0.267 and 0.800 0.0296 to 0.267 ≥ 0.800
<i>Glycine max</i>	Deformation of leaves Stunted growth Necrosis Mortality	≥ 0.141 ≥ 0.141 ≥ 0.353 0.353 to 2.21

* Effects were considered treatment related when > 2 replicates were influenced or mortality of > 10% occurred

Table A 2.6.2.2-2 Shoot height: NOEL, ED₂₅ and ED₅₀ values with confidence range (p)

Species	NOEL [L product/ha]	ED ₂₅ [L product/ha]	p = 95% [L/ha]	ED ₅₀ [L product/ha]	p = 95% [L/ha]
<i>Avena sativa</i>	0.883	3.23	2.55 - 4.27	> 5.52	-
<i>Tritium aestivum</i>	0.353	0.878	0.706 - 1.10	> 5.52	-
<i>Allium cepa</i>	0.800	1.83	1.58 - 2.14	> 2.40 [#]	-
<i>Brassica napus</i>	2.21	4.94	3.82 - > 5.52	> 5.52	-
<i>Raphanus sativus</i>	0.267	> 2.40 [#]	-	> 2.40 [#]	-
<i>Linum usitatissimum</i>	0.267	1.02	0.862 - 1.33	1.76	1.40 - 2.05
<i>Helianthus annuus</i>	0.0889	0.226	0.176 - 0.281	0.582	0.480 - 0.739
<i>Lactuca sativa</i>	0.267	1.08	0.680 - 1.55	> 2.40 [#]	-
<i>Lycopersicon esculentum</i>	0.0889	0.242	0.183 - 0.309	0.566	0.471 - 0.698
<i>Glycine max</i>	< 0.141	< 0.141	-	5.21	3.70 - > 5.52

- not determinable

[#] For higher tested application rates > 70% mortality occurred

Table A 2.6.2.2-3 Shoot fresh weight: NOEL, ED₂₅ and ED₅₀ values with confidence range (p)

Species	NOEL [L product/ha]	ED ₂₅ [L product/ha]	p = 95% [L/ha]	ED ₅₀ [L product/ha]	p = 95% [L/ha]
<i>Avena sativa</i>	0.353	0.855	0.450 - 1.33	2.30	1.72 - 3.32
<i>Tritium aestivum</i>	< 0.141	0.369	< 0.141 - 0.593	0.977	0.753 - 1.23
<i>Allium cepa</i>	0.800	0.872	0.596 - 1.36	1.38	1.01 - 1.80
<i>Brassica napus</i>	2.21	2.63	2.29 - 2.99	3.66	3.23 - 4.17
<i>Raphanus sativus</i>	0.0889	0.278	0.179 - 0.409	0.674	0.536 - 0.825
<i>Linum usitatissimum</i>	0.267	0.576	0.482 - 0.679	0.973	0.825 - 1.18
<i>Helianthus annuus</i>	0.0889	0.218	0.171 - 0.269	0.372	0.302 - 0.476
<i>Lactuca sativa</i>	0.0889	0.289	0.205 - 0.386	0.591	0.457 - 0.779
<i>Lycopersicon esculentum</i>	0.0296	0.0789	0.0594 - 0.102	0.146	0.114 - 0.185
<i>Glycine max</i>	< 0.141	0.868	0.679 - 1.08	2.07	1.82 - 2.40

- not determinable

CONCLUSION

The effects of Ethofumesate/Phenmedipham 125/125 g/L EC (HBZ10) on the vegetative vigour of 10 plant species (3 monocotyledons and 7 dicotyledons) was examined in comparison with a water control under greenhouse conditions over 21 days.

Lycopersicon esculentum was identified as most sensitive species. For shoot fresh weight, a statistically significant inhibition was observed at 0.0889, 0.267, 0.800, 2.40 L product/ha, resulting in a NOEL of 0.0296 L product/ha, the ER₅₀ was determined to be 0.146 L product/ha.

A 2.6.3 KCP 10.6.3 Extended laboratory studies on non-target plants

No new study is submitted.

A 2.7 KCP 10.7 Effects on other terrestrial organisms (flora and fauna)

No new study is submitted.

A 2.8 KCP 10.8 Monitoring data

No new study is submitted.