FINAL REGISTRATION REPORT

Part B

Section 9

Ecotoxicology

Detailed summary of the risk assessment

Product code: MEZ-HER 100 SC

Product name(s): MECORN 100 SC

Chemical active substance:

mesotrione, 100 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Pestila Sp. z o. o.

Submission date: October 2023, April 2024

MS Finalisation date: May 2024, August 2024

Version history

When	What
04.2024	Applicant’s update on data provided in RR of Callisto 100 SC
05.2024	Initial assessment by the zRMS
08.2024	The final Registration Report after 1st commenting period

Table of Contents

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)	kg or L product/ha a) max. rate per appl. b) max. total rate per crop/season	g or kg as/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	Poland	Maize	F	**1 L/ha susceptible** **Pigweed** *Amaranthus retroflexus* AMARE; **Field chamomile** *Anthemis arvensis* ANTAR; **Shepherd's purse** *Capsella bursa-pastoris* CAPBP; **Fat-hen** *Chenopodium album* CHEAL; **Common barnyard grass** *Echinochloa crus-galli* ECHCG; **Cleavers** *Galium aparine* GALAP; **Gallant soldier** *Galinsoga parviflora* GASPA; **Purple deadnettle** *Lamium purpureum* LAMPU; **Wild buckwheat** *Fallopia convolvulus* POLCO; **Common chickweed** *Stellaria media* STEME; **Fanweed** *Thlaspi arvense* THLAR; **Field pansy** *Viola arvensis* VIOAR **1L/ha Moderarely susceptible**	broadcast spraying	BBCH 14-15 Spring, post emergence	1 a) 1 b) 1	N/A	1 L/ha a) 1 L/ha b) 1 L/ha	100g mesotrione a) 100g mesotrione b) 100g mesotrione	200-300 L/ha	not relevant		A	A	R	A	A	A	R

				Common fumitory *Fumaria officinalis* FUMOF																
Interzonal uses (use as seed treatment, in greenhouses (or other closed places of plant production), as post-harvest treatment or for treatment of empty storage rooms)																				
Minor uses according to Article 51 (field uses)																				
Minor uses according to Article 51 (interzonal uses)																				

* 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

zRMS Final Conclusion:

Since report in dRR format is prepared by the Applicant, all remarks, comments, additional calculations and assessment done by the ZRMS are included in the commenting boxes or highlighted in gray.

All data referred to endpoints for active substance and metabolites are in line EFSA conclusion (EFSA Journal 2016;14(3):4419) and are accepted by evaluator. The proposed GAP of **Mecorn 100 SC** is covered by the assessment contained in plant protected product of **Callisto 100 SC** and is accepted for used in **Mecorn 100 SC.**

9.1.2 Grouping of intended uses for risk assessment

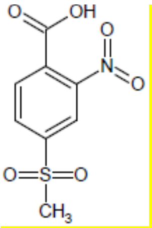
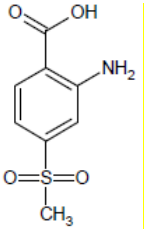
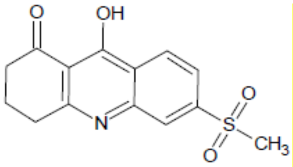
Not relevant. No new risk assessments submitted.

9.1.3 Consideration of metabolites

Information concerning metabolites relevant for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, this point origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

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 A12739A is indicated in the table.

Table 9.1-2 Metabolites of mesotrione

Metabolite	***Chemical structure***	***Molar mass***	***Maximum occurrence in compartments***	***Risk assessment required?***
NOA437130 (MNBA) *4-(methylsulfonyl)-2-nitrobenzoic acid*		*245*	*Soil: >10% of a.s (aerobic laboratory degradation and soil photolysis studies)* *Water: >5% of a.s. in 1 measurement* *Sediment: <5% of a.s.*	*Soil: Yes* *Water: Yes* *Sediment: No*
NOA422848 (AMBA) *2-amino-4-(methyl-sulfonyl) benzoic acid*		*215*	*Soil: >5% of a.s. in 2 sequential measurements (aerobic laboratory degradation studies and soil photolysis studies)* *Water: >10% of a.s.* *Sediment: >5% of a.s. in 2 sequential measurements*	*Soil: Yes* *Water: Yes* *Sediment: Yes*
SYN546974 *9-hydroxy-6-(methyl-sulfonyl)-3,4-dihydro-acridin-1(2H)-one*		*291*	*Soil: -* *Water: >5% of a.s. in 2 sequential measurements* *Sediment: >10% of a.s.*	*Soil: No* *Water: Yes* *Sediment: Yes*

9.2 Effects on birds (KCP 10.1.1)

Information concerning effects on birds for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, the point 9.2 origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

9.2.1 Toxicity data

Avian toxicity studies have been carried out with mesotrione. There are no potentially relevant metabolites for avian exposure. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on birds of A12739A were assessed as part of the EU assessment of mesotrione, where it was agreed that the provision of data on the formulation is not considered essential, because mammal studies give no indication of higher toxicity from the formulation A12739A, and the risk to birds from it can be adequately assessed from risk assessment for the active substance. The risk to birds from the proposed uses of A12739A will therefore be assessed using the endpoints for mesotrione.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process. Justifications are provided below with respect to the conversion of ppm endpoints to mg/kg bw/day endpoints.

Table 9.2-1: Endpoints and effect values relevant for the risk assessment for birds - mesotrione

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Bobwhite quail (Colinus virginianus)	*Mesotrione*	*Oral 1 d Acute*	*LD_{50} >2000 mg a.s./kg bw*	*EFSA Conclusion 2016 Rodgers, 1995a ZA1296/0535*
			Extrapolated: LD_{50} = 3776 mg a.s./kg bw	*See section 9.2.1.1*
~~*Mallard duck*~~	~~*Mesotrione*~~	~~*Oral 1 d Acute*~~	~~*LD_{50} >2000 mg a.s./kg bw*~~	~~*Hubbard et al. 2018 ZA1296_10605*~~
			~~*Extrapolated: LD_{50} = 3228 mg a.s./kg bw*~~	~~*See section 9.2.1.1*~~
Bobwhite quail (Colinus virginianus)	*Mesotrione*	*Dietary 8 d Short-term*	*LC_{50} >5200 mg a.s./kg diet*	*EFSA Conclusion 2016* [redacted]
Mallard duck (Anas platyrhynchos)	*Mesotrione*	*Dietary Reproductive toxicity*	*NOEL = 20.6 mg a.s./ kg bw/d (offspring effects on hatching and chick development)*	*EFSA Conclusion 2016* [redacted]

9.2.1.1 Justification for new endpoints

Extrapolation of acute endpoint for mesotrione used in the risk assessment

In the acute oral mesotrione toxicity study conducted with the bobwhite quail (Rodgers et al., 1995) no mortalities were observed and therefore the LD_{50} was reported as >2000 mg/kg bw. Under Point 2.1.2 of the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) a method has been proposed to extrapolate upwards the LD_{50} value. The extrapolation is carried out assuming a 50% binomial probability bound that mortality could have occurred but had simply been missed by chance in the test. The extrapolation factors are presented in Table 1 of the guidance document and are dependent upon the number of animals tested and whether no, or a single mortality, was observed in the study. The acute toxicity value has been extrapolated and is presented in the table below.

Table 9.2-2: Extrapolation of the acute oral toxicity value for mesotrione

Test substance	*Study*	*Test species*	*Experimental LD_{50} (mg/kg bw)*	*Number of animals tested*	*Number of mortalities*	*Extrapolation factor [a]*	*Corrected LD_{50} (mg/kg bw)*
Mesotrione	*Rogers et al., (1995a)*	*Bobwhite quail*	*>2000*	*10*	*0*	*1.888*	*3776*

[a] The extrapolation factor is presented in Table 1 of the guidance document (Point 2.1.2)

The extrapolated LD_{50} value for mesotrione of 3776 mg/kg bw will be used in the subsequent 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).

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the worst-case application rate (150 g mesotrione/ha) is used in the initial risk assessment.

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

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

Table 9.2-3: Screening Step assessment of the acute and long-term/reproductive risk for birds for all crop uses of A12739A - mesotrione

Active substance		*Mesotrione*					
Acute toxicity (mg/kg bw) ***TER criterion***		*3776* *10*					
GAP crop	***Application rate (g a.s./ha)***	***Crop scenario Growth stage***	***Indicator species***	***SV_{90}***	***MAF_{90}***	***DDD_{90} (mg/kg bw/d)***	***TER_a***
Maize, post-emergence BBCH 12-18	*1 x 150*	*Maize*	*Small omnivorous bird*	*158.8*	*1.0*	*23.8*	*158.7*
Reprod. Toxicity (mg/kg bw/d) ***TER criterion***		*20.6* *5*					
GAP crop	***Application rate (g a.s./ha)***	***Crop scenario Growth stage***	***Indicator species***	***SV_m***	***MAF_m × TWA***	***DDD_m (mg/kg bw/d)***	***TER_{lt}***
Maize, post-emergence BBCH 12-18	*1 x 150*	*Maize*	*Small omnivorous bird*	*64.8*	*1.0 × 0.53*	*5.15*	***4.0***

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 9.2-4: Tier 1 assessment of the long-term/reproductive risk for birds for all crop uses of A12739A - mesotrione

Active substance		*Mesotrione*					
Reprod. Toxicity (mg/kg bw/d) ***TER criterion***		*20.6* *5*					
GAP crop	***Application rate***	***Crop scenario Growth stage***	***Generic focal species***	***SV_m***	***MAF_m × TWA***	***DDD_m (mg/kg bw/d)***	***TER_{lt}***

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

	(g a.s./ha)						
Maize, post-emergence BBCH 12-18	*1 x 150*	*Maize BBCH 10-29*	*Medium granivorous bird "gamebird"*	*3.0*	*1.0 × 0.53*	*0.239*	*86*
		Maize leaf development BBCH 10-19	*Small insectivorous/worm feeding species "thrush"*	*5.7*	*1.0 × 0.53*	*0.453*	*45*
		Maize BBCH 10-29	*Small omnivorous bird "lark"*	*10.9*	*1.0 × 0.53*	*0.867*	*24*
		Maize BBCH 10-29	*Medium herbivorous/granivorous bird "pigeon"*	*22.7*	*1.0 × 0.53*	*1.80*	*11*
		Maize BBCH 10-19	*Small insectivorous bird "wagtail"*	*11.3*	*1.0 × 0.53*	*0.898*	*23*

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.

Mesotrione metabolites

Since metabolites are formed at <10% of parent levels in edible crop parts, and mammalian testing indicates that they are less toxic than the parent, it can be concluded that the risk to birds will be low and no further risk assessment was conducted in accordance with the conclusions in the final RAR (Mesotrione RAR 21, Vol. 3 CP Callisto 100 SC B-9 23/12/2015).

zRMS comments:

Birds
No data is provided in support of the application for authorization of **Mecorn 100 SC**.
The risk assessment for birds performed for Callisto 100 SC are suitable for the use of Mecorn 100 SC proposed in GAP.

On the basis of performed calculations for Callisto 100 SC, acceptable acute and long-term risk to birds may be concluded from proposed uses of Mecorn 100 SC.

The risk assessment for exposure via drinking water from puddles also showed acceptable risk.

9.2.2.2 Higher-tier risk assessment

Not 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 A12739A 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 (Koc <500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥500 L/kg).

With a K(f)oc of 50 (geomean; the worst-case is 14 in the final EFSA endpoints), mesotrione belongs to the group of less sorptive substances.

Effective application rate (g/ha)* **=**	*150*		
Acute toxicity (mg/kg bw) **=**	*3776*	*quotient =*	*0.04*
Reprod. toxicity (mg/kg bw/d) **=**	*20.6*	*quotient =*	*7.3*

* *Effective application rate = Maximum application rate x MAF. However in this case the MAF is not applicable as there is only a single application.*

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

zRMS comments:

Drinking water exposure
Screening evaluation of the risk resulting from exposure to mesotrione via drinking water is agreed by the zRMS. Acceptable risk may be concluded.

As in the course of the EU renewal of mesotrione it was concluded that its metabolites have similar or lower toxicity, specific evaluation of the drinking water risk was deemed not necessary and is considered to be covered by the evaluation performed for the active compound.

Screening evaluation of the risk resulting from exposure to mesotrione via drinking water is agreed by the zRMS. Acceptable risk may be concluded.

As in the course of the EU renewal of mesotrione it was concluded that its metabolites have similar or lower toxicity, specific evaluation of the drinking water risk was deemed not necessary and is considered to be covered by the evaluation performed for the active compound.

No data is provided in support of the application for authorization of **Mecorn 100 SC**.
The risk assessment for birds performed for Callisto 100 SC are suitable for the use of Mecorn 100 SC (100 g s.a./ha) proposed in GAP.

No additional risk assessment is required.

9.2.2.4 Effects of secondary poisoning

The log P_{OW} values of mesotrione and its main metabolites MNBA, AMBA and SYN546974 amount to 0.11, -1.3, 0.32 and 1.62 respectively and thus do not exceed the trigger value of 3. A risk assessment for effects due to secondary poisoning is not required.

The log P_{OW} values of mesotrione and its main metabolites MNBA, AMBA and SYN546974 amount to 0.11, -1.3, 0.32 and 1.62 respectively and thus do not exceed the trigger value of 3. A risk assessment for effects due to secondary poisoning is not required.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

9.2.2.5 Biomagnification in terrestrial food chains

Not relevant.

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

Not relevant.

9.2.4 Overall conclusions

The acute and long-term risks of A12739A to birds were assessed from toxicity exposure ratios between toxicity endpoints, estimated from studies with mesotrione and maximum residues occurring on food items following applications according to the proposed use pattern. The risk to birds from exposure via drinking water was also assessed. Risk of secondary poisoning for mesotrione was not assessed as the log P_{OW} is <3.0.

The TER values, calculated for recommended scenarios, all exceed the trigger value of 10 for acute risk and 5 for long-term risk, indicating that the risk to birds is acceptable following use of A12739A according to the proposed use pattern. The risk assessment for exposure via drinking water from puddles also showed acceptable risk.

zRMS comments: **Birds** No data is provided in support of the application for authorization of **Mecorn 100 SC**. The risk assessment for birds performed for Callisto 100 SC are suitable for the use of Mecorn 100 SC proposed in GAP. **On the basis of performed calculations for Callisto 100 SC, acceptable acute and long-term risk to birds may be concluded from proposed uses of Mecorn 100 SC. The refinement risk assessment for birds should be considered by MSs level.** The risk assessment for exposure via drinking water from puddles also showed acceptable risk.

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

Information concerning studies with mammals and risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired the point 9.3 origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

9.3.1 Toxicity data

Mammalian toxicity studies have been carried out with mesotrione. There are no potentially relevant metabolites for mammalian exposure. Full details of these studies are provided in the respective EU DAR and related documents.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Effects on mammals of A12739A were evaluated as part of the EU assessment of mesotrione.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process. Justifications regarding higher tier refinement endpoints are provided below.

Table 9.3-1: Endpoints and effect values relevant for the risk assessment for mammals - mesotrione

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Rat	*Mesotrione*	*Oral* *1 d* *Acute*	*LD_{50} >5000 mg a.s./kg bw*	*EFSA Conclusion 2016* [redacted]
Rat	*MNBA*	*Oral* *1 d* *Acute*	*LD_{50} >5000 mg/kg bw*	*EFSA Conclusion 2016* [redacted]
Rat	*AMBA*	*Oral* *1 d* *Acute*	*LD_{50} >5000 mg/kg bw*	*EFSA Conclusion 2016* [redacted]
Rat	*Mesotrione*	*Dietary* *Reproductive toxicity* *Three-generation study*	*NOAEL = 0.3 mg a.s./kg bw/d* *(decreased litter size in F_2)*	*EFSA Conclusion 2016* [redacted]
Mouse	*Mesotrione*	*Dietary* *Reproductive toxicity* *Two-generation study*	*NOAEL = 10 mg a.s./kg bw/d* *(reproductive effects)*	*RAR, B6, 2008* [redacted]
Rat	*Mesotrione*	*Dietary* *28d varying exposure study*	*NOEL = 2.4 mg a.s./kg bw/d* *(reversible tyrosenimic effects)*	*RAR, B6, 2008* [redacted]

Table 9.3-2: Endpoints and effect values relevant for the risk assessment for mammals – A12739A

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Rat	*A12739A*	*Oral* *1 d* *Acute*	*LD_{50} >2000 mg/kg bw*	*EFSA Conclusion 2016* [redacted]

9.3.1.1 Justification for new endpoints

Consideration of the long-term endpoint of mesotrione for use in risk assessment

The low NOEL for effects of mesotrione on mammals is unique to the rat, with unremarkable toxicity seen in the mouse, rabbit and dog. For refinement of risk to omnivorous mammals from mesotrione, where the mouse is the focal species for use in maize, the toxicity endpoint from the 2-generation mouse study (71 mg/kg bw/d) can be considered as a refinement. For the rat, the screening-level NOEL reported in the DAR of 0.3 mg/kg bw/day is based on effects in the F2 generation of a three-generation study of continuous exposure (140 days). This was agreed as the EU endpoint since the Expert Meeting stated that the ecological realism of exposure should not be taken into account for hazard characterisation. However, it is clear that exposure to mesotrione from a single application in maize in the spring will be limited to a short time period as the foliar DT_{50} is less than 1 day (North, 2016), and the mean soil DT_{50} is 34.3 days (non-normalised, EFSA Conclusion 2016). Therefore, a refined ecologically-relevant NOAEL endpoint of 1.2 mg/kg bw/day is proposed for the refined long term risk assessment for herbivorous mammals, based on the findings in the F_0 and F_1 generations of continuous exposure, based on modifications of reproductive and developmental parameters. During the EU review by the RMS, the reviewer stated: the ecotoxicity assessment will need to consider whether a reduction in litter size of 6.8% is acceptable for wild *populations. It should be noted that the reduction in litter size was not accompanied by a similar reduction in the numbers of offspring surviving or their development. It is therefore highly unlikely that this minor reduction is either biologically significant, or likely to have an impact at the population level. Furthermore, at the higher dose level of 100 ppm (12.3 mg/kg/day) the litter size was only marginally reduced and not significantly different compared to control values, indicating that the effect at 1.2 mg/kg bw/d is likely to be incidental. It is also considered highly unlikley that short-term exposure, for example at a critical developmental stage, would have caused the long-term effects seen in the F_2 generation, because similar effects at 1.2 mg/kg bw/d were not seen in the F_1 generation where short-term exposure would similarly have been experienced.*

For the mouse, in the EFSA conclusion, the conclusions for reproductive toxicity are:

- *Parental NOAEL: 10 mg/kg (50 ppm) based on increased tyrosine*
- *Reproductive NOAEL: 10 mg/kg based on reduced number of successful matings*
- *Offspring NOAEL: 2 mg/kg based on increased testes and kidney weight.*

The offspring NOAEL is not relevant to the wild mammal risk assessment as there is no evidence of organ malfunction and there is no impact on survival or reproduction of individuals, so would not lead to a population-level effect. Likewise, the parental NOAEL is again of no relevance to the survival of individuals or to the population, as in the absence of any adverse effect on the animal, it is just a biochemical measurement. However, the reproductive NOAEL could be of relevance to the population-level effects, so this is considered appropriate for the risk assessment (this endpoint is considered highly conservative as there is no dose response for this endpoint or a statistically significant difference).

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 Mammals and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438; hereafter referred to as EFSA/2009/1438).

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.

Table 9.3-3: Screening Step assessment of the acute and long-term/reproductive risk for mammals for all crop uses of A12739A - mesotrione

Active substance		*Mesotrione*					
Acute toxicity (mg/kg bw) ***TER criterion***		*>5000* *10*					
GAP crop, growth stage	***Application rate (g a.s./ha)***	***Crop scenario***	***Indicator species***	***SV_{90}***	***MAF_{90}***	***DDD_{90} (mg/kg bw/d)***	***TER_a***
Maize, post-emergence BBCH 12-18	*1 x 150*	*Maize*	*Small herbivorous mammal*	*136.4*	*1.0*	*20.5*	*>240*
Reprod. Toxicity (mg/kg bw/d) ***TER criterion***		*0.3* *5*					
GAP crop, growth stage	***Application rate (g a.s./ha)***	***Crop scenario***	***Indicator species***	***SV_m***	***MAF_m × TWA***	***DDD_m (mg/kg bw/d)***	***TER_{lt}***

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Maize, post-emergence BBCH 12-18	*1 x 100*	*Maize*	*Small herbivorous mammal*	*72.3*	*1.0 × 0.53*	*3.83*	***0.078***
Maize, post-emergence BBCH 12-18	*1 x 150*	*Maize*	*Small herbivorous mammal*	*72.3*	*1.0 × 0.53*	*5.75*	***0.052***

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 9.3-4: ***Tier 1 assessment of the long-term/reproductive risk for mammals for all crop uses of A12739A - mesotrione***

Active substance		*Mesotrione*					
Reprod. Toxicity (mg/kg bw/d) ***TER criterion***		*0.3 (lowest);* *5*					
GAP crop, growth stage	***Application rate (g a.s./ha)***	***Crop scenario Growth stage***	***Generic Focal species***	***SV_m***	***MAF_m × TWA***	***DDD_m (mg/kg bw/d)***	***TER_{lt}***
Maize, post-emergence BBCH 12-18	*1 x 100*	*Maize BBCH 10-19*	*Small insectivorous mammal "shrew"*	*4.2*	*1.0 × 0.53*	*0.223*	***1.3*** ~~*5.4*~~ ~~*45*~~
		Maize BBCH 10-29	*Small herbivorous mammal "vole"*	*72.3*	*1.0 × 0.53*	*3.83*	***0.078*** ~~*0.31*~~ ~~*2.6*~~
		Maize BBCH 10-29	*Small omnivorous mammal "mouse"*	*7.8*	*1.0 × 0.53*	*0.413*	***0.73*** ~~*2.9*~~ ~~*24*~~
	1 x 150	*Maize BBCH 10-19*	*Small insectivorous mammal "shrew"*	*4.2*	*1.0 × 0.53*	*0.334*	***0.90*** ~~*3.6*~~ ~~*30*~~
		Maize BBCH 10-29	*Small herbivorous mammal "vole"*	*72.3*	*1.0 × 0.53*	*5.75*	***0.052*** ~~*0.21*~~ ~~*1.7*~~
		Maize BBCH 10-29	*Small omnivorous mammal "mouse"*	*7.8*	*1.0 × 0.53*	*0.620*	***0.48*** ~~*1.9*~~ ~~*16*~~

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.

Mesotrione metabolites

Since metabolites are formed at <10% of parent level in edible crop parts and mammalian testing indicates that they are less toxic than the parent, it can be concluded that the risk to mammals will be low and no further risk assessment was conducted in accordance with the conclusions in the final RAR (Mesotrione RAR 21, Vol. 3 CP Callisto 100 SC B-9 23/12/2015).

Table 9.3-5: Screening Step assessment of the acute risk for mammals for all crop uses of A12739A - A12739A

Product		*A12739A*					
Acute toxicity (mg/kg bw) **TER criterion**		*>2000* *10*					
GAP crop, growth stage	**Application rate (g/ha)**	**Crop scenario**	**Indicator species**	**SV_{90}**	**MAF_{90}**	**DDD_{90} (mg/kg bw/d)**	**TER_a**
Maize, post-emergence BBCH 12-18	*1 x 1090[a]*	*Maize*	*Small herbivorous mammal*	*136.4*	*1.0*	*149*	*>13*
	1 x 1635[a]	*Maize*	*Small herbivorous mammal*	*136.4*	*1.0*	*223*	***>9.0***

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.
[a] A12739A is applied as 1.0 and 1.5 L/ha; density of A12739A is 1.09 g/ml

An acceptable risk is indicated at the screening level for the lower proposed use rate of A12739A.

Table 9.3-6: Tier 1 assessment of the acute risk for mammals for all crop uses of A12739A - A12739A

Product		*A12739A*					
Acute toxicity (mg/kg bw) **TER criterion**		*>2000* *10*					
GAP crop, growth stage	**Application rate (g/ha)**	**Crop scenario Growth stage**	**Generic Focal species**	**SV_{90}**	**MAF_{90}**	**DDD_{90} (mg/kg bw/d)**	**TER_a**
Maize, post-emergence BBCH 12-18	*1 x 1635[a]*	*Maize BBCH 10-19*	*Small insectivorous mammal “shrew”*	*7.6*	*1.0*	*12.4*	*>160*
		Maize BBCH 10-29	*Small herbivorous mammal “vole”*	*136.4*	*1.0*	*223*	***>9.0***
		Maize BBCH 10-29	*Small omnivorous mammal “mouse”*	*17.2*	*1.0*	*28.7*	*>70*

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.
[a] A12739A is applied as 1.5 L; density of A12739A is 1.09 g/mL

9.3.2.2 Higher-tier risk assessment

A12739A acute risk assessment for the higher application rate (1.5 L A12739A/ha)

*The acute risk assessment for herbivorous mammals has been refined here, based on the more realistic medium herbivorous mammal, the brown hare Lepus europaeus. The hare is the focal herbivorous species identified for early maize fields, as demonstrated in the report by **Alvarez (2019)**, referenced in the long-term risk assessment section below.*

The bodyweight for the hare reported in Appendix A of the Guidance document is 3800g, whilst the realistic bodyweight measured in maize fields at the proposed timing of application is 4130g (please see Alvarez 2019 for a full discussion). The FIR/bw can then be calculated using the equation provided in Appendix G of the Guidance document.

$$FIR = \left(\frac{DEE}{FE * \left(1 - \frac{MC}{100}\right) * \left(\frac{AE}{100}\right)} \right) \quad \text{[g fresh weight/d]}$$

In which

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

$$\log DEE = \log a + b \times \log bw$$

Table 9.3-7: ***Calculation of food intake rate for the hare considering a single item diet in post-emergence maize***

Food item	***Hare bodyweight***	***DEE***	***FIR***	***FIR/bw***
Maize shoots (grasses/ cereals)	*3800 g*	*2363*	*1210.7*	*0.32* [a]
Non-grass herbs	*3800g*	*2363*	*1468.1*	*0.39* [b]
Maize shoots (grasses/ cereals)	*4130g*	*2508.4*	*1284.94*	*0.31*
Non-grass herbs	*4130g*	*2508.4*	*1558.2*	*0.38*

Table 9.3-8: ***Higher-tier assessment of the acute risk for mammals due to the use of A12739A in maize – refined parameters (*) are further described and justified in the text***

Intended use	*Maize*					
Product	*A12739A*					
Application rate (g/ha)	*1 x 1635*[a]					
Acute toxicity (mg/kg bw)	*>2000*					
TER criterion	*10*					
Focal species	***Food category, % in diet***	***FIR/bw***	***RUD_{90} × DF (mg/kg food)***	***MAF_{90}***	***DDD_{90} (mg/kg bw/d)***	***TER_a***
*Brown hare Lepus europaeus **	*Grass + cereals, 100%*	*0.32*[b]	*102.3*[c] *× 1*	*1.0*	*53.5*	*>37*
	Non-grass herbs, 100%	*0.39*[d]	*70.3*[c] *× 1*	*1.0*	*44.8*	*>45*

FIR/bw: Food intake rate per body weight; RUD: residue unit dose; DF: deposition factor (considering possible interception by the crop); MAF: multiple application factor; DDD: daily dietary dose; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.
[a] *A12739A is applied as 1.5 L; density of A12739A is 1.09 g/mL*
[b] *Calculated above, and the same as the FIR/bw given for the herbivorous brown hare Lepus europaeus 3800 g bodyweight, feeding on 100% grass in the Grassland scenario in Appendix A of the EFSA Guidance document.*
[c] *default RUD values from Appendix F of the EFSA Guidance document*
[d] *Taken from Appendix A of the EFSA Guidance document. The FIR/bw given for the herbivorous brown hare Lepus europaeus 3800 g bodyweight, feeding on 100% plant matter (non-grass herbs) in the Vineyard scenario is 0.39.*

Chronic / Long-term risk assessment

A refined risk assessment investigating the potential long-term risk is presented in the confidential report referenced below:

Report:	[redacted]*(2019) A12739A Central Zone: refined risk assessments for mammals. Syngenta, Jealott's Hill, Bracknell, United Kingdom. Syngenta Unpublished Report (Syngenta File No. A12739A_11105)*

Since the data provided by the Applicant of Callisto 100 SC was not sufficient for the assessment this point the zRMS comments have been placed in this document as a supplement of Chronic / Long-term risk assessment (written in italics, highlighted in yellow). These data are applicable for MEZ-HER 100 SC which is comparable in composition with Callisto 100 SC as well as it is recommended to use in the same crops, dosees and time as Callisto 100 SC.

zRMS comments for Callisto 100 SC:
The Applicant performed extensive refinement of the risk to the wood mouse and brown hare with consideration of the refined PT, PD and residue decline data. However, all refinement options together with their justification were presented in the separate document (Alvarez, 2019) and in the dRR only the final assessment has been presented.
The document by Alvarez (2019) has been reviewed by the zRMS and it was noted that some parameters were refined based on the literature data or studies that were not provided in support of this submission

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

and their reliability could not be thus verified by the zRMS. As copying of the overall assessment from [redacted] being a pdf file would be too time consuming, the zRMS decided to perform its own risk refinement based on agreed parameters, copying from Alvarez (2019) only data that could be validated and considered in the performed evaluation. Calculations presented in Tables 9.3-9 and 9.3-10 above were struck through as not fully agreed and the zRMS refinement of the risk is presented below.

The Applicant is kindly reminded that the Core Assessment should be a stand-alone document, where all data considered in evaluation are summarised and all refinement options are presented together with their justification. This enables the zRMS to comment on considered parameters and facilitates concerned Member States independent validation of the data.

Summary of refinement options

Focal species
In the course of the EU review it was agreed that the relevant focal species for maize at BBCH 12-18 is wood mouse and brown hare. No further consideration of this refinement option is required, as it is in line with the conclusion taken at the EU level.

PT values

Wood mouse
At the EU level PT value of 0.139 was agreed for the wood mouse. Additional study to further refine the PT for the wood mouse was submitted by the Applicant ([redacted] 2016, KCP 10.1.2.2/05), however the study was performed in the Southern France and is thus not relevant for evaluation performed for the Central Zone. Results of the study were not considered for risk refinement purposes and EU agreed PT of 0.139 is used by the zRMS.

Brown hare
No study enabling PT refinement was available at the EU level. In support of this submission the Applicant provided study by [redacted] monitoring brown hares in two Central Zone countries (Germany and Hungary). As 21 individuals were found to be crop consumers, it was agreed by the zRMS that the overall 90th percentile PT value is sufficiently robust for purposes of the risk refinement. For details of the study evaluation, please refer to Appendix 2, KCP 10.1.2.2/07.

Additional study by [redacted] (2015, KCP 10.1.2.2/03) was also provided to further refine the PT value. Nevertheless, this study was already evaluated by zRMS (UK) during first zonal evaluation of formulation Calaris (owned by the same Applicant) and considered as unreliable. ~~at the EU level and considered as unreliable.~~ Taking this into account, its results were not used in the risk refinement.

In Alvarez (2019) also results of the study by [redacted] were taken into account in derivation of the PT value. The study was not submitted in support of this evaluation, but according to information provided by the Applicant, it was already considered during zonal evaluations of several formulations and accepted (by e.g. The Netherlands). On the other hand, this study was taken into account in support of evaluation of first zonal evaluation of formulation Calaris owned by the same Applicant. The zRMS (UK) could not review the study, as it was not submitted, but it was noted that the Applicant used percentage maize in the home range of monitored hares in order to derive PT. Following conclusion was taken by the UK ecotoxicology expert:

The zRMS has considered the proposed refinement to the PT however the study [redacted]) has not been submitted or evaluated. It is also noted the values provided are not PT values and the zRMS does not agree with the assumption that the percentage of maize in a home range provides an estimate for PT. Combined with the low sample size and that the consumers and potential consumers can not be calculated the suggested refinement to PT based on this study is not acceptable

The zRMS for re-evaluation of formulation Callisto agrees with this conclusion and is also of the opinion that consideration of percentage maize in the home range is not relevant measure to derive PT values. Taking this into account, results of the study by [redacted] are not reliable to be used for the risk refinement purposes.

Overall, the 90th percentile PT of 0.62 from study by [redacted] was considered in refinement performed by the zRMS. In case the Applicant would like to further refine the PT value for the brown hare, the translation of the study by [redacted] or at least detailed summary, including all information necessary for validation of the results, must be provided.
The translation of the summary of the study by [redacted] has been submitted by the Applicant and is now presented in Appendix 2, KCP 10.1.2.2/12. The overview by the zRMS confirmed the supposition of UK (zRMS for first evaluation of Calaris), that based on results of the study by [redacted] it was assumed that the percentages of maize in a home range of radio-tracked individuals are equivalent to the PT values. However, according to EFSA (2009), PT should be expressed as the amount of (potential) foraging time in the crop expressed as a proportion of the total time spent (potentially) foraging in the day. For this reason values based on results of study by [redacted] cannot be considered to be PT values, as such approach may lead to underestimation of the time the individual hare spent actually foraging in maize. It cannot be excluded that for example animal with 20% of maize within the home range actually spends e.g. 50 or 60% of its daily foraging time feeding in maize, which would lead to PT of 0.5 or 0.6, clearly exceeding the home range percentage. Taking this into account, approach taken is highly uncertain and percentage of maize in a home range of tracked individuals cannot be considered to be equivalent to PT values. Therefore results of study by [redacted] are not considered further as being not relevant for derivation of PT values.

PD values

Wood mouse
In the document by [redacted] the Applicant proposed two diets to be considered for purposes of the risk refinement.

One was the default diet as indicated in EFSA (2009), consisting of 25% weeds, 50% weed seeds and 25% of ground arthropods. It is noted that this default diet was considered during EU renewal of mesotrione.

As a second option the diet derived in May [redacted] and presented in Mammal Bible ([redacted]) was proposed. Overview of the various diets of the wood mouse in May available in Mammal Bible is provided below.

Reference	***% volume in stomach contents***				***Study site***
	Plant material	***Insects***	***Oligochaetes***	***Other***	
Gorman & Zubaid 1993a	*75*	*15*	*5*		*UK (woodland site)*
Gorman & Zubaid 1993b	*10*	*56*	*15*		*UK (sand-dune site)*
Pelz 1989	***16***	***10***	***40***	***Cereal grain (30%) Dicot seeds (4%)***	***Arable farm site in Rhineland, Germany (n=16)***
Rogers & Gorman 1995	*72 (monocots) 5 (dicots)*	*13*	*10*		*Set aside land, UK*

Wattts 1968	*4*	*88 (nearly all examples were leaf-eating caterpillars)*	*0*	*Seed endosperm (7%)*	*Wytham woods, UK*

The diet derived by Pelz (1989) was considered by the Applicant most relevant as it was obtained in the arable area. However, from the Mammal Bible it is not known if maize fields were present at the test site and if derived diet is relevant for the intended uses of Callisto. This is particularly important as the wood mouse is an opportunistic omnivore and its diet will highly depend on the landscape composition. In order to address this issue the publication by Pelz (1989) was consulted. The study was carried out from 1980 to 1986 and in the paper the map of the study area in 1984 is given and reproduced below.

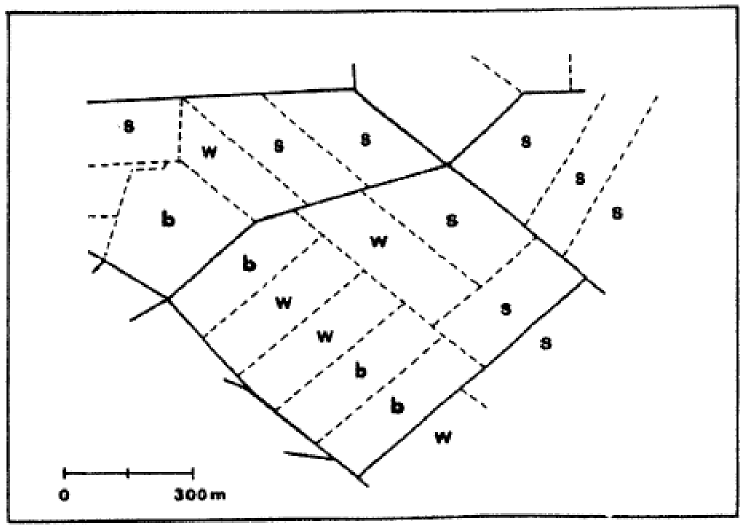


Figure 3.1 Map of the study area in the Rhineland in spring 1984. Solid lines – field paths; broken lines – field boundaries; b – winter barley; s – sugar beet; w – winter wheat.

From the above figure it is evident that the test site (at least in 1984) comprised of cereal and sugar beet fields with no maize fields present. No maps are present for remaining years, but taking into account that the study aimed at investigation of the damage by the wood mouse to sugar beet seeds and potential reduction of this damage due to the presence of cereals it may be expected that sugar beet and cereal fields represented high proportion of the area over the whole period of the study. High proportion of cereal fields explains also significant amount of cereal grain found in the mice stomachs and it is not known with what food item it would be replaced in case maize fields were present at high proportion in the test area. Taking all this into account the zRMS is of the opinion that the study by [redacted] *is not relevant to refine the diet of the wood mouse exposed following application of Callisto to maize.*

Overall, it was decided by the zRMS to perform refinement of the risk using approach taken at the EU level, i.e. with assumption of the standard diet of the wood mouse consisting of 25% weeds, 50% weed seeds and 25% of ground arthropods as indicated in EFSA (2009)

Brown hare
The brown hare diet was refined by the Applicant in [redacted] *on the basis of results of several publications, however neither was submitted in support of this evaluation and for this reason their reliability and relevance for intended uses of Callisto in maize could not be validated by the zRMS.*
In addition to that it was pointed out by the Applicant that the brown hare diet relevant for maize is indicated in the Northern Zone Guidance Document. The derived PD values were based on published data from studies carried out in Sweden (Frylestam 1980a), England (Tapper and Barnes 1986), France

(Chapuis 1990) and Denmark (Olesen & Asferg 2006; Hansen 1990). Following PD values are recommended:

Crop	***Growth stage***	***Season***	***PD (fresh weight)***		
			Monocotyledons (cereals, grasses)	*Dicotyledons (leafy crops, non-grass weeds)*	*Bush berry plants (buds, leaves)*
Maize	*BBCH 10-19*	*Spring*	*0.84*	*0.16*	*-*
	BBCH 10-39	*Summer*	*0.72*	*0.28*	*-*

In opinion of the zRMS, the PD values derived for spring may be also used for purposes of the evaluation performed in the Central Zone, as they were based on results of the studies performed in Member States of all zones, including Central Zone. Furthermore, all publications were already assessed, validated and agreed by the ecotoxicology experts of the Northern Zone and there is no reason to challenge derived conclusions.

Moreover, in opinion of the zRMS it is highly unlikely that the brown hare would feed exclusively on maize shoots, which is confirmed by various publications. For illustrative purposes table from Alvarez (2019) presenting diet of brown hares presented in [redacted] *is reproduced below.* [redacted] *summarised data from a study by Onderscheka et al. (1981) that was investigating hare diet from analysis of botanical composition of stomach contents. This study looked at stomach contents of 366 hares in 8 regions of Austria. Please note that the publication was not submitted by the Applicant so could not be fully validated by the zRMS, however results summarised below are presented as supportive information that the brown hare feed on dicotyledonous plants and that the diet composition as proposed by the Northern Zone Guidance Document is relevant.*

Botanic composition of the stomach contents of brown hares (annual average in %) in different areas of Austria (Zörner 1989)

Number of stomachs	***16***	***33***	***32***	***16***	***57***	***70***	***84***	***58***
Territory	***Wiener Neustadt***	***Theresienfeld***	***Weikersdorf***	***Sollenau***	***Zurndorf-Süd***	***Zurndorf-Nord***	***Schrems***	***Meires***
Cultivated plants								
Barley	*7.3*	*11.8*	*7.6*	*13.1*	*6.1*	*5.2*	*2.7*	*10.4*
Wheat	*2.4*	*-*	*1.1*	*0.0*	*16.2*	*15.5*	*0.0*	*8.4*
Oats	*1.9*	*2.0*	*3.1*	*1.4*	*0.2*	*0.0*	*3.2*	*8.9*
Rye	*17.1*	*21.5*	*19.0*	*18.3*	*0.6*	*3.3*	*23.7*	*11.4*
Maize	*11.6*	*14.2*	*11.5*	*13.6*	*4.8*	*9.2*	*0.0*	*0.0*
Beet	*4.9*	*-*	*9.1*	*5.7*	*-*	*3.7*	*0.0*	*0.0*
Alfalfa	*5.1*	*3.7*	*6.1*	*2.8*	*1.0*	*0.2*	*-*	*-*
Canola	*-*	*0.0*	*0.0*	*0.0*	*2.3*	*-*	*1.0*	*0.0*
Soybeans	*-*	*-*	*-*	*-*	*1.2*	*0.3*	*-*	*-*
Red clover	*-*	*-*	*-*	*-*	*-*	*-*	*12.5*	*16.6*
Potatoes	*-*	*-*	*-*	*-*	*-*	*-*	*0.1*	*0.1*
Total	*50.3*	*53.2*	*57.5*	*54.9*	*32.4*	*37.4*	*43.2*	*55.8*
Non-cultivated plants								
Grasses	*11.8*	*13.8*	*10.0*	*9.9*	*21.6*	*26.0*	*39.7*	*29.1*
Faboidea	*11.3*	*6.0*	*9.4*	*7.8*	*1.5*	*0.3*	*2.0*	*4.3*
Asteraceae	*2.7*	*4.5*	*1.8*	*5.6*	*4.0*	*3.2*	*5.4*	*4.2*
Brassicaceae	*2.3*	*4.2*	*1.8*	*0.4*	*1.2*	*0.0*	*0.0*	*0.2*
Plantain	*2.4*	*2.1*	*3.7*	*5.0*	*2.2*	*1.7*	*0.7*	*0.0*

Other occurring sporadically	*7.4*	*8.7*	*6.3*	*5.3*	*16.9*	*13.3*	*4.5*	*3.1*
Total	*37.9*	*39.3*	*33.0*	*34.0*	*47.4*	*44.5*	*52.3*	*40.9*
Supplemental food								
Cabbage					*1.2*	*2.6*		
Carrots					*5.1*	*1.5*		
Indeteminable	*10.5*	*5.5*	*5.1*	*8.1*	*13.6*	*12.5*	*3.8*	*2.5*
Animal hair	*1.3*	*2.0*	*4.4*	*3.0*	*0.3*	*1.5*	*0.7*	*0.8*

From the above table it is evident that brown hare do feed on dicotyledonous plants, although monocots represent the major part of their diet. It may be also seen that maize is definitely not the preferred food of the brown hare.

Taking this into account the zRMS is of the opinion that PD values of 0.84 and 0.16 for monocots and dicots, respectively, as proposed by the Northern Zone Guidance Document are sufficiently supported by the available data and may be used also in evaluation performed for the Central Zone.
Nevertheless, for concerned Member States that would not accept the proposed PD refinement, additional calculations are also performed for the worst case assumption that the brown hare would feed exclusively on maize shoots.

Food Intake Rate

Wood mouse
The FIR/bw for the wood mouse was performed by the Applicant in [redacted] *with consideration of the bodyweight of 21.7 g, as indicated in EFSA (2009) and the mixed diet indicated in EFSA guidance. Calculation was performed in line with indications of Appendix G of EFSA (2009) and is presented below.*

Maize	April-May	Plant material [f]	Ground arthropods	Weed seeds
Fraction of food item in mixed diet [a]	PD_i fresh (%)	25%	25%	50%
Food energy of food item [i] in mixed diet [b]	FE (kJ/dry g)	17.6	22.7	21.7
Moisture content of food item [i] in mixed diet [b]	MC (%)	76.4%	68.8%	9.9
Assimilation efficiency of food item [i] in mixed diet [c]	AE (%)	47%	87%	84%
Food energy of food item in diet [d]	FE_{item},fresh (kJ/g fresh weight)	0.488	1.54	8.21
Food energy of total mixed diet [d]	FE_{total},fresh (kJ/g fresh weight)	10.2		
Daily energy expenditure [d]	DEE (kJ/day)	59		
Food intake rate of total mixed diet [d]	FIR_{total}, fresh (g fresh weight/day)	5.76		
b.w. [e]	(g)	21.7		
FIR/b.w.	(g fresh weight/b.w./day)	0.27		

[a] PD for Wood mouse Tier 1 EFSA mixed diet
[b] From Table 3 of Appendix G in EFSA (2009)
[c] From Table 4 of Appendix G in EFSA (2009)
[d] Calculated according to EFSA (2009; Appendix G)
[e] Body weight of wood mouse from the EFSA Guidance
[f] Plant material is assumed to be = maize shoots (using the default values for grasses and cereal shoots)

As all parameters are agreed by the zRMS, the FIR/be of 0.27 will be used in the risk refinement.

Brown hare
The FIR/bw for the brown hare was calculated by the Applicant in [redacted] with consideration of the bodyweight of 3800 g, as indicated in EFSA (2009) and the mixed diet (PD of 0.84 and 0.16 for monocots and dicots, respectively). Calculation was performed in line with indications of Appendix G of EFSA (2009) and is presented below.

Maize		April-May	
		Maize shoots [f]	Non-grass herbs
Fraction of food item in mixed diet [a]	PD_i fresh (%)	84%	16%
Food energy of food item [i] in mixed diet [b]	FE (kJ/dry g)	17.6	17.8
Moisture content of food item [i] in mixed diet [b]	MC (%)	76.4	88.1
Assimilation efficiency of food item [i] in mixed diet [c]	AE (%)	47	76
Food energy of food item in diet [d]	FE_{item},fresh (kJ/g fresh weight)	1.640	0.258
Food energy of total mixed diet [d]	FE_{total},fresh (kJ/g fresh weight)	1.897	
Daily energy expenditure [d]	DEE (kJ/day)	2363.4	
Food intake rate of total mixed diet [d]	FIR_{total}, fresh (g fresh weight/day)	1245.61	
b.w. [e]	(g)	3800	
FIR/b.w.	(g fresh weight/b.w./day)	0.328	

[a] PD for the hare according to published papers, as discussed above
[b] From Table 3 of Appendix G in EFSA (2009)
[c] From Table 4 of Appendix G in EFSA (2009)
[d] Calculated according to EFSA (2009; Appendix G)
[e] Body weight of brown hare from either the EFSA Guidance (3800g)
[f] Monocot plant material is assumed to be = maize shoots (using the default values for grasses and cereal shoots)

As all parameters are agreed by the zRMS, the FIR/be of 0.328 will be used in the risk refinement.

For brown hare feeding exclusively with maize shoots, the FIR/bw of 0.32 as calculated in Table 9.3-7 with consideration of the bodyweight of 3800 g will be used.

Residue decline and fTWA

Maize
In order to determine the DT_{50} value in maize, a residue decline study by [redacted] has been submitted by the Applicant. The study is considered acceptable and due to data from only 5 trials it is proposed by the zRMS to use the worst case DT_{50} of 0.803 days for purposes of refinement of fTWA, which is 0.055. For evaluation of the study, please refer to Appendix 2, KCP 10.1.2.2/06.

Weeds
In order to determine the DT_{50} value in weeds, a residue decline study by [redacted] performed on clover has been submitted by the Applicant. The study is considered acceptable and due to reliable DT_{50} values obtained in 10 trials it is proposed by the zRMS to use the geometric mean DT_{50} of 2.19 days for purposes of refinement of fTWA, which is 0.150.
For evaluation of the study, please refer to Appendix 2, KCP 10.1.2.2/11.

RUD values

Default RUD values in line with EFSA (2009) are used for particular diet components.

During the commenting period additional information regarding potential refinement of the mean RUD value in maize has been provided by the Applicant. It was pointed out that the default RUD values indicated in EFSA (2009) for maize actually originate from the residue trials performed on grass+cereals with no maize trials included in derivation of the RUD. In order to derive RUD values relevant for maize, xxx analysed a large dataset of industry dietary residue trials performed for spray *applications of pesticides in maize at BBCH 10-19 (436 trials: 255 EU-N; 181 EU-S). The initial residues were converted to RUD values using the application rate. Mean and 90th percentile RUD values were calculated across all European trials and subsets covering the Northern and Southern residue regions, in order to check for any potential effect of region on RUD outcome. The methodology used followed approach taken to derive the default RUD values for grass+cerals in EFSA (2009). Based on obtained results, the mean RUD of 46.8 mg/kg was derived for maize and may potentially be used for purposes of the risk assessment, especially it actually originates from the sufficient dataset derived from residue trials in maize and is more relevant than RUD derived for grass+cereals, excluding residue trials in maize.*

It is, however, noted that very limited information on the study by [redacted] been provided by the Applicant and no background documents were presented. Taking this into account the zRMS could not confirm validity of the provided RUD value and this refinement option must be further considered at the national level. The short summary of study by [redacted] is provided in Appendix 2, KCP 10.1.2.2/13.

Nevertheless, refinement of the risk to focal species based on these refined RUD values in maize is presented below for illustrative purposes, in addition to calculations based on default RUD originating from grass+cereals trials.

Deposition factor

In [redacted] it was proposed by the Applicant to use the deposition factor of 0.75 for weeds, which will be partially shaded by maize crops at BBCH 12-18. However, according to EFSA (2009) consideration of deposition factor is relevant for maize at principal growth stages ≥3. Taking this into account consideration of the deposition factor for early post-emergence application of Callisto is not acceptable.

Refined TER calculations

Wood mouse

Intended use	***Maize, 1 × 1.5 L product/ha***							
Active substance/product	*mesotrione*							
Application rate (g a.s./ha)	*1 × 150*							
Reprod. toxicity (mg/kg bw/d)	*0.3*							
TER criterion	*5*							
Crop scenario Growth stage	***Generic focal species***	***PD/diet type***	***FIR/bw***	***RUD_m***	***MAF_m × TWA***	***PT***	***DDD_m (mg/kg bw/d)***	***TER_{lt}***
BBCH 10 - 29	*Small omnivorous mammal "mouse"*	*0.25 (maize)*	*0.27*	*54.2*	*1.0 × 0.055*	*0.139*	*0.004*	
		0.5 (seeds)		*40.2*	*1.0 × 0.53*		*0.06*	
		0.25 (arthropods)		*3.5 [1)]*	*1.0 × 0.53*		*0.003*	
						Sum of DDD_m	*0.067*	***4.5***

[1)] according to Appendix A of EFSA (2009) RUD values for arthropods with interception are relevant for scenario maize at BBCH 10-29

Intended use	***Maize, 1 × 1.0 L product/ha***
Active substance/product	*mesotrione*
Application rate (g a.s./ha)	*1 × 100*
Reprod. toxicity (mg/kg bw/d)	*0.3*

TER criterion		*5*						
Crop scenario Growth stage	**Generic focal species**	**PD/diet type**	**FIR/bw**	**RUD_m**	**MAF_m × TWA**	**PT**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
BBCH 10 - 29	*Small omnivorous mammal "mouse"*	*0.25 (maize)*	*0.27*	*54.2*	*1.0 × 0.055*	*0.139*	*0.003*	
		0.5 (seeds)		*40.2*	*1.0 × 0.53*		*0.04*	
		0.25 (arthropods)		*3.5* [1)]	*1.0 × 0.53*		*0.001*	
						Sum of DDD_m	*0.044*	*6.8*

[1)] according to Appendix A of EFSA (2009) RUD values for arthropods with interception are relevant for scenario maize at BBCH 10-29

Performed calculations demonstrated acceptable risk to the wood mouse following application of Callisto at the lower application rate corresponding to 100 g mesotrione/ha. Unacceptable risk was concluded for higher application rate of 150 g mesotrione/ha.

Brown hare

Intended use **Active substance/product** **Application rate (g a.s./ha)**		***Maize, 1 × 1.5 L product/ha*** *mesotrione* *1 × 150*						
Reprod. toxicity (mg/kg bw/d) **TER criterion**		*0.3* *5*						
Crop scenario Growth stage	**Focal species**	**PD/diet type**	**FIR/bw**	**RUD_m**	**MAF_m × TWA**	**PT**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
BBCH 10 - 29	*Brown hare*	*0.84 (maize)*	*0.328*	*54.2*	*1.0 × 0.055*	*0.62*	*0.076*	
		0.16 (dicot weeds)		*28.7*	*1.0 × 0.150*		*0.021*	
						Sum of DDD_m	*0.097*	***3.1***
BBCH 10 - 29	*Brown hare*	*1.0 (maize)*	*0.32*	*54.2*	*1.0 × 0.055*	*0.62*	*0.089*	***3.4***

Intended use **Active substance/product** **Application rate (g a.s./ha)**		***Maize, 1 × 1.0 L product/ha*** *mesotrione* *1 × 100*						
Reprod. toxicity (mg/kg bw/d) **TER criterion**		*0.3* *5*						
Crop scenario Growth stage	**Focal species**	**PD/diet type**	**FIR/bw**	**RUD_m**	**MAF_m × TWA**	**PT**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
BBCH 10 - 29	*Brown hare*	*0.84 (maize)*	*0.328*	*54.2*	*1.0 × 0.055*	*0.62*	*0.051*	
		0.16 (dicot weeds)		*28.7*	*1.0 × 0.150*		*0.014*	

						Sum of DDD_m	0.065	**4.6**
BBCH 10 - 29	Brown hare	1.0 (maize)	0.32	54.2	1.0 × 0.055	0.62	0.059	5.1

Risk assessment based on refined parameters demonstrated unacceptable risk to the brown hare from exposure to mesotrione applied at 150 g a.s./ha from both, mixed and single diet.
For lower application rate acceptable risk could be demonstrated for hares feeding exclusively on maize shoots, but unacceptable risk was demonstrated for hares with a TER slightly below the trigger of 5 when a mixed diet was considered. This shows that consideration of the single diet not necessarily represents worst case.

As mentioned above, analysis of the industry residue data in maize at BBCH 10-19 performed by [redacted] *demonstrated that default mean RUD value of 54.2 mg/kg derived for grass+cereals may be replaced by 46.8 mg/kg derive specifically for maize. The TER values calculated with consideration of this value are presented below for illustrative purposes.*

Wood mouse (RUD in maize set to 46.8 mg/kg)

Intended use **Active substance/product** **Application rate (g a.s./ha)**		**Maize, 1 × 1.5 L product/ha** mesotrione 1 × 150						
Reprod. toxicity (mg/kg bw/d) **TER criterion**		0.3 5						
Crop scenario Growth stage	**Generic focal species**	**PD/diet type**	**FIR/bw**	**RUD_m**	**MAF_m × TWA**	**PT**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
BBCH 10 - 29	Small omnivorous mammal “mouse”	0.25 (maize)	0.27	46.8	1.0 × 0.055	0.139	0.0036	
		0.5 (seeds)		40.2	1.0 × 0.53		0.06	
		0.25 (arthropods)		3.5 [1)]	1.0 × 0.53		0.003	
						Sum of DDD_m	0.0666	**4.5**

[1)] *according to Appendix A of EFSA (2009) RUD values for arthropods with interception are relevant for scenario maize at BBCH 10-29*

Intended use **Active substance/product** **Application rate (g a.s./ha)**		**Maize, 1 × 1.0 L product/ha** mesotrione 1 × 100						
Reprod. toxicity (mg/kg bw/d) **TER criterion**		0.3 5						
Crop scenario Growth stage	**Generic focal species**	**PD/diet type**	**FIR/bw**	**RUD_m**	**MAF_m × TWA**	**PT**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
BBCH 10 - 29	Small omnivorous mammal “mouse”	0.25 (maize)	0.27	46.8	1.0 × 0.055	0.139	0.002	
		0.5 (seeds)		40.2	1.0 × 0.53		0.04	
		0.25 (arthropods)		3.5 [1)]	1.0 × 0.53		0.001	

Sum of DDD_m	*0.043*	*7.0*

[1)] according to Appendix A of EFSA (2009) RUD values for arthropods with interception are relevant for scenario maize at BBCH 10-29

Performed calculations based on more relevant RUD value in maize confirmed acceptable risk to the wood mouse following application of Callisto at the lower application rate corresponding to 100 g mesotrione/ha. In case of higher application rate the refined RUD had only marginal impact on calculated DDD and hence on the TER. Acceptable risk from higher application rate of 150 g mesotrione/ha could not be concluded and needs further refinement.

Brown hare (RUD in maize set to 46.8 mg/kg)

Intended use	***Maize, 1 × 1.5 L product/ha***							
Active substance/product	*mesotrione*							
Application rate (g a.s./ha)	*1 × 150*							
Reprod. toxicity (mg/kg bw/d)	*0.3*							
TER criterion	*5*							
Crop scenario Growth stage	***Focal species***	***PD/diet type***	***FIR/bw***	***RUD_m***	***MAF_m × TWA***	***PT***	***DDD_m (mg/kg bw/d)***	***TER_{lt}***
BBCH 10 - 29	*Brown hare*	*0.84 (maize)*	*0.328*	*46.8*	*1.0 × 0.055*	*0.62*	*0.066*	
		0.16 (dicot weeds)		*28.7*	*1.0 × 0.150*		*0.021*	
						Sum of DDD_m	*0.087*	***3.4***
BBCH 10 - 29	*Brown hare*	*1.0 (maize)*	*0.32*	*46.8*	*1.0 × 0.055*	*0.62*	*0.077*	***3.9***

Intended use	***Maize, 1 × 1.0 L product/ha***							
Active substance/product	*mesotrione*							
Application rate (g a.s./ha)	*1 × 100*							
Reprod. toxicity (mg/kg bw/d)	*0.3*							
TER criterion	*5*							
Crop scenario Growth stage	***Focal species***	***PD/diet type***	***FIR/bw***	***RUD_m***	***MAF_m × TWA***	***PT***	***DDD_m (mg/kg bw/d)***	***TER_{lt}***
BBCH 10 - 29	*Brown hare*	*0.84 (maize)*	*0.328*	*46.8*	*1.0 × 0.055*	*0.62*	*0.044*	
		0.16 (dicot weeds)		*28.7*	*1.0 × 0.150*		*0.014*	
						Sum of DDD_m	*0.058*	*5.2*
BBCH 10 - 29	*Brown hare*	*1.0 (maize)*	*0.32*	*46.8*	*1.0 × 0.055*	*0.62*	*0.051*	*5.9*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

In case refinement of RUD is accepted by cMS, acceptable risk from the lower rate of 100 g a.s./ha may be concluded for brown hare feeding on both, mixed diet and maize shoots and no further consideration is required. For higher application rate the risk is still unresolved for brown hare feeding on both, mixed diet and maize shoots.

Nevertheless, calculations based on the refined RUD value needs to be confirmed at the national level.

It is noted that in order to refine the risk to the brown hare, the population modelling performed using POLARIS was provided by the Applicant [redacted]). The comprehensive summary of the modelling was not provided by the Applicant, the general summary of most important parameters and obtained results is provided by the zRMS below.

In parametrisation of the model three toxicity studies evaluated at the EU level were considered:

1. *28-day dynamic exposure study in rat [redacted]*
2. *Acute oral toxicity study with rat by [redacted]*
3. *Multigenerational study with rat by [redacted] (from this study the NOAEL of 0.3 mg a.s./kg bw/d was derived and used in the risk assessment). From this study crucial parameters related to the bodyweight reduction, litter size reduction and reduced pup survival were considered.*

The exposure was calculated with consideration of the application rate of 1x150, 2x150 and 5x150 g a.s./ha and default values indicated in EFSA (2009) for FIR/bw, RUD and foliar DT50. Deposition factor of 1 was considered.

The application dates were determined using the AppDate tool with consideration of the groundwater scenarios.

Body weight reductions were calculated using the 21d TWA exposure and the dose-response curve calculated on the basis of results of the study by Milburn (1997). Body weight reductions alone may have no influence on population density or structure. However, as described above, individuals with a body weight of 2884g or less on 31st of October may not survive winter. Therefore, in all simulations these animals were assumed to die immediately. This natural threshold could also include unexposed young individuals which were not old enough to have a body weight above this threshold.
The reduction of litter size was simulated at the time of birth. This was done by calculating the 21 d TWA concentration for each individual hare using the default EFSA (2009) values. Then, based on this concentration and on the respective dose response curves derived on the basis of results of the study by [redacted] the proportion was calculated by which litter size is reduced. Regarding the increased pup mortality, this effect was also simulated as a reduced litter size at birth. Hence, when birth was simulated, litter size was reduced twice: (1) according to the dose-response of the effect reduction of litter size; and (2) according to the dose-response of the effect increased pup mortality (based on Milburn, 1997). This means, increased pup mortality was assumed to occur at birth for simplicity. This assumption had no influence on the model results, since brown hares do not stop reproduction during lactation.

For validation of the PT values derived by the model, results of the study by Grimm & Katzschner (2019, KCP 10.1.2.2/07) were used. It is, however, noted that due to the small size of locations in Germany, only part of the study performed in Hungary was taken into account with only 2 out of 3 test sites. It is noted by the zRMS that part of the study performed in Germany resulted with higher 90th percentile PT comparing to part performed in Hungary and for this reason it is questioned if consideration of only two sites from Hungary was sufficient for proper validation of the model. Nevertheless, PT values simulated by the model were above 0.9 for about 30% of all hares, which clearly represents worst case as in the study by Grimm & Katzschner (2019) only one of all monitored hares had PT >0.9 and one had PT of 0.89 (both in Germany). For remaining hares the PT values ranged from 0.02 to 0.63.

The worst-case character of various landscapes for population level risk assessments of brown hares has previously been evaluated in Kleinmann and Wang (2017). In this publication it has been found that PT values of brown hares in maize are higher when the treated habitat is distributed equally over the *entire landscape (compared to a landscape with clusters of treated habitat). The worst landscape in Kleinmann and Wang (2017), resulting in the highest PT values, was a landscape from Lincolnshire (UK), in which hares spent a large proportion of their time foraging in fields since they were surrounded by suitable off-crop habitat in which they could rest. This landscape has been adapted for a risk assessment in maize.*

For the risk assessment it was assumed conservatively that 30% of the landscape area is composed of maize. Other habitats were winter wheat, winter, barley, woodland, pastures, oilseed rape, field margins, hedgerows and roads (see figure below).

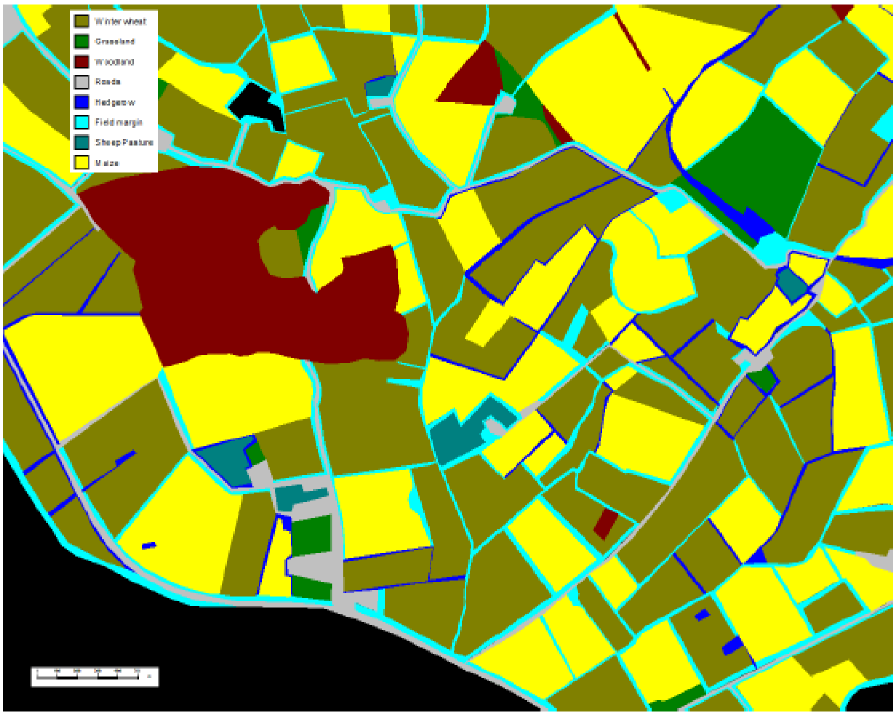
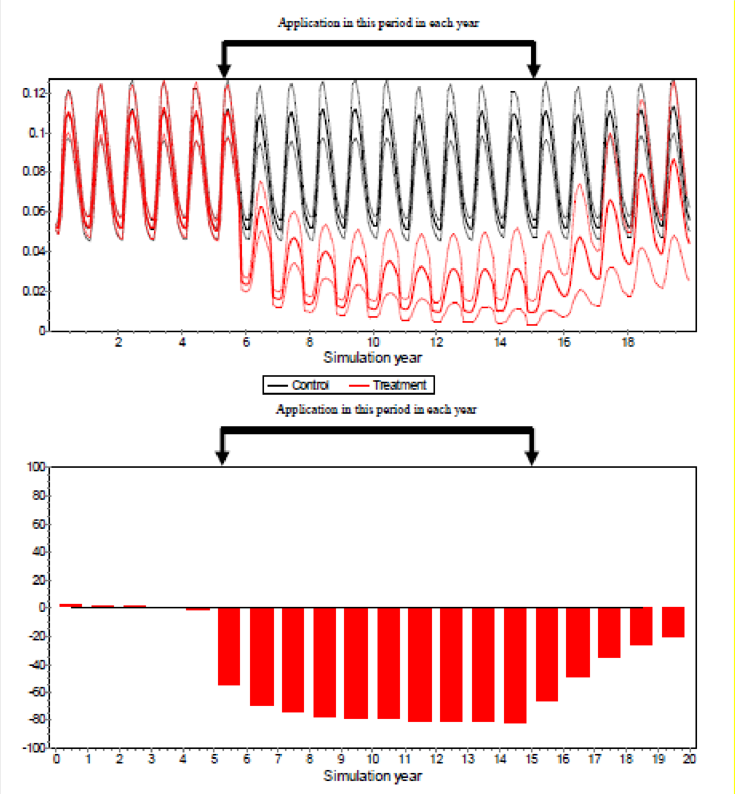


Figure 5. Habitat composition of the landscape from Lincolnshire, which has been used for the risk assessment.

In order to demonstrate that the model is able to detect effects, additional 90 simulations for 20-years were performed for a toxic reference substance with assumption of 25% mortality and 25% reduced litter size for 21 days. Effects were applied in the entire landscape (all habitats). Additionally, the body weight of all individuals in maize fields was reduced by 5% per day for 21 d starting at 1st of October. This corresponds to an overall weight reduction of about 65%. Clear effects at the population level could be *observed. As an example the graph presenting population density over 20 years assuming 5% bodyweight reduction for individual in maize for 21 days is presented below:*



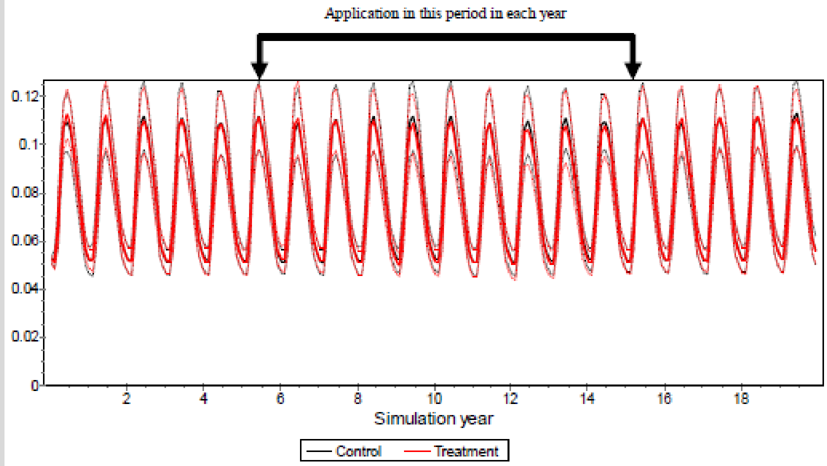
Maximal and minimal differences of densities of treatment vs. control simulations at the end of the year (31st Dec) for years in which the toxic reference was applied are presented in the table below.

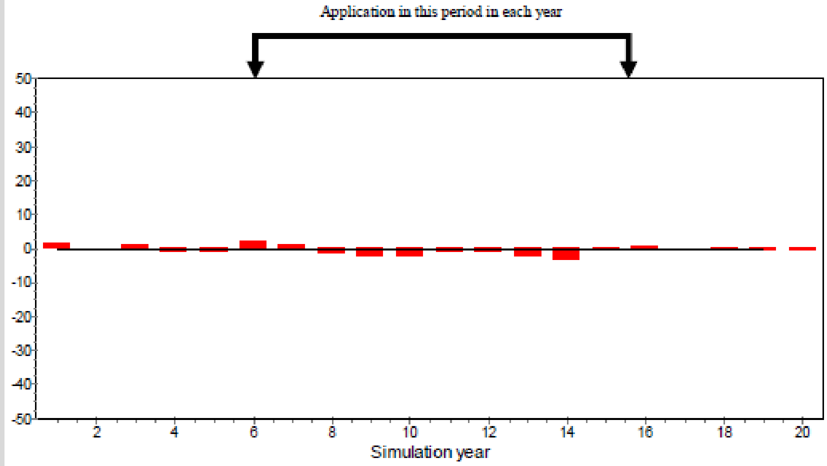
Toxic reference	Max. difference to control	Min. difference to control[1]	Recovery after years
25% additional mortality	-39.63	-20.86	3
25% reduced litter size for 21 d	-18.56	-7.19	2
5% body weight reduction per day in maize for 21 d (overall ~65% reduction)	-82.64	-55.51	>5

[1] Values >0 indicate that density in the treatment was higher than in the control.

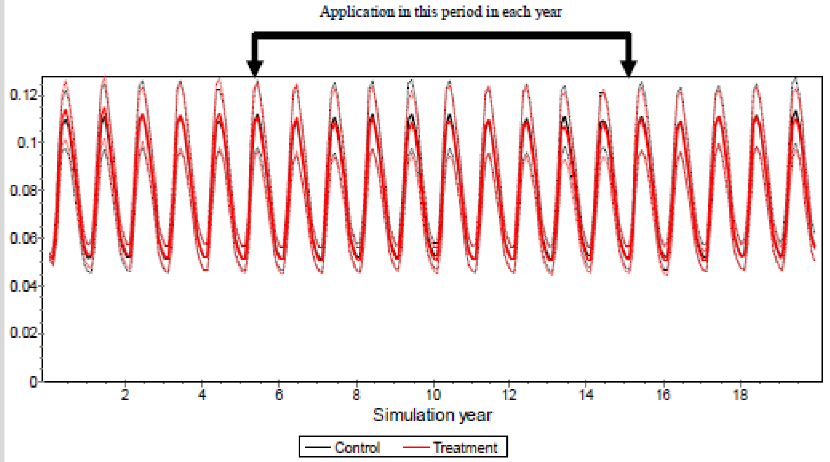
Results obtained for simulations performed for mesotrione

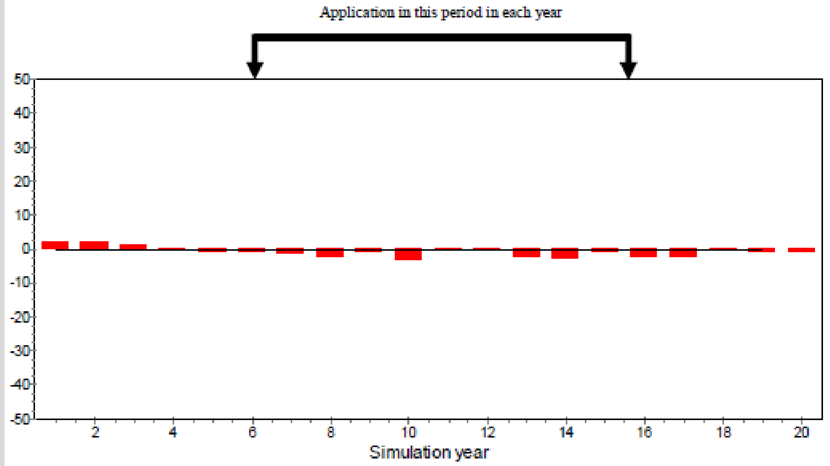
The population densities over 20 years assuming 1x, 2x and 5x the maximum intended application rate of Callisto are copied from the modelling report below. Dashed lines indicate standard deviations.



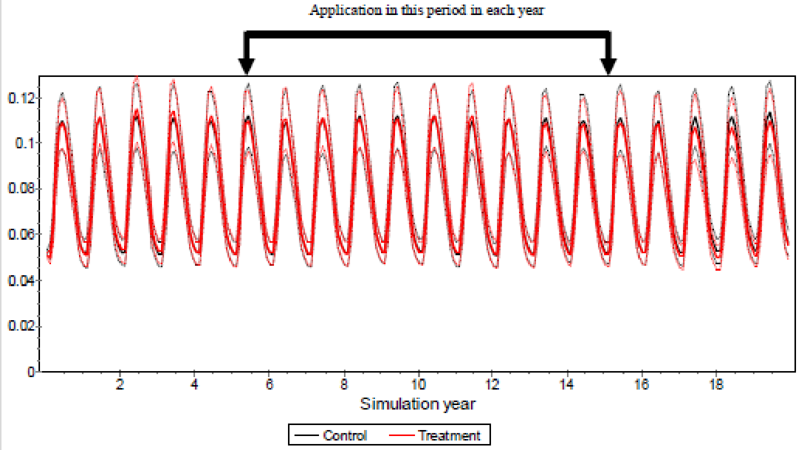


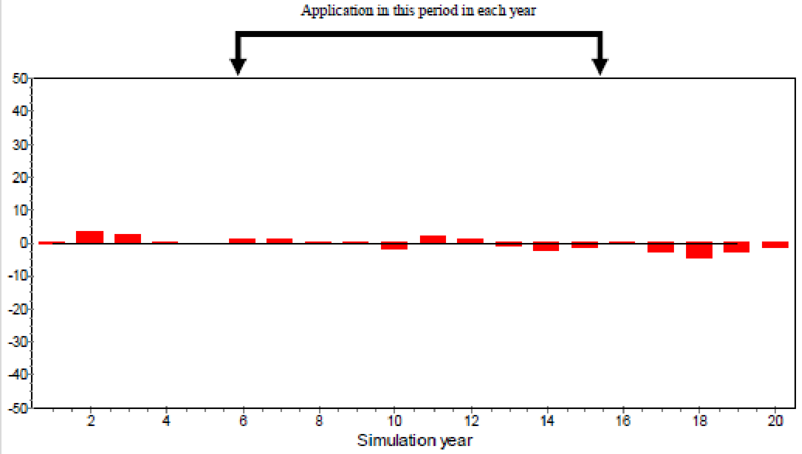
1x150 g mesotrione/ha





2x150 g mesotrione/ha





5x150 g mesotrione/ha

Maximal and minimal differences of densities of treatment vs. control simulations at the end of the year (31st Dec) for years in which the toxic reference was applied are presented in the table below.

	Max. difference to control	Min. difference to control [1]	Recovery after years
1x AR	-3.35	1.84	0 (no effect)
2x AR	-3.40	0.42	0 (no effect)
5x AR	-2.38	2.10	0 (no effect)

1 Values >0 indicate that density in the treatment was higher than in the control.

Overall, performed population modelling demonstrates that application of Callisto at 150 g a.s./ha (or even 5 times this rate) is not expected to have adverse effects to the brown hare at the population level.

In general the zRMS has some reservations to address the risk on the basis of population modelling as currently no validated models or criteria for their evaluation in the context of the regulatory risk assessment exist. Furthermore it is noted that the modelling was performed with assumption that the bodyweight reduction of 24.1% will have no impact at the population level. This conclusion was based on the literature review performed by Brauer & Wang (2016, KCP 10.1.2.2/10). However, the literature review mentioned was focused on determination of impact of bodyweight reduction on survival and reproduction of rabbits, so it is not known if the same trigger for bodyweight reduction could be applied for the brown hare. On the other hand, in the population modelling it was assumed that all individuals with bodyweight of 2884 g (i.e. default 3800 g reduced by 24.1%) observed on 31st of October will not survive the winter. This seems to be very conservative assumption that could balance the uncertainty related to the trigger weight reduction determined for the rabbit. It is also noted that the bodyweight of 3800 g is a default value indicated by EFSA (2009), while according to the Mammal Bible the brown hare weight ranges from 2900 to 3500 g (males) and from 3100 to 3750 g (females). This further confirms *that the assumptions made in the model are conservative, as in reality assumed trigger bodyweight of 2884 g would be only marginally lower than the minimum normal weight of males and females.*

In opinion of the zRMS the performed population modelling (Kleinmann, 2019a) ~~is acceptable despite~~ has some uncertainties, which are however balanced by other conservative assumptions. Nevertheless, due to absence of the clear criteria for consideration of results of such modelling in the regulatory risk assessment, the zRMS is of the opinion that ~~it~~ in general, population modelling may be used rather to support acceptable risk in case when the deterministic risk assessment results with TER values close to the trigger. This approach has been internally agreed by the Polish authorities and is used on the regular basis during the national authorisations. Taking this into account it is concluded by the zRMS that despite uncertainties mentioned, results of the population modelling by Kleinmann (2019a) are sufficient to support acceptable risk for the lower application rate of Callisto at 100 g a.s./ha with deterministic risk assessment resulting with TER values of 4.6 and 5.1 for mixed and single diet, respectively.
For higher application rate of 150 g a.s./ha the TER values of 3.1 and 3.4 for mixed and single diet, respectively, are clearly below the trigger and the risk is considered to be not sufficiently resolved.

Concerned Member States must decide on acceptability and applicability of population modelling in their countries and acceptability of the risk to the brown hare from both application rates at the product authorisation.

The Applicant is requested to provide comprehensive summary of the report by Kleinmann (2019a) in order to aid concerned Member States more detailed evaluation of the performed population modelling. Despite this request, the summary was not provided by the Applicant so it could not be presented in this updated version of the Core Assessment. Nevertheless, as already mentioned above, in absence of the commonly agreed approach towards evaluation of population modelling and implementation of its results into the regulatory risk assessment, each cMS has to review the population modelling by Kleinmann (2019a) and decide on its acceptability and applicability at the national level. This concerns also all other accompanying documents considered for parametrisation of the model, including paper by Brauer and Wang (2016). The zRMS evaluation should be thus treated as illustrative rather than conclusive.
It should be also noted that during the commenting period the new population modelling based on modified parameters agreed with The Netherlands has been submitted by the Applicant (Kleinmann, 2020). This new modelling was performed using the same concept as in Kleinmann (2019a), but it addressed concerns of The Netherlands principally on: the implementation of toxicity dose-response curves which they suggested should be implemented as threshold levels rather than extrapolated; on the worst-case nature of the landscape assessed; and on the extremely high EMFs required to demonstrate effects. There were also a number of clarifications on the parameterisation data.
This new report was indicated as an updated Kleinmann (2019a), but due to the modified parameters it would require completely new evaluation which was not possible within the given timeframes, which could be adjusted in case the zRMS was informed about the ongoing discussion with The Netherlands or about intention to perform additional population modelling.
As no such information was provided by the Applicant, at this stage the zRMS may only indicate that there is such a new modelling, which may be potentially less uncertain. Nevertheless, its acceptability and applicability must be decided at the national level, similarly as in case of Kleinmann (2019a), since in absence of the common agreement on evaluation of population modelling at the EU level and within the Central Zone, no final conclusion may be taken at the zonal level based on such data. The summary of Kleinmann (2020) is provided in Appendix 2, KCP 10.1.2.2/14 to aid preliminary review by the cMS.

Overall conclusions on the dietary risk assessment for mammals

In opinion of the zRMS the risk to mammals from application of Callisto at 100 g a.s./ha is sufficiently addressed on the basis of the available data.

Further refinement is, however, deemed necessary for higher application rate of 150 g a.s./ha. It is the view of the zRMS that this could be done using the endpoint calculated using benchmark dose approach, *which is considered to be more reliable way for derivation of an endpoint comparing to the standard NOAEL determination. Nevertheless, as indicated in point 9.3.1.1 above, acceptability of endpoint derived using this approach may vary among Member States and should be thus addressed at the national level. Alternatively, the Applicant may provide respective calculations to the zRMS for evaluation and concerned Member States may then decide on acceptability of this approach.*

Concerned Member States must decide on acceptability and applicability of all refinement options considered in the risk refinement as well as population modelling in their countries at the product authorisation.

Please note also that there is possibility for application of Callisto at application rate between 100 and 150 g a.s./ha (e.g. 120 g a.s./ha). However, as such rate was not included in the GAP evaluated in area of ecotoxicology and was thus not considered by the zRMS, this possibility has to be dealt with by concerned Member States at the national product authorisation.

zRMS comments:

Mammals
No data is provided in support of the application for authorization of **Mecorn 100 SC**.
The risk assessment for mammals performed for Callisto 100 SC are suitable for the use of Mecorn 100 SC proposed in GAP.

On the basis of performed calculations for Callisto 100 SC, acceptable acute and long-term risk to mammals may be concluded from proposed uses of Mecorn 100 SC.

According to the Registration Report for **Callisto 100 SC** the acute and long-term risk assessment for birds and mammals have been accepted. On the basis of performed calculations in **Callisto 100 SC** report, acceptable acute and long-term risk to mammals may be concluded from proposed uses of **Mecorn 100 SC.** No additional risk assessment is required.

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} ≥500 L/kg).

*With a K(f)oc of 50 (geomean; the worst-case is 14 in the final EFSA endpoints), mesotrione belongs to the group of less sorptive substances. Here, the maximum use rate of 1 x 150 g a.s./ha has been used to cover the risk to mammals from all intended uses (see **Błąd! Nie można odnaleźć źródła odwołania.**).*

Effective application rate (g/ha) =*	*150*		
Acute toxicity (mg/kg bw) =	*>5000*	*quotient =*	*<0.030*
Reprod. toxicity (mg/kg bw/d) =	*0.3 (NOEL)*	*quotient =*	***500***

** Effective application rate = Maximum application rate x MAF. However, in this case the MAF is not applicable as there is only a single application.*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

The resulting ratio for acute risk falls below the trigger of 50 indicating that further assessment of the acute risk to mammals from drinking water from puddles is not required for mesotrione.

For the chronic risk since the ratio of effective application rate (in g/ha) to relevant endpoint (in mg/kg bw/d) exceeds the critical value of 50 for at least one use scenario, a quantitative risk assessment (calculation of TER values) is necessary.

The predicted environmental concentration in puddles is calculated as follows in accordance with the EFSA Guidance Document:

$$PEC_{puddle} = \frac{AR/10}{1000\ (w + Koc\ x\ s)}$$

where:
AR = application rate (g/ha); divisor of 10 to achieve rate in mg/m²
w = 0.02 (pore water term; volume)
s = 0.0015 (soil term: volume, density, organic carbon content)

Table 9.3-9: Assessment of the risk for mammals due to exposure to mesotrione via contaminated drinking water in puddles

Intended use	*Maize*					
Active substance	*Mesotrione*					
Application rate (g/ha)	*1 × 100 and 1 × 150*					
Reprod. toxicity (mg/kg bw/d)	*0.3 (NOEL)*					
TER criterion	*5*					
Soil-relevant applic. rate (g/ha)	***K_{oc} (L/kg)***	***PEC_{puddle} (mg/L)***	***DW uptake (L/kg bw/d)***	***Daily dose (mg/kg bw/d)***	***Endpoint (mg/kg bw/d)***	***TER_{lt}***
100	*50 (geomean)*	*0.105*	*0.24*	*0.0252*	*0.3* ~~1.2~~	*12* ~~48~~
100	*14 (worst-case in the EFSA conclusion) [a]*	*0.244*	*0.24*	*0.0586*	*0.3* ~~1.2~~	*5.1* ~~20~~
150	*50 (geomean)*	*0.158*	*0.24*	*0.0379*	*0.3* ~~1.2~~	*7.9* ~~32~~
150	*14 (worst-case in the EFSA conclusion) [a]*	*0.366*	*0.24*	*0.0878*	***0.3*** ~~1.2~~	***3.4*** ~~14~~

PEC_{puddle}: concentration in puddles; DW: drinking water; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.
[a] The final DAR states: "As the adsorption is pH dependent a worst-case value should be used for risk assessment rather than a mean"

For the proposed use of 100 g a.s./ha the resulting TER values are above the trigger of 5 indicating acceptable chronic risk to mammals from drinking water from puddles.

Since the data provided by the Applicant of Callisto 100 SC was not sufficient for the assessment this point the zRMS comments have been placed in this document as a supplement of drinking water exposure assessment (written in italics, highlighted in yellow). These data are applicable for MEZ-HER 100 SC which is comparable in composition with Callisto 100 SC as well as it is recommended to use in the same crops, doses and time as Callisto 100 SC.

zRMS comments in Callisto 100 SC report: *The screening evaluation of the risk resulting from exposure to mesotrione via drinking water is agreed by the zRMS. Acceptable acute risk could be concluded for both application rates, but TER calculation was deemed necessary for the long-term risk. Risk assessment presented in Table 9.3-11 above is agreed by the zRMS. Acceptable chronic risk via drinking water could be concluded for lower application rate of 100 g a.s./ha.*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

For higher application rate refinement of the risk was deemed necessary and – as in case of higher tier dietary risk assessment – it was presented in Alvarez (2019) with no refinement options and justification of considered parameters presented in the dRR.
Nevertheless, the refinement presented in Alvarez (2019) was not evaluated by the zRMS in detail as unacceptable dietary risk was concluded for application rate of 150 g a.s./ha anyway, so additional refinement performed for drinking water exposure would not result with conclusion on acceptable use of Callisto at 150 g a.s./ha.

However, short overview of proposed refinement options is presented below.

Option 1

First option was refinement of the risk performed with consideration of the water content in various food items in the wood mouse diet to estimate the actual water demand. The zRMS does not agree with this approach as there are no data demonstrating that the wood mouse is the only small mammal species that would potentially drink water from puddles on the field treated with mesotrione, especially puddles may be also formed at the field margins or even outside the field, where can be utilised by other mammalian species with higher water demands.
During the commenting period the Applicant indicated that the wood mouse was identified as the small mammal focal species in maize and given its low body weight it is considered suitable for assessing the risk from puddles located in-field. The editable summary of the performed calculations as presented in Alvarez (2019) was submitted and is presented below for reference (text in italics).

The default drinking water assessment is based on a granivorous mouse eating 100% cereal seeds. As discussed above, the focal species for the proposed maize use is the wood mouse with a post-emergence diet of 25% maize, 25% insects and 50% seeds; and the brown hare, with a 100% herbivorous diet.
In accordance with Table 19 of Appendix L of the EFSA Guidance, grasses and cereal shoots contain 76.4% moisture; arthropods 68.8% moisture; whilst weed seeds contain only 9.9% moisture.
The realistic water needs for the omnivorous wood mouse will be calculated in accordance with Appendix K of the EFSA bird and mammal guidance document.

Drinking water consumption for omnivorous wood mouse

Food type	Energetic content of food (kJ/g wet wt)	Assimilation efficiency (%)	Energetic content of food, weighted by assimilation efficiency (kJ/g wet wt)	Portion of different food items in diet mix (% of diet wet weight)	Energy uptake per gram of each diet item [a] (kJ/g wet wt)	DEE (kJ)	FIR Daily food consumption of different food items [b] (g wet wt/day)
Weed seeds	*19.55*	*84*	*16.42*	*50*	*8.21*	-	*2.87*
Insects	*7.08*	*87*	*6.16*	*25*	*1.54*	-	*1.44*
Maize	*4.15*	*47*	*1.95*	*25*	*0.448*		*1.44*
Total	-	-	-	*100*	*10.2*	*58.83*	*5.75*

a Energy uptake for food item (kJ/g wet wt) = Energy content of food weighted by assimilation efficiency (kJ/g) $\times \frac{\text{proportion of food item in diet}}{100}$

b Daily consumption of food item (g wet wt/d) $= \frac{\text{DEE (kJ)}}{\text{Energy uptake/ g of total diet (kJ/g)}} \times \frac{\text{proportion of food item in diet}}{100}$

Calculation of water in the mixed diet for the 21.7g wood mouse (as per Appendix K) and remaining water need

Food type	FIR Daily food consumption of different food items [b] (g wet wt/day)	Moisture content (%)	Food water (mL)	Metabolic water [a] (mL)	Flux (mL/d) [b]	DWR [c]	DWR/bw
Weed seeds	*2.87*	*9.9*	*0.28*				
Insects	*1.44*	*68.8*	*0.99*				
Maize	*1.44*	*76.4*	*1.10*				

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Total			*2.37*	*1.58*	*7.4*	*3.45*	*0.16*

[a] Metabolic water is calculated using the following equation:
Metabolic water (ml) = DEE (kJ) x 0.0269 mL/kJ (mean value; DEFRA 2007 as referenced in Appendix K); thus for the Wood mouse metabolic water = 58.83 x 0.0269 = 1.59 mL.
[b] Daily water flux for a wood mouse, as given in Appendix K, derived from:
log10(WF) = -0.110+0.734x log110 (bw) for non-dessert species
[c] The drinking water rate requirement = total water flux (ml/d) – (food water + metabolic water) = 7.4 – (2.05+1.59)

The realistic water need considering a mixed diet is then used in the calculation of the DDD and refined TER values, below.

Assessment of the risk for mammals due to exposure to mesotrione via contaminated drinking water in puddles in-field

Intended use	*Maize*					
Active substance	*Mesotrione*					
Application rate (g/ha)	*1x 150*					
Reprod. toxicity (mg/kg bw/d)	*0.3 (NOEL)*					
TER criterion	*5*					
Soil-relevant applic. rate (g/ha)	***Koc (L/kg)***	***PEC_{puddle} (mg/L)***	***DW uptake (L/kg bw/d)***	***Daily dose (mg/kg bw/d)***	***Endpoint (mg/kg bw/d)***	***TER_{lt}***
150	*50 (geomean)*	*0.158*	*0.16*	*0.0253*	*0.3*	*12*
150	*14 (worst case in the EFSA conclusion) [a]*	*0.366*	*0.16*	*0.0585*	*0.3*	*5.1*

PEC_{puddle}: concentration in puddles; DW: drinking water; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.
[a] The final DAR states: "As the adsorption is pH dependent a worst case value should be used for risk assessment rather than a mean"

An acceptable risk is indicated in all cases when considering the focal species' realistic diet.

Applicant's calculation provided above were checked by the zRMS and are confirmed to be performed correctly.
In general, the zRMS agrees that from the small mammalian species only the wood mouse was identified to be relevant in early maize. Furthermore, in the first step of the drinking water assessment it is assumed that the indicator species will feed exclusively on seeds, which in case of the wood mouse is highly unlikely, especially as at the time of application of Callisto (May-June) there will be high availability of insects, earthworms and plants which form high proportion of the wood mouse diet. Therefore the performed above refinement of the risk based on the default diet and water content in particular food items may be potentially sufficient. However, as indicated in EFSA (2009), due to the incidental nature of puddle occurrence on agricultural fields, the potential for refinement of the assessment using the 'ecological parameters' for indicator/focal species is deemed very limited. The indication of EFSA (2009) refers particularly to PT values, however in opinion of the zRMS it may be extended also to other parameters, including the diet composition, which is not foreseen by EFSA (2009) as a refinement option of the risk via drinking water. It has to be noted that with TER only marginally above trigger (5.1) even slight increase of proportion of seeds in the diet composition may lead to an unacceptable risk. On the other hand, increase of percentage of vegetation or earthworms (not considered at all) in the diet will significantly reduce the water demand and will give larger margin of safety. Nevertheless, the zRMS has some concerns that due to not fully recognised proportion of seeds in the wood mouse diet the refinement provided above may be not fully protective and for this reason consideration of the run-off concentration of the active substance from relevant FOCUS Step 3 scenarios is considered to be more relevant approach, especially it is indicated in EFSA (2009) as relevant refinement option. Additional information regarding consideration of this approach in refinement of the risk to the wood mouse via drinking water after application of Callisto at 150 g a.s./ha is presented below (Option 2). Nevertheless, concerned Member States may wish to consider the refinement based on the wood mouse diet at the product authorisation.

Option 2

The another option was consideration of the FOCUS run-off concentrations, in line with EFSA (2009). This option was not checked by the zRMS in detail, but being in line with the guidance document it could be potentially accepted. Unfortunately, the concentration of mesotrione carried in the run-off water could not be validated as these values are not routinely reported in area of Section 8 and for this reason the TOXSWA reports would need to be provided in order to enable validation of the considered concentrations and confirmation that they actually represent worst case.
During the commenting period editable document presenting summary of this refinement option was provided by the Applicant and is presented below (text in italics).

The EFSA Guidance states:
"Puddle scenario
Refinements to the exposure part of this scenario can be made by using runoff concentrations directly from relevant FOCUS step 3 scenarios."
Thus the PEC_{sw} values from run-off scenarios are presented below to represent the PEC_{puddle} and these are used to refine the daily dose and TER values in the table below. Please note that the PEC_{puddle} is derived from the runoff estimates only, and is therefore not the standard PEC_{sw} presented in the aquatic section as calculated after dilution in a standard water body.

Derivation of PEC_{puddle} (PEC_{runoff}) from FOCUS modelling files

A puddle PEC_{max} was calculated by using the runoff concentrations generated at Step 3. The puddle PECmax was calculated for the use that gave the highest PECsw at FOCUS Step 3 for each 'R' scenario in the report:

Report:	*Ibrahim L. (2017a) Mesotrione - A European Environmental Fate Assessment for Parent Using the FOCUS Surface Water Models at Steps 3 to 4 Following Spray Application to Maize and an Analysis of its FOCUS Step 3 and 4 Exposure Patterns Using the EPAT Tool. RIFCON GmbH, Report No. 1520528-2 (Syngenta File No. ZA1296_10482/VV-630286)* *Modelling report: Syngenta file No.: VV-859308*

*To calculate puddle PECmax concentration the application year chosen by PAT and displayed in the *.p2t file was noted. The *.zts file was taken for the scenario required which displays the daily summed RUNF and RFLX1 values (runoff depth cm/day and pesticide runoff flux g/cm^2/day respectively). The units are defined in the PRZM user manual (Suárez 2005). However in the plotting variable section of the *.inp a factor is defined and applied to the default output. These factors are 10 and 1x 10^7 for RUNF and RFLX1respectively. The RUNF and RFLX1 figures from the *.zts file are converted to l/ha and ug/ha. The runoff concentration in ug/L calculated for each day using the formula below:*

$$\text{Daily Puddle PEC R/O concentration (ug/L)} = \frac{\text{RFLX1}(\mu g/ha)}{\text{RUNF}(L/ha)}$$

From the summarised daily concentrations, the maximum value for the application year chosen was taken and reported as the PEC_{puddle}.

A table summarising the conversion factors used is shown below:

Conversion Factors used in the calculation of the daily run off concentrations from the FOCUS PRZM *.zts file

Variable	***Default Unit***	***Factor applied to default unit from *.inp***	***Equivalent units for recording in *.zts file***	***Conversion to***	***Factors used in the unit conversion***
RUNF	*cm/day*	*10*	*mm*	*L/ha[a]*	*x 10,000*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

RFLX1	*g/cm²/day*	*1x10⁷*	*dg/ha*	*µg/ha*	*x 10 (to convert to g/ha)* *x 1000000 (to convert to ug/ha)*

[a] 1mm depth of rainfall over 1 hectare = 10,000 litres

An example calculation for any one chosen day is shown below:

*An example single line output from the *.zts file*

```
TSRTIME SERIES OUTPUT FILES
 TSR  FOCUS_PRZM_SW_4.3.1, 27 Apr. 2015           PRZM 4.63 Apr. 2015
 TSR                  RUNF      ESLS      PRCP      INFL      RFLX1        EFLX1        TPAP
TSR PRZ  1984  4 18    2.794     4.318     30.00     2.230     0.7626E-01   0.1070E-03   0.000
```

To calculate the daily RUNF value in L/ha

RUNF = 2.794 mm/day

1mm depth of rainfall over 1 hectare = 10,000 litres

∴ 1ha =2.794 x 10000
= 27940 L/ha

To calculate the daily RFLX1 value in µg/ha

RFLX1 = 0.7626E-01 dg/ha x 10
= 0.7626 g/ha x 1000000
= 7.626E+05 µg/ha

To calculate the daily run off concentration in µg/L

Daily run off concentration = 7.626E+05 µg/ha / 27940 L/ha

= 27.2942 µg/l

The daily run off concentration is calculated for each individual day in the application year and the runoff concentration taken from the maximum of the daily figure in the application year. This is reported below.

Mesotrione: PEC$_{puddle}$ derived from the run-off component from FOCUS Surface Water Step 3

Scenario	Waterbody	Crop	App'n rate (g/ha)	Timing	Application year	Parameter Combination	Entry route	PECsw max (µg/L)	Puddle PECmax [R/O conc max] (µg/L)
R1	*Pond*	*Maize*	*150*	*Post emergence*	*01 Mar 1984- 28 Feb 1985*	*Acidic*	*Runoff*	*0.113*	*27.66*
R1	*Stream*	*Maize*	*150*	*Post emergence*	*01 Mar 1984- 28 Feb 1985*	*Acidic*	*Runoff*	*2.40*	*27.66*
R2	*Stream*	*Maize*	*150*	*Post emergence*	*01 Mar 1977- 28 Feb 1978*	*Neutral*	*Runoff*	*3.28*	*20.98*
R3	*Stream*	*Maize*	*150*	*Post emergence*	*01 Mar 1980- 28 Feb 1981*	*Neutral*	*Runoff*	*5.93*	*30.59*
R4	*Stream*	*Maize*	*150*	*Post emergence*	*01 Mar 1984- 28 Feb 1985*	*Neutral*	*Runoff*	*6.26*	*31.59*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Suárez 2005: PRZM-3, A Model for Predicting Pesticide and Nitrogen Fate in the Crop Root and Unsaturated Soil Zones: Users Manual for Release 3.12.2

The assessment presented below, as originally submitted, represents a worst-case of exposure as the maximum initial PEC has been used, instead of the 21d TWA as recommended in the EFSA Guidance document for chronic assessment. Please note that the values for R1 are higher in the original calculations than the ones presented above, and this is because a different pH scenario was worst-case. The old worst-case ones are considered in the assessment below and indicate a large margin of safety.

Mesotrione: PEC$_{puddle}$ derived from the run-off component from FOCUS

Scenario	Waterbody	Crop	Application rate	entry route	Puddle PECmax [R/O conc max] (µg/L)
R1	Pond	Maize	150	Runoff	38.26
R1	Stream	Maize	150	Runoff	38.26
R2	Stream	Maize	150	Runoff	20.98
R3	Stream	Maize	150	Runoff	30.60
R4	Stream	Maize	150	Runoff	31.58

Mesotrione: refined assessment of the risk for mammals off-crop due to exposure to mesotrione via contaminated drinking water in puddles using FOCUS and using the default EFSA mammal scenario

Intended use **Active substance** **Application rate (g/ha)**		*Maize* *Mesotrione* *1 × 150*				
Reprod. toxicity (mg/kg bw/d) **TER criterion**		*0.3 (NOEL)* *5*				
Soil-relevant applic. rate (g/ha)	**Scenario**	**FOCUS PECrunoff (PEC$_{puddle}$) (mg/L)**	**DW uptake (L/kg bw/d)**	**Daily dose (mg/kg bw/d)**	**Reprod. toxicity (mg/kg bw/d)**	**TER$_{lt}$**
150	*R1/Pond*	*0.03826*	*0.24*	*0.00918*	*0.3*	*33*
	R1/Stream	*0.03826*	*0.24*	*0.00918*		*33*
	R2/Stream	*0.02098*	*0.24*	*0.00504*		*60*
	R3/Stream	*0.03060*	*0.24*	*0.00734*		*41*
	R4/Stream	*0.03158*	*0.24*	*0.00758*		*40*

PEC$_{puddle}$: concentration in puddles; DW: drinking water; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger

The approach taken by the Applicant in calculation of the concentration of mesotrione in puddles from run-off concentration is in general agreed by the zRMS. It is, however noted, that PRZM files could not be checked as due to some technical error they could not be extracted from the ZIP archive for review. It is noted that there are some differences in PEC$_{puddle}$ calculated from R1 scenario and presented in two tables above – in the second table the PEC$_{puddle}$ is clearly higher (38.26 µg/L) comparing to the first table, where PEC$_{puddle}$ of 27.66 µg/L is reported. The higher value was taken for TER calculation. Nevertheless, the reason for this difference is not clear and it was not explained by the Applicant and the zRMS could not check this calculation due to technical reason indicated above.
Nevertheless, as the dietary chronic risk to the wood mouse from application of Callisto at 150 g a.s./ha was not sufficiently resolved, in case the Applicant would like to authorise this application rate in some Member States, additional evaluation would be necessary at the national level anyway. The correctness of the PEC$_{puddle}$ based on run-off concentration could be then confirmed at the national level.
Overall, acceptable chronic risk to the wood mouse from drinking water following application of 150 g a.s./ha will be concluded in case PEC$_{puddle}$ are calculated accurately, which has to be confirmed at the national product authorisation.

Option 3
A third option was also presented, based on consideration of the dependency between pH and soil sorption of mesotrione. With consideration of the linear relationship, acceptable risk could be concluded

up to and including pH of 7.3. For pH 7.4 and higher, unacceptable TER values were calculated. For alkaline soils the risk was further refined using the wood mouse water demand calculated with consideration of the particular diet components. However, consideration of the wood mouse diet in the risk refinement is not agreed by the zRMS for reasons already indicated above (see option one).

As the refined risk assessment presented in Table 9.3-12 is not agreed by the zRMS, it has been struck through and shaded. The same concerns calculations based on NOAEL of 1.2 mg a.s./kg bw/d, as proposed refinement of the endpoint was not agreed by the zRMS (for details, please refer to point 9.3.1.1 of this document).

Overall, acceptable risk is concluded for mammals exposed via drinking water following application of Callisto at 100 g a.s./ha.

For higher application rate at 150 g a.s./ha further refinement is required or respective information from the FOCUS modelling. Although this information was provided by the Applicant and acceptable risk could be potentially concluded, due to technical failure the PRZM files could not be checked by the zRMS and will have to be validated at the national product authorisation, in case the Applicant will request authorisation of this higher rate of Callisto.

The Applicant is kindly reminded that the Core Assessment should be a stand-alone document, where all data considered in evaluation are summarised and all refinement options are presented together with their justification. This enables the zRMS to comment on considered parameters and facilitates concerned Member States independent validation of the data. Taking this into account, in case further refinement of the drinking water risk assessment is provided, this has to be prepared in an editable document, so it may be copied and inserted into the Core Assessment.

As in the course of the EU renewal of mesotrione it was concluded that its metabolites have similar or lower toxicity, specific evaluation of the drinking water risk was deemed not necessary and is considered to be covered by the evaluation performed for the active compound.

zRMS comments:

Drinking water exposure
Screening evaluation of the risk resulting from exposure to mesotrione via drinking water is agreed by the zRMS. Acceptable risk may be concluded.

As in the course of the EU renewal of mesotrione it was concluded that its metabolites have similar or lower toxicity, specific evaluation of the drinking water risk was deemed not necessary and is considered to be covered by the evaluation performed for the active compound.

Screening evaluation of the risk resulting from exposure to mesotrione via drinking water is agreed by the zRMS. Acceptable risk may be concluded.

As in the course of the EU renewal of mesotrione it was concluded that its metabolites have similar or lower toxicity, specific evaluation of the drinking water risk was deemed not necessary and is considered to be covered by the evaluation performed for the active compound.

No data is provided in support of the application for authorization of **Mecorn 100 SC**.
The risk assessment for mammals performed for Callisto 100 SC are suitable for the use of Mecorn 100 SC (100 g s.a./ha) proposed in GAP.

No additional risk assessment is required.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

9.3.2.4 Effects of secondary poisoning

The log P_{OW} values of mesotrione and its main metabolites MNBA, AMBA and SYN546974 amount to 0.11, -1.3, 0.32 and 1.62 respectively and thus do not exceed the trigger value of 3. A risk assessment for effects due to secondary poisoning is not required.

The log P_{OW} values of mesotrione and its main metabolites MNBA, AMBA and SYN546974 amount to 0.11, -1.3, 0.32 and 1.62 respectively and thus do not exceed the trigger value of 3. A risk assessment for effects due to secondary poisoning is not required.

9.3.2.5 Biomagnification in terrestrial food chains

Not relevant.

9.3.3 Risk assessment for baits, pellets, granules, prills or treated seed

Not relevant.

9.3.4 Overall conclusions

The acute and long-term risks of A12739A to mammals were assessed from toxicity exposure ratios between toxicity endpoints, estimated from studies with A12739A and mesotrione, and maximum residues occurring on food items following applications according to the proposed use pattern. The risk to mammals from exposure via drinking water was also assessed. Risk of secondary poisoning for mesotrione was not assessed as the log P_{OW} is <3.0.

The TER values, calculated for recommended scenarios, all exceed the trigger values of 10 for acute risk, indicating that the risk to mammals is acceptable following use of A12739A according to the proposed use pattern. Also the risk assessment for exposure via drinking water from puddles showed acceptable risk.

The long-term risk of mesotrione to herbivorous and omnivorous mammals was refined by identifying the brown hare and wood mouse as relevant focal species, refining the residues in potential food items, considering the realistic amount of time spent foraging in early maize fields (PT), and considering population modelling for the brown hare.

zRMS comments:

Mammals
No data is provided in support of the application for authorization of **Mecorn 100 SC**.
The risk assessment for mammals performed for Callisto 100 SC are suitable for the use of Mecorn 100 SC proposed in GAP.

On the basis of performed calculations for Callisto 100 SC, acceptable acute and long-term risk to mammals may be concluded from proposed uses of Mecorn 100 SC. The refinement risk assessment for mammals should be considered by MSs level.

The risk assessment for exposure via drinking water from puddles also showed acceptable risk.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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 mesotrione, consequently no further assessment of potential effects on reptiles and amphibians will be presented in this document.

zRMS comments: Accepted.

9.5 Effects on aquatic organisms (KCP 10.2)

Information concerning effects on aquatic organisms relevant for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, this point origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

9.5.1 Toxicity data

Studies on the toxicity to aquatic organisms have been carried out with mesotrione and its potentially relevant metabolites. Full details of these studies are provided in the respective EU DAR and related documents, as well as in Appendix 2 of this document (new studies).

Effects of A12739A on aquatic organisms were evaluated as part of the EU assessment of mesotrione.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process. There are some deviations for which justifications are provided below.

Table 9.5-1: Endpoints and effect values relevant for the risk assessment for aquatic organisms – mesotrione and potentially relevant metabolites

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Oncorhynchus mykiss	*Mesotrione*	*96 h, s*	*LC_{50} >120 mg a.s./L $_{s}$*	*EFSA Conclusion 2016* [redacted]
Oncorhynchus mykiss	*MNBA*	*96 h, s*	*LC_{50} >120 mg a.s./L $_{s}$*	*EFSA Conclusion 2016* [redacted]
Oncorhynchus mykiss	*AMBA*	*96 h, s*	*LC_{50} = 150 mg a.s./L $_{s}$*	*EFSA Conclusion 2016* [redacted]
Pimephales promelas	*Mesotrione*	*36 d chronic, f*	*NOEC = 12.5 mg a.s./L $_{mm}$*	*EFSA Conclusion 2016* [redacted]
Daphnia magna	*Mesotrione*	*48 h, s*	*EC_{50} >622 mg a.s./L $_{mm}$*	*EFSA Conclusion 2016 Gentle and Hamer, 1995 ZA1296/0561*
Daphnia magna	*MNBA*	*48 h, s*	*EC_{50} = 130 mg a.s./L $_{nom}$*	*EFSA Conclusion 2016 Kent and Shillabeer, 1997 ZA1296/0531*
Daphnia magna	*AMBA*	*48 h, s*	*EC_{50} = 160 mg a.s./L $_{nom}$*	*EFSA Conclusion 2016 Magor and Gore, 1998b R44276/0018*
Daphnia magna	*Mesotrione*	*21 d, ss*	*NOEC = 180 mg a.s./L $_{mm}$*	*EFSA Conclusion 2016 Morris et al., 1996 ZA1296/0564*
Pseudokirchneriella subcapitata	*Mesotrione*	*120 h, s*	*E_rC_{50} = 13 mg a.s./L $_{mm}$ E_bC_{50} = 3.5 mg a.s./L $_{mm}$*	*EFSA Conclusion 2016 Shillabeer et al., 1997 ZA1296/0186*
Pseudokirchneriella subcapitata	*MNBA*	*72 h, s*	*E_rC_{50} = 42 mg a.s./L $_{mm}$ E_bC_{50} = 38 mg a.s./L $_{mm}$*	*EFSA Conclusion 2016 Smyth et al., 1997b ZA1296/0533*
Pseudokirchneriella subcapitata	*AMBA*	*72 h, s*	*E_rC_{50} = 14 mg a.s./L $_{mm}$ E_bC_{50} = 9.4 mg a.s./L $_{mm}$*	*EFSA Conclusion 2016 Smyth et al., 1998 R44276/0019*
Lemna gibba	*Mesotrione*	*14 d, ss*	*E_bC_{50} frond no.= 0.022 mg a.s./L $_{mm}$*	*EFSA Conclusion 2016 Smyth et al., 1997c*

Species	*Substance*	*Exposure system*	*Results*	*Reference*
			E_bC_{50} dry weight = 0.0077 mg a.s./L $_{mm}$	*ZA1296/0182*
Lemna gibba	*Mesotrione*	*7 d, ss*	*E_rC_{50} frond no or biomass = 0.0241 mg a.s./L nom* *E_bC_{50} yield = 0.0045 mg a.s./L nom*	*Hengsberger and Wydra, 2015* *ZA1296_10438*
Myriophyllum spicatum	*Mesotrione*	*14d, ss*	*E_rC_{50} total shoot length = 0.0287 mg a.s./L nom* *E_yC_{50} yield = 0.00255 mg a.s./L nom*	*Gonsior 2017* *ZA1296_10504*
Aquatic macrophytes	*Mesotrione*	*Geometric mean*	*E_rC_{50} = 0.0263 mg a.s./L* *E_yC_{50} = 0.00339 mg a.s./L*	*See section 9.5.1.1*
Lemna gibba	*MNBA*	*7 d, ss*	*E_rC_{50} >97 mg a.s./L $_T$* *E_yC_{50} >97 mg a.s./L $_T$*	*EFSA Conclusion 2016* *Liedtke, 2013a* *CA3511_10001*
Lemna gibba	*AMBA*	*7 d, ss*	*E_rC_{50} >90 mg a.s./L $_T$* *E_yC_{50} >90 mg a.s./L $_T$*	*EFSA Conclusion 2016* *Liedtke, 2013b* *R044276_10001.*
Lemna gibba	*SYN546974*	*7 d, ss*	*E_rC_{50} >95 mg a.s./L $_{nom}$* *E_yC_{50} = 93 mg a.s./L $_{nom}$*	*EFSA Conclusion 2016* *Liedtke, 2013c* *SYN546974_10001*
Higher-tier studies (micro- or mesocosm studies)				
None				

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 T:based on time-weighted mean measured concentrations

Table 9.5-2: Endpoints and effect values relevant for the risk assessment for aquatic organisms – A12739A

Species	*Substance*	*Exposure system*	*Results*	*Reference*
Cyprinus carpio	*A12739A*	*96 h, s*	*LC_{50} = 71 mg product/L $_{nom}$*	*EFSA Conclusion 2016* [redacted]
Daphnia magna	*A12739A*	*48 h, s*	*EC_{50} = 49 mg product/L $_{nom}$*	*EFSA Conclusion 2016* *Ricketts and Langridge, 2005* *ZA1296/2042*
Pseudokirchneriella subcapitata	*A12739A*	*96 h, s*	*E_rC_{50} > 100 mg product/L $_{nom}$* *E_bC_{50} = 72 mg product/L $_{nom}$*	*EFSA Conclusion 2016* *Volz, 2005* *ZA1296/2049*
Lemna gibba	*A12739A*	*7 d, ss*	*E_rC_{50} = 0.117 mg product/L $_{nom}$* *E_yC_{50} = 0.0269 mg product/L $_{nom}$*	*EFSA Conclusion 2016* *Zawadsky, 2013* *A12739A_10273*

s: static; ss: semi-static; f: flow-through; nom: based on nominal concentrations

9.5.1.1 Justification for new endpoints

According to the recommendations in 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), focus on growth rate endpoints for algae and aquatic plants are recommended for European risk assessment. The advantage of using the growth rate endpoints is that growth rate is less dependent on study duration and is relevant to 'recovery potential'.

Based on the recommendations from the EFSA Aquatic Guidance, Syngenta propose that the worst-case E_rC_{50} values for A12739A, mesotrione and its metabolites are used in the algal and aquatic plant risk assessments. This approach is widely accepted for algae. However, it is recognised that some regulatory authorities may have reservations about the use of E_rC_{50} values for macrophyte risk assessment when these are less conservative than $E_{b\ or\ y}C_{50}$ values, and therefore the $E_{b\ or\ y}C_{50}$ values will also be assessed.

Lemna endpoint for mesotrione

The laboratory study for Lemna was repeated due to issues in the original study submitted in which concentrations were not maintained within 20% of nominal throughout the exposure period, and endpoints were not reported in terms of growth rate. The new 7d study (Hengsberger & Wydra 2015) fulfils all the current acceptability criteria, and concentrations were maintained within 20% of nominal throughout the study. The biomass endpoints of the Hengsberger & Wydra study (2015, $E_bC_{50\ dry\ weight}$ = 0.0052 mg a.s./L) and the previous study of Smyth et al. (1997c, E_bC_{50} = 0.0077 mg a.s./L) are very similar, and the new endpoints will be used in the risk assessment, in preference, as they are considered more reliable.

Myriophyllum endpoint for mesotrione

In the EU review a data gap was identified for a dicot aquatic macrophyte, and therefore a new test has been carried out with Myriophyllum spicatum. The results for Lemna and Myriophyllum are remarkable similar as shown in the table above, indicating that there is no indication of selectivity to dicot or monocot aquatic macrophytes.

Use of geomean values for macrophyte risk assessment

In accordance with the Aquatic Guidance document ('Tier 2a'), the geometric mean of endpoints can be used when there are data from more than 1 species, and when these differ by less than a factor of 10. Since data are available from studies with Myriophyllum and Lemna, the geometric mean E_rC_{50} and E_yC_{50} can be used.

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).

For mesotrione and its metabolites, PEC_{SW} values were calculated for acidic soils (pH 5.1), neutral soils (pH 6.5) and alkaline soils (pH 7 to 9). In a risk envelope approach the maximum PEC_{SW} values arising from any of the three soil types were used in the risk assessment.

In the tables below, for A12739A, mesotrione and relevant metabolites, the regulatory acceptable concentrations (RACs) were derived by taking into account relevant endpoint values and the default safety factors in accordance with the EFSA Aquatic Guidance.

Table 9.5-3: Derivation of RAC values used in the Tier 1 risk assessment – mesotrione and relevant metabolites

Species	***Substance***	***Exposure system***	***Results (µg/L)***	***Assessment Safety factor***	***RAC (µg/L)***
Oncorhynchus mykiss	*Mesotrione*	*96h, s*	*LC_{50} >120 000*	*100*	*>1200*
Oncorhynchus mykiss	*MNBA*	*96h, s*	*LC_{50} >120 000*	*100*	*>1200*
Oncorhynchus mykiss	*AMBA*	*96h, s*	*LC_{50} = 150 000*	*100*	*1500*
Pimephales promelas	*Mesotrione*	*36d chronic, f*	*NOEC = 12500*	*10*	*1250*
Daphnia magna	*Mesotrione*	*48h, s*	*EC_{50} >622 000*	*100*	*>6220*

Species	***Substance***	***Exposure system***	***Results (µg/L)***	***Assessment Safety factor***	***RAC (µg/L)***
Daphnia magna	*MNBA*	*48h, s*	*EC_{50} = 130 000*	*100*	*1300*
Daphnia magna	*AMBA*	*48h, s*	*EC_{50} = 160 000*	*100*	*1600*
Daphnia magna	*Mesotrione*	*21d, ss*	*NOEC = 180 000*	*10*	*18000*
Pseudokirchneriella subcapitata	*Mesotrione*	*120h, s*	*E_rC_{50} = 13 000*	*10*	*1300*
Pseudokirchneriella subcapitata	*MNBA*	*72h, s*	*E_rC_{50} = 42 000*	*10*	*4200*
Pseudokirchneriella subcapitata	*AMBA*	*72h, s*	*E_rC_{50} = 14 000*	*10*	*1400*
Lemna gibba	*Mesotrione*	*7d, ss*	*ErC50 = 24.1 EbC50 = 4.^{5a}*	*10*	*2.41 0.45*
Myriophyllum spicatum	*Mesotrione*	*14d, ss*	*ErC50 = 28.7 EbC50 = 2.55[a]*	*10*	*2.87 0.255*
Macrophytes	*Mesotrione*	*Geometric mean*	*ErC50 = 26.3 EbC50 = 3.39[a]*	*10*	*2.63 0.339*
Lemna gibba	*MNBA*	*7d, ss*	*E_rC_{50} or E_yC_{50} >97 000[a]*	*10*	*>9700*
Lemna gibba	*AMBA*	*7d, ss*	*E_rC_{50} or E_yC_{50} >90 000[a]*	*10*	*>9000*
Lemna gibba	*SYN546974*	*7d, ss*	*E_rC_{50} >95 000 E_yC_{50} = 93 000[a]*	*10*	*>9500 9300*

d: days; h: hours; s: static; ss: semi-static; f: flow-through; RAC: Regulatory acceptable concentration
[a] Based on the recommendations from the EFSA Aquatic Guidance, Syngenta propose that the worst case E_rC_{50} values are used in the algal and aquatic plant risk assessments. This approach is widely accepted for algae. However, it is recognised that some regulatory authorities may have reservations about the use of E_rC_{50} values for macrophyte risk assessment when these are less conservative than $E_{b\ or\ y}C_{50}$ values, and therefore the $E_{b\ or\ y}C_{50}$ values will also be assessed

Table 9.5-4: Derivation of RAC values used in the Tier 1 risk assessment – A12739A

Species	***Substance***	***Exposure system***	***Results (µg/L)***	***Assessment Safety factor***	***RAC (µg/L)***
Cyprinus carpio	*A12739A*	*96h, s*	*LC_{50} = 71000*	*100*	*710*
Daphnia magna	*A12739A*	*48h, s*	*EC_{50} = 49000*	*100*	*490*
Pseudokirchneriella subcapitata	*A12739A*	*96h, s*	*E_rC_{50} > 100000*	*10*	*>10000*
Lemna gibba	*A12739A*	*7d, ss*	*E_rC_{50} = 117 E_yC_{50} = 26.9[a]*	*10*	*11.7 2.69*

s: static; ss: semi-static; RAC: Regulatory acceptable concentration
[a] Based on the recommendations from the EFSA Aquatic Guidance, Syngenta propose that the worst case E_rC_{50} values are used in the algal and aquatic plant risk assessments. This approach is widely accepted for algae. However, it is recognised that some regulatory authorities may have reservations about the use of E_rC_{50} values for macrophyte risk assessment when these are less conservative than $E_{b\ or\ y}C_{50}$ values, and therefore the $E_{b\ or\ y}C_{50}$ values will also be assessed.

In the following tables, the ratios between predicted environmental concentrations in surface water bodies (PECSW, PECSED) and regulatory acceptable concentrations (RAC) for aquatic organisms are given per intended use for each FOCUS scenario and each organism group.

Mesotrione

Table 9.5-5: Aquatic organisms: acceptability of risk (PEC/RAC <1) for mesotrione for each organism group based on maximum FOCUS PEC_{SW} calculations for the use of A12739A in maize (1 x 100 g a.s./ha, post-emergence)

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte (lowest E_rC_{50})***	***Aquatic macrophyte (lowest E_yC_{50})***
RAC (µg/L)		*>1200*	*1250*	*>6220*	*18000*	*1300*	*2.41* ~~2.8~~	*0.255* ~~0.301~~
FOCUS Scenario	***PEC_{gl-max} (µg/L)***							
Step 1								
	33.5	*<0.028*	*0.027*	*<0.0054*	*0.0019*	*0.026*	***13.9*** ~~12~~	***131*** ~~110~~
Step 2								
N-Europe	*4.38*	*	*	*	*	*	***1.8*** ~~1.6~~	***17*** ~~15~~
S-Europe	*8.22*	*	*	*	*	*	***3.4*** ~~2.9~~	***32*** ~~27~~
Step 3								
D3/Ditch	*0.525*	*	*	*	*	*	*0.22* ~~0.19~~	***2.1*** ~~1.7~~
D4/Pond	*0.056*	*	*	*	*	*	*0.023* ~~0.020~~	*0.22* ~~0.19~~
D4/Stream	*0.451*	*	*	*	*	*	*0.19* ~~0.16~~	***1.8*** ~~1.5~~
D5/Pond	*0.031*	*	*	*	*	*	*0.013* ~~0.010~~	*0.12* ~~0.10~~
D5/Stream	*0.459*	*	*	*	*	*	*0.19* ~~0.16~~	***1.8*** ~~1.5~~
D6/Ditch	*0.527*	*	*	*	*	*	*0.22* ~~0.19~~	***2.1*** ~~1.8~~
R1/Pond	*0.076*	*	*	*	*	*	*0.032* ~~0.03~~	*0.30* ~~0.25~~
R1/Stream	*1.60*	*	*	*	*	*	*0.66* ~~0.57~~	***6.3*** ~~5.3~~
R2/Stream	*2.16*	*	*	*	*	*	*0.90* ~~0.77~~	***8.5*** ~~7.2~~
R3/Stream	*3.94*	*	*	*	*	*	***1.6*** ~~1.4~~	***15*** ~~13~~
R4/Stream	*4.16*	*	*	*	*	*	***1.7*** ~~1.5~~	***16*** ~~14~~

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** No further assessment is required as an acceptable risk has been demonstrated in a more conservative FOCUS scenario*

For macrophytes, calculated PEC/RAC ratios did not indicate an acceptable risk to aquatic macrophytes in FOCUS Steps 1 and 2, and in the R3/Stream and R4/Stream scenarios in Step 3 considering the E_rC_{50}, or all ditch and stream scenarios considering the E_yC_{50}. Therefore, further refinement is required. The risk to macrophytes will be refined by considering mitigation at Step 4.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Table 9.5-6: Aquatic organisms: acceptability of risk (PEC/RAC <1) for mesotrione for each organism group based on maximum FOCUS PEC_{SW} calculations for the use of A12739A in maize (1 x 150 g a.s./ha, post-emergence)

Group		***Fish acute***	***Fish prolonged***	***Inverteb. acute***	***Inverteb. prolonged***	***Algae***	***Aquatic macrophyte (lowest E_rC_{50})***	***Aquatic macrophyte (lowest E_yC_{50})***
RAC (µg/L)		*>1200*	*1250*	*>6220*	*18000*	*1300*	2.41 ~~2.8~~	0.255 ~~0.301~~
FOCUS Scenario	***PEC_{gl-max} (µg/L)***							
Step 1								
	50.2	*<0.042*	*0.040*	*<0.0081*	*0.0028*	*0.039*	**21** ~~18~~	**197** ~~170~~
Step 2								
N-Euope	*6.56*	*	*	*	*	*	**2.7** ~~2.3~~	**26** ~~22~~
S-Europe	*12.3*	*	*	*	*	*	**5.1** ~~4.4~~	**48** ~~41~~
Step 3								
D3/Ditch	*0.787*	*	*	*	*	*	0.33 ~~0.28~~	**3.1** ~~2.6~~
D4/Pond	*0.084*	*	*	*	*	*	0.035 ~~0.030~~	0.33 ~~0.28~~
D4/Stream	*0.677*	*	*	*	*	*	0.28 ~~0.24~~	**2.7** ~~2.3~~
D5/Pond	*0.047*	*	*	*	*	*	0.02 ~~0.02~~	0.18 ~~0.16~~
D5/Stream	*0.689*	*	*	*	*	*	0.29 ~~0.25~~	**2.7** ~~2.3~~
D6/Ditch	*0.791*	*	*	*	*	*	0.33 ~~0.28~~	**3.1** ~~2.6~~
R1/Pond	*0.113*	*	*	*	*	*	0.05 ~~0.040~~	0.44 ~~0.38~~
R1/Stream	*2.40*	*	*	*	*	*	0.996 ~~0.86~~	**9.4** ~~8.0~~
R2/Stream	*3.28*	*	*	*	*	*	**1.4** ~~1.2~~	**13** ~~11~~
R3/Stream	*5.93*	*	*	*	*	*	**2.5** ~~2.1~~	**23** ~~20~~
R4/Stream	*6.26*	*	*	*	*	*	**2.6** ~~2.2~~	**25** ~~21~~

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
** No further assessment is required as an acceptable risk has been demonstrated in a more conservative FOCUS scenario*

For macrophytes, calculated PEC/RAC ratios did not indicate an acceptable risk to aquatic macrophytes in FOCUS Steps 1 and 2, and in the R2/Stream, R3/Stream and R4/Stream scenarios in Step 3 considering the E_rC_{50}, or all ditch and stream scenarios considering the E_yC_{50}. Therefore, further refinement is required. The risk to macrophytes will be refined by considering mitigation at Step 4.

Refinement of risk for macrophytes considering FOCUS Step 4

Table 9.5-7: Aquatic macrophytes: refined higher-tier risk assessment for acceptability of risk (PEC/RAC < 1) for mesotrione based on mitigation at FOCUS Step 4 following application of mesotrione to maize at 1 x 100 g a.s./ha, post-emergence

Group						***Aquatic macrophyte E_rC_{50}***	***Aquatic macrophyte E_yC_{50}***
RAC (µg/L)						*Tier 1 RAC based on E_rC_{50} = 2.41*	*Tier 1 RAC based on E_yC_{50} = 0.255*
Application regime	***FOCUS Scenario***	***Vegetative filter strip (m)*** [a]	***No spray buffer (m)***	***Nozzle reduction (%)***	***PEC (µg/L)***	***PEC/RAC***	***PEC/RAC***
1 x 100 g a.s./ha, post-emergence	***Step 4***						
	D3/ditch (neutral scenario)	*-*	*-*	*50*	*0.263*	***	***1.03***
		-	*5*	*-*	*0.172*	***	*0.68*
		10 (L&M)	*10*	*-*	*0.091*	***	*0.36*
	D4/stream (acidic scenario)	*-*	*-*	*50*	*0.227*	***	*0.89*
		-	*5*	*-*	*0.191*	***	*0.75*
		10 (L&M)	*10*	*-*	*0.102*	***	*0.40*
	D5/stream (acidic scenario)	*-*	*-*	*50*	*0.235*	***	*0.92*
		-	*5*	*-*	*0.199*	***	*0.78*
		10 (L&M)	*10*	*-*	*0.111*	***	*0.44*
	D6/ditch (acidic scenario)	*-*	*-*	*50*	*0.265*	***	***1.04***
		-	*5*	*-*	*0.175*	***	*0.69*
		10 (L&M)	*10*	*-*	*0.094*	***	*0.37*
	R1/stream (acidic scenario)	*-*	*-*	*50*	*1.60*	***	***6.3***
		-	*5*	*-*	*1.60*	***	***6.3***
		10 (L&M)	*10*	*-*	*0.724*	***	***2.8***
		20 (L&M)	*20*	*-*	*0.379*	***	***1.5***
	R2/stream (neutral scenario)	*-*	*-*	*50*	*2.16*	***	***8.5***
		-	*5*	*-*	*2.16*	***	***8.5***
		10 (L&M)	*10*	*-*	*0.952*	***	***3.7***
		20 (L&M)	*20*	*-*	*0.493*	***	***1.9***
	R3/stream (neutral scenario)	*-*	*-*	*50*	*3.94*	***1.6***	***15.5***
		-	*5*	*-*	*3.94*	***1.6***	***15.5***
		10 (L&M)	*10*	*-*	*1.78*	*0.74*	***7.0***
		20 (L&M)	*20*	*-*	*0.931*	*0.39*	***3.7***
	R4/stream (neutral scenario)	*-*	*-*	*50*	*4.16*	***1.7***	***16.3***
		-	*5*	*-*	*4.16*	***1.7***	***16.3***
		10 (L&M)	*10*	*-*	*1.89*	*0.78*	***7.4***

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Group						***Aquatic macrophyte E_rC_{50}***	***Aquatic macrophyte E_yC_{50}***
RAC (µg/L)						*Tier 1 RAC based on E_rC_{50} = 2.41*	*Tier 1 RAC based on E_yC_{50} = 0.255*
Application regime	***FOCUS Scenario***	***Vegetative filter strip (m)*** [a]	***No spray buffer (m)***	***Nozzle reduction (%)***	***PEC (µg/L)***	***PEC/RAC***	***PEC/RAC***
		20 (L&M)	*20*	*-*	*0.992*	*0.41*	***3.9***

[a] L&M = mitigation according to FOCUS Landscape and Mitigation V1 (2007); reduction for 10 / 20 m buffer is 60 / 80 % in runoff flux and volume and 85 / 95 % in sediment flux and mass
PEC/RAC ratios above the relevant trigger of 1 are shown in ***bold***
** No further assessment is required as an acceptable risk has been demonstrated in a more conservative FOCUS scenario*

The comparison of the refined PEC and RAC values indicates acceptable risk to aquatic macrophytes following 1 application of 100 g mesotrione/ha to maize post-emergence as follows:

- *D scenarios, considering the E_yC_{50}: when a 5 m buffer is considered*
- *R scenarios:*
  - *Considering the E_rC_{50}:*
    - *R3 and R4: when a 10 m vegetated buffer zone according to FOCUS Landscape and Mitigation V1 (2007) buffer is considered*
  - *Considering the E_yC_{50}:*
    - *R1, R2, R3, R4: require further consideration.*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Table 9.5-8: Aquatic macrophytes: refined higher-tier risk assessment for acceptability of risk (PEC/RAC < 1) for mesotrione based on mitigation at FOCUS Step 4 following application of mesotrione to maize at 1 x 150 g a.s./ha, post-emergence

Group						**Aquatic macrophyte E_rC_{50}**	**Aquatic macrophyte E_yC_{50}**
RAC (µg/L)						Tier 1 RAC based on E_rC_{50} = 2.41 ~~2.8~~	Tier 1 RAC based on E_yC_{50} = 0.255 ~~0.301~~
Application regime	**FOCUS Scenario**	**Vegetative filter strip (m)** [a]	**No spray buffer (m)**	**Nozzle reduction (%)**	**PEC (µg/L)**	**PEC/RAC**	**PEC/RAC**
1 x 150 g a.s./ha, post-emergence	**Step 4**						
	D3/ditch (all soil scenarios)	-	-	50	0.394	*	**1.5** ~~1.3~~
		-	5	-	0.258	*	**1.01** ~~0.86~~
		10 (L&M)	10	-	0.137	*	0.54 ~~0.46~~
	D4/stream (acidic scenario)	-	-	50	0.340	*	**1.3** ~~1.1~~
		-	5	-	0.287	*	**1.1** ~~0.95~~
		10 (L&M)	10	-	0.154	*	0.60 ~~0.51~~
	D5/stream (acidic scenario)	-	-	50	0.353	*	**1.4** ~~1.2~~
		-	5	-	0.300	*	**1.2** ~~1.0~~
		10 (L&M)	10	-	0.167	*	0.66 ~~0.55~~
	D6/ditch (acidic scenario)	-	-	50	0.398	*	**1.6** ~~1.3~~
		-	5	-	0.262	*	**1.03** ~~0.87~~
		10 (L&M)	10	-	0.141	*	0.55 ~~0.47~~
	R1/stream (acidic scenario)	-	-	50	2.40	*	**9.4** ~~8.0~~
		-	5	-	2.40	*	**9.4** ~~8.0~~
		10 (L&M)	10	-	1.09	*	**4.3** ~~3.6~~
		20 (L&M)	20	-	0.567	*	**2.2** ~~1.9~~
	R2/stream (neutral scenario)	-	-	50	3.28	**1.4** ~~1.2~~	**12.9** ~~11~~
		-	5	-	3.28	**1.4** ~~1.2~~	**12.9** ~~11~~
		10 (L&M)	10	-	1.45	0.60 ~~0.52~~	**5.7** ~~4.8~~
		20 (L&M)	20	-	0.749	0.31 ~~0.27~~	**2.9** ~~2.5~~
	R3/stream (neutral scenario)	-	-	50	5.93	**2.5** ~~2.1~~	**23.3** ~~20~~
		-	5	-	5.93	**2.5** ~~2.1~~	**23.3** ~~20~~
		10 (L&M)	10	-	2.68	**1.11** ~~0.96~~	**10.5** ~~8.9~~
		20 (L&M)	20	-	1.40	0.58 ~~0.50~~	**5.5** ~~4.7~~
	R4/stream (neutral scenario)	-	-	50	6.26	**2.6** ~~2.2~~	**24.5** ~~21~~
		-	5	-	6.26	**2.6** ~~2.2~~	**24.5** ~~21~~
		10 (L&M)	10	-	2.85	**1.2** ~~1.0~~	**11.2** ~~9.5~~
		20 (L&M)	20	-	1.49	0.62 ~~0.53~~	**5.8** ~~5.0~~

[a] L&M = mitigation according to FOCUS Landscape and Mitigation V1 (2007); reduction for 10 / 20 m buffer is 60 / 80 % in runoff flux and volume and 85 / 95 % in sediment flux and mass
PEC/RAC ratios above the relevant trigger of 1 are shown in **bold**
* No further assessment is required as an acceptable risk has been demonstrated in a more conservative FOCUS scenario

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

The comparison of the refined PEC and RAC values indicates acceptable risk to aquatic macrophytes following 1 application of 150 g mesotrione/ha to maize post-emergence as follows:

- *D scenarios, considering the E_yC_{50}: when a 10 ~~5~~ m buffer is considered for D3, D4, D5, D6.*
- *R scenarios:*
  - *Considering the E_rC_{50}:*
    - *R2: when a 10 m vegetated buffer zone according to FOCUS Landscape and Mitigation V1 (2007) buffer is considered*
    - *R3, R4: when a 10 m vegetated buffer zone according to FOCUS Landscape and Mitigation V1 (2007) buffer is considered*
  - *Considering the E_yC_{50}:*
    - *R1, R2 and R4: require further consideration.*

Mesotrione metabolite MNBA

Table 9.5-9: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for the mesotrione metabolite MNBA for each organism group based on maximum FOCUS PEC_{SW} calculations for the maximum use of A12739A in maize (1.5 L A12739A/ha)

Group		***Fish acute***	***Inverteb. acute***	***Algae***	***Aquatic macrophyte (based on E_rC_{50} or E_yC_{50})***
RAC (µg/L)		*>1200*	*1300*	*4200*	*>9700*
FOCUS Scenario	***PEC $_{gl-max}$ (µg/L)***				
Step 1					
	23.3	*<0.019*	*0.018*	*0.0055*	*<0.0024*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Mesotrione metabolite AMBA

Table 9.5-10: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for the mesotrione metabolite AMBA for each organism group based on maximum FOCUS PEC_{SW} calculations for the maximum use of A12739A in maize (1.5 L A12739A/ha)

Group		***Fish acute***	***Inverteb. acute***	***Algae***	***Aquatic macrophyte (based on E_rC_{50} or E_yC_{50})***
RAC (µg/L)		*1500*	*1600*	*1400*	*>9000*
FOCUS Scenario	***PEC $_{gl-max}$ (µg/L)***				
Step 1					
	10.8	*0.0072*	*0.0068*	*0.0077*	*<0.0012*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

Mesotrione metabolite SYN546974

Table 9.5-11: Aquatic organisms: acceptability of risk (PEC/RAC < 1) for the mesotrione metabolite SYN546974 for each organism group based on maximum FOCUS PEC$_{SW}$ calculations for the maximum use of A12739A in maize (1.5 L A12739A/ha)

Group		***Aquatic macrophyte (based on E_rC_{50})***	***Aquatic macrophyte (based on E_yC_{50})***
RAC (µg/L)		*>9500*	*9300*
FOCUS Scenario	***PEC $_{gl-max}$ (µg/L)***		
Step 1			
	1.60	*<0.00017*	*0.00017*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold

A12739A

Table 9.5-12: Aquatic organisms: initial and higher-tier risk assessment for acceptability of risk (PEC/RAC <1) for A12739A considering exposure mitigation measures for the different proposed uses in maize

Group				***Fish acute***	***Inverteb. acute***	***Algae***	***Aquatic macrophyte (based on E_rC_{50})***	***Aquatic macrophyte (based on E_yC_{50})***
RAC (µg/L)				*710*	*490*	*>10000*	*11.7*	*2.69*
Application rate	***Spray drift buffer (m)***	***Drift-reducing nozzles (%)***	***PEC (µg/L)***	*PEC/RAC*	*PEC/RAC*	*PEC/RAC*	*PEC/RAC*	*PEC/RAC*
1 x 1.0 L A12739A/ha (1 x 1.090 kg A12739A/ha [a])	*1*	*-*	*10.1*	*0.014*	*0.021*	*<0.0010*	*0.86*	***3.8***
	1	*50*	*5.03*	*-*	*-*	*-*	*-*	***1.9***
	1	*75*	*2.52*	*-*	*-*	*-*	*-*	*0.94*
	5	*-*	*2.07*	*-*	*-*	*-*	*-*	*0.77*
1 x 1.5 L A12739A/ha (1 x 1.635 kg A12739A/ha [a])	*1*	*-*	*15.1*	*0.021*	*0.031*	*<0.0015*	***1.3***	***5.6***
	1	*50*	*7.55*	*-*	*-*	*-*	*0.65*	***2.8***
	1	*75*	*3.77*	*-*	*-*	*-*	*-*	***1.4***
	1	*90*	*1.51*	*-*	*-*	*-*	*-*	*0.56*
	5	*-*	*3.11*	*-*	*-*	*-*	*0.27*	***1.2***
	5	*50*	*1.55*	*-*	*-*	*-*	*-*	*0.58*
	10	*-*	*1.58*	*-*	*-*	*-*	*-*	*0.59*

PEC: Predicted environmental concentration; RAC: Regulatory acceptable concentration; PEC/RAC ratios above the relevant trigger of 1 are shown in bold
[a] Assuming a formulation density of 1.09 g cm^{-3}

The comparison of the refined PEC and RAC values indicate acceptable risk to aquatic organisms following 1 application of 1.0 L A12739A/ha to maize without *mitigations when considering the E_rC_{50} RAC. When considering the E_yC_{50} RAC, an acceptable risk is indicated with the following mitigation options: either 75% drift reducing nozzles; or a 5 m buffer.*

The comparison of the refined PEC and RAC values indicate acceptable risk to aquatic organisms following 1 application of 1.5 L A12739A/ha to maize considering a 5 m buffer or 50% drift reducing nozzles when considering the E_rC_{50} RAC. When considering the E_yC_{50} RAC, an acceptable risk is indicated with the following mitigation options: 90% drift reducing nozzles; or a 5 m buffer + 50% drift-reducing nozzles; or a 10 m buffer.

9.5.3 Overall conclusions

The PEC/RAC ratios for A12739A, mesotrione and its metabolites are less than the trigger value of 1, indicating that the risk to aquatic organisms is acceptable following use of A12739A according to the proposed use pattern when considering the following mitigation measures as presented in the tables below. Since Syngenta proposes that the E_rC_{50} values should be used for macrophyte risk assessment in accordance with the Aquatic Guidance Document, these endpoints have been used to summarise the mitigation below. Mitigations addressing the use of the $E_{b\ or\ y}C_{50}$ are available in the main text.

Table 9.5-13: Overall proposed mitigation measures for A12739A applied at 1 x 1.0 L/ha in maize (100 g mesotrione/ha)

Test substance	Appl. rate (g/ha)	Organism	A or C	FOCUS scenario									
				D1	D2	D3	D4	D5	D6	R1	R2	R3	R4
A12739A	1090	Fish	A			- [a]							
Mesotrione	100	Fish	A			-	-	-	-	-	-	-	-
Mesotrione	100	Fish	C			-	-	-	-	-	-	-	-
A12739A	1090	Aq inverts	A			- [a]							
Mesotrione	100	Aq inverts	A			-	-	-	-	-	-	-	-
Mesotrione	100	Aq inverts	C			-	-	-	-	-	-	-	-
A12739A	1090	Algae	C			- [a]							
Mesotrione	100	Algae	C			-	-	-	-	-	-	-	-
A12739A	1090	Macrophytes	C			- [a]							
Mesotrione	100	Macrophytes	C			-	-	-	-	-	-	E_rC_{50}: 10 m VFS (L&M)	E_rC_{50}: 10 m VFS (L&M)

A = acute, C = chronic
An empty/grey field means that the scenario is not relevant to the crop group
"-"mitigation measures are not required for this scenario
VFS (L&M) = vegetative filter strip according with FOCUS Landscape and Mitigation V1 (2007)
[a] spray drift entry; drift value according to Rautmann at al. (2001)

Table 9.5-14: Overall proposed mitigation measures for A12739A applied at 1 x 1.5 L/ha in maize (150 g mesotrione/ha)

Test substance	Appl. rate (g/ha)	Organism	A or C	FOCUS scenario									
				D1	D2	D3	D4	D5	D6	R1	R2	R3	R4
A12739A	1635	Fish	A			- [a]							
Mesotrione	150	Fish	A			-	-	-	-	-	-	-	-
Mesotrione	150	Fish	C			-	-	-	-	-	-	-	-
A12739A	1635	Aq inverts	A			- [a]							
Mesotrione	150	Aq inverts	A			-	-	-	-	-	-	-	-
Mesotrione	150	Aq inverts	C			-	-	-	-	-	-	-	-
A12739A	1635	Algae	C			- [a]							
Mesotrione	150	Algae	C			-	-	-	-	-	-	-	-
A12739A	1635	Macrophytes	C			50% DR; or 5 m SD [a]							
Mesotrione	150	Macrophytes	C			-	-	-	-	-	E_rC_{50}: 10 m VFS (L&M)	E_rC_{50}: 20 m VFS (L&M)	E_rC_{50}: 20 m VFS (L&M)

A = acute, C = chronic
An empty/grey field means that the scenario is not relevant to the crop group
"-"mitigation measures are not required for this scenario
SD = spray drift buffer; VFS (L&M) = vegetative filter strip according with FOCUS Landscape and Mitigation V1 (2007)
DR = drift reducing nozzles
[a] spray drift entry; drift value according to Rautmann at al. (2001)

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

zRMS comments:

Aquatic organisms
No data is provided in support of the application for authorization of **Mecorn 100 SC**.
The risk assessment for aquatic organisms performed for Callisto 100 SC are suitable for the use of Mecorn 100 SC proposed in GAP.

On the basis of performed calculations for Callisto 100 SC, acceptable risk to aquatic organisms may be concluded from proposed uses of Mecorn 100 SC.

The PECsw/sed performed for Callisto 100 SC are suitable for the use of Mecorn 100 SC proposed in GAP.

The input parameters considered by the Applicant for surface water modelling were agreed by the zRMS.

In order to mitigate the risk, Step 4 simulations were performed with assumption of 5, 10 and 20 m spray drift buffer and 10 m and 20 m vegetative filter strips (for run-off scenarios) or 50% nozzle reduction. The run-off reduction was assumed in line with FOCUS Landscape and Mitigation recommendations (FOCUS, 2007).

Based on the risk assessment for **Callisto 100 SC**, a safe use for intended uses for **Mecorn 100 SC** could be identified, provided that appropriate risk mitigation measures are taken into account. The risk mitigation measures should be considered at MSs level. No additional risk assessment is required.

PL
Acceptable risk with no need for mitigation measures was demonstrated in scenarios representative for Poland (D3, D4 and R1) for application rate of 1.0 L/ha (corresponding to 100 g a.s./ha).

9.6 Effects on bees (KCP 10.3.1)

Information concerning effects on bees relevant for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, this point origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

9.6.1 Toxicity data

Studies on the toxicity to bees have been carried out with mesotrione. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on bees of A12739A were evaluated as part of the EU assessment of mesotrione.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.6-1: Endpoints and effect values relevant for the risk assessment for bees - mesotrione

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Apis mellifera	*Mesotrione*	*48h Oral*	*LD_{50} >11 µg a.s./bee*	*EFSA Conclusion 2016 Jackson and Gough, 1995 ZA1296/0540*
Apis mellifera	*Mesotrione*	*48h Contact*	*LD_{50} >100 µg a.s./bee*	*EFSA Conclusion 2016 Jackson and Gough, 1995 ZA1296/0540*
Apis mellifera	*Mesotrione (formulated as A12739A)*	*Semi-chronic larval toxicity (7 day study)*	*LD_{50} = 118.5 µg a.s./larva NOED = 57.8 µg a.s./larva*	*EFSA Conclusion 2016 Kleebaum, 2013 A12739A_10464 [a]*
Apis mellifera	*Mesotrione (formulated as A12739A)*	*Chronic adult toxicity (10 days)*	*LD_{50} = 19.2 µg a.s./bee/day NOED = 8.1 µg a.s./bee/day*	*EFSA Conclusion 2016 Kleebaum, 2013a A12739A_10465 [a]*
Higher-tier studies (tunnel test, field studies)				
Not relevant				

[a] These studies have been submitted to fulfil the data requirements under Commission Regulation (EU) No 283/2013; but they are not used in this risk assessment as they are not considered under the currently notified risk assessment guidance.

Table 9.6-2: Endpoints and effect values relevant for the risk assessment for bees – A12739A

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Apis mellifera	*A12739A*	*48h Oral*	*LD_{50} = 877.4 µg/bee*	*EFSA Conclusion 2016 Franke 2013 A12739A_10015*
Apis mellifera	*A12739A*	*96h Contact*	*LD_{50} = 578.2 µg/bee*	*EFSA Conclusion 2016 Franke 2013 A12739A_10015*

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Higher-tier studies (tunnel test, field studies)				

9.6.1.1 Justification for new endpoints

Additional toxicity studies performed with mesotrione were not necessary as sufficient data package including studies on chronic toxicity of Callisto to adult bees and larvae, is available from the EU review.

9.6.2 Risk assessment

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the worst-case application rate of 1.5 L A12739A/ha (corresponding to 150 g mesotrione/ha) is used in the risk assessment.

Table 9.6-3: Crop groupings and critical use patterns relevant to the use of A12739A

Test substance	***GAP crop species***	***Application category***	***Critical use pattern***		
			Rate (g a.s./ha)	***No. of apps***	***App. Interval (days***
A12739A	*Maize BBCH 12-18*	*Downward spray*	*150*	*1*	*N/A*

9.6.2.1 Hazard quotients for bees

The risk assessment performed by the Applicant in line with EFSA (2013) was not validated by the zRMS, as according to conclusions of the Central Zone Steering Committee, recommendations of EFSA (2013) should not be considered for the zonal evaluations until the guidance is noted at the EU level. Taking this into account, the risk assessment in the Core Assessment should be performed in line with recommendations of the current guidance, i.e. SANCO/10329/2002 rev 2 final. Respective calculations are thus presented in table below.

Intended use	*Maize, 1 × 1.5 L product/ha*		
Active substance	*mesotrione*		
Application rate (g a.s./ha)	*1 × 150*		
Test design	***LD_{50} (lab.) (µg a.s/bee)***	***Single application rate (g a.s./ha)***	***Q_{HO}, Q_{HC} criterion: $Q_H \leq 50$***
Oral toxicity	*>11*	*150*	*<13.6*
Contact toxicity	*>100*		*<1.5*
Product	*Callisto*		
Application rate (g product/ha)	*1 × 1642.5 (based on relative density of 1.095 g/mL)*		
Test design	***LD_{50} (lab.) (µg product/bee)***	***Single application rate (g product/ha)***	***Q_{HO}, Q_{HC} criterion: $Q_H \leq 50$***
Oral toxicity	*877.4*	*1642.5*	*1.9*
Contact toxicity	*578.2*		*2.8*

All calculated HQ values are below the trigger of 50 indicating acceptable risk to bees from intended uses of Callisto.

Risk from metabolites

*In accordance with the **EFSA Guidance Document on the risk assessment of plant protection products on bees (EFSA, 2013)** as the identified metabolites of mesotrione are formed in amounts of <10% then the risk assessment is considered covered by the parent and so further assessment is not required.*

9.6.2.2 Higher-tier risk assessment for bees (tunnel test, field studies)

Not relevant.

9.6.3 Effects on bumble bees

Regarding Polish guidelines for registrations in art. 33 based on art. 34 Regulation 1107/2009 studies on bumblebees are not required.
No data or information is currently available for bumble bees.

9.6.4 Effects on solitary bees

No data or information is currently available for solitary bees.
For solitary bees there are currently no validated accepted test guidelines or guidance documents available. Ring tests are ongoing for the Osmia acute (contact and oral) study and semi field test design. Studies on solitary bees are not required under Regulation (EC) No 1107/2009, therefore currently there is no data requirement for these study types.

9.6.5 Overall conclusions

The acute risk of Callisto to honeybees was re-assessed by the zRMS from hazard quotients following SANCO/10329/2002 rev 2 final, estimated from acute oral and contact studies with Callisto, mesotrione and the maximum single application rate of 150 g mesotrione/ha.

All the calculated hazard quotients are less than the relevant trigger of 50, indicating that the acute oral and contact risk to bees is acceptable following use of Callisto according to the proposed use pattern.

zRMS comments:

The risk assessment for bees evaluated in **Callisto 100 SC** cover use of **Mecorn 100 SC.**

The acute toxicity data for mesotrione and Callisto (A12739A) are in line with EU agreed endpoints reported in EFSA Journal 2016;14(3):4419. The chronic toxicity of Callisto to adult bees as well as toxicity of the formulation to larvae are also in agreement with EU agreed values. All the calculated hazard quotients are less than the relevant trigger of 50, indicating that the acute oral and contact risk to bees is acceptable following use of Callisto according to the proposed use pattern.

In addition to that, the Applicant submitted studies on chronic toxicity of mesotrione to adult bees and larvae (Wendling, 2018 and Eckert, 2016). It is, however, noted that data regarding chronic toxicity to adult bees and larvae obtained in studies performed with the representative formulation (Callisto) were deemed sufficient at the EU level and no data gap in this area was identified in EFSA Journal 2016;14(3):4419. Taking this into account it may be concluded that data requirements as set by the Commission Regulation (EU) No 284/2013 are fulfilled and no additional studies are deemed necessary. Additional studies performed with the active substance were thus not evaluated by the zRMS as sufficient data package is already available from the EU review. Concerned Member States that require risk assessment performed in line with EFSA bee guidance (2013) may utilize the EU toxicity data available for the formulated product.

The risk assessment based on this studies should be considered when GD for Bees, 2013 is implemented at EU level. Final decision should be taken into account at MSs level.

9.7 Effects on arthropods other than bees (KCP 10.3.2)

Information concerning effects on arthropods other than bees relevant for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, this point origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

9.7.1 Toxicity data

Studies on the toxicity to non-target arthropods have been carried out with the representative solo formulation of mesotrione. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on non-target arthropods of A12739A were evaluated as part of the EU assessment of mesotrione.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.7-1: Endpoints and effect values relevant for the risk assessment for non-target arthropods - mesotrione

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Typhlodromus pyri (protonymphs)	*A12739A*	*Laboratory test glass plates (2D)*	*LR_{50} = 93.11 g a.s./ha* *ER_{50} >81 g a.s./ha*	*EFSA Conclusion 2016* *Fallowfield, 2012* *A12739A_10010*
Aphidius rhopalosiphi (adults)	*A12739A*	*Laboratory test glass plates (2D)*	*LR_{50} = 43.56 g a.s./ha* *ER_{50} >25.6 g a.s./ha*	*EFSA Conclusion 2016* *Stevens, 2012* *A12739A_10008*
Typhlodromus pyri (protonymphs)	*A12739A*	*Extended laboratory test maize leaves (2D)*	*LR_{50} >300 g a.s./ha* *ER_{50} >150 g a.s./ha*	*EFSA Conclusion 2016* *Fallowfield, 2013* *A12739A_10020*
Aphidius rhopalosiphi (adults)	*A12739A*	*Extended laboratory test barley leaves (3D)*	*LR_{50} >225 g a.s./ha* *ER_{50} >225 g a.s./ha*	*EFSA Conclusion 2016* *Stevens, 2013* *A12739A_10276*
Aleochara bilineata (adults)	*A12739A*	*Extended laboratory test sand (2D)*	*ER_{50} >200 g a.s./ha*	*EFSA Conclusion 2016* *Tew, 2013* *A12739A_10275*
Pardosa sp. (adults)	*A12739A*	*Extended laboratory test soil (2D)*	*LR_{50} >150 g a.s./ha* *ER_{50} >150 g a.s./ha*	*EFSA Conclusion 2016* *Vaughan, 2013* *A12739A_10388*

9.7.1.1 Justification for new endpoints

Not relevant.

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

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the worst-case application rate of 1.5 L A12739A/ha (corresponding to 150 g mesotrione/ha) is used in the risk assessment.

The $PER_{in\text{-}field}$ values according to ESCORT 2 were calculated as:

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

Table 9.7-2: First- and higher-tier assessment of the in-field risk for non-target arthropods due to the maximum use of A12739A in maize (BBCH 12-18)

Intended use	*Maize*		
Active substance	*Mesotrione*		
Application rate (g/ha)	*1 × 150*		
MAF	*1 (foliar) / 1 (soil)*		
Test species Tier I	***LR_{50} (lab.) (g/ha)***	***$PER_{in\text{-}field}$ (g/ha)***	***$HQ_{in\text{-}field}$ criterion: HQ ≤ 2***
Aphidius rhopalosiphi	*43.56*	*150 (foliar)* *150 (soil)*	***3.4** (foliar)* ***3.4** (soil)*
Typhlodromus pyri	*93.11*	*150 (foliar)* *150 (soil)*	*1.6 (foliar)* *1.6 (soil)*
Test species Higher-tier	***ER_{50} (g/ha)***	***$PER_{in\text{-}field}$ (g/ha)***	***$PER_{in\text{-}field}$ below ER_{50}?***
Aphidius rhopalosiphi	*>225*	*150 (foliar)* *150 (soil)*	*Yes*
Typhlodromus pyri	*>150*	*150 (foliar)* *150 (soil)*	*Yes*
Aleochara bilineata	*>200*	*150 (foliar)* *150 (soil)*	*Yes*
Pardosa sp.	*>150*	*150 (foliar)* *150 (soil)*	*Yes*

MAF: Multiple application factor; PER: Predicted environmental rate; HQ: Hazard quotient; Criteria values shown in bold breach the relevant trigger.

The HQ values of the Tier I risk assessment for T. pyri are below the trigger of 2, indicating that the risk to in-field non-target arthropods is acceptable following the use of A12739A according to the proposed use pattern. However, the HQ values for A. rhopalosiphi are greater than the trigger of 2 for Tier I tests indicating a potential risk to sensitive non-target arthropods within the field, which needs to be assessed further.

The Tier II, extended laboratory study for A. rhopalosiphi showed acceptable in-field risk to non-target arthropods following the use of A12739A according to the proposed use pattern. A test with an additional species is triggered by the Tier I risk assessment for Aphidius, and therefore a test has been carried out on the relevant ground-dwelling beetle Aleochara bilineata since application is early post-emergence. In addition tests with T. pyri and Pardosa have been carried out. The toxicity endpoints for T. pyri, A. bilineata and Pardosa are greater than the soil and foliar PER values, indicating that the risk to in-field non-target arthropods is acceptable following use of A12739A according to the proposed use pattern.

9.7.2.2 Risk assessment for off-field exposure

The $PER_{off\text{-}field}$ value according to ESCORT 2 was calculated as:

$PER_{off\text{-}field}$ = Application rate × MAF × (drift factor ÷ VDF (vegetation distribution factor)).

Note - The model used to estimate spray drift was developed for drift onto a two-dimensional water surface and, as such, does not account for interception and dilution by three-dimensional vegetation in off-crop areas. Therefore, a vegetation distribution factor (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 VDF of 10 is recommended by ESCORT 2. For 3-dimensional studies, i.e. where spray treatment is applied onto whole plants, the VDF of 10 is not used, as any dilution over the 3-dimensional vegetation surface is accounted for in the study design.

The corrected $PER_{off\text{-}field}$ value according to ESCORT 2 was calculated as:

corr. $PER_{off\text{-}field}$ = $PER_{off\text{-}field}$ × correction factor

Note - ESCORT 2 recommends that a correction factor is applied to study data to account for extrapolation from testing just two representative species, to the species diversity expected in off-crop areas. A correction factor of 10 is applied for Tier I data. A correction factor of 5 is applied to Tier II data.

Table 9.7-3: First- and higher-tier assessment of the off-field risk for non-target arthropods due to the maximum use of A12739A in maize (BBCH 12-18)

Intended use		*Maize*				
Active substance		*Mesotrione*				
Application rate (g/ha)		*1 × 150*				
MAF		*1*				
Drift rate (%)		*2.77%*				
VDF		*10 (2D) / none (3D)*				
Test species Tier I	***LR_{50} (lab.) (g/ha)***	***Drift factor***	***$PER_{off\text{-}field}$ (g/ha)***	***CF***	***Corrected $PER_{off\text{-}field}$ (g/ha)***	***$HQ_{off\text{-}field}$ criterion: HQ ≤ 2***
Aphidius rhopalosiphi	*43.56*	*0.0277*	*0.831* ~~0.416~~	*10*	*8.31* ~~4.16~~	*0.19* ~~0.096~~
Typhlodromus pyri	*93.11*	*0.0277*	*0.831* ~~0.416~~	*10*	*8.31* ~~4.16~~	*0.09* ~~0.045~~
Test species Higher-tier	***ER_{50} (g/ha)***	***Drift factor***	***$PER_{off\text{-}field}$ (g/ha)***	***CF***	***Corrected $PER_{off\text{-}field}$ (g/ha)***	***corr. $PER_{off\text{-}field}$ below ER_{50}?***
Aphidius rhopalosiphi	*>225*	*0.0277*	*4.16*	*5*	*20.8*	*Yes*
Typhlodromus pyri	*>150*	*0.0277*	*0.831* ~~0.416~~	*5*	*4.16* ~~2.08~~	*Yes*
Aleochara bilineata	*>200*	*0.0277*	*0.831* ~~0.416~~	*5*	*4.16* ~~2.08~~	*Yes*
Pardosa sp.	*>150*	*0.0277*	*0.831* ~~0.416~~	*5*	*4.16* ~~2.08~~	*Yes*

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 HQ values of the Tier I risk assessment for T. pyri and A. rhopalosiphi are below the trigger of 2, indicating that the risk to off-field non-target arthropods is acceptable following the use of A12739A according to the proposed use pattern.

Also, the Tier II, extended laboratory studies for A. rhopalosiphi, T. pyri, Aleochara bilineata and Pardosa showed acceptable off-field risk to non-target arthropods following the use of A12739A according to the proposed use pattern.

9.7.2.3 Additional higher-tier risk assessment

Not relevant.

9.7.2.4 Risk mitigation measures

No risk mitigation needed.

9.7.3 Overall conclusions

At Tier I, the in-field and off-field HQ values for Typhlodromus pyri were below the trigger value for the worst-case use scenario (1 x 150 g a.s./ha in maize) indicating acceptable risk. However, the in-field HQ values for Aphidius rhopalosiphi were above the trigger value and required further refinement.
The Tier II, extended laboratory studies showed acceptable foliar in-field and off-field effects from foliar applications of A12739A for A. rhopalosiphi, T. pyri, Aleochara bilineata and Pardosa for the worst-case use scenario (1 x 150 g a.s./ha in maize). The risk to non-target arthropods is therefore acceptable following use of A12739A according to the proposed use pattern.

zRMS comments: **Non-target arthropods other than bees** No data is provided in support of the application for authorization of **Mecorn 100 SC**. The intended uses in GAP for the formulation Product **Callisto 100 SC** are within those considered acceptable for registration of **Mecorn 100 SC**. No unacceptable effects are anticipated on communities of terrestrial non-target arthropods due to the use of **Mecorn 100 SC** according proposed use in GAP.

9.8 Effects on non-target soil meso- and macrofauna (KCP 10.4)

Information concerning effects on non-target soil meso- and macrofauna relevant for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, this point origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

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 mesotrione and its relevant metabolites in soil. Full details of these studies are provided in the respective EU DAR and related documents as well as in Appendix 2 of this document (new studies).

Effects on earthworms and other non-target soil organisms (meso- and macrofauna) of A12739A were evaluated as part of the EU assessment of mesotrione. 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 in line with the results of the EU review process with some minor deviations. Justifications are provided below.

Table 9.8-1: Endpoints and effect values relevant for the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) – mesotrione and relevant soil metabolites

Species	***Substance***	***Exposure system***	***Results***	***Reference***
Chronic				
Eisenia fetida	*Mesotrione (formulated as A12739A)*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 10.85 mg a.s./kg dw EC_{10} = 5.91 mg a.s./kg dw*	*EFSA Conclusion 2016 Friedrich, 2011 A12739A_10000*
Eisenia fetida	*MNBA*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 1050 mg/kg dw EC_{10} >1050 mg/kg dw*	*EFSA Conclusion 2016 Friedrich, 2013a CA3511_10002*
Eisenia fetida	*AMBA*	*Mixed into substrate 56 d, chronic 10 % peat content*	*NOEC = 1050 mg/kg dw EC_{10} = 1050 mg/kg dw*	*EFSA Conclusion 2016 Friedrich, 2013b R044276_10002*
Folsomia candida	*Mesotrione (formulated as A12739A)*	*Mixed into substrate 28 d[b], chronic 5 % peat content*	*NOEC = 50.5 mg a.s./kg dw [a] EC_{10} = 37.5 mg a.s./kg dw [a]*	*EFSA Conclusion 2016 Friedrich, 2013c A12739A_10013*
Folsomia candida	*MNBA*	*Mixed into substrate 28 d, chronic 5 % peat content*	*NOEC = 100 mg/kg dw*	*Dickinson, 2015 CA3511_10011*
Hypoaspis aculeifer	*Mesotrione (formulated as A12739A)*	*Mixed into substrate 14 d[c], chronic 5 % peat content*	*NOEC = 90.9 mg a.s./kg dw [a] EC_{10} > 90.9 mg a.s./kg dw [a]*	*EFSA Conclusion 2016 Schulz, 2013 A12739A_10014*
Hypoaspis aculeifer	*MNBA*	*Mixed into substrate 14 d, chronic 5 % peat content*	*NOEC = 1050 mg/kg dw EC_{10} could not be calculated*	*Ramsden, 2015 CA3511_10010*
Field studies				
Not relevant				
Litter bag test				
Not relevant				

[a] The endpoints are reported as NOEC (reproduction) Collembola = 556 mg A12739A/kg and NOEC for Hypoaspis = 1000 mg A12739A/kg; these have been converted to the mesotrione content considering it is present as 9.09% w/w

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

[b] *Please note that in the EFSA conclusion this is incorrectly stated as 14d, but this is a 28d test, as stated in the RAR*
[c] *Please note that in the EFSA conclusion this is incorrectly stated as 28d, but this is a 14d test, as stated in the RAR*

9.8.1.1 Justification for new endpoints

Since Annex I submission new studies with mesotrione metabolites have been performed to fulfil the new data requirements under 1107/2009, and as a result there are new endpoints for use in the risk assessment. These studies are summarised in Table 9.8-1.

9.8.2 Risk assessment

The evaluation of the risk to 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 Section 8 (Environmental Fate), Chapter 8.7.2. According to the assessment of environmental-fate data, multi-annual accumulation in soil does not need to be considered for mesotrione.

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the worst-case application rate of 1.635 kg A12739A/ha (corresponding to 150 g mesotrione/ha) is used in the risk assessment. The relevant endpoints for A12739A, mesotrione and relevant metabolites are compared to the maximum PEC_{soil}.

Table 9.8-2: First-tier assessment of the acute and chronic risk for earthworms and other non-target soil organisms (meso- and macrofauna) due to the maximum use of A12739A in maize (BBCH 12-18) – mesotrione and its relevant metabolites

Intended use	*Maize*		
Chronic effects on earthworms			
Test substance	***NOEC (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***TER_{lt} (criterion TER ≥ 5)***
Mesotrione	*EC_{10} = 5.91*	*0.150*	*39*
MNBA	*1050*	*0.062*	*16935*
AMBA	*1050*	*0.011*	*95000*
Chronic effects on other soil macro- and mesofauna (Folsomia)			
Test substance	***NOEC (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***TER_{lt} (criterion TER ≥ 5)***
Mesotrione	*37.5*	*0.150*	*250*
MNBA	*100*	*0.062*	*1613*
AMBA	*3.75 [a]*	*0.011*	*341*
Chronic effects on other soil macro- and mesofauna (Hypoaspis)			
Test substance	***NOEC (mg/kg dw)***	***PEC_{soil} (mg/kg dw)***	***TER_{lt} (criterion TER ≥ 5)***
Mesotrione	*90.9*	*0.150*	*610*
MNBA	*1050*	*0.062*	*16935*
AMBA	*9.09 [a]*	*0.011*	*830*

PEC: Predicted environmental concentration; TER: toxicity to exposure ratio
[a] *Tests with AMBA have not been carried out, and the risk assessment has been performed on the basis of the endpoint for the parent divided by 10.*

9.8.2.2 Higher-tier risk assessment

Not relevant.

9.8.3 Overall conclusions

Earthworms

The long-term risk of A12739A to earthworms was assessed from long-term toxicity exposure ratios (TERs) between the selected toxicity endpoints for A12739A, mesotrione and its relevant metabolites, and the maximum PEC_{soil}. The chronic TER values for A12739A, mesotrione and its metabolites are greater than the Regulation (EU) 546/2011 trigger of 5, indicating that the risk to earthworms is acceptable following use of A12739A, according to the proposed use pattern.

Other soil macro-organisms

The risk of A12739A to other non-target soil macro-organisms, as represented by Collembola and Hypoaspis, was assessed from long-term TERs between the selected no-effect concentrations, derived from laboratory tests on mesotrione (formulated as A12739A) and its metabolites, and the maximum PEC_{soil}. The TER_{LT} values for mesotrione (formulated as A12739A) and its metabolites are all greater than the recommended trigger value of 5, indicating that the risk to soil macro-organisms, as represented by Collembola and Hypoaspis, is acceptable following use of A12739A according to the proposed use pattern.

zRMS comments: **Effect on non-target soil meso- and macrofauna** No data is provided in support of the application for authorization of **Mecorn 100 SC**. The intended uses product **Callisto 100 SC** are within those considered acceptable for registration of **Mecorn 100 SC**. The long-term risk assessment presented for earthworms and other soil non-target macro-organisms based on the endpoints from the studies performed on formulation of **Callisto 100 SC.** The risk assessment is appropriate to be used for **Mecorn 100 SC**. Use of **Mecorn 100 SC** is not expected to pose risk to soil macro-organisms. No additional risk assessment is not required.

9.9 Effects on soil microbial activity (KCP 10.5)

Information concerning effects on soil microbial activity relevant for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, this point origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

9.9.1 Toxicity data

Studies of the effects on soil microorganisms have been carried out with mesotrione and its relevant soil metabolites. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on soil microorganisms of A12739A were evaluated as part of the EU assessment of mesotrione.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.9-1: Endpoints and effect values relevant to the risk assessment for soil microorganisms – mesotrione and its metabolites

Endpoint	***Substance***	***Exposure system***	***Results***	***Reference***
N-mineralisation	*Mesotrione (tested as formulation A12739A)*	*28 d, aerobic*	*Nitrate formation rate 5.84 mg A12739A/kg soil dw 7.8 % (< 25 % effect at up to 0.53 mg a.s./kg soil dw)*	*EFSA Conclusion 2016 Schulz, 2013a A12739A_10024*
N-mineralisation	*MNBA*	*28 d, aerobic*	*Nitrate formation rate 1.13 mg/kg soil dw -7.6 % (< 25 % effect at up to 1.13 mg/kg soil dw)*	*EFSA Conclusion 2016 Schulz, 2013b CA3511_10000*
N-mineralisation	*AMBA*	*28 d, aerobic*	*Nitrate formation rate 1.13 mg/kg soil dw -4.8 % (< 25 % effect at up to 1.13 mg/kg soil dw)*	*EFSA Conclusion 2016 Schulz, 2013b CA3511_10000*

**Please note that Carbon transformation is no longer a data requirement*

9.9.1.1 Justification for new endpoints

Not relevant.

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 Section 8 (Environmental Fate), Chapter 8.7.2, and were already used in the risk assessment for earthworms and other non-target soil organisms (meso- and macrofauna) (see 0).

To achieve a concise risk assessment, the risk envelope approach is applied. Here, the worst-case application rate of 1.635 kg A12739A/ha (corresponding to 150 g mesotrione/ha) is used in the risk assessment.

Table 9.9-2: Assessment of the risk for effects on soil micro-organisms due to the use of A12739A in maize (BBCH 12-18) – mesotrione and its soil metabolites

Intended use	*Maize BBCH 12-18*		
N-mineralisation			
Test substance	***Max. conc. with effects ≤ 25 % (mg a.s./kg dw)***	***PEC_{soil} (mg a.s./kg dw)***	***Risk acceptable?***
Mesotrione	*0.53 (at 28d)*	*0.150*	*Yes*
MNBA	*1.13 (at 28 d)*	*0.062*	*Yes*
AMBA	*1.13 (at 28 d)*	*0.011*	*Yes*

9.9.3 Overall conclusions

The risk of mesotrione (formulated as A12739A) and its metabolites to soil micro-organisms was evaluated by comparison of the maximum concentrations with effects <25% derived from laboratory tests, with maximum PEC_{soil}.
All the effect levels exceeded the relevant PEC_{soil} values, indicating that the risk to soil micro-organisms is acceptable following the use of A12739A according to the proposed use patterns.

zRMS comments:
Effects on soil microbial activity
No data is provided in support of the application for authorization of **Mecorn 100 SC**. The intended uses product **Callisto 100 SC** are within those considered acceptable for registration of **Mecorn 100 SC**. The risk assessment presented for micro-organisms on the endpoints from the studies performed on formulation of **Callisto 100 SC** has been accepted for **Mecorn 100 SC**. The risk assessment is appropriate to be used for **Mecorn 100 SC**. According to the Registration Report for **Callisto 100 SC** the risk assessment for microorganisms have been accepted. On the basis of performed calculations in **Callisto 100 SC** report, acceptable risk assessment to microorganisms may be concluded from proposed uses of **Mecorn 100 SC**. The risk to soil micro-organisms from uses of **Mecorn 100 SC** is expected to be low. No additional risk assessment is not required.

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

Information concerning effects on non-target terrestrial plants relevant for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, this point origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

9.10.1 Toxicity data

Studies on the toxicity to non-target terrestrial plants have been carried out with mesotrione. Full details of these studies are provided in the respective EU DAR and related documents.

Effects on non-target terrestrial plants of A12739A were evaluated as part of the EU assessment of mesotrione.

The selection of studies and endpoints for the risk assessment is in line with the results of the EU review process.

Table 9.10-1: Endpoints and effect values relevant for the risk assessment for non-target terrestrial plants - mesotrione

Species	***Substance***	***Exposure system***	***Results***	***Reference***
9 – 20 NTP species	*AMBA and MNBA*	*Screening study*	*NOEC = 4000 g/ha*	*Renewal Assessment Report, 11 Vol.3 CA B-9 (11/11/2015)* *Shribbs, 1997* *ZA1296/0189*
Lactuca sativa d	*A12739A*	*21 d* *Seedling emergence*	*ER_{50} biomass = 13.8 g a.s./ha*	*EFSA Conclusion 2016* *Porch et al., 2003* *ZA1296/1144*
Lactuca sativa d	*A12739A*	*21 d* *Vegetative vigour*	*ER_{50} biomass = 0.883 g a.s./ha*	*EFSA Conclusion 2016* *Porch et al., 2003a* *ZA1296/1145*
Species Sensitivity Distribution (SSD)	*A12739A*	*21 d* *Vegetative vigour*	*HC_5 = 0.173 g a.s./ha*	*EFSA Conclusion 2016*

d: dicotyledonous

9.10.1.1 Justification for new endpoints

Not relevant.

9.10.2 Risk assessment

9.10.2.1 Tier-1 risk assessment (based 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 $PER_{off\ field}$ was calculated as Application rate × drift factor

Table 9.10-2: Assessment of the risk for non-target plants due to the use of A12739A in maize (1 x 100 g a.s./ha, BBCH 12-18)

Intended use	*Maize*			
Active substance	*Mesotrione*			
Application rate (g/ha)	*1 × 100*			
Drift rate (%)	*2.77% at 1 m*			
MAF	*1*			
Test species	***ER_{50} (g/ha)***	***Drift factor***	***$PER_{off-field}$ (g/ha)***	***TER criterion: TER ≥ 5***
Lactuca sativa (most sensitive species, seedling emergence)	*13.8*	*0.0277*	*2.77*	*5.0*

Lactuca sativa (most sensitive species, vegetative vigour)	*0.883*	*0.0277*	*2.77*	***0.32***
	HC_{05} (g/ha)	***Drift factor***	***$PER_{off-field}$ (g/ha)***	***TER criterion: TER ≥ 1***
HC_{05} vegetative vigour	*0.173*	*0.0277*	*2.77*	***0.062***

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

Table 9.10-3: Assessment of the risk for non-target plants due to the use of A12739A in maize (1 x 150 g a.s./ha, BBCH 12-18)

Intended use	*Maize*			
Active substance	*Mesotrione*			
Application rate (g/ha)	*1 × 150*			
Drift rate (%)	*2.77% at 1 m*			
MAF	*1*			
Test species	***ER_{50} (g/ha)***	***Drift factor***	***$PER_{off-field}$ (g/ha)***	***TER criterion: TER ≥ 5***
Lactuca sativa (most sensitive species, seedling emergence)	*13.8*	*0.0277*	*4.16*	***3.3***
Lactuca sativa (most sensitive species, vegetative vigour)	*0.883*	*0.0277*	*4.16*	***0.21***
	HC_{05} (g/ha)	***Drift factor***	***$PER_{off-field}$ (g/ha)***	***TER criterion: TER ≥ 1***
HC_{05} vegetative vigour	*0.173*	*0.0277*	*4.16*	***0.042***

MAF: Multiple application factor; PER: Predicted environmental rate; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

9.10.2.3 Higher-tier risk assessment

Three semi-field studies were conducted, investigating four species. The endpoints are summarised in the EFSA Conclusion 2016 of mesotrione. The RAR concluded that the results despite some drawbacks were conservative and therefore could be considered:

"As the evaluator noted all of the endpoints from both the Tier 2 and semi-field studies could be conservative as they were derived from the total weight of surviving plants in a replicate to determine biomass. Ideally, these results would be reported as weight per surviving plant. As this would then remove the effect of mortality from these variables. Using the total weight per replicate for species where mortality has occurred will result in more conservative and variable data. If no mortality occurred the values would represent true parameter estimates.

*This information regarding the higher tier semi-field studies is provided for information. **Member states may wish to consider these points when determining suitable risk mitigation measures for non-target plants.** No formal risk assessment or TER values have been produced with this data, as an acceptable risk has already been demonstrated by the Tier 2 SSD risk assessment. Semi field data is only available for only four species whilst ten NTPs were assessed in the Tier 2 risk assessment (deterministic and SSD). Therefore, the Tier 2 risk assessment is based on the more comprehensive set of information".*

The higher tier semi field studies were carried out on the 4 most sensitive species from the Tier 2 studies. The endpoints as proposed in the RAR are:

Cucumber C. sativus: Early growth stage 21-Days after treatment $ER_{50\ biomass}$ = 0.714 g a.s./ha

Lettuce L. sativa: Early growth stage 21-Days after treatment $ER_{50\ biomass}$ = 1.65 g a.s./ha

Tomato L. esculentum: Middle growth stage 35-Days after treatment $ER_{50\ biomass}$ = 4.46 g a.s./ha

Turnip Brassica rapa: Early growth stage 21-Days after treatment $ER_{50\ biomass}$ = 1.70 g a.s./ha

Since only 4 species are available these data are not suitable for calculation of an HC_5. Instead, it is proposed to use either the lowest value with a reduced assessment factor of 2 since these tests concentrated on the known most sensitive species; or to use the geomean of the higher tier data giving an $ER_{50\ geomean}$ = 1.73 g a.s./ha.

9.10.2.4 Risk mitigation measures

In order to reduce the off-field exposure, risk mitigation measures can be implemented. These correspond to unsprayed in-field buffer strips of a given width and/or the usage of drift reducing nozzles. The results of the risk assessment using typical mitigation measures (no-spray buffer zones of 5, 10, 20 m or 30 m; drift-reducing nozzles with reduction by 50 %, 75 %, or 90 %) are summarised in the following tables.

Table 9.10-4: Risk assessment for non-target terrestrial plants due to the use of A12739A in maize (1 x 100 g a.s./ha, BBCH 12-18) considering risk mitigation (in-field no-spray buffer zones, and drift-reducing nozzles)

Intended use		Maize			
Active substance		Mesotrione			
Application rate (g/ha)		1 × 100			
MAF		1			
Buffer strip (m)	**Drift rate (%)**	**$PER_{off-field}$ (g/ha)**	**$PER_{off-field}$ 50 % drift red. (g/ha)**	**$PER_{off-field}$ 75 % drift red. (g/ha)**	**$PER_{off-field}$ 90 % drift red. (g/ha)**
1	2.77	2.77	1.39	0.693	0.277
5	0.57	0.570	0.285	0.143	0.0570
10	0.29	0.290	0.145	0.0725	0.0290
20	0.15	0.150	0.0750	0.0375	0.0150
30	0.100	0.100	0.0500	0.0250	0.0100
Toxicity value ER_{50} = 0.883 g/ha *Lactuca sativa* (most sensitive species, vegetative vigour)		**TER** **criterion: TER ≥ 5**			
1		**0.32**	**0.64**	**1.3**	**3.2**
5		**1.5**	**3.1**	6.2	15
10		**3.0**	6.1	12	30
20		5.9	12	24	59
30		8.8	18	35	88
Toxicity value HC_{05} = 0.173 g/ha (most sensitive distribution, vegetative vigour)		**TER** **criterion: TER ≥ 1**			
1		**0.062**	**0.12**	**0.25**	**0.62**
5		**0.30**	**0.61**	1.2	3.0
10		**0.60**	1.2	2.4	6.0
20		1.2	2.3	4.6	12
30		1.7	3.5	6.9	17

MAF: Multiple application factor; PER: Predicted environmental rates; TER: toxicity to exposure ratio. TER values shown in bold fall below the relevant trigger.

9.10.3 Overall conclusions

The first tier risk assessment in which TER values were calculated from worst-case endpoints from seedling emergence and vegetative vigour studies with 10 species and a $PER_{off-field}$ value at 1 m from the treated crop, indicated a potential risk to off-field non-target plants. The risk was refined using a probabilistic risk assessment, and considering mitigation with buffers and spray drift reduction technology.

Since the data provided by the Applicant of Callisto 100 SC was not sufficient for the assessment this point the zRMS comments have been placed in this document as a supplement of drinking water exposure assessment (written in italics, highlighted in yellow). These data are applicable for MEZ-HER 100 SC which is comparable in composition with Callisto 100 SC as well as it is recommended to use in the same crops, doses and time as Callisto 100 SC.

zRMS comments in Callisto 100 SC:

The refinement of the risk based on the results of semi-field studies was not agreed by the zRMS and for this reason the risk mitigation measures were determined based on lowest ER_{50} derived from standard toxicity studies and HC_5 values.

On the basis of performed calculations following risk mitigation measures are required to protect non-target terrestrial plants:

1. *For application rate of 100 g a.s./ha:*
    - *20 m unsprayed buffer zone to non-agricultural land, or*
    - *10 m unsprayed buffer zone to non-agricultural land combined with reduction of the spray drift by 50%, or*
    - *reduction of the spray drift by 75%.*
2. *For application rate of 150 g a.s./ha:*
    - *30 m unsprayed buffer zone to non-agricultural land, or*
    - *20 m unsprayed buffer zone to non-agricultural land combined with reduction of the spray drift by 50%, or*
    - *10 m unsprayed buffer zone to non-agricultural land combined with reduction of the spray drift by 75%, or*
    - *5 m unsprayed buffer zone to non-agricultural land combined with reduction of the spray drift by 90%.*

zRMS comments:

Non-target plants:

No data is provided in support of the application for authorization of **Mecorn 100 SC**. The intended uses product **Callisto 100 SC** are within those considered acceptable for registration of **Mecorn 100 SC**. The risk assessment presented for non-target plants on the endpoints from the studies performed on formulation of **Callisto 100 SC** has been accepted for **Mecorn 100 SC**. The risk assessment is appropriate to be used for **Mecorn 100 SC**. According to the Registration Report for **Callisto 100 SC** the risk assessment for non-target plants have been accepted. On the basis of performed calculations in **Callisto 100 SC** report, acceptable risk assessment to non-target plants may be concluded from proposed uses of **Mecorn 100 SC**.

On the basis of performed calculations following risk mitigation measures are required to protect non-target terrestrial plants:

- 20 m unsprayed buffer zone to non-agricultural land, or
- 10 m unsprayed buffer zone to non-agricultural land combined with reduction of the spray drift by 50%, or
- reduction of the spray drift by 75%.

Concerned Member States must decide on applicability of the indicated mitigation measures at the product authorisation in their countries.

The risk assessment for non-target plants should be considered by MSs level.

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

Tests on other non-target species are not required.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

9.12 Monitoring data (KCP 10.8)

There are no other relevant data for the active substance or product on organisms in the environment generated from monitoring schemes.

9.13 Classification and Labelling

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the classification and labelling with regard to ecotoxicological data is proposed is included in table below.

MEZ-HER 100 SC has the same recipe as the reference product Callisto 100 SC and the classification of MEZ-HER 100 SC was proposed on the basis of the reference product classification as well as calculation method. The proposed classification of the product MEZ-HER 100 SC is:

Table 9.13-1: Justified proposals for classification and labelling for MEZ-HER 100 SC according to Regulation (EC) No 1272/2008

Hazard class(es), categories:	**Aquatic Acute 1, H400** **Aquatic Chronic 1, H410**
Hazard pictograms or Code(s) for hazard pictogram(s):	 GHS09
Signal word:	Warning
Hazard statement(s):	H410 - Very toxic to aquatic life with long lasting effects.
Precautionary statement(s):	P391 - Collect spillage.
Additional labelling phrases:	EUH401 - To avoid risks to human health and the environment, comply with the instructions for use.

zRMS comments:
The CLP classification presented above is agreed by zRMS.

Following labelling is proposed with regard to effects on aquatic environment:

Hazard pictograms:	GHS09 
Signal word:	Warning
Hazard statement(s):	H410 - Very toxic to aquatic life with long lasting effects
Precautionary statement(s):	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

Tables considered not relevant can be deleted as appropriate.

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

List of data submitted by the applicant and relied on

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

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

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 10.1.2.2 / 07	[redacted]	*2010*	*Exposure of mammals in maize fields in France - Attractiveness of maize fields and relevant species* *Syngenta* [redacted] *GLP* *not published* [redacted]	*N*	*SYN*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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 / 08	[redacted]	*2005*	*Generic field monitoring of birds and mammals on maize and beet fields in Austria* [redacted] *GLP* *not published* *Syngenta File No N/1155*	*Y*	*BCS*
KCP 10.1.2.2 / 09	[redacted]	*2014*	*Generic field study on small mammals - focal species and wood mouse (Apodemus sylvaticus) PT in maize fields in Germany* [redacted] *GLP* *not published* *Syngenta File No NA_13410*	*Y*	*OXN*
KCP 7.1.1 / 01	[redacted]	*2005*	*Mesotrione 100 G/L SC Formulation (A12739A):* [redacted] *GLP* *not published* *Syngenta File No ZA1296/1921*	*Y*	*SYN*
KCP 10.2 / 01	[redacted]	*2005*	*Mesotrione 100 g/L SC formulation (A12739A):* [redacted] *GLP* *not published* *Syngenta File No ZA1296/1803*	*N*	*SYN*
KCP 10.2 / 02	*Ricketts D., Langridge G.*	*2005*	*Mesotrione 100 g/L SC (A12739A): Acute toxicity to the Cladoceran Daphnia magna under static conditions* *Syngenta Crop Protection AG, Basel, Switzerland* *Syngenta - Jealott's Hill International, Bracknell, Berkshire, United Kingdom, RJ3714B* *GLP* *not published* *Syngenta File No ZA1296/2042*	*N*	*SYN*
KCP 10.2 / 03	*Volz E.*	*2005*	*Mesotrione 100 SC Formulation (A12739A): Toxicity to Pseudokirchneriella subcapitata (formerly Selenastrum capricornutum) in a 96-hour algal growth inhibition test* *Syngenta Crop Protection AG, Basel, Switzerland* *RCC Ltd., Itingen, Switzerland, A18325* *GLP* *not published* *Syngenta File No ZA1296/2049*	*N*	*SYN*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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 / 04	*Zawadsky C.*	*2013*	*Mesotrione SC (A12739A) - Assessment of Toxic Effects on the duckweed Lemna gibba in a 7 day Semi-Static Test and 14 day Recovery Period* *Syngenta Crop Protection AG, Basel, Switzerland* *Eurofins Agroscience Services EcoChem GmbH, N-Osch., Germany, S12-03986* *GLP* *not published* *Syngenta File No A12739A_10273*	*N*	*SYN*
KCP 10.3.1 / 01	*Kleebaum K.*	*2013*	*Mesotrione SC (A12739A) - Semi-chronic toxicity to the honeybee larvae Apis mellifera L. under laboratory conditions (in vitro)* *Syngenta Crop Protection AG, Basel, Switzerland* *BioChem Agrar, Gerichshain, Germany, 13 10 48 073 B* *GLP* *not published* *Syngenta File No A12739A_10464*	*N*	*SYN*
KCP 10.3.1 / 02	*Kleebaum K.*	*2013a*	*Mesotrione SC (A12739A) - Chronic toxicity to the honeybee Apis mellifera L. in a 10 day continuous laboratory feeding study* *Syngenta Crop Protection AG, Basel, Switzerland* *BioChem Agrar, Gerichshain, Germany, 13 10 48 074 B* *GLP* *not published* *Syngenta File No A12739A_10465*	*N*	*SYN*
KCP 10.3.1 / 03	*Franke M.*	*2013*	*Mesotrione SC (A12739A) - Acute toxicity to the honeybee Apis mellifera L. under laboratory conditions* *Syngenta Crop Protection AG, Basel, Switzerland* *BioChem Agrar, Gerichshain, Germany, 13 10 48 001 B* *GLP* *not published* *Syngenta File No A12739A_10015*	*N*	*SYN*
KCP 10.3.2 / 01	*Fallowfield L.*	*2012*	*Mesotrione SC (A12739A) - A rate-response laboratory bioassay of the effects of fresh residues on the predatory mite, Typhlodromus pyri (Acari: Phytoseiidae)* *Syngenta Crop Protection AG, Basel, Switzerland* *Mambo-Tox Ltd., Southampton, United Kingdom, SYN-12-41* *GLP* *not published* *Syngenta File No A12739A_10010*	*N*	*SYN*

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 / 02	*Stevens J.*	*2012*	*Mesotrione SC (A12739A) - A rate-response laboratory bioassay of the effects of fresh residues on the parasitic wasp Aphidius rhopalosiphi (Hymenoptera, Braconidae)* *Syngenta Crop Protection AG, Basel, Switzerland* *Mambo-Tox Ltd., Southampton, United Kingdom, SYN-12-42* *GLP* *not published* *Syngenta File No A12739A_10008*	*N*	*SYN*
KCP 10.3.2 / 03	*Fallowfield L.*	*2013*	*Mesotrione SC (A12739A) - A rate-response extended laboratory bioassay of the effects of fresh residues on the predatory mite Typhlodromus pyri (Acari: Phytoseiidae)* *Syngenta Crop Protection AG, Basel, Switzerland* *Mambo-Tox Ltd., Southampton, United Kingdom, SYN-13-4* *GLP* *not published* *Syngenta File No A12739A_10020*	*N*	*SYN*
KCP 10.3.2 / 04	*Stevens J.*	*2013*	*Mesotrione SC (A12739A) - A rate-response extended laboratory bioassay of the effects of fresh residues on the parasitic wasp Aphidius rhopalosiphi (Hymenoptera, Braconidae)* *Syngenta Crop Protection AG, Basel, Switzerland* *Mambo-Tox Ltd., Southampton, United Kingdom, SYN-13-5* *GLP* *not published* *Syngenta File No A12739A_10276*	*N*	*SYN*
KCP 10.3.2 / 05	*Tew G.*	*2013*	*Mesotrione SC (A12739A) - A rate-response extended laboratory test to evaluate the effects of fresh residues on the rove beetle Aleochara bilineata (Coleoptera; Staphylinidae)* *Syngenta Crop Protection AG, Basel, Switzerland* *Mambo-Tox Ltd., Southampton, United Kingdom, SYN-13-6* *GLP* *not published* *Syngenta File No A12739A_10275*	*N*	*SYN*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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 / 06	*Vaughan R.*	*2013*	*Mesotrione SC (A12739A) - A rate-response extended laboratory test to determine the effects of fresh residues on spiders of the genus Pardosa (Araneae, Lycosidae)* *Syngenta Crop Protection AG, Basel, Switzerland* *Mambo-Tox Ltd., Southampton, United Kingdom, SYN-13-7* *GLP* *not published* *Syngenta File No A12739A_10388*	*N*	*SYN*
KCP 10.4 / 01	*Friedrich S.*	*2011*	*Mesotrione SC (A12739A) - Sublethal toxicity to the earthworm Eisenia fetida in artificial soil* *Syngenta - Jealott's Hill, Bracknell, United Kingdom* *BioChem Agrar, Gerichshain, Germany, 11 10 48 003 S* *GLP* *not published* *Syngenta File No A12739A_10000*	*N*	*SYN*
KCP 10.4 / 02	*Friedrich S.*	*2013*	*Mesotrione SC (A12739A) - Effects on the Reproduction of the Collembolan Folsomia candida* *Syngenta Crop Protection AG, Basel, Switzerland* *BioChem Agrar, Gerichshain, Germany, 13 10 48 009 S* *GLP* *not published* *Syngenta File No A12739A_10013*	*N*	*SYN*
KCP 10.4 / 03	*Schulz L.*	*2013*	*Mesotrione SC (A12739A) - Effects on the Reproduction of the Predatory Mite Hypoaspis aculeife* *Syngenta Crop Protection AG, Basel, Switzerland* *BioChem Agrar, Gerichshain, Germany, 13 10 48 010 S* *GLP* *not published* *Syngenta File No A12739A_10014*	*N*	*SYN*
KCP 10.5 / 01	*Schulz L.*	*2014*	*Mesotrione SC (A12739A) - Effects on the Activity of Soil Microflora (Nitrogen and Carbon Transformation Tests)* *Syngenta Crop Protection AG, Basel, Switzerland* *BioChem Agrar, Gerichshain, Germany, 13 10 48 006 C/N* *GLP* *not published* *Syngenta File No A12739A_10024*	*N*	*SYN*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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 10.6 / 01	*Porch J., Martin K., Krueger H.*	*2003*	*ZA1296 (Mesotrione): The toxicity effects of a 100 g/litre SC formulation (A12739A) on the seedling emergence of ten species of plants* *Syngenta Crop Protection AG, Basel, Switzerland* *Wildlife International Ltd., Easton MD, USA, 528-152* *GLP* *not published* *Syngenta File No ZA1296/1144*	*N*	*SYN*
KCP 10.6 / 02	*Porch J., Martin K., Krueger H.*	*2003a*	*ZA1296 (Mesotrione): The toxicity effects of a 100 g/litre SC formulation (A12739A) on the vegetative vigour of ten species of plants* *Syngenta Crop Protection AG, Basel, Switzerland* *Wildlife International Ltd., Easton MD, USA, 528-153* *GLP* *not published* *Syngenta File No ZA1296/1145*	*N*	*SYN*

The following tables are to be completed by MS

List of data submitted by the applicant and not relied on

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

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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
KCP 10.1.1 / 01	*Hubbard PM, Davis RJ, Temple DL*	*2018*	*Mesotrione - An Acute Oral Toxicity Study with the Mallard Using a Sequential Testing Procedure* *Syngenta Crop Protection AG, Basel, Switzerland* *EAG, Inc. 8598 Commerce Drive Easton, MD 21601 USA* *GLP* *not published* *Syngenta File No ZA1296/10605*	*Y*	*SYN*
KCP 10.1.2/01	*Alvarez T.*	*2019*	*Mesotrione: refined risk assessment for mammals in the central zone* *Syngenta European Product Registration, Basel, Switzerland* *Not GLP* *not published* *Syngenta File No A12739A_11105* ***This is CONFIDENTIAL INFORMATION****	*N*	*SYN*
KCP 10.1.2.2 / 02	*Prescott C.*	*2004*	*The assessment of Wood mouse acceptance /avoidance of different crop seeds when presented in free feeding conditions to individually caged animals in a six hour no-choice situation; and to monitor the incidence of de-husking for each seed type.* *Syngenta Crop Protection AG, Basel, Switzerland* *University of Reading, Reading, United Kingdom, VPU/04/026 2033623* *Not GLP* *not published* *Syngenta File No N/1014*	*N*	*SYN*
KCP 10.1.2.2 / 03	*Siebert U., Voight U., Zaccaroni M.*	*2013*	*Generic field monitoring of hares in a mixed landscape in Germany* *Syngenta Crop Protection AG, Basel, Switzerland* *BCS DocID: M475145-01-1, BAR/FS069* *Not GLP* *not published* *Syngenta File No NA_13449*	*Y*	*BCS*
KCP 10.1.2.2 / 04	*Voigt U., Zaccaroni M.*	*2015*	*Generic field monitoring of hares in a mixed landscape in Germany - Jacobs index* *Bayer Crop Science AG, Monheim, Germany* *BAR/FS069* *Not GLP* *not published* *Syngenta File No NA_13997*	*N*	*BCS*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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 / 05	*Dittrich R., Benito M.*	*2016*	*Occurrence and PT of Wood mice in pre- and post-emergence maize fields in France, southern zone.* *Syngenta Crop Protection AG, Basel, Switzerland* *tier3 solutions GmbH, Leverkusen, Germany, NA_14235, B15064* *Not GLP* *not published* *Syngenta File No NA_14237*	*N*	*BCS*
KCP 10.1.2.2 / 01	*Fulling O., Sainz-Elipe S.*	*2015*	*Generic field study on the presence and abundance of common voles in maize fields in Northern France* *BASF Ltd., Ludwigshafen, Germany* *774934* *GLP* *not published* *Syngenta File No NA_13749*	*Y*	*BASF*
KCP 10.1.2.2 / 06	*North L.*	*2016*	*Mesotrione - Foliage Decline with A12739A on Maize in Northern France and the United Kingdom in 2015* *Syngenta Crop Protection AG, Basel, Switzerland* *Eurofins Agroscience Services Ltd, Wilson, UK, S15-02057* *GLP* *not published* *Syngenta File No A12739A_11065*	*N*	*SYN*
KCP 10.1.2.2/07	*Grimm T & Katzschner I*	*2019*	*Generic monitoring of European hares to determine proportion of time spent foraging in early maize in Central Europe. RIFCON GmbH, Goldbeckstr. 13, 69493 Hirschberg, Germany* *Report No. R1740045* *GLP, Unpublished* *Syngenta File No. NA_14950*	*N*	*SYN*
KCP 10.1.2.2/08	*Kleinmann J*	*2019*	*Comparison of POLARIS Brown hare and ALMaSS Brown hare for use in Pesticide Risk assessments. WSC Scientific GmbH, Dossenheimer Landstrasse 9/1 69121 Heidelberg Germany Report Number 18014-SYN-1.* *Syngenta File No. A20718J_10072* ***This is CONFIDENTIAL INFORMATION****	*N*	*SYN*
KCP 10.1.2.2/09	*Kleinmann J.*	*2019a*	*Mesotrione - Population-level risk assessment for the brown hare: use in maize. WSC Scientific GmbH, Dossenheimer Landstrasse 9/1 69121 Heidelberg Germany. Report Number 18014-SYN-2.* *Syngenta File No. A20718J_10073* ***This is CONFIDENTIAL INFORMATION****	*N*	*SYN*
KCP	*Brauer M. & Wang M.*	*2016*	*Effects of body weight reduction on survival and reproduction in rabbits (Oryctolagus cuniculus; L.) WSC Scientific*	*N*	*WSC*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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
10.1.2.2/10			*GmbH, Dossenheimer Landstrasse 9/1 69121 Heidelberg Germany. Report No. 15070-WSC* *Syngenta File No. NA_14946* ***This is CONFIDENTIAL INFORMATION****		
KCP 10.1.2.2/11	*Allen L.*	*2019*	*Mesotrione – Mesotrione – Foliage Decline Study on Clover in Hungary, Germany, United Kingdom, Northern France and Belgium in 2018.* *CEMAS, Imperial House, Oaklands Park, Wokingham, Berkshire, RG41 2FD, , UK* *Report No. CEMR-8397* *GLP, Unpublished* *Syngenta File No. A12738A_10535*	*N*	*SYN*
KCP 10.1.2.2 / 12	*Späth V.*	*1989*	*Untersuchungen zur Populationsökologie des Feldhasen (Lepus europaeus Pallas) in der Oberrheinebene* *Translation: Studies on the Population Ecology of the Field Hare (Lepus europaeus PALLAS) in the Upper Rhine Plain* *PhD thesis, University of Freiburg, Freiburg im Breisgau.* *Not GLP* *published* *Syngenta File No. VV-243592*	*N*	*-*
KCP 10.1.2.2 / 13	*Murfitt R., Foudoulakis M., Ebeling M., Guth K., Brugger K.*	*2015*	*Measured residues on maize foliage for use in bird and mammal risk assessment'* *Syngenta, Bracknell, UK; and others.* *Poster presented at SETAC Barcelona, 2015* *Not GLP* *published*	*N*	*-*
KCP 10.1.2.2 / 14	*Kleinmann J.*	*2020*	*Kleinmann J. (2020) Mesotrione - Population-level risk assessment for the brown hare: use in maize. Report Number 18014-SYN-4. WSC Scientific GmbH, Dossenheimer Landstrasse 9/1 69121 Heidelberg Germany.* *Syngenta File No. VV-847099* *Not GLP* *not published*	*N*	*SYN*
KCP 10.2.1 / 01	*Hengsberger A., Wydra V. (report amendment 2; Kosak L., Wydra V.)*	*2015 (amend.2 2016)*	*Mesotrione wet paste (ZA1296) - Toxicity to the aquatic plant Lemna gibba in a semi-static growth inhibition test with a subsequent recovery period* *Syngenta Crop Protection AG, Basel, Switzerland* *IBACON GmbH, Rossdorf, Germany, 105732240* *GLP* *not published* *Syngenta File No ZA1296_10438*	*N*	*SYN*

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 / 02	*Hengsberger A., Wydra V.*	*2015a*	*Mesotrione wet paste (ZA1296) - Toxicity to the aquatic plant Lemna gibba in a reciprocal growth inhibition test* *Syngenta Crop Protection AG, Basel, Switzerland* *IBACON GmbH, Rossdorf, Germany, 105731240* *GLP* *not published* *Syngenta File No ZA1296_10436*	*N*	*SYN*
KCP 10.2.1 / 03	*Gonsior G.*	*2017*	*Mesotrione - Growth inhibition of Myriophyllum spicatum in a water/sediment system* *Syngenta Crop Protection AG, Basel, Switzerland* *Eurofins Agroscience Services EcoChem GmbH, N-Osch., Germany, S16-06273* *GLP* *not published* *Syngenta File No ZA1296_10504*	*N*	*SYN*
KCP 10.3.1.2/01	*Wendling, K.*	*2018*	*Mesotrione - Honey Bee (Apis mellifera L.) Chronic Oral Toxicity Test 10 Day Feeding Test in the Laboratory,* *Eurofins Agroscience Services Ecotox GmbH, Eutinger Str. 24, 75223 Niefern-Öschelbronn, Germany* *Report Number S18-03658* *GLP, Unpublished* *Syngenta file No. ZA1296_10608*	*N*	*SYN*
KCP 10.3.1.3/01	*Eckert, J.*	*2016*	*Mesotrione - Honey bee (Apis mellifera L.) Larval Toxicity Test (Repeated Exposure through to Adult Emergence),* *Eurofins Agroscience Services Ecotox GmbH, Eutinger Str. 24, 75223 Niefern-Öschelbronn, Germany* *Report Number S16-00332* *GLP, Unpublished* *Syngenta file No. ZA1296_10465*	*N*	*SYN*
KCP 10.4.2.1 / 01	*Dickinson R.*	*2015*	*R169649 - Collembola (Folsomia candida) Reproduction Test in Soil* *Syngenta Crop Protection AG, Basel, Switzerland* *AgroChemex Ltd, Manningtree, United Kingdom, ENV-14-015* *GLP* *not published* *Syngenta File No CA3511_10011*	*N*	*SYN*
KCP 10.4.2.1 / 02	*Ramsden C.*	*2015*	*R169649 - Predatory Mite (Hypoaspis (Geolaelaps) aculeifer) Reproduction Test in Soil* *Syngenta Crop Protection AG, Basel, Switzerland* *AgroChemex Ltd, Manningtree, United Kingdom, ENV-14-012* *GLP* *not published*	*N*	*SYN*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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
			Syngenta File No CA3511_10010		

Appendix 2 Detailed evaluation of the new studies

No new additional studies have been submitted.
Information concerning detailed evaluation of the new studies relevant for risk assessment is included in RR for the reference product Callisto 100 SC. Since compositions of MEZ-HER 100 SC and Callisto 100 SC (product code: A12739A) are comparable, as well as data protection for Callisto 100 SC data has been expired, this point origins from RR of Callisto 100 SC of 21.09.2020 (written in italics, highlighted in yellow). For the full view of evaluation the zRMS comments have been also included to this document (written in italics, highlighted in yellow). These data have been assessed and accepted as well as are applicable for evaluation MEZ-HER 100 SC.

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

Comments of zRMS:	*The study summarised below was a new vertebrate study not required to finalise the risk assessment. No data gap in area of avian toxicity testing was identified in EFSA Journal 2016;14(3):4419. Taking this into account, the study was not evaluated and not considered in the risk assessment.* *The summary is thus struck through and shaded.*

Reference:	*KCP 10.1.1.1/01*
Report	*Hubbard PM, Davis RJ, Temple DL (2018). Mesotrione - An Acute Oral Toxicity Study with the Mallard Using a Sequential Testing Procedure. EAG, Inc. 8598 Commerce Drive Easton, MD 21601 USA* *Unpublished report number 528B-574. Experimental period June 28th 2018 to July 13th 2018* *(Syngenta File No. ZA1296_10605)*
Guideline(s):	*OECD Draft Guideline 223*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Not evaluated as submission of additional vertebrate study is not justified*
Duplication (if vertebrate study)	*No*

A 2.1.1.2 KCP 10.1.1.2 Higher tier data on birds

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

A 2.1.2.2 KCP 10.1.2.2 Higher tier data on mammals

zRMS comments: *The full summaries of the higher tier studies were not provided by the Applicant below. Instead, the reference was made to document by Alvarez (2019). In opinion of the zRMS, full summaries of studies considered for purposes of the risk refinement should be presented in the Core assessment in order to facilitate concerned Member States independent validation of their results. For this reason summaries of additional studies evaluated by the zRMS and considered in the risk assessment were completed below.*

Comments of zRMS:	*During the EU review it was already concluded that the common vole is not relevant focal species for maize at BBCH 12-18. Taking this into account, additional data supporting this conclusion were not necessary and the study by Fulling & Sainz-Elipe (2015) was not evaluated by the zRMS.*

Reference:	*KCP 10.1.2.2/01*
Report	*Fulling O. & Sainz-Elipe S. (2015) Generic field study on the presence and abundance of common voles in maize fields in Northern France, unpubl. tier3 solutions GmbH Report No. B15009* *Syngenta file No NA_13749 (Data owned by BASF, available to Syngenta by data agreement)*
Guideline(s):	*No guideline applicable. The study is consistent with guidance provided in EFSA Journal 2009; 7(12).*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Not evaluated; focal species for maize at BBCH 12-18 were already confirmed at the EU level*
Duplication (if vertebrate study)	*No*

Comments of zRMS:	*Reason for submission of the study by Prescott (2004) is unclear to the zRMS as its results were not used in the risk refinement.* *The study just confirms that wood mouse may feed on seeds, prefer some seeds over others and de-husk part of the seeds. All this information is already known from literature. It should be also noted that the risk assessment for the wood mouse is performed with consideration of weed seeds representing part of the diet, while the weed seeds were not included in the study, so it cannot be concluded if the wood mouse would de-husk weed seeds.* *As results of the study were not used in the risk assessment, the study was not evaluated by the zRMS in detail. However, the summary has been completed by the zRMS and retained below so concerned Member States could see that results of the study do not provide any particularly useful or new information that could be implemented into the risk refinement.*

Reference:	*KCP 10.1.2.2/02*
Report	*Prescott C. (2004). The assessment of Wood mouse acceptance /avoidance of different crop seeds when presented in free feeding conditions to individually caged animals in a six hour no-choice situation; and to monitor the incidence of de-husking for each seed type. University of Reading VPU Report. The Vertebrate Pests Unit School of Animal and Microbial Sciences, The University of Reading, Whiteknights, Reading. RG6 6AJ. UK. Syngenta study VPU/04/026. Syngenta File No. N/1014 (Data owned by Syngenta)*
Guideline(s):	*No guidelines available, but following recommendations in the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) and its appendices*
Deviations:	*No*
GLP:	*No*
Acceptability:	*Not evaluated as not used in the risk assessment*
Duplication (if vertebrate study)	*No*

Comments of zRMS:	*The study by Voigt & Zaccaroni (2013) was already evaluated by zRMS (UK) during zonal assessment of formulation Calaris (see Core Assessment, Part B, Section 6 of February 2018 available on CIRCABC). Following conclusions were derived:* *This was a non-GLP study conducted by the University of Veterinary Medicine, Hannover. The study assessed PT values for hares in Germany between March and June 2012. The*

	study area consisted of a number of crops including: cereals, sugar beet, maize, oilseed rape, bare soil and off crop. The following observations were noted by the zRMS. *As stated in EFSA bird and mammal guidance 2009 ideally the mammals would be visually observed when determining PT values. In this study the PT values were calculated based solely on GPS co-ordinates every 10 minutes and assumptions as to whether the hares are foraging. This adds major uncertainty to the study results.* *It was noted that none of the individuals tracked were still alive at the end of the study and there were technical issues meaning data was missing from eight individuals (33% of those initially tagged). These issues reduce the reliability of the study.* *The zRMS has only considered the PT results relevant to maize and in-line with the proposed use of 'Calaris' i.e. BBCH 11-18. In order to conduct a conservative risk assessment the zRMS has considered the 'worst case' consumer only (i.e. PT > 0) values. Only three PT values were above 0 in the target crop at the correct growth phase. Furthermore there were only two individuals as one was tracked in multiple weeks.* *According to the study author the hares demonstrated a low attraction to maize. However the zRMS considers this could be due to the relatively low amount of maize habitat in the study area during the study which reached a maximum of 16.5%. The low proportion of maize fields in the study site also adds uncertainty as to whether this study can be considered a reasonable 'worst-case' for assessing applications to maize in the central zone.* *Based on the low number of individuals (n = 2) and the other deficiencies noted above the zRMS does not consider this study suitable for risk assessment* *The zRMS for re-evaluation of formulation Callisto (PL) fully agrees with conclusions of the United Kingdom and confirms that results of the study are not suitable for the risk refinement purposes.* *As complete study summary supplemented with additional zRMS (UK) information was available in the mentioned zonal report for Calaris, it was copied and provided below in order to facilitate concerned Member States independent review and submission of the comments.*

Reference:	*KCP 10.1.2.2/03*
Report	*Voigt U., Zaccaroni M. (2013) Generic field monitoring of hares in a mixed landscape in Germany, Report Number BAR/FS069, University Of Veterinary Medicine Hannover, Bünteweg 2 30559 Hannover Germany. (Syngenta File No. NA_13449) Study owner BCS, Syngenta have access.*
Guideline(s):	*No guidelines available, but following recommendations in the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) and its appendices*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Already evaluated by zRMS (UK) during zonal assessment of formulation Calaris (see Core Assessment, Part B, Section 6 finalised in February 2018). Results of the study were considered unreliable.*
Duplication (if vertebrate study)	*No*

Comments of zRMS:	*Due to various deficiencies, the study by Voigt & Zaccaroni (2013), summarised above in KCP 10.1.2.2/03, is considered not suitable for the risk refinement purposes. Taking this into account, calculation of Jacobs Indices based on results of this study is also unreliable and was thus not evaluated by the zRMS.*

Reference:	*KCP 10.1.2.2/04*
Report	*Voigt U., Zaccaroni M. (2015) Generic field monitoring of hares in a mixed landscape in Germany – Jacobs Index; Report Number BAR/FS069, University of Veterinary Medicine*

	Hannover, Bünteweg 2 30559 Hannover Germany. (Syngenta File No. NA_13997) Study owner BCS, Syngenta have access.
Guideline(s):	*No guidelines available*
Deviations:	*No*
GLP:	*No*
Acceptability:	*Not evaluated as study by Voigt & Zaccaroni (2015) considered as not sufficiently reliable to be implemented into the risk assessment (see evaluation of the study in KCP 10.1.2.2/03 above).*
Duplication (if vertebrate study)	*No*

Comments of zRMS:	*The study by Dittrich & Benito (2016) was performed in the Southern France (department of Ariège and HauteGaronne, region of Midi-Pyrénées) so it results are not representative for conditions of the Central Zone. Taking this into account the study was not evaluated by the zRMS and not considered for purposes of the risk refinement.*

Reference:	*KCP 10.1.2.2/05*
Report	*Dittrich R. and Benito M.M. (2016) Occurrence and PT of Wood mice in pre- and post-emergence maize fields in France, southern zone. Report Number B15064. tier3 solutions GmbH, Kolberger Str. 61-63, 51381 Leverkusen, Germany* *Study owner Bayer – Syngenta has access* *(Syngenta File No. NA_14235 ~~14237~~)*
Guideline(s):	*No guidelines available*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Not evaluated as not representative for the Central Zone (study performed in the Southern France).*
Duplication (if vertebrate study)	*No*

Comments of zRMS:	*The aim of the study by Grimm & Katzschner (2019) was to determine the proportion of time the brown hares spent potentially foraging in early germinated maize fields (BBCH <20).* *The study was well performed and is considered acceptable by the zRMS. The full study summary has been provided by the zRMS below in order to facilitate concerned Member States independent review and submission of the comments.* *Initial site selection in the study was based on the presence of the European hare, high proportions of maize fields within the landscape and the suitability for performing radio-tracking. To increase representativeness and variability of landscape parameters among Central European maize growing areas, two different study areas in two different countries and five different study sites were chosen in areas of high proportions of maize within Central Europe. The region used for the study represented typical maize growing region in Germany and Hungary and may be thus considered representative for conditions of the Central Zone. However, concerned Member States may wish to re-consider representativeness of the conditions of the study for agronomic conditions in their countries.* *At test sites the maize fields represented on average 36% of the landscape surface within the investigated hares home ranges and at some test sites their proportion in the total landscape exceeded 45 or even 50%.* *The study was performed at early stages of maize and included BBCH from 00 to 19. However, as the aim of the study was to determine the time that brown hares potentially feed*

	on maize shoots, results for fields with BBCH <09 were excluded from calculation of PT values. *For purposes of the radio-tracking, 23 individual adult brown hares were trapped and equipped with the radio tags. Trapping locations were chosen in areas with high number of maize/future maize fields and hares were captured either in such fields or nearby (e.g. in adjacent off-crop structures or neighbouring fields).* *The total weight of the hare collar was about 40 g, representing approximately 1% of the bodyweight of the tagged animals. Due to the low weight of the tags (far below the recommended maximum of 5% of the total bodyweight) it was not expected that they would have influence the animals' behaviour. Visual observations confirmed normal behaviour of the animals. In order to give animal time to acclimatize, the radio-tracking started no earlier than 2 days after tagging with single check telemetry of the individuals.* *During the telemetry sessions each individual was tracked continuously for 24 hours, which is in line with recommendations of EFSA (2009). During this time all movements between different habitats and changes of the behaviour (e.g. foraging, resting) were recorded. In addition to that, animals were observed with binoculars, scopes and night observation devices.* *During radio-tracking without visual contact, all instances of an active signal were interpreted as potential foraging behaviour and thus included in the calculation of PT values. However, based on the behaviour confirmed by visual contacts during the 24h telemetry, animals foraged for just 32.0% of their visually observed time and showed active behaviour other than foraging in 18.5% of the time. Therefore, the time spent potentially foraging in maize is rather overestimated for this habitat. This confirms that the PT values are conservative and rather overestimate the actual PT values for early maize (BBCH growth stages up to 20) than being a minimum value.* *In general, results of the study indicate that brown hares do utilise early maize fields as the feeding habitat. During the 24-hours radio-tracking session most of 23 radio-tagged hares were observed in maize fields with individual PT values ranging from 0.02 to 0.94. One individual (or signal) could not be tracked after tagging and most probably the animal left the study site. One individual was found at the end of May far outside the study site. To increase the number of radio-tracking sessions and to cover wider range of BBCH stages, two individuals were radio-tracked twice, giving 23 radio-tracking sessions in total. One session was excluded from further calculations as being not "consumer session" (animal was never located in a maize field being active during the session, had no maize in the 24h home range and was not caught on a maize field).* *Taking into account that 21 individuals (i.e. >20 recommended by EFSA, 2009) were observed potentially foraging during radio-tracking sessions (with one animal observed twice), in opinion of the zRMS the 90th percentile PT value is sufficiently reliable and may be used for purposes of the refinement of the risk for the brown hare.* *It should be noted that PT values were derived for maize stages ranging from BBCH 09 to 19, while formulation Callisto is intended to applied at BBCH 11-18 ~~12-18~~. Nevertheless, obtained results show that different BBCH growth stages up to <20 did not have an impact on the use of maize as foraging habitat by the brown hare. Taking this into account, the overall 90th percentile PT of 0.62 is considered acceptable for purposes of refinement of the risk to the brown hare exposed after application of Callisto according to the intended use pattern. Concerned Member States may wish to re-consider this value.* *Following the commenting period additional information regarding the test sites, the habitat proportions as well as the number of individual animals radio-tracked were added to the study summary.* *It was also questioned by AT, if it was appropriate to calculate the 90th percentile PT for the whole study period, as more tracking sessions were performed at BBCH <15, while less were performed at BBCH >15.* *First of all it should be noted that that in EFSA (2009) the BBCH 10-19 is treated as a single period for early maize with no differentiation for single stages, which is captured in the study by Grimm and Katzschner (2019).*

	Furthermore, in opinion of the zRMS, available results show that PT values for the whole period of study were comparable. For example, the maximum PT of 0.89 derived for BBCH 12-14 is close to maximum PT of 0.94, derived for BBCH 15-19. *The next highest value of 0.56 for BBCH 10-11 (derived in both, Germany and in Hungary) is close to 0.63 at BBCH 15-19. The lowest PT of 0.23 for BBCH 15-16 is even lower than several PT values for BBCH 10-15.* *In addition to that, the mean PT values of 0.35 and 0.39 were calculated for BBCH <15 (16 sessions) and >15 (6 sessions), respectively, which demonstrates that derived PT values have not depended on the growth stage.* *Therefore, in our opinion, PT values calculated for the whole period of study are comparable and may be merged in order to derive single 90th percentile PT.* *AT raised also concerns regarding several low PT values derived for 5 individuals. The zRMS would like to point out that animals for which low PT values were calculated spent more time in other habitats (e.g. meadow, for which the 90th percentile PT of 0.76 was calculated in the study report, respective table has been added to the study summary). With together 23 animals radio-tracked variable habitat preference could be expected but even with several low values (i.e. 5 animals with PT <0.1) the derived 90th percentile PT is more robust than the maximum PT taken from the study where telemetry data are available for only e.g. 6 animals, which is frequently seen in such studies, especially older ones.*

Reference:	*KCP 10.1.2.2/07*
Report	*T Grimm and I Katzschner (2019) Generic monitoring of European hares to determine proportion of time spent foraging in early maize in Central Europe* *Syngenta Limited; unpubl. RIFCON GmbH report No. R1740045, March 2019.* *Syngenta File No. NA_14950*
Guideline(s):	*No official test guideline(s) available at present* *Conducted under consideration of the EFSA Guidance Document on Risk Assessment for Birds & Mammals (EFSA 2009).*
Deviations:	*Not relevant*
GLP:	*Yes*
Acceptability:	*Acceptable*
Duplication *(if vertebrate study)*	*No*

Executive Summary

The aim of this generic study was to investigate the use of maize fields as foraging habitat by Brown hare (Lepus europaeus) in the Central Europe. Focus was the determination of respective PT values (i.e. proportion of diet obtained in treated area, calculated as proportion of potentially foraging time spent in maize fields by hares) during the early growing period of maize via continuous 24-hour radio-tracking sessions of multiple individual hares. In total, radio-tracking sessions of 21 individual hares at five study sites were performed during the early crop development of maize in Central Europe. Radio-tracking sessions were performed from late April until early June 2018. The number of conducted 24h telemetry sessions was 23 (17 in Germany, six in Hungary), since two individuals were radio tracked twice.
The calculated single PT values ranged from 0.02 to 0.94 resulting in an average of 0.36 (±0.26) and 90th percentile of 0.62. Calculated PT values did not differ substantially between different study sites; mean values were slightly higher in Germany (0.38) than in Hungary (0.31).

Materials

Test Material	*No substance was tested.*
Test organisms	
Species:	*European brown hare (Lepus europaeus)*
Crop:	*Maize, BBCH 00-19*
Test design	

Replication: *5 study sites*
Duration of study: *3 months*

Study Design and Methods

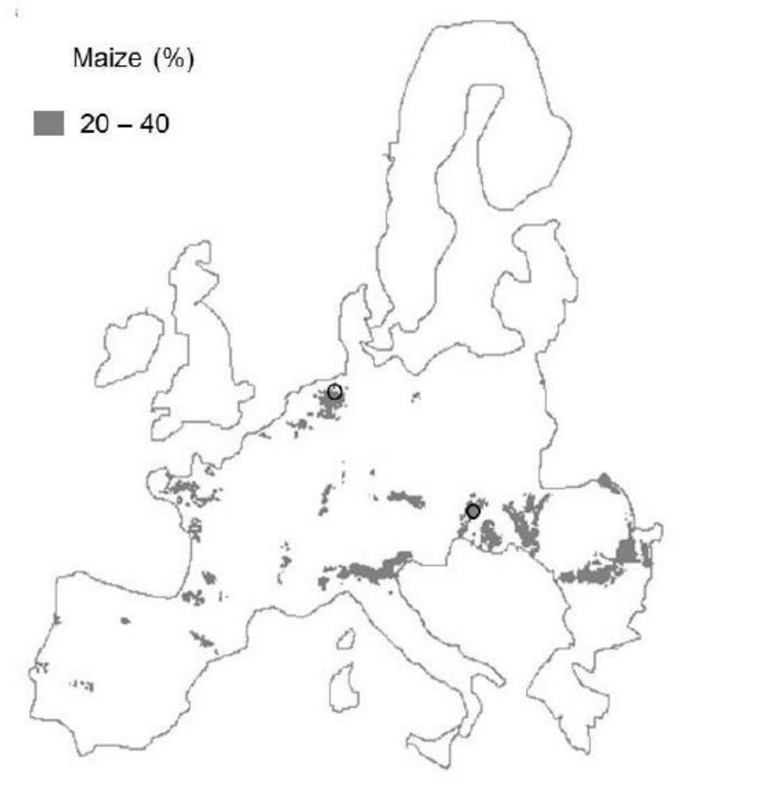
Experimental dates: April - June 2018

Study sites

The study was conducted in five study sites in Central Europe in two main areas for maize growing (with on average 36 % of the landscape surface within the home ranges of the investigated hares comprising maize). Three study sites were located in Lower Saxony (Germany), near Holtrop, Rastede and Burhafe, and two study sites were located in the administrative county Győr-Moson-Sopron (Hungary), one near Szany and one close to Bösarkany. Detailed information regarding the test locations is given in the below table.

Country	***Study site***	***Location of the study site***		
		Coordinate system	***Easting***	***Northing***
Germany	*Rastede*	*WGS 84 UTM 32 U*	*0447698*	*5902051*
	Burhafe	*WGS 84 UTM 32 U*	*0415313*	*5938465*
	Holtrop	*WGS 84 UTM 32 U*	*0404171*	*5920188*
Hungary	*Bösarkany*	*WGS 84 UTM 33 T*	*0665111*	*5284131*
	Szany	*WGS 84 UTM 33 T*	*0672548*	*5256137*

The proportion of maize of the total landscape surface even exceeded 45% (in the study site Rastede, Germany) and 50 % (in the study site Bösarkany, Hungary) which represents the highest coverage of maize on regional scale known in Central Europe. The crop cover map of maize in Europe (with proportion of maize >20%) together with test sites location (marked with black circles) is presented on figure below.



modified map
Source: Report on the activities realized within the Service Level Agreement between JRC and EFSA as a support of the FATE and ECOREGION Working Groups of EFSA PPR (SLA/EFSA-JRC/2008/01) 2010

Crop cover map of maize in Europe and location of the study sites (the map presents all areas in Europe in which the proportion of maize cover of the total land surface is more than 20%)

Review of habitat proportions based on all habitats within the outermost locations during 24h telemetry of all individuals per study site is given in table below.

Country	*Study site*	*Habitat [%]*						
		*Arable crops other than maize **	*Forest/hedges*	*Others ***	*Meadow*	*Maize*		
						Total maize	*Post-emergence*	*Pre-emergence*
Germany	*Burhafe*	*0.26*	*7.02*	*1.21*	*76.74*	*14.76*	*14.76*	*0.00*
	Holtrop	*2.87*	*16.53*	*6.60*	*42.61*	*31.39*	*29.81*	*1.59*
	Rastede	*0.00*	*16.85*	*5.75*	*30.95*	*46.45*	*46.45*	*0.00*
	Total G	***1.75***	***16.33***	***6.12***	***39.54***	***36.26***	***35.29***	***0.96***
Hungary	*Bösarkany*	*34.02*	*8.36*	*1.83*	*1.32*	*54.48*	*44.91*	*9.57*
	Szany	*63.74*	*9.26*	*2.83*	*0.63*	*23.54*	*22.27*	*1.27*
	Total H	***51.71***	***8.89***	***2.42***	***0.91***	***36.06***	***31.44***	***4.63***
Total		***23.83***	***13.05***	***4.48***	***22.47***	***36.17***	***33.59***	***2.58***

** Cereal, lucerne, sunflower, oilseed rape, other crops (e.g. potato), stubble and ploughed fields*
*** Streets, settlements, water*

The proportion of maize and other arable land within the study sites and number of sessions per study site are presented in the table below.

Country	*Study site*	*Habitat [%]*			*No of 24h telemetry sessions*
		*Arable crop other than maize **	*Meadow*	*Maize ***	
Germany	*Burhafe*	*0.28*	*83.63*	*16.09*	*1*
	Holtrop	*3.74*	*55.43*	*40.84*	*10*
	Rastede	*0.00*	*39.99*	*60.01*	*5*
	Total Germany	***2.26***	***50.98***	***46.75***	***16***
Hungary	*Bösarkany*	*37.88*	*1.47*	*60.65*	*3*
	Szany	*72.51*	*0.71*	*26.78*	*3*
	Total Hungary	***58.31***	***1.02***	***40.67***	***6***
Total		***28.90***	***27.24***	***43.86***	***22***

** Cereal, lucerne, sunflower, oilseed rape, other crops (e.g. potato), stubble and ploughed fields*
*** Including pre-emergence maize fields*

The vegetation status of maize in the study sites was recorded using BBCH growth stage scale. The study sites, comprising the area around the trapping locations of the tagged animals and the positions in which they were recorded during single checks and 24h telemetry, were mapped. Surveys of drilled maize fields before the emergence of maize plants showed that virtually no weeds occurred on these fields, indicating that pre-emergence maize fields are likely to be unattractive habitats for hares due to their lack of food and cover.

Trapping

The majority of animals were trapped and fitted with radio tags at the beginning of the Field Phase (i.e. before the drilling of maize). All tracked hares were captured either on future maize fields (i.e. fields to become maize fields later once drilled), already drilled maize fields or nearby in off-crop structures around such maize fields.
Hares were trapped using series of nets. The animals were chased into these nets by beaters walking towards the net line.
Each trapped animal was sexed, weighed and equipped with a radio tag (Biotrack Ltd., UK; www.biotrack.co.uk) and released at the trapping site.

Radio-tracking

For radio-tracking, animals were located with Yagi antennas according to two different approaches: single check telemetry and 24h telemetry.
For single check telemetry each animal was located once at the beginning (after all hares were tagged) and the end of the entire Field Phase (when 24h telemetry was finished) in order to survey its presence in the respective study site during the entire Field Phase.
During 24h telemetry sessions the animal was radio-tracked continuously for 24 hours by two observers, locating the animal from two different positions, which allowed triangulating the animal's exact position.

Each change of habitat (if possible) and/or each change of behaviour (i.e. active/inactive) was recorded with time and bearing angle to the signal of the animal. The 24h telemetry sessions were conducted when the BBCH growth stages of the maize fields were <20. Main focus was given to the period of emergence until the end of leaf development (i.e. BBCH growth stages 09 to 19).

In order to confirm the animals' behaviour based on the radio signals, animals were observed with binoculars, scopes and night observation devices to get 'visual contact' whenever possible.

Calculation of PT

For each telemetry session, the proportion of diet obtained in maize fields (PT) was calculated as the proportion of the 'potentially foraging' time the individual hare spent in that crop. Thus, the 'time potentially foraging' is the sum of the time periods covered by behavioural categories when foraging could not be excluded. All instances when the animal was definitely known to be performing non-foraging activities (e.g. resting or fighting) were excluded from PT calculations.

A mean PT value (± standard deviation) and 90th percentile values were calculated based on all single PT values. In addition, the total visual contact time and the respective behaviour categories during 24h telemetry were calculated in order to compare behaviour categories based on radio-tracking signals with behaviour confirmed via visual contact.

Results and Discussion

In total, radio-tracking sessions of 21 individual hares at five study sites were performed during the early crop development of maize in Central Europe. Radio-tracking sessions were performed from late April until early June 2018. The number of conducted 24h telemetry sessions was 23 (17 in Germany, six in Hungary), since two individuals were radio tracked twice. One session had to be excluded from analysis, as this session was not considered as a 'consumer session' since the animal was never located being 'active' in a maize field during the session, had no maize in the 24h home range, and was not caught on a maize field.

Maize fields covered on average approximately 36% of the total landscape surface and 44% of the arable land surface within the 24h home ranges of hares in all study sites.

The calculated single PT values ranged from 0.02 to 0.94 resulting in an average of 0.36 (±0.26) and 90th percentile of 0.62. Calculated PT values did not differ substantially between different study sites; mean values were slightly higher in Germany (0.38) than in Hungary (0.31).

Drilled maize fields which were not yet emerged were checked in each study site for the occurrence of weeds at the beginning of the Field Phase (except of Szany, where all maize fields, except one, were already emerged). Fields that were still not emerged prior to the start of 24h radio-tracking were checked for weed occurrence again (one field in Holtrop, one field in Szany and two fields in Bösarkany). Each survey showed that no weeds occurred on not yet emerged maize fields in the five study sites. Therefore since hares on those fields could not be foraging, those results were excluded from the PT analysis. This is clear from the photographs included in the report.

Calculated PT values of hares in maize fields in early BBCH growth stages (BBCH growth stage <20) in Central Europe

Country	***Session ID***	***PT***	***Animal No***	***Date (dd.mm.2018)***	***BBCH for maize fields inside the 24h home range***
Germany	*398_GER_01*	*0.56*	*14_G*	*18.05.*	*10-11*
	398_GER_02	*0.40*	*18_G*	*19.05.*	*09-11*
	398_GER_03	*0.17*	*23_G*	*20.05.*	*10-12*
	398_GER_04	*0.08*	*20_G*	*23.05.*	*11-12*
	398_GER_05	*0.50*	*17_G*	*22.05.*	*11-12*
	398_GER_06	*0.09*	*13_G*	*23.05.*	*12*
	398_GER_07	*0.08*	*19_G*	*22.05.*	*11*
	398_GER_08	*0.02*	*21_G*	*24.05.*	*12*
	398_GER_09	*0.44*	*15_G*	*25.05.*	*13*
	398_GER_10	*0.41*	*16_G*	*26.05.*	*13*
	398_GER_12	*0.18*	*1_G*	*27.05.*	*12-14*
	398_GER_13	*0.89*	*5_G*	*28.05.*	*12-14*
	398_GER_14	*0.37*	*4_G*	*30.05.*	*13*
	398_GER_15	*0.26*	*3_G*	*01.06.*	*15-16*
	398_GER_16	*0.94*	*5_G*	*04.06.*	*15-19*
	398_GER_17	*0.63*	*1_G*	*05.06.*	*15-19*
Hungary	*398_HU_01*	*0.42*	*15_H*	*29.04.*	*10-13*
	398_HU_02	*0.38*	*14_H*	*30.04.*	*13*
	398_HU_03	*0.56*	*13_H*	*02.05.*	*13-14*
	398_HU_04	*0.28*	*1_H*	*13.05.*	*13-15*
	398_HU_05	*0.21*	*2_H*	*14.05.*	*14-15*
	398_HU_06	*0.02*	*3_H*	*15.05.*	*15*
Mean		***0.36***	*-*	*-*	*-*
90th percentile		***0.62***	*-*	*-*	*-*
SD		***0.26***	*-*	*-*	*-*

The total visual contact time during all 24h-telemetry sessions was 68 hours and 39 minutes which reflects 12% of the total radio tracking time of 552 hours. In 49% of the visually observed time, hares were classified as resting. The active behaviour during visual contact was classified as 'foraging behaviour' for 32% and as 'other behaviour' (such as e.g. fighting, running or grooming) for 19%.

For 5 animals low PT values were calculated in maize (PT <0.1), but it should be pointed out that these animals preferred other habitats than maize fields. In order to support this information, PT values calculated for different habitats are presented in table below.

Calculated PT values of hares in various habitats in the study

Country	***Session ID***	***PT maize***	***PT meadow ****	***PT all other habitats***	***Date (dd.mm.2018)***	***Animal No***
Germany	*398_GER_01*	*0.56*	*0.24*	*0.20*	*18.05.*	*14_G*
	398_GER_02	*0.40*	*0.44*	*0.16*	*19.05.*	*18_G*
	398_GER_03	*0.17*	*0.76*	*0.07*	*20.05.*	*23_G*
	398_GER_04	*0.08*	*0.51*	*0.41*	*23.05.*	*20_G*
	398_GER_05	*0.50*	*0.32*	*0.18*	*22.05.*	*17_G*
	398_GER_06	*0.09*	*0.75*	*0.16*	*23.05.*	*13_G*
	398_GER_07	*0.08*	*0.62*	*0.30*	*22.05.*	*19_G*
	398_GER_08	*0.02*	*0.73*	*0.25*	*24.05.*	*21_G*
	398_GER_09	*0.44*	*0.46*	*0.10*	*25.05.*	*15_G*
	398_GER_10	*0.41*	*0.14*	*0.45*	*26.05.*	*16_G*
	398_GER_11		*0.80*	*0.20*	*27.05.*	*22_G*
	398_GER_12	*0.18*	*0.52*	*0.30*	*27.05.*	*1_G*
	398_GER_13	*0.89*	*0.07*	*0.04*	*28.05.*	*5_G*
	398_GER_14	*0.37*	*0.53*	*0.10*	*30.05.*	*4_G*
	398_GER_15	*0.26*	*0.66*	*0.08*	*01.06.*	*3_G*
	398_GER_16	*0.94*	*0.05*	*0.01*	*04.06.*	*5_G*
	398_GER_17	*0.63*	*0.32*	*0.05*	*05.06.*	*1_G*
Hungary	*398_HU_01*	*0.42*	*-*	*0.58*	*29.04.*	*15_H*
	398_HU_02	*0.38*	*-*	*0.62*	*30.04.*	*14_H*
	398_HU_03	*0.56*	*-*	*0.44*	*02.05.*	*13_H*
	398_HU_04	*0.28*	*-*	*0.69*	*13.05.*	*1_H*
	398_HU_05	*0.21*	*-*	*0.79*	*14.05.*	*2_H*
	398_HU_06	*0.02*	*-*	*0.98*	*15.05.*	*3_H*
Mean		*0.36*	*0.47 **	*0.31*	*-*	*-*
90th percentile		*0.62*	*0.76 **	*0.68*	*-*	*-*
SD		*0.26*	*0.24 **	*0.27*	*-*	*-*

** For 'PT meadow' values are given for sessions conducted in Germany only due to the low proportion of meadows in Hungary. Hence mean, 90$_{th}$ percentile and SD values are calculated based on the sessions in Germany only.*

Conclusion

This study demonstrated that maize fields, at pre-emergence growth stage, are in general not relevant foraging habitats for hares.
This report gives most appropriate, reliable and robust PT values for European hares using maize fields during early growth stages (BBCH growth stages < 20) in Central Europe for the use in wildlife risk assessments according to the recommendations of EFSA (2009). Values were calculated under worst-case assumptions (such as highest maize proportions in the study areas, data evaluation of 'consumers' only and therefore high exposure risk for each individual) and the PT values are considered to be conservative.

Comments of zRMS:	*The comprehensive summary of the comparison of both models was not provided by the Applicant and it was not possible for the zRMS to copy all the relevant information.* *Nevertheless, the conclusions provided below reflect the overall assessment of both models and it may be concluded that POLARIS model is more suitable to perform the regulatory risk assessment, especially there is possibility for parametrisation in line with EFSA (2009).*

Reference:	*KCP 10.1.2.2/08*
Report	*Kleinmann J (2019) Comparison of POLARIS Brown hare and ALMaSS Brown hare for use in Pesticide Risk assessments. WSC Scientific GmbH, Dossenheimer Landstrasse 9/1 69121 Heidelberg Germany.Report Number 18014-SYN-1. MWc, Germany.* *Syngenta File No. A20718J_10072*
Guideline(s):	*Conducted under consideration of the EFSA Guidance Document on Risk Assessment for Birds & Mammals (EFSA 2009).* *Also the good modelling practice guideline*
Deviations:	*No*
GLP:	*Yes*

Acceptability:	*Conclusions of the author are agreed by the zRMS*
Duplication (if vertebrate study)	*No*

Conclusion:

Two individual based population models on Brown hare (Lepus europeaus) are published in the scientific literature. These are ALMaSS Brown hare, published by Topping et al. (2010) and POLARIS Brown hare, published by Kleinmann and Wang (2017). In order to evaluate if these models are suitable for the pesticide risk assessment and which strengths each model offers, both models have been evaluated and compared to each other. This comparison included: (i) model documentation, (ii) conceptual differences, (iii) parameterisation, (iv) implementation of the models in a computer program and (v) validation of the model.

For both models documentation is available. However, while for one model documentation for POLARIS Brown hare is available which includes all relevant information, for ALMaSS information needed to be collected from different sources and the documentation overall was much less detailed and sometimes missing (information could partly be found only in the C++ source code). Regarding the conceptual differences of the models, the largest difference was that most processes in ALMaSS Brown hare are based on energy budgets of individual hares. This energy budget simulation results in a much more complex model compared to POLARIS Brown hare, in which no individual energy budgets are simulated. In contrast, individual variation results from the combination of parameter distributions derived from the literature.

Overall, ALMaSS Brown hare seems to be developed for academic purposes (e.g. to evaluate the effect of changing landscape structure or management; Topping et al., 2003) whereas POLARIS Brown hare was developed specifically for the purpose of conducting pesticide risk assessments according to EFSA (2009). This is also reflected in the parameterisation and validation. In particular the validation of ALMaSS Brown hare is very short and mainly conducted using patterns from population density and growth, while the authors of POLARIS Brown hare aimed to cover all parts of brown hare biology (reproduction, survival, population density, growth and spatial behaviour) that they considered relevant for the risk assessment. Also, the implementation of the models reflects their purpose. A graphical user interface (GUI) is available for POLARIS Brown hare which also includes a dedicated risk assessment module for the risk assessment according to EFSA (2009). However, for ALMaSS no GUI is available and scenarios need to be parameterised in text files; no risk assessment module is available so effects from pesticide treatment need to be hardcoded) and results of analysis need to be analysed using separate software tools.

In conclusion, both models are able to produce results which can be analysed in the context of a population level risk assessment. While for POLARIS the model structure, parametrisation, validation, etc. is described in detail in the model documentation and while risk assessments can be done relatively easily using the GUI, the documentation of ALMaSS Brown hare is incomplete and a risk assessment cannot be done easily. From the available ALMaSS documentation it is hard for risk assessors and regulators to evaluate the model and the results of a risk assessment regarding their uncertainty and validity.

Comments of zRMS:	*The population modelling for brown hare performed using POLARIS model was evaluated by the zRMS and due to some deficiencies identified it is considered to be supportive information. No comprehensive summary was presented by the Applicant in the dRR and for this reason the key input parameters and deficiencies identified were shortly described by the zRMS in the commenting box in point 9.3.2.2 of this document. Results are also presented there together with the evaluation of the performed modelling. It should be, however, noted that in absence of the commonly agreed approach towards evaluation of population modelling and implementation of its results into the regulatory risk assessment, each cMS has to review the population modelling by Kleinmann (2019a) and decide on its acceptability and applicability at the national level. The zRMS evaluation should be thus treated as illustrative rather than conclusive.* *The Applicant is requested to provide the extent summary in an editable form in order to enable the zRMS its inclusion in the Core Assessment for reference of concerned Member*

	States. Despite this request, the summary was not provided by the Applicant so it could not be presented in this updated version of the Core Assessment. *The Applicant is also kindly reminded that the Core Assessment should be a stand-alone document, where all data considered in evaluation are summarised and all refinement options are presented together with their justification. This enables the zRMS to comment on considered parameters and facilitates concerned Member States independent validation of the data.*

Reference:	*KCP 10.1.2.2/09*
Report	*Kleinmann J (2019a) Mesotrione - Population-level risk assessment for the brown hare: use in maize. Report Number 18014-SYN-2. WSC Scientific GmbH, Dossenheimer Landstrasse 9/1 69121 Heidelberg Germany.* *Syngenta File No. A20718J_10073*
Guideline(s):	*Conducted under consideration of the EFSA Guidance Document on Risk Assessment for Birds & Mammals (EFSA 2009).* *Also the good modelling practice guideline*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Considered as supportive information, evaluation of the zRMS and more detailed information on input parameters are presented in point 9.3.2.2 of this document*
Duplication (if vertebrate study)	*No*

Conclusion:

This report details a population-level risk assessment which has been conducted for the herbicide mesotrione, applied in maize at a rate of 1 x 150 g a.s./ha, to address the chronic risk to brown hare (Lepus europaeus).

Simulations were conducted with the population model for the brown hare implemented in the commercial software POLARIS. This population model was developed in line with a recent EFSA opinion on good modelling practice (EFSA, 2014). The model, which has recently been published (Kleinmann and Wang, 2017a), is validated and documented in detail, including parameterisation, model verification, calibration, sensitivity analysis and validation. The entities of the model are the landscape and the individual hares. The landscape consists of multiple habitats, each characterised by habitat type (e.g. grassland) and amount of food resources. Individuals are characterised by the state variables: age, gender, developmental stage (lactating offspring, subadult, adult), reproductive status (breeding or non-breeding), fertility (fertile, infertile; applies to females only), pregnancy. Exposure is simulated for each individual according to its daily movement. Most processes defined in the model are updated in daily time steps for each individual. However, movement is simulated on a smaller time step, depending on the individual daily walking distance.

Based on a recent publication of Kleinmann and Wang (2017a) in which the worst-case character of landscapes for brown hare risk assessments has been evaluated, a landscape was selected for application in maize. This landscape was characterised by a high proportion of maize fields (30% of the landscape consisted of maize) in a mixed agricultural landscape. Since brown hares densities are low compared to other small mammals (<10 hares per 100 ha) a relatively large simulation landscape (>1000ha) is necessary for the evaluation in order to obtain robust population sizes. The suitability of the landscape for use in risk assessment was confirmed by applying a hypothetical 'toxic standard' i.e. by applying e.g. 25% mortality, 25% reduced pup production or 5% reduced body weight per day for all hares in maize fields. Results showed that this landscape was sufficiently sensitive to detect effects. Additionally, a comparison of PT values from model simulations and PT values from a field study demonstrated that the simulations produced realistic, but slightly worst-case PT.

The parameterisation of adverse effects due to application of mesotrione was based on the findings from a multi-generation study in rat (Milburn, 1997). For the simulations the endpoints decreased body weight, reduced litter size and reduced pup survival were considered. Exposure of each hare was calculated using default values from the EFSA (2009) and considering a default DT_{50} value of 10 days for ground vegetation in maize (EFSA, 2009). Simulations were run for 20 years. During these 20 years, applications were simulated for 10 years (year 6 to 15). Population level effects were assessed based on a comparison of the exposed population density to the untreated control density at the end of each of the 10 years with treatment.

*Simulations with the population model showed that for an **E**xposure **M**ultiplication **F**actor (EMF) up to 5x the maximum intended application rate of mesotrione of 150 g/ha no relevant effects (above the limit of detection of 5%) were observed. The results from this risk assessment can be considered worst case for the following reasons: First, in the two-generation study by Milburn (1996 exposure over 28 weeks) animals were continuously exposed to mesotrione over several months while exposure in the field is predicted to be much shorter because of the low substance specific foliar DT_{50} ($DT_{50} \leq 2.05$ d; references in Alvarez, 2019). Second, a landscape with a high proportion of maize fields was considered; the worst-case character of this landscape had previously been confirmed. Third, a closed population with no immigration was considered in modelling, hence there was no possibility of recovery by immigration. Overall, the risk assessment includes a margin of safety of >19. Based on these results no unacceptable effects are expected for real populations at the maximum intended application rate under worst-case field conditions and hence a negligible risk can be concluded.*

Overall it can be concluded that no unacceptable risk to brown hare populations is expected following application of mesotrione in maize at 150 g a.s./ha.

Comments of zRMS:	*As in case of other higher tier studies, no comprehensive summary was presented by the Applicant in the dRR and for this reason some additional information has been copied from the paper by the zRMS and inserted below.* *Nevertheless, as the paper is actually 48 pages literature review including multiple tables and figures, it was not possible for the zRMS to provide here all the relevant data. Instead, a table with summary of all considered papers and figure presenting results of meta-analysis are presented.* *It should be noted that results of the review by Brauer & Wang (2016) were used for parametrisation of the model used in population modelling. However, in absence of the commonly agreed approach towards evaluation of population modelling and implementation of its results into the regulatory risk assessment, each cMS has to review the population modelling by Kleinmann (2019a) and decide on its acceptability and applicability at the national level. This concerns also all other accompanying documents considered for parametrisation of the model, including paper by Brauer and Wang (2016). Therefore the zRMS evaluation should be treated as illustrative rather than conclusive.* *The Applicant is kindly reminded that the Core Assessment should be a stand-alone document, where all data considered in evaluation are summarised and all refinement options are presented together with their justification. This enables the zRMS to comment on considered parameters and facilitates concerned Member States independent validation of the data.* *Despite request for submission of the comprehensive summary, it was not provided by the Applicant so it could not be presented in this updated version of the Core Assessment.*

Reference:	*KCP 10.1.2.2/10*
Report	*Brauer M. & Wang M. (2016) Effects of body weight reduction on survival and reproduction in rabbits (Oryctolagus cuniculus; L.) WSC Scientific GmbH, Dossenheimer Landstrasse 9/1 69121 Heidelberg Germany. Report No. 15070-WSC* *Syngenta File No. NA_14946*
Guideline(s):	*Not applicable*

Deviations:	*No*
GLP:	*Not applicable*
Acceptability:	*Acceptable as supportive information, but its acceptability and applicability must be confirmed by concerned Member States at the national product authorisation*
Duplication (if vertebrate study)	*No*

Executive Summary

The present study extends the findings of a previous literature study conducted for small farmland mammals (Brauer and Wang, 2014) with data for European rabbit (Oryctolagus cuniculus). This previous study aimed at understanding how reduced body weight may affect population relevant parameters, such as mortality or reproduction based on public literature data (laboratory and field data), re-evaluations of raw data and an overall meta-analysis. Brauer and Wang (2014) had been found that lower body weight only resulted in reduced survival or reproduction when weight was >20% reduced. Below this level no adverse, but sometimes even positive effects were observed (e.g. on survival).

Study Design and Methods

A literature research was conducted focussing on effects of reduced body weight on survival and reproduction of rabbits. The review was conducted based on scientific journals and monographs. The following key words were used and combined with the species name Oryctolagus cuniculus or rabbit:

- *body weight, weight loss, growth, starvation, deprivation, nutritional influences, diet, feed, food supply, caloric, restriction, protein, health*
- *litter size, offspring, reproduction, sexual maturation, breeding, pregnant, puberty, pups, adults, energy, intake, survival, mortality, longevity, behaviour, development*
- *population, ecology, laboratory, field*

Only articles in which body weight was quantified could be used for a detailed review. To ensure that effects described in laboratory studies were not caused due to application or administration of substances, only laboratory studies with reduced or restricted diets were used. Similarly, no field studies were considered in which effects might have been caused by the application of substances or where impacts by agricultural practices were apparent. When necessary, raw data were analysed in detail in order to conduct additional analyses or to test hypotheses. Whenever suitable data were available only in graphs, data were extracted by scanning. Results were reported separately for effects on survival and effects on reproduction (effects on litter size, offspring survival and puberty).

Results

*No adverse effects of reduced body weight were found on survival unless the reduction reached **24.1%** (only relevant for over-winter survival; when body weight falls below 1100 g). The body weight threshold can be considered to be a rather conservative (worst-case) since the data from which Wallage-Drees and Michielsen (1989) deduce this threshold do not clearly support that animals below 1100 g died. They only show that in autumn (September/October) there were more juvenile rabbits below 1100 g than at the end of the winter four months later (January/February). Individual growth of juveniles was not taken into account. Beyond this level rabbits in winter seemed to start to starve (at least in dune habitat; Wallage-Drees and Michielsen, 1989). Effects on reproduction due to low female body weight were not found in any study, e.g. Adams (1975) found no effects on any reproductive parameters in low-weight females (-19.5% lower body than average) and he found also postnatal survival being excellent. Litter size decreased with decreasing female body weight (Brambell, 1944). However, for smaller litters the survival to maturity was larger (Rödel et al., 2009). Hence lower body weight does not negatively influence the number of surviving offspring, since the overall production of young is not affected (on the contrary, the overall production of young is slightly increased for lower body weight). Furthermore, having larger litters also results in a greater depletion of body stores of females, which is detrimental for future reproduction. Regarding birth weight, a reduction of 24.8% had a negative impact on offspring survival during the first three weeks (8.8% additional mortality; Poigner et al., 2000). Below this level no effects were observed. The main effect of birth body weight was a relative one, animals which are less heavy than littermates have a competitive* *disadvantage, which reduces their chance to find a teat. Castellini et al. (2003) stated that the milk availability determined the mortality rate but not the reduced body weight itself, which was only an indirect effects caused by reduced milk intake. Lactation is a highly competitive period, which is a key process for natural selection and pups that are heavier or stronger compared to litter mates have a higher chance to survive. Higher litter size decreases the chance of pups to survive to maturity because of an increasing competition between littermates. Similar to the survival of adults (see above), deaths in litters only occurred when the body weight was strongly reduced, leading to starvation (about 29.2% body weight reduction, Bautista et al., 2008). According to various authors, other factors then body weight regulate the survival and reproduction in rabbits under field conditions. The main factors are predation, food quality, population density and seasonal or yearly variations.*

These results are in line with previous findings from a literature review complemented by a meta-analysis for small farmland mammals (Brauer and Wang, 2014). Brauer and Wang (2014) found, that a lower body weight up to 20% had no significant effects on mortality and reproduction in small mammals (e.g. wood mouse, common vole, and others). The results of the present report demonstrate that in rabbits no adverse effects on survival or reproduction were found unless body weight was lower than about 24% or more.

All results of this report are summarised in figure below. A summary of considered literature paper is given in the table that follows.

***Figure:** Effect summary of reduced body/birth weight on survival and reproduction in rabbits. The arrows show the limit of body weight reduction for natural winter survival in dune habitat (*, low food availability, worst case) and pups dying during lactation due to starvation in the laboratory (**).*

Conlcusion

Overall, a reduction of body weight was shown to affect survival or reproduction parameters of rabbits only when it was reduced by >24%. Beyond this level no negative effects were found.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Table: Summary of all studies regarding differences of body weight and observed effects on survival and reproduction

Reference	***Body/Birth weight in control group [g]***	***Percent body/birth weight difference [%]***	***Observed effect***	***Description***
Effects on survival				
Wallage-Drees and Michielsen (1989)	*Mean juveniles winter body weight: 1450*	*Juveniles: -24.1*	*At this level no negative impact on over winter survival (juveniles); below this level reduced winter survival (not quantified by Wallage-Drees and Michielsen, 1989)*	*Winter body weight threshold (about 1100 g) for over-winter survival reported for a dune land habitat with limited food resources (in agricultural land this threshold is probably lower due to better food availability)*
Poigner et al. (2000)	*Mean normal birth weight: 54.4*	*Pups: -24.8*	*8.8% additional mortality during lactation*	*No positive effects on survival with 22.0% increased birth weight compared to normal birth weight.*
Effects on reproduction				
Adams (1975)	*Mean female body weight: 1305*	*Females: -19.5*	*No negative impact on several reproduction parameters*	*The body weight difference in females was up to 650 g between individuals. However, the author reported pregnancies in all except one female, normal gestation lengths and only two females showed resorption. Furthermore, Adams (1975) stated that overall postnatal survival was excellent.*
Trout and Smith (1995)	*Paunched female body weight on clay soil: 1291.0*	*Females: -9.3 (sand)*	*No negative impact on reproduction*	*No effect on number of implanted embryos and annual reproductive productivity. Soil type (food availability), population density and breeding season length were the main factors determining annual productivity*
	Paunched female body weight on clay soil: 1291.0	*Females: -2.9 (chalk)*	*No negative impact on reproduction*	
Fortun-Lamothe et al. (1996)	*Empty female body weight on day 28 of pregnancy (starch diet): 2985*	*Females: -5.5*	*No impact on foetal survival during pregnancy*	*Different diets for females with different energy content did not affect foetal survival or weight.*
Fortun-Lamothe et al. (2000)	*Mean kit birth weight in litters with 4 pups: 60.0*	*Pups: -5.5*	*No impact on pup survival during lactation*	*Mortality rate during lactation was not significant different for lighter pups.*
	Mean pup body weight at weaning in litters with 4 pups: 607	*Pups: -25.7*	*No impact on pup survival at weaning*	

Meo et al. (2004)	*Mean birth weight: 70.3*	*Pups: -35.5*	*4.1% additional mortality during lactation (not significant)*	*Mortality rates during the pre-weaning period did not differ significantly among the two groups.*
Bautista et al. (2008)	*The authors only stated that starved animals had 29.2% lower weight compared to surviving pups (weight of surviving pups not given).*	*Pups: -29.2*	*Mortality during lactation due to starvation*	*Competition between litter mates for the mother's milk was the main factor for pup survival.*

Foliage decline study used to refine the risk assessment:

Comments of zRMS:	*Preliminary results of the study by North (2016) has been provided during the renewal process of mesotrione and initial assessment was performed by the RMS. It was concluded that the study is acceptable and detailed kinetic evaluation may provide reliable DT_{50} that may be used for purposes of the risk refinement. This was, however, not performed, as during the EU review trials in the Northern France were still ongoing.* *Since then, the study was finalised and submitted in support of re-evaluation of Callisto at the zonal level. The study is considered acceptable. The kinetic evaluation of the study was presented in Alvarez (2019) and is included below the study summary by the zRMS.* *Following the commenting period more extent information regarding the test locations and weather conditions was added to the study summary.*

Reference:	*KCP 10.1.2.2/06*
Report	*North L (2016). Mesotrione – Foliage Decline Study with A12739A on Maize in Northern France and the United Kingdom in 2015. Report Number S15-02057. Eurofins Agroscience Services Ltd., Slade Lane, Wilson, Melbourne, Derbyshire, DE73 8AG, UK. Syngenta File No. A12739A_11065*
Guideline(s):	*Commission of the European Communities, General Recommendations for the Design, Preparation and Realization of Residue Trials; 7029/VI/95 (rev. 5, working document).* *OECD Guidelines for the Testing of Chemicals – Crop Field Trial, No. 509, OECD, Paris 2009.* *OECD Guidance Document on Crop Field Trials, Series on Pesticides No. 66 and Series on Testing and Assessment No. 164, ENV/JM/MONO(2011)50.* *OECD Guidance Document on Overview of Residue Chemistry Studies (as revised 2009), Series on Testing and Assessment (No. 64) and Series on Pesticides (No. 32), ENV/JM/MONO(2009)31.* *Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009.* *OECD Guidance Document on Pesticide Residue Analytical Methods, ENV/JM/MONO(2007)17 (Unclassified, 13 Aug 2007).*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Acceptable*
Duplication (if vertebrate study)	*No*

Executive Summary

Five residue decline field trials on maize were successfully conducted in Northern France and the United Kingdom during 2015. Each trial consisted of a control and a treated plot, with the exception of trial

S15-02057-05, where the control samples were taken from the treated plot immediately prior to application of the formulation.
To plot P1, mesotrione was applied to maize as A12739A, an emulsifiable concentrate (EC) formulation containing 100 g mesotrione per litre. One application was made at 150 g a.s./ha for mesotrione at BBCH 14-16.

Following the application, treated maize whole plant samples were collected at < 1 hour after application (HAA) , 4 HAA, 10 HAA, 24 HAA, 34 HAA, 48-51 HAA, 72-78 HAA and 96-99 HAA, with untreated maize whole plant samples being collected < 1 hour before application (HBA).
(Nominal sampling intervals for treated maize whole plant samples: < 1 HAA, 4 HAA, 10 HAA, 24 HAA, 34 HAA, 48 HAA, 72 HAA, and 96 HAA).

Samples were analysed for mesotrione and its metabolite MNBA.
The study design as detailed above was successfully carried out leading to the following conclusions.
Residues of mesotrione in treated maize whole plant samples taken at < 1 hour after application (HAA) were in the range 3.09 to 14.99 mg/kg, at 4 HAA were in the range 2.74 to 12.63 mg/kg, at 10 HAA were in the range 2.05 to 8.61 mg/kg, at 24 HAA were in the range 0.91 to 4.30 mg/kg, at 34 HAA were in the range 0.50 to 2.95 mg/kg, at 48-51 HAA were in the range 0.36 to 1.37 mg/kg, at 72-78 HAA were in the range below the limit of quantification (LOQ: 0.01 mg/kg) to 0.63 mg/kg, and at 96-99 HAA were in the range 0.06 to 0.13 mg/kg.

Residues of MNBA in treated maize whole plant samples taken at < 1 hour after application (HAA) were in the range below the limit of quantification (LOQ: 0.01 mg/kg) to 0.05 mg/kg, at 4 HAA were in the range 0.04 to 0.25 mg/kg, at 10 HAA were in the range 0.07 to 0.36 mg/kg, at 24 HAA were in the range 0.07 to 0.37 mg/kg, at 34 HAA were in the range 0.05 to 0.37 mg/kg, at 48-51 HAA were in the range 0.06 to 0.35 mg/kg, at 72-78 HAA were in the range below the limit of quantification (LOQ: 0.01 mg/kg) to 0.17 mg/kg, and at 96-99 HAA were in the range 0.04 to 0.11 mg/kg.

No residues of mesotrione and MNBA were detected at or above the limit of quantification (LOQ: 0.01 mg/kg) in any of the untreated maize whole plant samples taken in this study.

Materials

Test system	*The following test system is representative of the crop group required for product registration. Maize (Zea Mays)* *EPPO code ref. ZEAMX*	
Test Item(s)	*Formulation – Company Code*	*A12739A*
	Formulation Content and Type	*100 EC*
	Batch No.	*SAV5A15007*
	Valid until:	*Mar 2018*
	Active ingredient	*Mesotrione*
	Nominal Content in Formulation (nominal)	*100 g/L*
	Actual Content in Formulation (actual)	*99.3 g/L*
	Stability	*The test item is assumed to be stable for the period of use in the study, pending concurrent batch re-analysis*

Study Design and Methods

Five residue field trials on maize were conducted in Northern France and the United Kingdom in 2015. Details regarding the trials locations and distance to the closest test site are given in table below.

Trial number	***Location***	***Post code***	***Longitude:***	***Latitude:***	***Distance to closest site***
S15-02057-01	*Lancashire, UK*	*WN6 9QG*	*-2.7203*	*53.594*	*44km*
S15-02057-06	*Lancashire, UK*	*BB7 4NJ*	*-2.3322*	*53.932*	*44km*
S15-02057-03	*Derbyshire, UK*	*DE6 5BL*	*-1.6392*	*52.936*	*33km*
S15-02057-04	*Leicestershire*	*LE11 3QU*	*-1.2524*	*52.758*	*33km*
S15-02057-05	*Alsace, France*	*Stotzheim 7140*	*7.4995*	*48.3716*	*>100 km*

Details of the application of mesotrione as formulation A12739A to maize in Trials S15-02057-01, S15-02057-03, S15-02057-04, S15-02057-05, S15-02057-06 are summarised in the table below.

Table A 1: ***Treatment details for Trial S15-02057-01, S15-02057-03, S15-02057-04, S15-02057-05, S15-02057-06***

Trial. S15-02057-	*Applications*	*Application date(s)*	*Formulation Code*	*Product rate (L/ha)*	*Actual spray volume (L/ha)*	*Growth stage at application (BBCH)*	*AI application rate (g mesotrione/ha)*	
							Actual	*Target*
-01	*1*	*09/07/2015*	*A12739A*	*1.45*	*193*	*15-16*	*145*	*150*
-03	*1*	*23/06.2015*	*A12739A*	*1.58*	*212*	*14-16*	*158*	*150*
-04	*1*	*09/07/2015*	*A12739A*	*1.48*	*197*	*16*	*148*	*150*
-05	*1*	*25/08/2015*	*A12739A*	*1.53*	*257*	*15*	*153*	*150*
-06	*1*	*14/07/2015*	*A12739A*	*1.47*	*196*	*15-16*	*147*	*150*

There was no rainfall within 48 hours of the application being made at all trial sites, with the exception of trial S15-02059-04, which experienced 0.2 mm of rainfall on the day of application. Detailed weather data are presented in table below. In each trial the weather station was located on the test site.

Date	*Air temperature [°C]*			*Precipitation [mm]*	*Humidity [%]*			*Soil*		*Solar [MJ]*
	Min	*Max*	*Daily average*		*Min*	*Max*	*Daily average*	*Av. temp. at 10 cm [°C]*	*Moisture at 10 cm [m^3/m^3]*	
Trial S15-02057-01 (UK)										
09 Jul 2015	*8.9*	*15.2*	*12.3*	*0*	*52.5*	*82.2*	*66.1*	*15.3*	*0.46*	*34.8*
10 Jul 2015	*11.6*	*24.3*	*17.1*	*0*	*45.5*	*85.6*	*63.0*	*16.8*	*0.45*	*32.9*
11 Jul 2015	*13.9*	*18.3*	*15.4*	*0*	*55.1*	*87.1*	*73.9*	*17.7*	*0.44*	*21.0*
12 Jul 2015	*13.3*	*16.6*	*15.0*	*0*	*64.2*	*88.7*	*76.7*	*17.0*	*0.44*	*25.9*
13 Jul 2015	*13.0*	*16.6*	*13.7*	*1.8*	*76.2*	*87.5*	*82.5*	*16.9*	*0.44*	*20.9*
Trial S15-02057-03 (UK)										
23 Jun 2015	*8.1*	*19.4*	*14.2*	*0*	*52.4*	*93.0*	*71.9*	*16.0*	*0.36*	*16.4*
24 Jun 2015	*9.8*	*20.5*	*15.4*	*0*	*49.5*	*95.0*	*75.1*	*18.2*	*0.36*	*19.8*
25 Jun 2015	*10.7*	*22.2*	*16.8*	*0*	*56.9*	*95.8*	*77.5*	*18.8*	*0.36*	*12.6*
26 Jun 2015	*12.3*	*19.5*	*16.1*	*2.4*	*74.8*	*93.3*	*82.4*	*18.6*	*0.36*	*7.0*
27 Jun 2015	*10.6*	*21.5*	*16.4*	*0*	*46.6*	*96.4*	*73.5*	*18.3*	*0.35*	*19.9*
Trial S15-02057-04 (UK)										
09 Jul 2015	*9.3*	*19.9*	*14.4*	*0.2*	*Reported values indicate that humidity at this test site was erroneously reported in the report. In absence of raw data verification was not possible*			*15.5*	*0.46*	*0.30 **
10 Jul 2015	*9.5*	*25.0*	*18.4*	*0*				*16.8*	*0.45*	*0.26 **
11 Jul 2015	*14.7*	*22.1*	*18.4*	*0.2*				*17.7*	*0.44*	*0.16 **
12 Jul 2015	*13.6*	*22.3*	*17.4*	*2.6*				*17.0*	*0.44*	*0.19 **
13 Jul 2015	*13.7*	*19.6*	*16.6*	*3.4*				*16.9*	*0.44*	*0.16 **
Trial S15-02057-06 (UK)										
14 Jul 2015	*8.3*	*18.7*	*13.5*	*0*	*55.3*	*89.1*	*75.2*	*17.3*	*0.34*	*26.4*
15 Jul 2015	*7.8*	*18.2*	*13.0*	*0*	*49.3*	*88.0*	*68.0*	*16.9*	*0.31*	*34.5*
16 Jul 2015	*6.1*	*20.9*	*13.5*	*0*	*47.7*	*88.6*	*67.5*	*16.9*	*0.28*	*33.7*
17 Jul 2015	*12.6*	*18.0*	*15.3*	*0.4*	*49.4*	*83.0*	*67.1*	*17.3*	*0.27*	*31.6*
18 Jul 2015	*10.1*	*18.3*	*14.2*	*0*	*48.0*	*84.9*	*62.9*	*16.6*	*0.26*	*37.1*
Trial S15-02057-05 (N-FR)										
25 Aug 2015	*12.0*	*22.8*	*17.2*	*0*	*37.3*	*94.4*	*62.6*	*19.0*	*0.29*	*2248.2*
26 Aug 2015	*9.9*	*27.6*	*18.5*	*0*	*36.0*	*96.9*	*71.5*	*19.7*	*0.27*	*2284.2*
27 Aug 2015	*14.3*	*30.9*	*23.1*	*0*	*37.7*	*94.8*	*65.2*	*21.6*	*0.26*	*2017.8*
28 Aug 2015	*17.9*	*28.9*	*22.8*	*0*	*51.5*	*98.5*	*77.8*	*23.6*	*0.25*	*1465.2*
29 Aug 2015	*14.9*	*31.1*	*22.3*	*0*	*47.3*	*100.0*	*81.5*	*24.1*	*0.25*	*1852.2*

** At this test site solar is given in W/m^2*

Selection of samples to be analysed and shipment:

Following the application, treated maize whole plant samples were collected at < 1 hour after application (HAA) , 4 HAA, 10 HAA, 24 HAA, 34 HAA, 48-51 HAA, 72-78 HAA and 96-99 HAA, with untreated maize whole plant samples being collected < 1 hour before application (HBA).
(Nominal sampling intervals for treated maize whole plant samples: < 1 HAA, 4 HAA, 10 HAA, 24 HAA, 34 HAA, 48 HAA, 72 HAA, and 96 HAA).

Specimens were kept deep frozen at or below -18°C during transport and storage prior to analysis.

Residue analysis

The analytical phase was conducted at the Eurofins Agroscience Services facility located in France, using method GRM007.11A. The Limit of Quantification (LOQ) required was 0.01mg/kg for mesotrione and its metabolite MNBA.

Results

Table A 2: Results of Analysis of Field Trial Samples for Mesotrione

Number and Nominal Rate of Application (g a.s./ha)	***Sampling Interval (hours)***	***Crop Part***	***Mesotrione Residue (mg/kg)***				
			Trial S15-02057-01 (UK)	***Trial S15-02057-03 (UK)***	***Trial S15-02057-04 (UK)***	***Trial S15-02057-05 (France)***	***Trial S15-02057-06 (UK)***
1 x 150	*< 1 HAA*	*Whole plant*	*7.09*	*13.96*	*4.24*	*14.99*	*3.09*
1 x 150	*4 HAA*	*Whole plant*	*8.48*	*7.75*	*2.98*	*12.63*	*2.74*
1 x 150	*10 HAA*	*Whole plant*	*4.11*	*6.25*	*3.33*	*8.61*	*2.05*
1 x 150	*24 HAA*	*Whole plant*	*3.86*	*3.57*	*1.69*	*4.30*	*0.91*
1 x 150	*34 HAA*	*Whole plant*	*2.79*	*2.95*	*0.50*	*2.19*	*0.80*
1 x 150	*48-51 HAA*	*Whole plant*	*0.92*	*1.37*	*0.41*	*1.07*	*0.36*
1 x 150	*72-78 HAA*	*Whole plant*	*0.16*	*0.63*	*0.14*	*0.31*	*< 0.01*
1 x 150	*96-99 HAA*	*Whole plant*	*0.12*	*0.11*	*0.06*	*0.13*	*0.10*
Control	*< 1 HBA*	*Whole plant*	*< 0.01*	*< 0.01*	*< 0.01*	*< 0.01*	*< 0.01*

HBA: hours before application, HAA: hours after application
No correction of results for either control residues or recovery values has been performed

Table A 3: Results of Analysis of Field Trial Samples for MNBA

Number and Nominal Rate of Application (g a.s./ha)	***Sampling Interval (hours)***	***Crop Part***	***MNBA Residue (mg/kg)***				
			Trial S15-02057-01	***Trial S15-02057-03***	***Trial S15-02057-04***	***Trial S15-02057-05***	***Trial S15-02057-06***
1 x 150	*< 1 HAA*	*Whole plant*	*0.02*	*0.05*	*< 0.01*	*0.05*	*0.01*
1 x 150	*4 HAA*	*Whole plant*	*0.10*	*0.13*	*0.04*	*0.25*	*0.05*
1 x 150	*10 HAA*	*Whole plant*	*0.10*	*0.22*	*0.07*	*0.36*	*0.09*
1 x 150	*24 HAA*	*Whole plant*	*0.15*	*0.23*	*0.07*	*0.37*	*0.10*
1 x 150	*34 HAA*	*Whole plant*	*0.15*	*0.20*	*0.05*	*0.37*	*0.12*
1 x 150	*48-51 HAA*	*Whole plant*	*0.13*	*0.24*	*0.06*	*0.35*	*0.09*
1 x 150	*72-78 HAA*	*Whole plant*	*0.07*	*0.17*	*0.05*	*0.12*	*< 0.01*
1 x 150	*96-99 HAA*	*Whole plant*	*0.06*	*0.10*	*0.04*	*0.11*	*0.08*
Control	*< 1 HBA*	*Whole plant*	*< 0.01*	*< 0.01*	*< 0.01*	*< 0.01*	*< 0.01*

HBA: hours before application, HAA: hours after application
No correction of results for either control residues or recovery values has been performed

Conclusions

Residues of mesotrione in treated maize whole plant samples taken at < 1 hour after application (HAA) were in the range 3.09 to 14.99 mg/kg, at 4 HAA were in the range 2.74 to 12.63 mg/kg, at 10 HAA were in the range 2.05 to 8.61 mg/kg, at 24 HAA were in the range 0.91 to 4.30 mg/kg, at 34 HAA were in the range 0.50 to 2.95 mg/kg, at 48-51 HAA were in the range 0.36 to 1.37 mg/kg, at 72-78 HAA were in the range below the limit of quantification (LOQ: 0.01 mg/kg) to 0.63 mg/kg, and at 96-99 HAA were in the range 0.06 to 0.13 mg/kg.

Residues of MNBA in treated maize whole plant samples taken at < 1 hour after application (HAA) were in the range below the limit of quantification (LOQ: 0.01 mg/kg) to 0.05 mg/kg, at 4 HAA were in the range 0.04 to 0.25 mg/kg, at 10 HAA were in the range 0.07 to 0.36 mg/kg, at 24 HAA were in the range 0.07 to 0.37 mg/kg, at 34 HAA were in the range 0.05 to 0.37 mg/kg, at 48-51 HAA were in the range 0.06 to 0.35 mg/kg, at 72-78 HAA were in the range below the limit of quantification (LOQ: 0.01 mg/kg) to 0.17 mg/kg, and at 96-99 HAA were in the range 0.04 to 0.11 mg/kg.

No residues of mesotrione and MNBA were detected at or above the limit of quantification (LOQ: 0.01 mg/kg) in any of the untreated maize whole plant samples taken in this study.

zRMS comments:
The kinetic evaluation of the study by North (2016) as presented in Alvarez (2019) has been provided by the zRMS below.
In general, the kinetic evaluation is considered acceptable. It is noted that kinetic evaluation was performed only using SFO, while other models could give improvement of fits in trials S15-02057-01 and S15-02057-03.
The Chi^2 error in trials S15-02057-01, S15-02057-03 and S15-02057-04 was >15%, however Chi^2 above 15% is not the reason for rejection of obtained results when the statistical analyses and visual fits are acceptable. As this is the case for trials mentioned and in general, SFO kinetics is preferred to derive DT_{50} values for residue decline trials in plants, consideration of only SFO is accepted by the zRMS. As results from 5 trials performed in only 2 countries are available (of which one is Northern France not belonging to the Central Zone, although conditions in Northern France are similar to the Central Europe), it is proposed by the zRMS to use the worst case DT_{50} of 0.803 days for purposes of the risk refinement.

Approach taken by the zRMS was questioned during the commenting period as being overly conservative. It was pointed out by AT that

[...] Based on the EFSA guidance on birds and mammals along with the outcome of the general PRAPER 185 (2019), it has been agreed that for residue decline on plants at least four independent DT50 values are required (at sufficient geographical distances, e.g. 100 km as a thumb rule) from the concerned regulatory zone in line with the intended use. If at least 4 such DT50 values are available, then a geometric mean can be calculated and used in the risk assessment. [...]

The zRMS would like to point out following issues:

- *In the UK the distance between particular sites was in range 33-44 km, so DT_{50} values derived from UK sites cannot be considered to be fully independent when the minimum distance of 100 km is taken into account.*
- *4 out of 5 trials were performed in the UK and only single trial was performed in the Northern France, which does not belong to the Central Zone. Although extrapolation from the Northern France to the Central Zone is possible, it is noted that temperature and radiation were clearly higher than at the UK sites. This could be due to different months (in UK studies were performed in June-July, while in France in August), but this difference adds some additional uncertainty.*
- *As no other country was involved in testing and majority of test sites was located in the UK, the zRMS has some concerns whether the variability in degradation between particular countries was sufficiently addressed.*
- *Dossier for Callisto was submitted before EFSA Supporting publication 2019:EN-1673 was issued, so its recommendations do not apply to assessment of this product. It should be, however, noted that until the meeting on general recurring issues in ecotoxicology was carried out in 2018, it was only agreed that minimum 4 residue decline trials are required to refine the default DT_{50} value, while no common approach has been developed at either EU or the Central Zone level with regard to the minimum number of residue decline trials required to*

derive the geometric mean DT_{50}. Some Member States considered 4 trials as sufficient, while at least 10 trials were required by other Member States. In addition to that, due to the time constraints not all aspects of the derivation of the relevant DT_{50} in plant material were discussed during the meeting in 2018. Nevertheless, in point 6 of Appendix F it is indicated that used of the worst case DT_{50} should be considered when the dataset presents limited reliability, which for reasons described above is the case for residue trials by North (2016).

Despite deficiencies mentioned above, obtained results clearly demonstrated that DT_{50} of mesotrione for plant material is much shorter than the default 10 days and this information should be accounted for in the risk assessment. Nevertheless, as the general rules regarding independency of trials were not fulfilled and the variability of degradation in particular countries was not sufficiently covered, in opinion of the zRMS the more conservative approach should be taken with the worst case DT_{50} of 0.803 days used in the risk refinement.

The kinetic evaluation of results of the study by North (2016) was performed using CAKE ver. 3.2 program. Overall summary of derived DT_{50} and DT_{90} values is presented in table below. The visual fits together with statistical evaluation are presented below, separately for each trial. Please note that evaluation of the visual fits was done by the zRMS.

Trial	***DT_{50} [days]***	***DT_{90} [days]***	***Remarks***
S15-02057-01 (UK)	***0.803***	*2.67*	*Acceptable, acceptable visual fit, some potential for improvement*
S15-02057-03 (UK)	*0.512*	*1.7*	*Acceptable, acceptable visual fit but potential for improvement*
S15-02057-04 (UK)	*0.663*	*2.2*	*Acceptable, good visual fit, some potential for improvement*
S15-02057-05 (N-FR)	*0.636*	*2.11*	*Acceptable, good visual fit*
S15-02057-06 (UK)	*0.531*	*1.76*	*Acceptable, excellent visual*

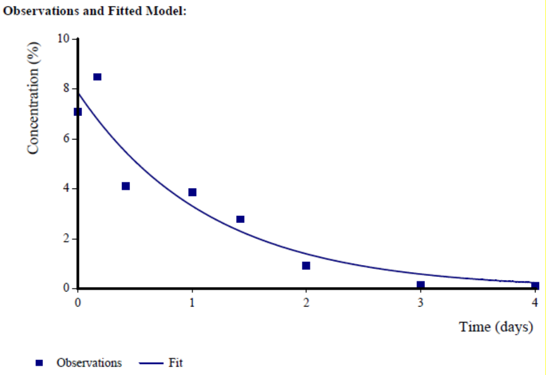
*Value in **bold** is proposed by the zRMS for the risk refinement purposes*

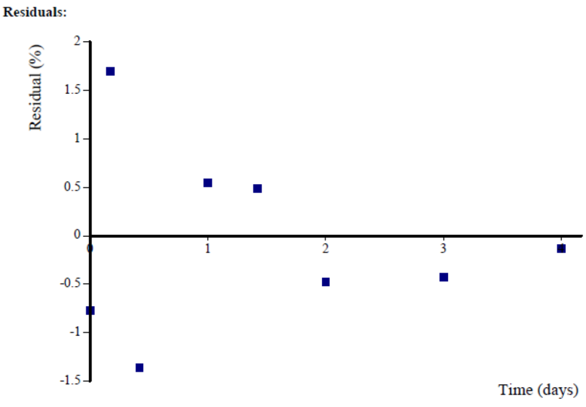
Trial S15-02057-01 (UK)

Dissipation parameters of mesotrione in maize (trial S15-02057-01)

Kinetic model	***Compound***	***VA***	***χ^2 error (%)***	***t-test***	***DT_{50} (d)***	***DT_{90} (d)***
SFO	*Mesotrione*	*+*	*20.5*	*0.0022*	*0.803*	*2.67*

estimation of visual fits: +++ excellent ++ good + acceptable - unacceptable



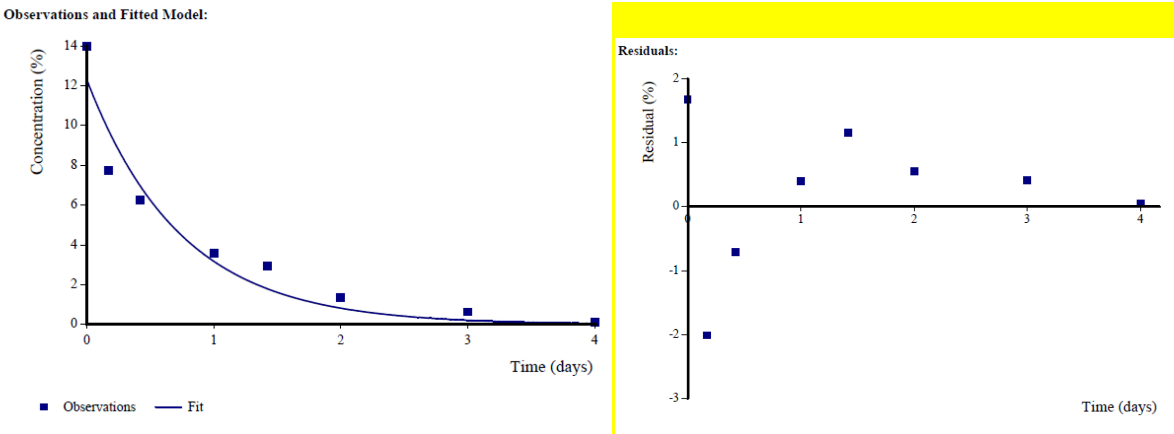


Trial S15-02057-03 (UK)

Dissipation parameters of mesotrione in maize (trial S15-02057-03)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*+*	*18.8*	*0.0011*	*0.512*	*1.7*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable

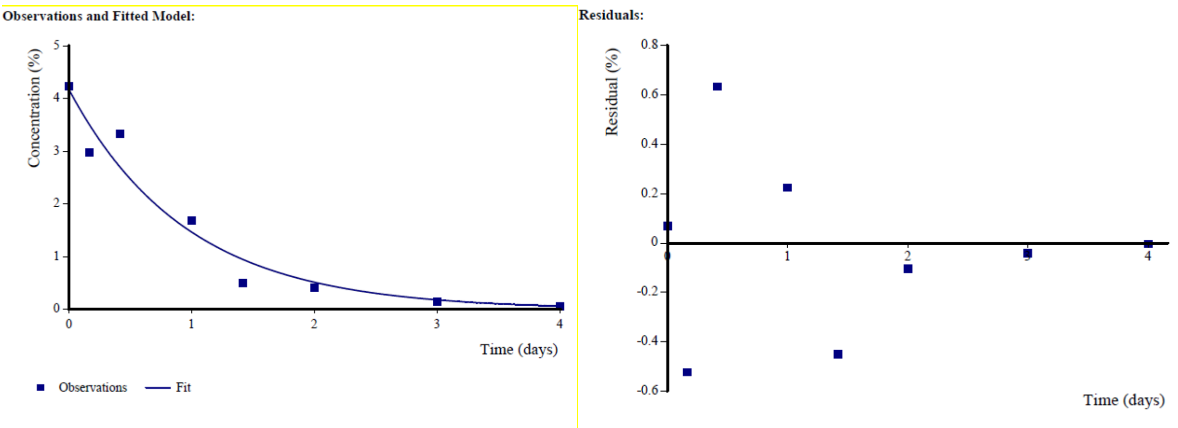


Trial S15-02057-04 (UK)

Dissipation parameters of mesotrione in maize (trial S15-02057-04)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*++*	*16.4*	*5.55E-004*	*0.663*	*2.2*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable

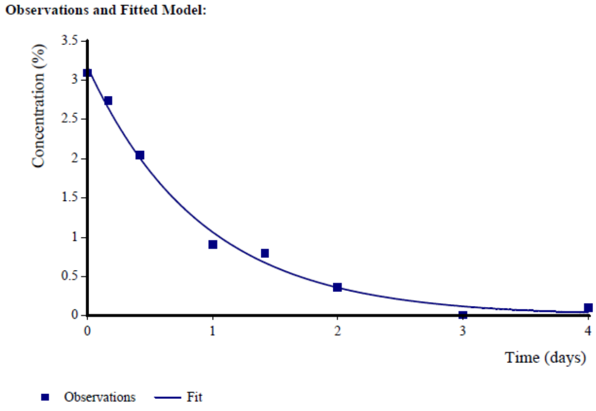


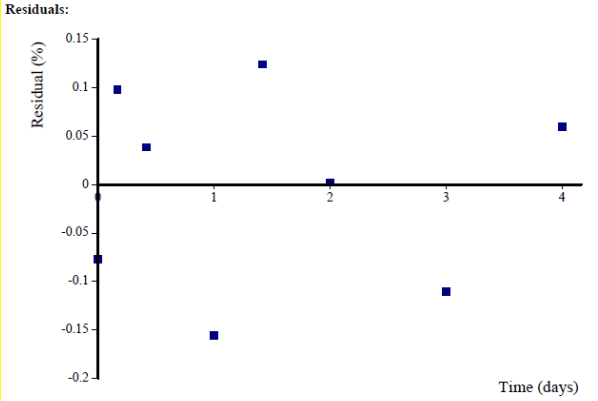
Trial S15-02057-05 (France)

Dissipation parameters of mesotrione in maize (trial S15-02057-05)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*++*	*6.02*	*1.99E-006*	*0.636*	*2.11*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable



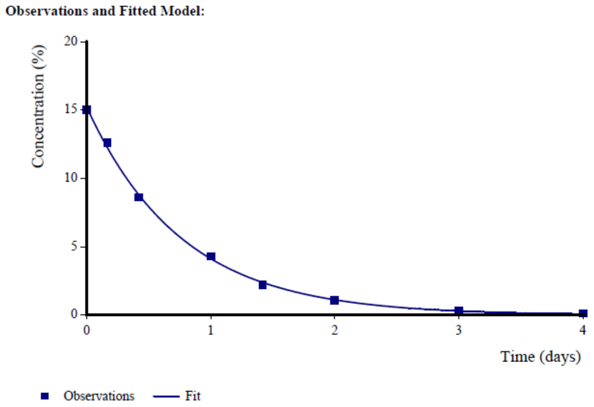


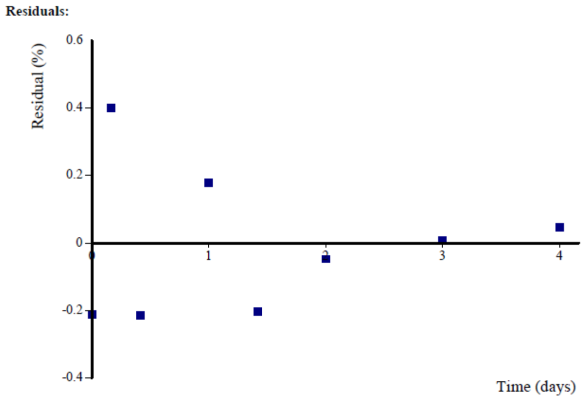
Trial S15-02057-06 (UK)

Dissipation parameters of mesotrione in maize (trial S15-02057-06)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*+++*	*2.92*	*2.18E-008*	*0.531*	*1.76*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable





*****

Comments of zRMS:	*The residue trials were performed in various Central Zone countries (UK, Hungary, Germany, Poland and Belgium) as well as in one Southern Zone country (Northern France). However, in opinion of the zRMS, environmental conditions in the Northern France are comparable with conditions of the Central Zone and for this reason results for this trial may be included in the overall analysis.* *The aim of the study was determination of the decline of the residues of mesotrione on clover, which may be considered as representative species for dicotyledonous weeds consumed by birds and mammals.* *The study was not performed with Callisto, but with another mesotrione SC formulation (A12738A) containing 480 g mesotrione/L. However, the application rate was in line with the maximum rate proposed for Callisto.* *In most of trials the application was made to early growth stages of clover (BBCH 15-18). In two trials the application was performed at BBCH 12-61 or 12-81 (it is not specified in the report at which stage exactly the product was applied). Nevertheless, the study does not need to simulate the growth stages of the target crop (maize), as at the time of application weeds may be at various growth stages. Furthermore, residues in trials performed at later BBBCH stages were at level comparable with trials where the product was applied earlier, which gives additional reassurance that the residue decline on clover does not depend on the growth stage.* *Due to expected rapid decline of mesotrione, intensive sampling was performed during the first days after application, with two samplings performed on the day of application. The sampling schedule gave together 8 data points for each trial, which is sufficient to perfom the reliable kinetic analysis.* *In some trials residues during first 24 hours were quite variable with slightly higher residue levels observed on later samplings. No explanation regarding this issue was provided in the study report. In some trials the variability of residues resulted with poor or unacceptable kinetic fits (see comments regarding kinetic evaluation below the study summary).* *Overall, the study is considered acceptable. The kinetic evaluation of the study was presented in Alvarez (2019) and is included below the study summary by the zRMS.*

Reference:	*KCP 10.1.2.2/11*
Report	*Allen L. (2019). Mesotrione – Foliage Decline Study on Clover in Hungary, Germany, United Kingdom, Northern France and Belgium in 2018. Report Number CEMR-8397. CEMAS), Imperial House, Oaklands Park, Wokingham, Berkshire, RG41 2FD, UK. Syngenta File No. A12738A_10535*
Guideline(s):	*Commission of the European Communities, General Recommendations for the Design, Preparation and Realization of Residue Trials; 7029/VI/95 (rev. 5, working document).* *OECD Guidance Document on Crop Field Trials, Series on Pesticides No. 66 and Series on Testing and Assessment No. 164, ENV/JM/MONO(2011)50.* *OECD Guidance Document on Overview of Residue Chemistry Studies (as revised 2009), Series on Testing and Assessment (No. 64) and Series on Pesticides (No. 32), ENV/JM/MONO(2009)31.* *Guidelines and Criteria for the Preparation and Presentation of Complete Dossiers and of Summary Dossiers for the Inclusion of Active Substances in Regulations (EU) 283/2013 and 284/2013 implementing Regulation (EC) 1107/2009.* *OECD Guidelines for the Testing of Chemicals – Crop Field Trial, No. 509, OECD, Paris 2009.* *European Commission Guidance for Generating and Reporting Methods of Analysis in Support of Pre-registration Requirements for Annex II (Part A, Section 4) of Directive 91/414, SANCO/3029/99 revision 4 (11 Jul 2000).* *OECD Guidance Document on Pesticide Residue Analytical Methods, ENV/JM/MONO(2007)17 (Unclassified, 13 Aug 2007).* *The Application of the OECD Principles of GLP to the Organisation and Management of Multi-Site Studies, ENV/JM/MONO (2002) 9.* *OECD Series on Principles of GLP and Compliance Monitoring No. 1 (as revised in 1997)*

	"OECD Principles on Good Laboratory Practice", Paris 1998. ENV/MC/CHEM(98)17 and respective national regulations. *The national GLP requirements are based on the OECD Principles of Good Laboratory Practice, which are accepted by regulatory authorities throughout the European Community, the United States of America (FDA and EPA) and Japan (MHW, MAFF and METI) on the basis of intergovernmental agreements*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Acceptable*
Duplication (if vertebrate study)	*No*

Executive Summary

Twelve (10 + 2 contingency) foliar decline residue field trials on clover were planned, eleven (10 + 1 contingency) were successfully conducted in Northern France, Germany, Poland, Hungary, United Kingdom and Belgium during 2018. One trial was cancelled due to poor crop growth.

Mesotrione was applied to clover as A12738A, a suspension concentrate (SC) formulation containing nominal 480 g mesotrione per litre. One application, applied at BBCH 16-18 was made at a nominal rate of 150 g ai/ha for mesotrione, with the exception of trial SRDE18-001-037HR which was applied at BBCH 12-61 and trial SRDE18-002-037HR which was applied at BBCH 16-81. Untreated immature clover samples were taken from the plot at 0 DBA (days before application). Treated samples of immature clover were taken at 0, 8, 24, 32 and 48 HAA (hours after application) and at 3, 4 and 7 DAA (days after application).

Residue samples were shipped frozen to the analytical facility where they were analysed for mesotrione.

Residues of mesotrione in treated clover taken at < 1 hour after application (HAA) were in the range 3.63 to 11.97 mg/kg. At 8 HAA they were in the range 2.71 to 11.41 mg/kg, at 24 HAA in the range 2.28 to 11.02 mg/kg, at 32 HAA in the range 2.06 to 9.02 mg/kg, at 48 HAA they were in the range 1.78 to 7.14 mg/kg, at 3 days after application (DAA) they were in the range 0.22 – 6.06, 5 DAA in the range 0.08 – 4.37 and 7 DAA 0.05 – 1.70 mg/kg.

No residues of mesotrione and MNBA were detected at or above the limit of quantification (LOQ: 0.01 mg/kg) in any of the untreated clover whole plant samples taken in this study.

Materials

Test system	*The following test system is representative of the crop group required for product registration.* *Clover (Trifolium repens, Trifolium incarnatum, Trifolium alexandrinum)* *EPPO Code: TRFRE, TRFIN, TRFAL*	
Test Item(s)	*Formulation – Company Code*	*A12738A*
	Formulation Content and Type	*480 SC*
	Batch No.	*SAV7B17001*
	Valid until:	*30 April 2020*
	Active ingredient	*Mesotrione*
	Nominal Content in Formulation (nominal)	*480 g/L*
	Actual Content in Formulation (actual)	*474 g/L*
	Stability	*The test item is assumed to be stable for the period of use in the study, pending concurrent batch re-analysis*
Reference Item	*Name*	*Mesotrione*
	Batch No.	*492970*
	Valid until:	*29 Feb 2020*
	Purity	*99.5%*

Study Design and Methods

Eleven field trials on clover ~~maize~~ were conducted in Central Europe in 2018. Details regarding the trials locations are given in table below. The distance between locations in particular countries was >100 km.

Trial number	***Location***	***Post code***	***Longitude:***	***Latitude:***	***Distance between locations in one country***
SRHU18-053-037HR	*Kőszeg, HU*	*9730*	*16.549517*	*47.395936*	*~70 km*
SRHU18-054-037HR	*Zalalövő, HU*	*8999*	*16.592355*	*46.828378*	
SRPL18-014-037HR	*Jadowniki Bielskie, PL*	*88-400*	*17.813470*	*52.854237*	*>100 km*
SRPL18-015-037HR	*Łaźniki, PL*	*99-440*	*19.760421*	*52.207968*	
SRDE18-001-037HR	*Adlkofen, DE*	*84166*	*12.27524*	*48.554*	*>100 km*
SRDE18-002-037HR	*Untergruppenbach, DE*	*74199*	*9.15322*	*49.05253*	
SRUK18-001-037HR	*Pakenham, UK*	*IP31 2NG*	*0.49420*	*52.16525*	*~80 km*
SRUK18-002-037HR	*Spalding, UK*	*PE12 9QQ*	*0.11291*	*52.49582*	
SRFR18-010-037HR	*La Chapelle de Guinchay, N-FR*	*71570*	*4.771163*	*46.221286*	*~55 km*
SRFR18-011-037HR	*Simandre, N-FR*	*71290*	*5.003540*	*46.610062*	
G006-18H	*Saint-Amand, BE*	*6221*	*4.29554*	*50.30483*	*-*

Details of the application of mesotrione as formulation A12738A to clover are summarised in the table below.

Table A 4: Treatment details for Clover Trials

Trial	***Applications***	***Application date(s)***	***Formulation Code***	***Growth stage at application (BBCH)***	***AI application rate (g mesotrione/ha)***	
					Actual	***Target***
SRFR18-010-037HR	*1*	*24 May 2018*	*A12738A*	*18*	*155.2*	*150*
SRFR18-011-037HR	*1*	*9 Jul 2018*	*A12738A*	*16-18*	*148.1*	*150*
SRHU18-053-037HR	*1*	*18 Jun 2018*	*A12738A*	*16-18*	*154.6*	*150*
SRHU18-054-037HR	*1*	*18 Jun 2018*	*A12738A*	*16-18*	*155.1*	*150*
SRUK18-001-037HR	*1*	*9 May 2018*	*A12738A*	*16-17*	*157.5*	*150*
SRUK18-002-037HR	*1*	*6 Jul 2018*	*A12738A*	*15-17*	*139.5*	*150*
SRPL18-014-037HR	*1*	*7 May 2018*	*A12738A*	*16-18*	*154.4*	*150*
SRPL18-015-037HR	*1*	*8 May 2018*	*A12738A*	*16-18*	*151.3*	*150*
SRDE18-001-037HR	*1*	*25 Jun 2018*	*A12738A*	*12-61[a]*	*152.8*	*150*
SRDE18-002-037HR	*1*	*17 Jul 2018*	*A12738A*	*12-81[a]*	*155.5*	*150*
G006-18H	*1*	*18 Jun 2018*	*A12738A*	*16-17*	*149.5*	*150*

[a] Growth stage at application was 12-61 or 12-81 rather than 16-18 as stated in the study plan due to hot, dry weather conditions causing the crop to have a large range of growth stages. Minimal impact was anticipated as the analytical results were comparable to the other trials

There was no rainfall within 48 hours of the application being made at all trial sites. Detailed weather data are presented in tables below.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Trial	***Date***	***Air temperature [°C]***			***Precipitation***	***Weather station***	
		Min	***Max***	***Daily average***		***Name***	***Distance to the test site***
SRHU18-053-037HR (Hungary)	*18 Jun 2018*	*19*	*27*	*23*	*0*	*Shombately MO Station*	*23.3 km*
	19 Jun 2018	*18*	*28*	*23*	*0*		
	20 Jun 2018	*19*	*29*	*24*	*0*		
	21 Jun 2018	*16*	*30*	*23*	*14*		
	22 Jun 2018	*14*	*20*	*17*	*0*		
	23 Jun 2018	*7*	*20*	*13.5*	*0*		
	24 Jun 2018	*12*	*21*	*16.5*	*4*		
	25 Jun 2018	*13*	*19*	*16*	*0*		
	26 Jun 2018	*10*	*23*	*16.5*	*0*		
	27 Jun 2018	*13*	*22*	*17.5*	*6*		
	28 Jun 2018	*14*	*23*	*18.5*	*0*		
	29 Jun 2018	*19*	*27*	*23*	*0*		
	30 Jun 2018	*18*	*24*	*21*	*0*		
	01 Jul 2018	*9*	*21*	*15*	*0*		
	02 Jul 2018	*7*	*23*	*15*	*0*		
	03 Jul 2018	*11*	*27*	*19*	*0*		

Trial	***Date***	***Air temperature [°C]***			***Precipitation***	***Weather station***	
		Min	***Max***	***Daily average***		***Name***	***Distance to the test site***
SRHU18-054-037HR (Hungary)	*18 Jun 2018*	*17*	*26*	*21.5*	*0*	*Zalaegerszeg MO Station*	*20.0 km*
	19 Jun 2018	*17*	*27*	*22*	*0*		
	20 Jun 2018	*17*	*29*	*23*	*0*		
	21 Jun 2018	*17*	*30*	*23.5*	*4*		
	22 Jun 2018	*13*	*19*	*16*	*0*		
	23 Jun 2018	*7*	*19*	*13*	*0*		
	24 Jun 2018	*11*	*19*	*15*	*9*		
	25 Jun 2018	*12*	*19*	*15.5*	*1*		
	26 Jun 2018	*12*	*23*	*17.5*	*0*		
	27 Jun 2018	*13*	*22*	*17.5*	*6*		
	28 Jun 2018	*14*	*21*	*17.5*	*1*		
	29 Jun 2018	*18*	*25*	*21.5*	*3*		
	30 Jun 2018	*17*	*23*	*20*	*0*		
	01 Jul 2018	*9*	*21*	*15*	*0*		
	02 Jul 2018	*10*	*23*	*16.5*	*0*		
	03 Jul 2018	*13*	*26*	*19.5*	*0*		

Trial	***Date***	***Air temperature [°C]***			***Precipitation***	***Weather station***	
		Min	***Max***	***Daily average***		***Name***	***Distance to the test site***
SRPL18-014-037HR (Poland)	*07 May 2018*	*6.7*	*23.4*	*15*	*0*	*On-site weather station*	*50 m*
	08 May 2018	*10.4*	*25*	*17.7*	*0*		
	09 May 2018	*12.6*	*27.1*	*19.9*	*0*		
	10 May 2018	*15.6*	*27.5*	*21.6*	*0*		
	11 May 2018	*15.8*	*24.4*	*20.1*	*1.3*		
	12 May 2018	*14.6*	*24.7*	*19.6*	*0.3*		
	13 May 2018	*13.2*	*25.7*	*19.4*	*0*		
	14 May 2018	*14.5*	*22.2*	*18.3*	*0*		
	15 May 2018	*12.5*	*20.6*	*16.6*	*0.8*		
	16 May 2018	*14.1*	*21.7*	*17.9*	*0.3*		
	17 May 2018	*13.4*	*20.7*	*17.1*	*2.8*		
	18 May 2018	*11.6*	*21.1*	*16.4*	*0.8*		
	19 May 2018	*7.5*	*20.2*	*13.9*	*0*		
	20 May 2018	*7.4*	*21.6*	*14.4*	*0*		
	21 May 2018	*9.7*	*22.7*	*16.2*	*0*		

Trial	*Date*	*Air temperature [°C]*			*Precipitation*	*Weather station*	
		Min	*Max*	*Daily average*		*Name*	*Distance to the test site*
SRPL18-015-037HR (Poland)	*08 May 2018*	*8*	*24*	*16*	*0*	*On-site weather station*	*-*
	09 May 2018	*13*	*27*	*20*	*0*		
	10 May 2018	*14*	*27*	*20*	*0*		
	11 May 2018	*12*	*25*	*18*	*0*		
	12 May 2018	*14*	*24*	*19*	*0.2*		
	13 May 2018	*9*	*25*	*17*	*0*		
	14 May 2018	*9*	*20*	*14*	*0*		
	15 May 2018	*9*	*19*	*14*	*0*		
	16 May 2018	*13*	*18*	*16*	*1.2*		
	17 May 2018	*13*	*17*	*14*	*0*		
	18 May 2018	*12*	*17*	*14*	*0*		
	19 May 2018	*8*	*18*	*13*	*0*		
	20 May 2018	*10*	*20*	*15*	*0*		
	21 May 2018	*6*	*21*	*13*	*0*		
	22 May 2018	*9*	*22*	*16*	*0*		

Trial	*Date*	*Air temperature [°C]*			*Precipitation*	*Weather station*	
		Min	*Max*	*Daily average*		*Name*	*Distance to the test site*
SRDE18-001-037HR (Germany)	*25 Jun 208*	*10.2*	*20.1*	*Not provided*	*0*	*On-site weather station*	*-*
	26 Jun 208	*10*	*21.7*		*0*		
	27 Jun 208	*11.5*	*21.5*		*1.2*		
	28 Jun 208	*11.9*	*14.7*		*25.2*		
	29 Jun 208	*14.0*	*25.5*		*0.3*		
	30 Jun 208	*12.7*	*23.0*		*0*		
	01 Jul 2018	*10.5*	*21.1*		*0*		
	02 Jul 2018	*9.4*	*23.2*		*0*		
	03 Jul 2018	*12.4*	*26.2*		*0*		
	04 Jul 2018	*15.6*	*26.5*		*0.2*		
	05 Jul 2018	*14.0*	*27.4*		*0*		
	06 Jul 2018	*14.6*	*19.9*		*3.8*		
	07 Jul 2018	*13.4*	*24.0*		*0*		
	08 Jul 2018	*14.0*	*25.1*		*0*		
	09 Jul 2018	*14.3*	*25.2*		*0*		

Trial	*Date*	*Air temperature [°C]*			*Precipitation*	*Weather station*	
		Min	*Max*	*Daily average*		*Name*	*Distance to the test site*
SRDE18-002-037HR (Germany)	*19 Jul 2018*	*12.6*	*30.3*	*Not provided*	*0*	*On-site weather station*	*-*
	20 Jul 2018	*13.6*	*32.4*		*0*		
	21 Jul 2018	*16.7*	*22*		*1.8*		
	22 Jul 2018	*17.1*	*23.8*		*0.8*		
	23 Jul 2018	*16.3*	*28.9*		*0*		
	24 Jul 2018	*14.6*	*32.6*		*0*		
	25 Jul 2018	*15.7*	*34.4*		*0*		
	26 Jul 2018	*16.6*	*34*		*0*		
	27 Jul 2018	*14.7*	*33.2*		*0*		
	28 Jul 2018	*17.1*	*31.2*		*0*		
	29 Jul 2018	*16.7*	*32.3*		*0*		
	30 Jul 2018	*16.1*	*35*		*1.4*		

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Trial	*Date*	*Air temperature [°C]*			*Precipitation*	*Weather station*	
		Min	*Max*	*Daily average*		*Name*	*Distance to the test site*
SRUK18-001-037HR (UK)	*09 May 2018*	*9.8*	*20.7*	*15.6*	*0*	*On-site weather station*	*-*
	10 May 2018	*8.6*	*16.1*	*12.3*	*0.2*		
	11 May 2018	*7.2*	*16.8*	*12.5*	*0*		
	12 May 2018	*8.8*	*18.7*	*13.6*	*11.7*		
	13 May 2018	*8.4*	*16.0*	*12.3*	*0.5*		
	14 May 2018	*7.2*	*17.1*	*12.4*	*0*		
	15 May 2018	*8.8*	*20.2*	*13.9*	*0*		
	16 May 2018	*8.1*	*13.6*	*10.5*	*0*		
	17 May 2018	*4.7*	*14.6*	*9.8*	*0*		
	18 May 2018	*5.9*	*16.4*	*10.9*	*0*		
	19 May 2018	*2.2*	*18.4*	*11.2*	*0*		
	20 May 2018	*7.0*	*19.8*	*12.2*	*0*		
	21 May 2018	*6.0*	*21.9*	*14.5*	*0*		
	22 May 2018	*7.8*	*20.6*	*14*	*0*		
	23 May 2018	*9.3*	*18.2*	*12.5*	*0*		

Trial	*Date*	*Air temperature [°C]*			*Precipitation*	*Weather station*	
		Min	*Max*	*Daily average*		*Name*	*Distance to the test site*
SRUK18-002-037HR (UK)	*06 Jul 2018*	*14.2*	*23.8*	*18.5*	*0*	*On-site weather station*	*-*
	07 Jul 2018	*13.3*	*25.6*	*19.8*	*0*		
	08 Jul 2018	*11.4*	*25.9*	*19.0*	*0*		
	09 Jul 2018	*14.0*	*23.1*	*17.9*	*0*		
	10 Jul 2018	*13.2*	*18.9*	*15.2*	*0*		
	11 Jul 2018	*13.4*	*17.0*	*15.0*	*0*		
	12 Jul 2018	*13.4*	*20.4*	*15.6*	*0*		
	13 Jul 2018	*9.3*	*21.7*	*15.7*	*0*		
	14 Jul 2018	*11.1*	*27.7*	*19.7*	*0*		
	15 Jul 2018	*13.1*	*29.6*	*20.5*	*0*		
	16 Jul 2018	*11.8*	*27.4*	*20.6*	*0*		
	17 Jul 2018	*14.6*	*22.8*	*18.8*	*0*		
	18 Jul 2018	*9.3*	*23.3*	*17.6*	*0*		
	19 Jul 2018	*13.7*	*26.1*	*19.*	*0*		
	20 Jul 2018	*10.2*	*26.8*	*17.9*	*0*		

Trial	*Date*	*Air temperature [°C]*			*Precipitation*	*Weather station*	
		Min	*Max*	*Daily average*		*Name*	*Distance to the test site*
SRFR18-010-037HR (N-France)	*24 May 2018*	*10.7*	*27.3*	*18.7*	*0*	*On-site weather station*	*-*
	25 May 2018	*14.8*	*28.6*	*21.6*	*0*		
	26 May 2018	*15.9*	*29.3*	*22.4*	*0*		
	27 May 2018	*15.9*	*28.1*	*20.4*	*3.4*		
	28 May 2018	*14.8*	*25.2*	*18.4*	*2*		
	29 May 2018	*15.6*	*25.9*	*20.1*	*0.2*		
	30 May 2018	*13.8*	*27.2*	*19.3*	*0*		
	31 May 2018	*15.3*	*23.9*	*18.3*	*4.4*		
	01 Jun 2018	*13.5*	*24.8*	*18.4*	*7.6*		
	02 Jun 2018	*13.9*	*26.4*	*20.7*	*0*		
	03 Jun 2018	*16.4*	*27.9*	*20.7*	*8.2*		
	04 Jun 2018	*15.7*	*26.6*	*20.1*	*8.4*		
	05 Jun 2018	*16*	*27.3*	*20.7*	*18*		
	06 Jun 2018	*15.2*	*27.3*	*20.4*	*0*		
	07 Jun 2018	*15.7*	*25.2*	*20.5*	*0*		
	08 Jun 2018	*16.9*	*27.9*	*21*	*0.8*		

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Trial	*Date*	*Air temperature [°C]*			*Precipitation*	*Weather station*	
		Min	*Max*	*Daily average*		*Name*	*Distance to the test site*
SRFR18-011-037HR (N-France)	*09 Jul 2018*	*15.6*	*29.1*	*22.7*	*0*	*On-site weather station*	*-*
	10 Jul 2018	*15.8*	*26.7*	*21.5*	*0*		
	11 Jul 2018	*11.3*	*23.5*	*17.9*	*0*		
	12 Jul 2018	*10.8*	*26.9*	*19.3*	*0*		
	13 Jul 2018	*13.5*	*30*	*21.8*	*0*		
	14 Jul 2018	*15*	*30.2*	*22.7*	*0*		
	15 Jul 2018	*15.3*	*30.4*	*21.3*	*1*		
	16 Jul 2018	*12.7*	*29.7*	*20.8*	*0.4*		
	17 Jul 2018	*16.3*	*27.9*	*22.1*	*0*		
	18 Jul 2018	*12.6*	*29.5*	*22.1*	*0*		
	19 Jul 2018	*13.9*	*31.8*	*23.4*	*0*		
	20 Jul 2018	*16.3*	*28.3*	*21.5*	*5.4*		
	21 Jul 2018	*16.8*	*25.7*	*20.4*	*59.8*		
	22 Jul 2018	*15.8*	*27.3*	*21.4*	*0*		
	23 Jul 2018	*15.2*	*29.3*	*23.1*	*0*		
	24 Jul 2018	*16*	*30.9*	*23.6*	*0*		

Trial	*Date*	*Air temperature [°C]*			*Precipitation*	*Weather station*	
		Min	*Max*	*Daily average*		*Name*	*Distance to the test site*
G006-18H (Belgium)	*18 Jun 2018*	*14.3*	*20.5*	*17.1*	*0*	*WS-GP1-Station SGS01*	*200 m*
	19 Jun 2018	*13.3*	*20.4*	*17.2*	*0*		
	20 Jun 2018	*16.1*	*26.3*	*20.5*	*0*		
	21 Jun 2018	*7.5*	*17.6*	*14.4*	*0*		
	22 Jun 2018	*6*	*17.5*	*12.4*	*0*		
	23 Jun 2018	*6*	*19.7*	*13.9*	*0*		
	24 Jun 2018	*8.9*	*19.8*	*14.5*	*0*		
	25 Jun 2018	*10.8*	*22.9*	*16.5*	*0*		
	26 Jun 2018	*10.5*	*23.9*	*17.2*	*0*		
	27 Jun 2018	*11.7*	*25.9*	*19.6*	*0*		
	28 Jun 2018	*13.7*	*26.7*	*21.1*	*0*		
	29 Jun 2018	*14.7*	*27.7*	*21.8*	*0*		
	30 Jun 2018	*14.4*	*29.1*	*22.4*	*0*		
	01 Jul 2018	*15.7*	*28.5*	*22.2*	*0*		
	02 Jul 2018	*12.7*	*27.6*	*21.2*	*0*		

Selection of samples to be analysed and shipment:

Following the application, treated clover whole plant samples were collected at < 1 hour after application (HAA) , 8 HAA, 24 HAA, 32 HAA, 48 HAA, 3 days after application (DAA), 4 DAA and 7 DAA, with untreated clover whole plant samples being collected < 1 hour before application (HBA).
Specimens were kept deep frozen at or below -18°C during transport and storage prior to analysis.

Residue analysis

The analytical phase was conducted at the CEMAS facility located in the UK, using method GRM007.11A. The Limit of Quantification (LOQ) required was 0.01mg/kg for mesotrione.

Results

Table A 5: Results of Analysis of Field Trial Samples for Mesotrione

Time	*Mesotrione residues (mg/kg)*										
	SRUK18-001-037HR	*SRUK18-002-037HR*	*SRHU18-053-037HR*	*SRHU18-054-037HR*	*SRFR18-010-037HR*	*SRFR18-011-037HR*	*SRDE18-001-037HR*	*SRDE18-002-037HR*	*SRPL18-014-037HR*	*SRPL18-015-037HR*	*G006-18H*
0	*6.10*	*3.63*	*11.97*	*11.69*	*11.51*	*8.75*	*4.46*	*9.11*	*6.15*	*6.50*	*8.58*
8 HAA	*6.03*	*4.20*	*11.41*	*8.99*	*8.78*	*9.98*	*5.66*	*2.71*	*4.34*	*4.58*	*8.48*
24 HAA	*4.58*	*3.39*	*11.02*	*8.76*	*9.86*	*8.73*	*4.59*	*2.59*	*2.28*	*4.72*	*8.17*

32 HAA	*2.69*	*4.09*	*9.02*	*8.80*	*6.72*	*4.77*	*3.98*	*3.29*	*2.06*	*6.37*	*5.65*
48 HAA	*2.73*	*2.61*	*7.14*	*6.89*	*5.47*	*4.66*	*4.21*	*2.54*	*1.78*	*5.78*	*5.54*
72 HAA	*1.95*	*2.17*	*6.06*	*5.51*	*2.00*	*4.77*	*0.22*	*2.61*	*3.82*	*1.8*	*3.26*
96 HAA	*0.58*	*2.76*	*0.14*	*0.12*	*0.58*	*4.37*	*0.08*	*0.43*	*1.67*	*1.66*	*3.43*
168 HAA	*0.27*	*0.19*	*0.11*	*0.07*	*0.09*	*0.70*	*0.09*	*0.05*	*1.23*	*0.27*	*1.70*
0DBA	*<0.01*	*<0.01*	*<0.01*	*<0.01*	*<0.01*	*<0.01*	*<0.01*	*<0.01*	*<0.01*	*<0.01*	*<0.01*

DBA: days before application, HAA: hours after application
No correction of results for either control residues or recovery values has been performed

Conclusions

Residues of mesotrione in treated clover taken at < 1 hour after application (HAA) were in the range 3.63 to 11.97 mg/kg. At 8 HAA they were in the range 2.71 to 11.41 mg/kg, at 24 HAA in the range 2.28 to 11.02 mg/kg, at 32 HAA in the range 2.06 to 9.02 mg/kg, at 48 HAA they were in the range 1.78 to 7.14 mg/kg, at 3 days after application (DAA) they were in the range 0.22 – 6.06, 5 DAA in the range 0.08 – 4.37 and 7 DAA 0.05 – 1.70 mg/kg.
No residues of mesotrione were detected at or above the limit of quantification (LOQ: 0.01 mg/kg) in any of the untreated clover whole plant samples taken in this study.

zRMS comments:
The kinetic evaluation of the study by Allen (2019) as presented in Alvarez (2019) has been provided by the zRMS below.

In general, the kinetic evaluation is considered acceptable.

It is noted that kinetic evaluation was performed only using SFO, while other models could give improvement of fits in most of the trials (although in trial SRFR18-011-037HR potential for improvement is uncertain). Furthermore, improvement could be also possible with outliers removed or with consideration of residues analysed at 8 hours after application as initial residues (in most of trials maximum residues were observed at this sampling point and then decline of mesotrione was observed).

Kinetic fit for one trial performed in Germany (SRDE18-002-037HR) is, in opinion, of the zRMS, unacceptable, which is confirmed by very high Chi^2 (>40%). Nevertheless, there is potential for improvement using other models. Results for this trial are excluded from further considerations, as only unacceptable SFO fit is available.

The Chi^2 error in several trials was >15%, however Chi^2 above 15% is not the reason for rejection of obtained results when the statistical analyses and visual fits are acceptable. As this is the case for trials mentioned and in general, SFO kinetics is preferred to derive DT_{50} values for residue decline trials in plants, consideration of only SFO is accepted by the zRMS. As after exclusion of unacceptable fit results from 10 trials are available, it is proposed by the zRMS that mean DT_{50} value of 2.19 days may be used for purposes of the risk refinement.

The kinetic evaluation of results of the study by Allen (2019) was performed using CAKE ver. 3.2 program. Overall summary of derived DT_{50} and DT_{90} values is presented in table below. The visual fits together with statistical evaluation are presented below, separately for each trial. Please note that evaluation of the visual fits was done by the zRMS.

Trial	***DT_{50} [days]***	***DT_{90} [days]***	***Remarks***
SRUK18-001-037HR	*1.49*	*4.96*	*Acceptable, good visual fit*
SRUK18-002-037HR	*3.57*	*11.9*	*Acceptable, acceptable visual fit, DT_{90} overestimated by the model*
SRHU18-053-037HR	*1.99*	*6.61*	*Acceptable, acceptable visual fit*
SRHU18-054-037HR	*2.01*	*6.68*	*Acceptable, acceptable visual fit*

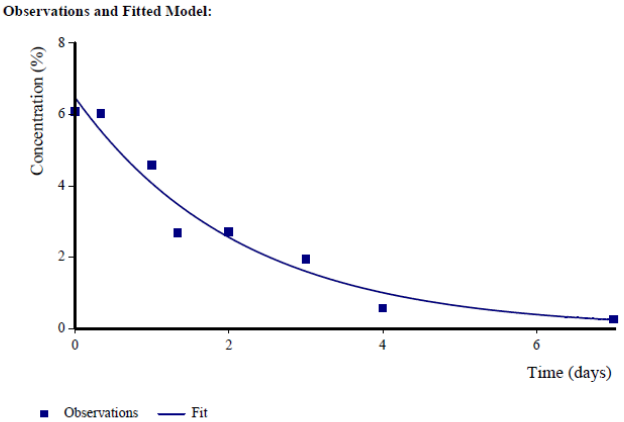
SRFR18-010-037HR	*1.55*	*5.13*	*Acceptable, good visual fit, but some potential for improvement*
SRFR18-011-037HR	*2.57*	*8.54*	*Acceptable but poor visual fit, improvement with bi-phasic models uncertain*
SRDE18-001-037HR	*1.77*	*5.89*	*Acceptable, but poor visual fit, clear potential for improvement using bi-phasic models*
SRDE18-002-037HR	*1.06*	*3.51*	*Unacceptable, unacceptable visual fit, Chi^2 >40%, but improvement possible using bi-phasic model*
SRPL18-014-037HR	*2.41*	*7.99*	*Acceptable but poor visual fit, improvement possible using bi-phasic model*
SRPL18-015-037-HR	*2.64*	*8.75*	*Acceptable but poor visual fit, improvement possible using bi-phasic model, DT_{50} overestimated by the model*
G006-18H	*2.65*	*8.8*	*Acceptable, good visual fit*
Geometric mean	***2.19***	***-***	***Results of trial SRDE18-002-037HR excluded from the calculation***

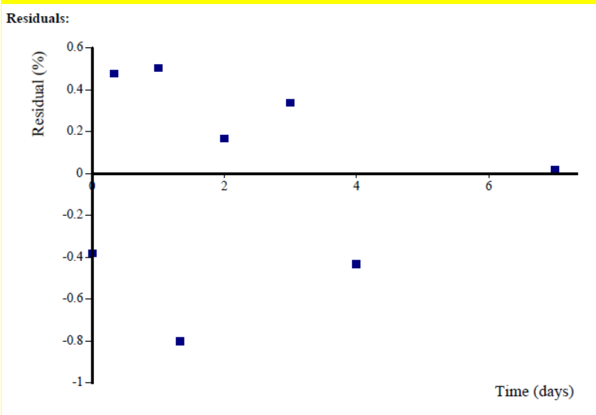
Trial SRUK18-001-037HR (UK)

Dissipation parameters of mesotrione in maize (trial SRUK18-001-037HR)

Kinetic model	***Compound***	***VA***	***χ^2 error (%)***	***t-test***	***DT_{50} (d)***	***DT_{90} (d)***
SFO	*Mesotrione*	*++*	*11.4*	*1.51E-004*	*1.49*	*4.96*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable



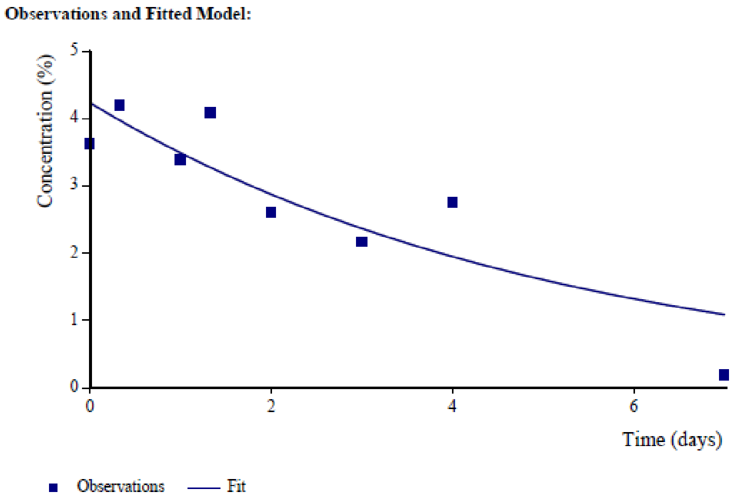


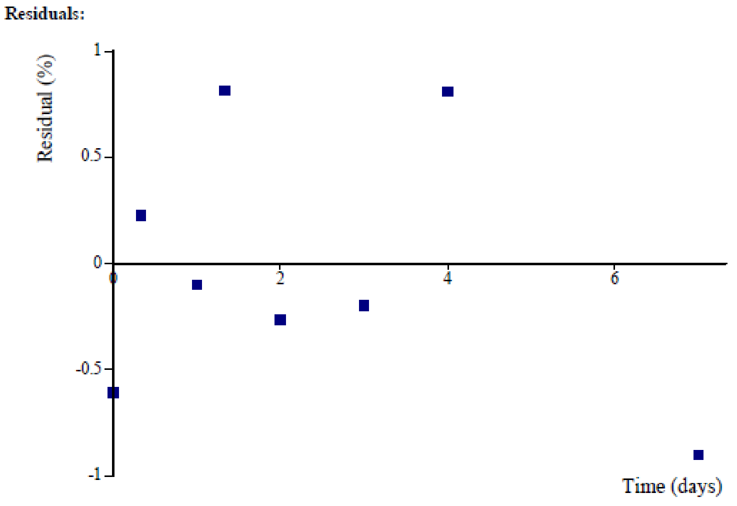
Trial SRUK18-002-037HR (UK)

Dissipation parameters of mesotrione in maize (trial SRUK18-002-037HR)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*+*	*16.0*	*0.0078*	*3.57*	*11.9*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable





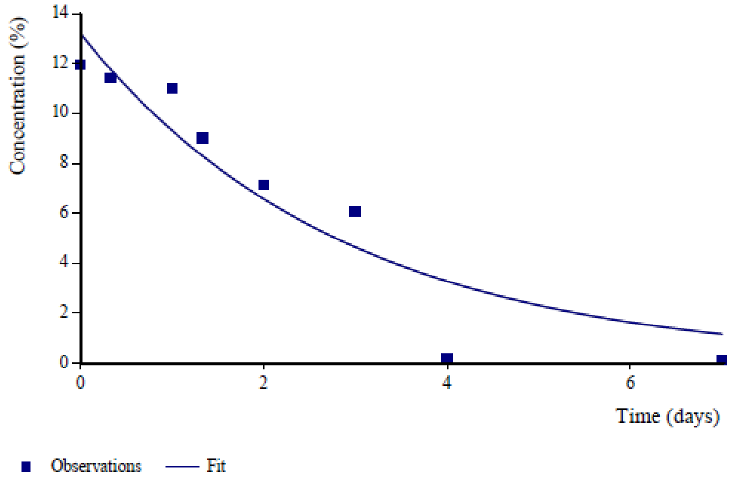
Trial SRHU18-053-037HR (Hungary)

Dissipation parameters of mesotrione in maize (trial SRHU18-053-037HR)

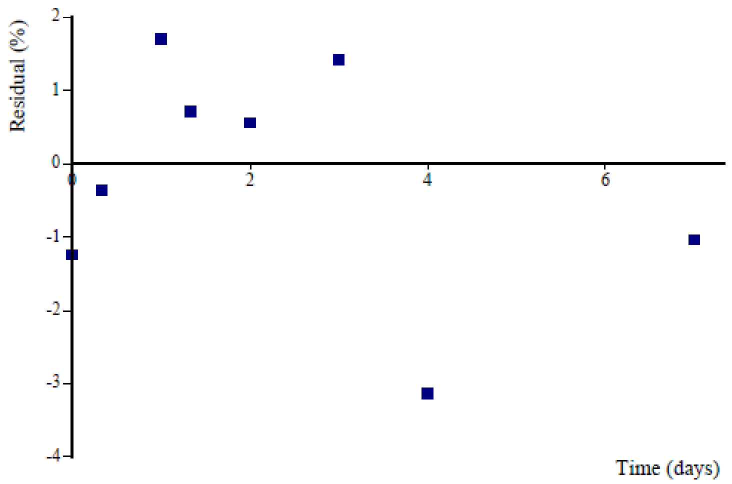
Kinetic model	***Compound***	***VA***	***χ^2 error (%)***	***t-test***	***DT_{50} (d)***	***DT_{90} (d)***
SFO	*Mesotrione*	*+*	*17.0*	*0.0022*	*1.99*	*6.61*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable

Observations and Fitted Model:



Residuals:

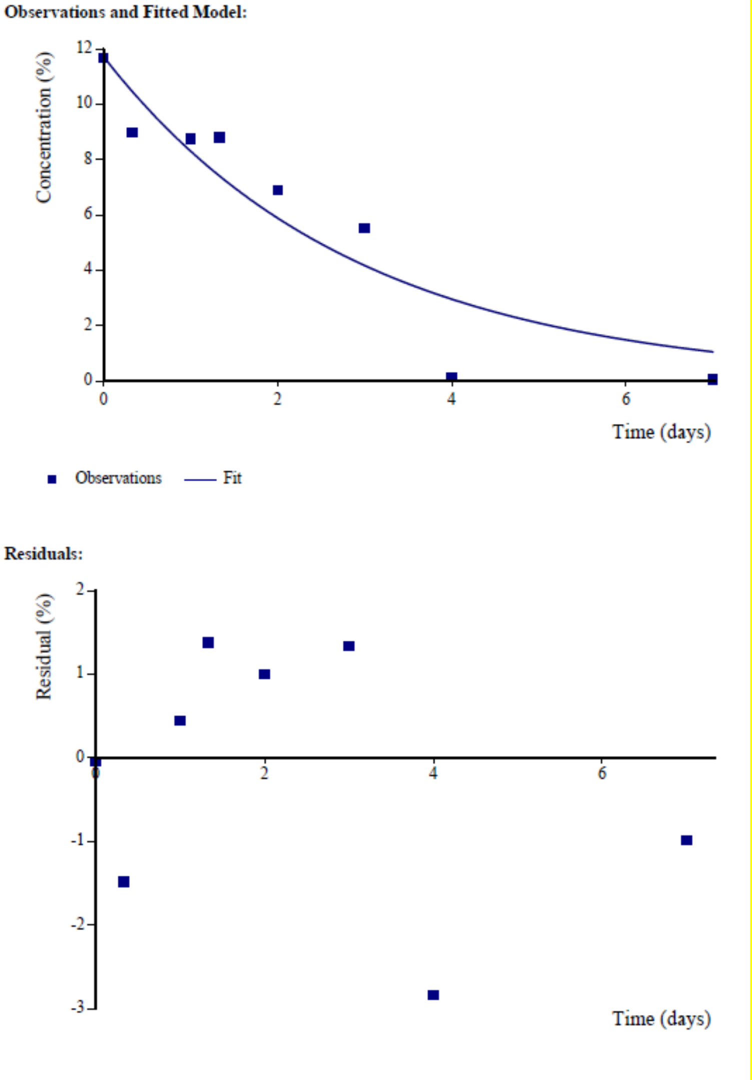


Trial SRHU18-054-037HR (Hungary)

Dissipation parameters of mesotrione in maize (trial SRHU18-054-037HR)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*+*	*17.8*	*0.082*	*2.01*	*6.68*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable

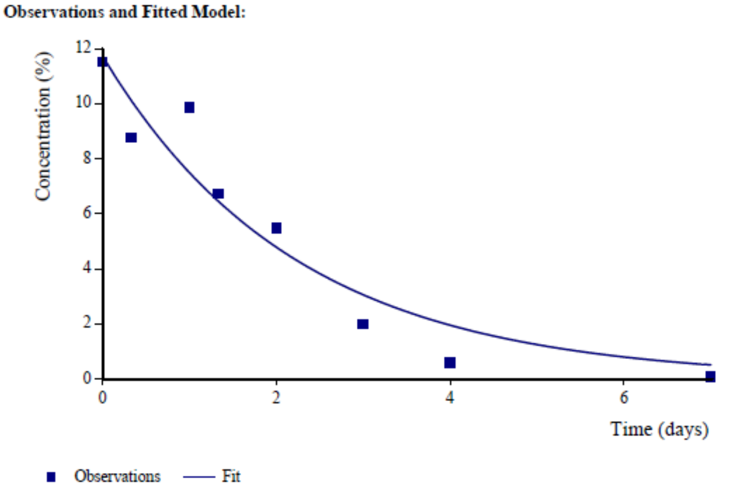


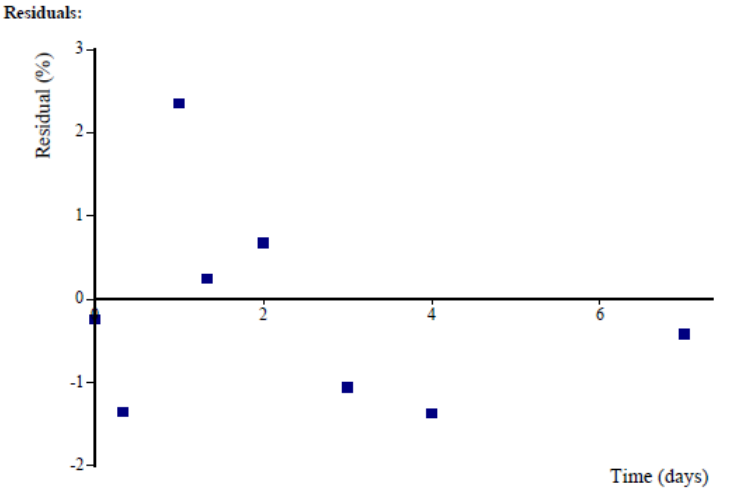
Trial SRFR18-010-037HR (N-France)

Dissipation parameters of mesotrione in maize (trial SRFR18-010-037HR)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*++*	*16.7*	*0.0011*	*1.55*	*5.13*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable





Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

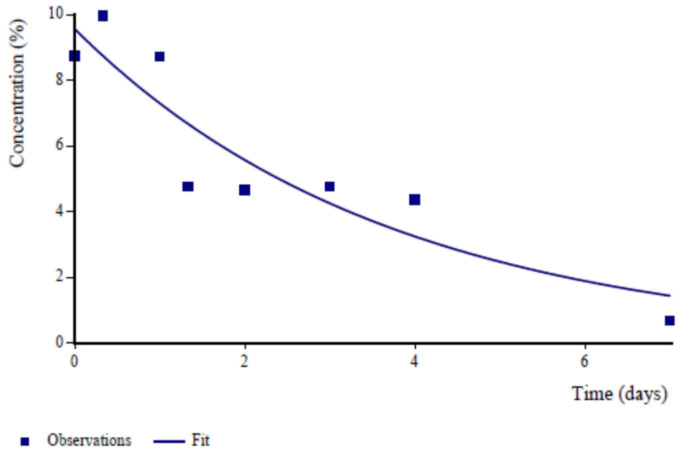
Trial SRFR18-011-037HR (N-France)

Dissipation parameters of mesotrione in maize (trial 3)

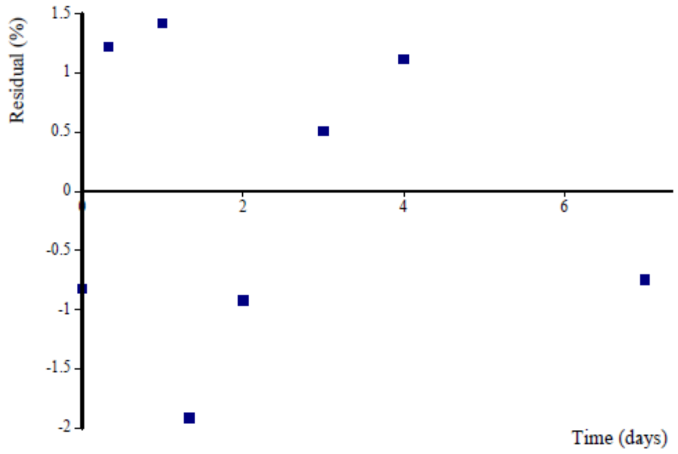
Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*o*	*15.8*	*0.0034*	*2.57*	*8.54*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable

Observations and Fitted Model:



Residuals:

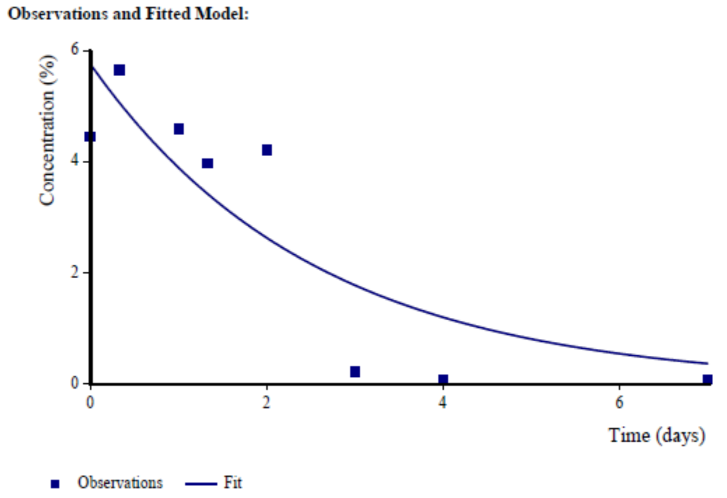


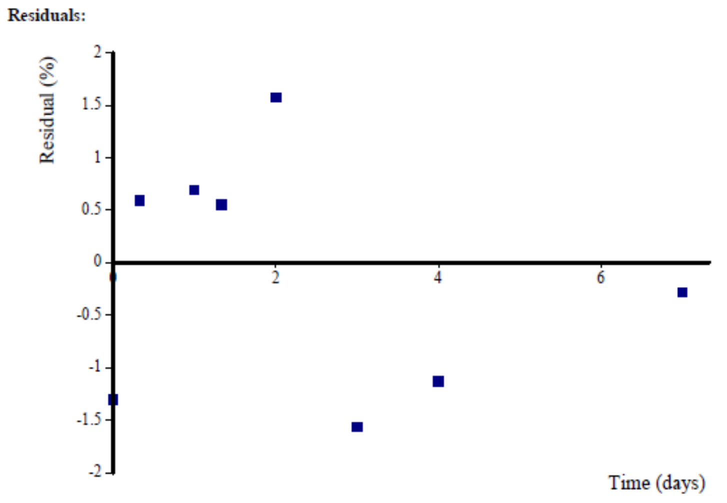
Trial SRDE18-001-037HR (Germany)

Dissipation parameters of mesotrione in maize (trial 3 SRDE18-001-037HR)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*o*	*29.2*	*0.016*	*1.77*	*5.89*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable





Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

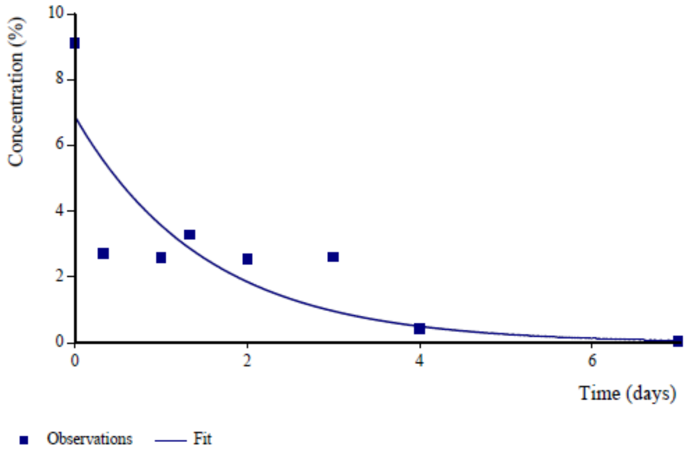
Trial SRDE18-002-037HR (Germany)

Dissipation parameters of mesotrione in maize (trial SRDE18-002-037HR)

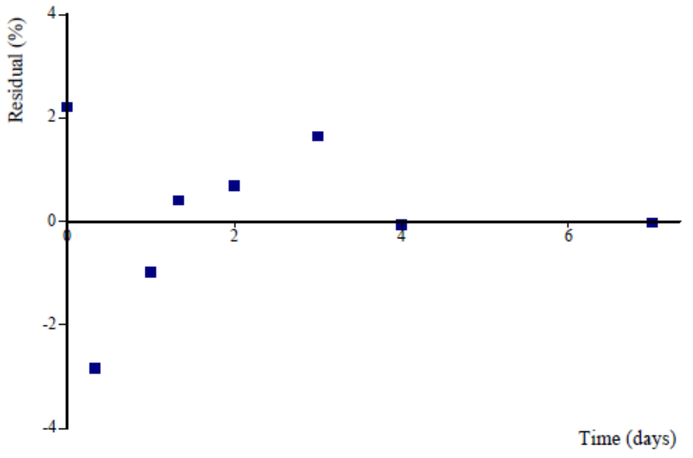
Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*-*	*40.2*	*0.027*	*1.06*	*3.51*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable

Observations and Fitted Model:



Residuals:



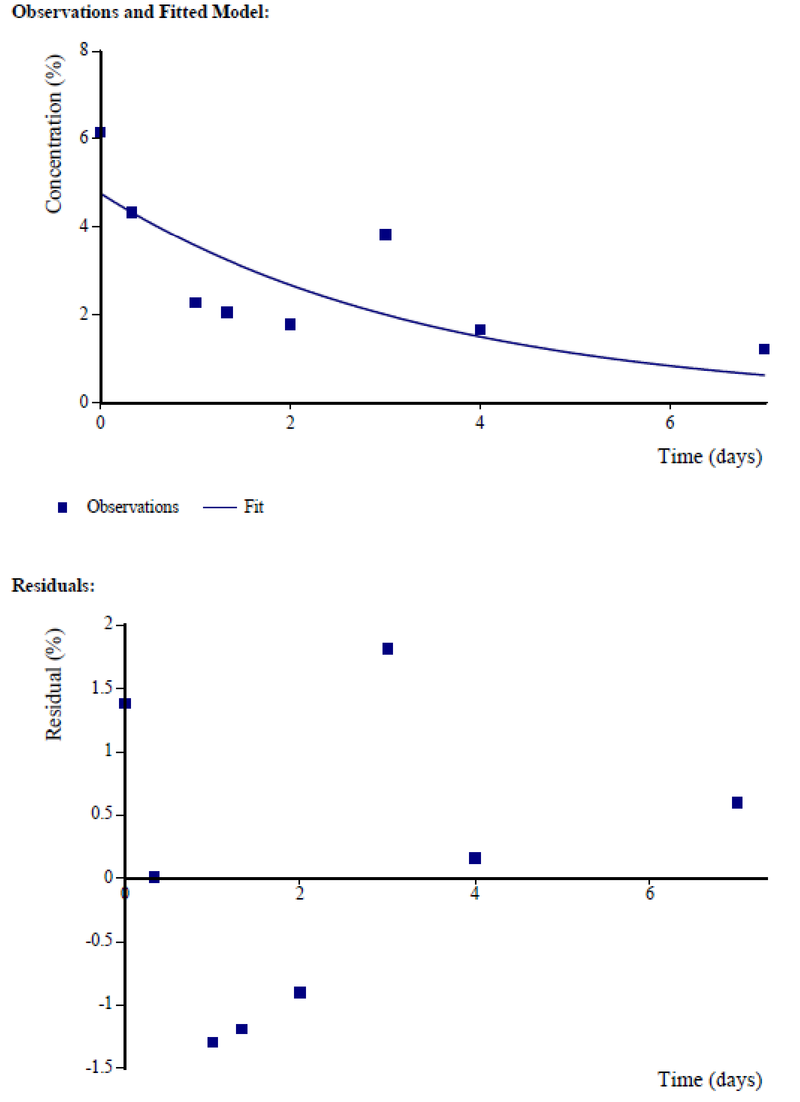
Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Trial SRPL18-014-037HR (Poland)

Dissipation parameters of mesotrione in maize (trial SRPL18-014-037HR)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*o*	*29.7*	*0.036*	*2.41*	*7.99*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable

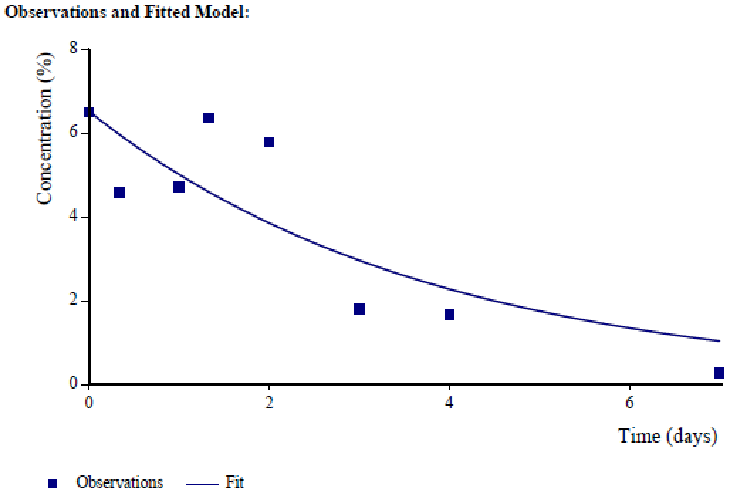


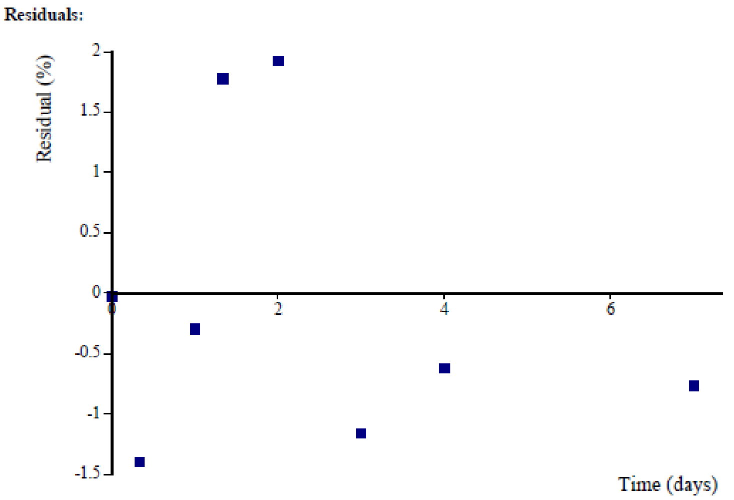
Trial SRPL18-015-037HR (Poland)

Dissipation parameters of mesotrione in maize (trial SRPL18-015-037HR)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*o*	*23.8*	*0.018*	*2.64*	*8.75*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable





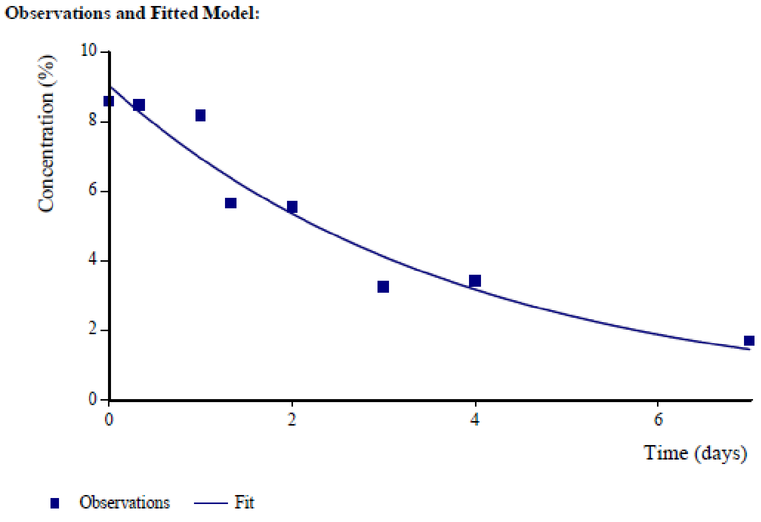
Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

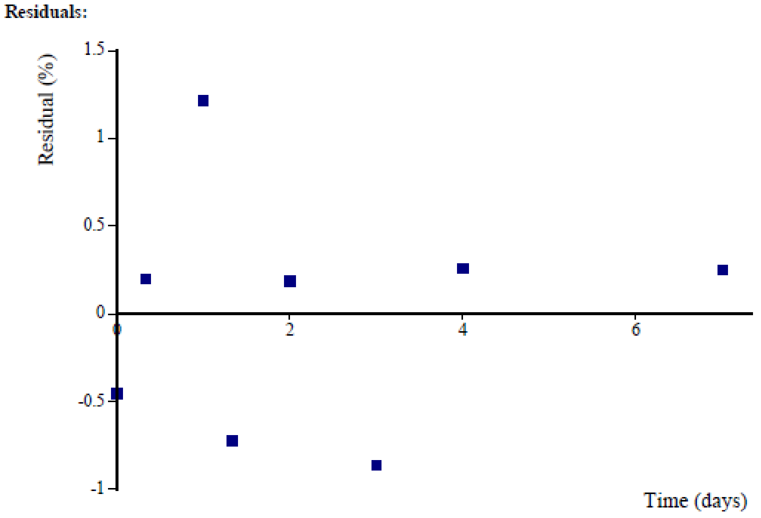
Trial G006-18H (Belgium)

Dissipation parameters of mesotrione in maize (trial 3)

Kinetic model	*Compound*	*VA*	*χ^2 error (%)*	*t-test*	*DT_{50} (d)*	*DT_{90} (d)*
SFO	*Mesotrione*	*++*	*8.94*	*2.08E-004*	*2.65*	*8.8*

estimation of visual fits: +++ excellent; ++ good; + acceptable; o poor; - unacceptable





The below studies have already been evaluated and considered adequate during the EU AIR review of mesotrione:

Comments of zRMS:	*The study has been already evaluated at the EU level and re-evaluation at the zonal level was deemed not necessary. For the study summary and respective evaluation, please refer to mesotrione RAR of 2015.*

Reference:	*KCP 10.1.2.2/07*
Report	*Funkenhaus A, Giessing B (2010) Exposure of mammals in maize fields in France - attractiveness of maize fields and relevant species. RIFCON GmbH, Im Neuenheimer Feld 517. D-69120 Heidelberg, Germany. Syngenta Unpublished Report No. R09012-2. Study No TK0003853* *Syngenta file No NA_11991 (Data owned by Syngenta)*
Guideline(s):	*No guidelines available, but following recommendations in the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) and its appendices*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Already evaluated at the EU level*
Duplication (if vertebrate study)	*No*

Comments of zRMS:	*The study has been already evaluated at the EU level and re-evaluation at the zonal level was deemed not necessary. For the study summary and respective evaluation, please refer to mesotrione RAR of 2015.*

Reference:	*KCP 10.1.2.2/08*
Report	*Wolf C (2005) Generic field monitoring of birds and mammals on maize and beet fields in Austria. Bayer CropScience AG. Unpublished Report No: WFC/FS 017, 20 January 2005.* [redacted]
Guideline(s):	*No guidelines available, but following recommendations in the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) and its appendices*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Already evaluated at the EU level*
Duplication (if vertebrate study)	*No*

Comments of zRMS:	*The study has been already evaluated at the EU level and re-evaluation at the zonal level was deemed not necessary. For the study summary and respective evaluation, please refer to mesotrione RAR of 2015.*

Reference:	*KCP 10.1.2.2/09*
Report	[redacted] *owner: Oxon Italia, S.p.A., Syngenta access)*
Guideline(s):	*No guidelines available, but following recommendations in the EFSA Guidance Document on Risk Assessment for Birds and Mammals (2009) and its appendices*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Yes*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Duplication (if vertebrate study)	*No*

Comments of zRMS:	*The study by Späth (1989) has been used by the Applicant to refine the PT value for the brown hare in maize fields. No summary of the study was available during the initial review by the zRMS and the study itself is written in German, so it was not possible to validate its results. It was noted that the study was, however, submitted in support of evaluation of first zonal evaluation of formulation Calaris owned by the same Applicant. Following conclusion was derived by the zRMS for Calaris (UK):* *The zRMS has considered the proposed refinement to the PT however the study (Späth 1989) has not been submitted or evaluated. It is also noted the values provided are not PT values and the zRMS does not agree with the assumption that the percentage of maize in a home range provides an estimate for PT. Combined with the low sample size and that the consumers and potential consumers can not be calculated the suggested refinement to PT based on this study is not acceptable* *Nevertheless, without the translated study summary it was not possible to verify conclusions of the UK evaluator and the Applicant was requested to provide respective document, which was submitted during the commenting period and is presented below.* *The overview by the zRMS confirmed the supposition of UK evaluator, that based on results of the study by Späth (1989) it was assumed that the percentages of maize in a home range of radio-tracked individuals are equivalent to the PT values. However, according to EFSA (2009), PT should be expressed as the amount of (potential) foraging time in the crop expressed as a proportion of the total time spent (potentially) foraging in the day. For this reason values based on results of study by Späth (1989) cannot be considered to be PT values, as such approach may lead to underestimation of the time the individual hare spent actually foraging in maize. It cannot be excluded that for example animal with 20% of maize within the home range actually spends e.g. 50 or 60% of its daily foraging time feeding in maize, which would lead to PT of 0.5 or 0.6, clearly exceeding the home range percentage. Taking this into account, approach taken is highly uncertain and percentage of maize in a home range of tracked individuals cannot be considered to be equivalent to PT values. Therefore results of study by Späth (1989) are considered to be not relevant for derivation of PT values and cannot be used to refine this parameter.*

Reference:	*KCP 10.1.2.2/12*
Report	*Späth V. (1989) Untersuchungen zur Populationsökologie des Feldhasen (Lepus europaeus Pallas) in der Oberrheinebene* *Translation: Studies on the Population Ecology of the Field Hare (Lepus europaeus PALLAS) in the Upper Rhine Plain* *PhD thesis, University of Freiburg, Freiburg im Breisgau.* *Syngenta File No. VV-243592*
Guideline(s):	*Not applicable*
Deviations:	*Not applicable*
GLP:	*No*
Acceptability:	*Study itself performed correctly, but not relevant for derivation of PT values*
Duplication (if vertebrate study)	*Not relevant (monitoring study)*

Executive summary

The aim of this work was to examine the extent to which hare densities in the Upper Rhine Plain in Germany are correlated with different landscape structure parameters and to what extent a causal explanation model can be developed to establish the existing population densities of the field hare. The study took place in an arable region mainly growing cereals and maize, but also some pasture and grassland.

Test Material	*Not applicable for generic field study*
Test design	
Test site:	*Upper Rhine Plain between Neuchâtel and Karlsruhe, Germany*
Replication:	*None*
Live-trapping test organisms	
Species:	*Brown hare (Lepus europaeus L.)*
Live trapping test design	
Type of trap:	*net*
Number of traps per plot:	*Not stated*
Duration of trapping session:	*Not stated*
Dates of live trapping tests:	*late winter 1984 to spring 1986*
Marking of individuals:	*Radio transmitter collars*
Radio-tracked test organisms	
Species:	*Brown hare (Lepus europaeus L.)*
Radio-tracking test design	
Number of individuals:	*21 hares fitted with collars*
Duration:	*late winter 1984 to spring 1986*
Environmental test conditions	
Temperature: ***Precipitation:*** ***Humidity:***	• *a mild and precipitous winter of 83/84* • *a subsequent dry, cold spring,* • *an average summer and* • *a rainy autumn* • *a cold and snowy winter of 84/85* • *a spring characterised by arctic cold snaps* • *a warm and dry summer and autumn of 1985.*
Plant protection treatments during test:	*Pesticide treatments were not managed so followed standard practices for the region*

Study Design and Methods

Field phase experimental dates: late winter 1984 to spring 1986

Aim: *The aim of this study was to investigate the habitat selection, activity pattern and home range distribution of the Brown hare in the Upper Rhine Plain between Neuchâtel and Karlsruhe which was selected as the study region in consultation with the hunters of Baden-Württemberg. Due to its arable use and favourable climate, this area is considered one of the "homelands" of the field hare, with comparatively high bag results.*

Study area: *The study region belongs to the "Southern, Middle and Northern Upper Rhine Lowlands" geographically and as a climate zone. In 1984, 17 study areas with a reference area of 2800 ha and in 1985 23 study areas with a reference area of 4009 ha were included in the investigations. This mixed area represents a typical landscape for growing grain in Central Europe, mainly cereals and maize. Moist, low-lying river valleys, i.e. unfavourable habitats from the outset, were not represented.*

***Method and parameters**: All the habitats in the study area were described through seasonal direct surveys in order to define any environment available for hares. In addition to the cultivated field crop types, the grain and maize fields were tested for the presence of field weeds. In this case, the areas treated with herbicides according to regulations could be separated from fields which had been alternatively treated, or had not been treated with herbicides, or which were only insufficiently treated with herbicides. The grain and maize fields with pronounced field weeds were specially marked in the maps and evaluated separately.*
During hunting area visits and hare counts, dates and data on soil cultivation measures, harvesting measures and vegetation development were continually maintained, so that structural changes to the landscape during the course of the year could be understood.

Using nine radio-tracked hares, specific land use mapping was carried out within the respective populated areas. The cultivation rates of the individual crop types were compiled for the subsequent periods of time, which are comparable in vegetation characteristics:

- *1 March to 15 May*
- *16 May to 20 July*
- *21 July to 5 September*
- *6 September to 31 December*

The temporal classification of the periods was based on the growth development of the main types of crops (grain and maize) and the process of harvesting and soil cultivation measures.
The grazing capacities of the individual months for an average hunting area for which the following land use has been adopted are shown below:

Winter grain	*30%*	*Volunteer grain*	*10%*
Winter barley	*10%*	*Catch crop*	*20%*
Weedy summer grain	*20%*	*Maize stubble*	*10%*
Grain	*10%*		
Maize	*30%*		
Other root crops	*10%*		
Meadow	*10%*		

The grazing capacity in midsummer and in autumn have been used as parameters for the identification of possible grazing shortages.

Determination of hare densities

Spotlighting with line transects was used as a method for determining the game densities of the field hare. With this observation and counting method, predefined routes are driven at night with a vehicle at walking speed, and the strips of ground to the left and right of the route are illuminated by spotlights. The headlights used have a practical operating distance of approximately 250 m in suitable terrain. The viewing distance up to which the hares were noted was generally 150 m. The route driven was chosen in such a way that the neighbouring line transects were continuous with each other. This method is particularly suitable for the field hare because the high level of activity of the hare during the early hours of the night, in conjunction with the reflective iris of its eyes, minimises the percentage of overlooked hares . Areas with visually impairing vegetation were searched with binoculars. For this purpose, especially during the vegetation period, the journey was interrupted every 100 m, in order to systematically search all semi-covered areas (up to a maximum vegetation height of 50 cm).

In the case of marked hares the counting accuracy was at a re-observation rate of 90%; the double observation rate per transect was 7.6% for marked animals.

Determination of grazing preferences

The spotlighting method using line transects was also used to record the distribution patterns of the hare on the individual types of crop.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

During the total counts in the period from November to mid-April a certain percentage of the hare population could thus be attributed to the types of crop present. Based on the comparison of the area proportion of the crop type concerned and the percentage of hares found there, conclusions can be drawn about the preference or avoidance of certain types of crop at specific times.

In the period from mid-April to about the beginning of November, only a partial area of the SA can be seen, and therefore only a certain proportion of the hare population can be recorded. While the area proportion of the observable types of crop is known, the observed proportion of the respective field hare population can only be reconstructed after determining the summer population in the month of September. The number of hares observed in one field type is correlated to the calculated total number for the respective point in time (assuming a linear incremental curve from the winter population, mid-April to the summer population, end of September).

From the total 23 study areas, 8 in 1984 and 13 in 1985 were examined year-round for the distribution of the field hares (approximately at 14-day intervals) using the spotlight counting method.

Capture, tagging and recapture of 21 hares

In the spring of 1984 and 1985, a total of 21 field hares were caught using nets and equipped with a collar transmitter. In addition to the collar transmitter, the animals also received a Rototag ear tag (light orange) with Scothlite tape adhered to it. The finding and observation of the tracked hares was made easier at night due to the reflective tape and was also possible within semi-covering plant populations. In order to receive the transmitter signals we used an H-antenna and a tracking receiver from the company Reichenbach. The signals were displayed acoustically via a built-in loudspeaker and as a pointer deflection on a built-in ammeter. The observation and monitoring of the tracked hares was generally carried out from the car.

The location was recorded on maps with a scale of 1: 5000, in which the land use of the study areas had already been recorded at the start of the investigation. In addition, the respective behaviour of the hares was logged in a diary-like manner with accurate times, so that knowledge could be gained not only about the size of the home range, but also on activity rhythm and grazing behaviour. The motion detectors allowed for concrete conclusions to be made on the activity of the field hare. The acoustic signals could be converted into certain behaviours of the relevant field hare by an experienced observer. It was thus possible to distinguish between grazing, sitting, lying and moving on the basis of the incoming signals.

The radio-tracked field hares were usually observed three times a week. The observation activity spanned from dusk to the morning hours. From the logs, the following was calculated:

1) *The distribution of the grazing time on individual field crop types*
2) *The seasonal order of the types of crops sought for cover*
3) *The percentage of boundary line grazing of the total grazing time for five hares*
4) *The size of seasonal core areas as the polygonal area obtained by connecting the extreme observation points during certain time periods. Boundary structures (roads, waterways, trees and shrubs) respected by the hares were, however, taken into account, so that there were, for example, concave boundaries of the home ranges.*
5) *The area of the habitat during the total observation period as the total area of the seasonal core areas.*

Out of the total of 23 radio-tracked individuals, 13 animals were able to be observed for more than 100 days (sometimes even over 200 days).

***Results and Discussion**:*

The total counts of the individual test areas carried out during the early hours of the night provide a density indication for each hunting area for the period from February to April (winter density, WD) and for the period from mid-August to October (summer density, SD). In most of the SAs the winter densities varied between 20 and 30 hares per 100 ha. The range of winter densities extended from 6 to 94 units per 100 ha. The range of summer densities extended from 16 to 127 units per 100 ha with an average of 44.2.

During the years 1984 and 1985, 21 field hares were equipped with collar transmitters and subsequently observed over a period of at least 12 and no more than 263 days. Within two weeks after their capture, four tracked hares had failed, three more transmitters could no longer be located less than 90 days after the capture. Out of the first four field hares, three animals were found dead or killed, the remaining four field hares were probably lost from the observation due to technical defects on the collar transmitters. In total, 13 tracked hares were observed for between three and nine months. The mean average value was 198 days.

Home ranges and observation period of radio-tracked hares

Study area	Field hare (Name)	Sex (m, f)	Observation period (Date, day)				Observation intensity (Minutes per month)	Home range (ha)
1984								
Au-Niederfeld	Willi *	m	20.03	-	15.11.	240	2890	17
	Lisbet	f	20.03	-	10.05	51	-	18
Durmersheim	Iwan *	m	19.03	-	22.08	156	2786	35
Würmersheim	Franz	m	30.04	-	04.07	65	-	16
	Rilke	m	30.04	-	10.05	10	-	-
	Großmann	m	29.10	-	01.02	94	-	16
Allmannsweier	Detlef	m	29.03	-	29.09	184	2104	29
	Beißer	m	12.04	-	17.10	188	2189	17
	Ida	f	12.04	-	30.09	171	2334	34
Herbolzheim	Elvira	f	11.04	-	24.09	166	409	36
Rheinhausen	Anna	f	18.04	-	30.04	12	-	-
1985								
Au-Niederfeld	Annie *	f	02.04	-	21.12	263	2444	6
	Dollie *	f	02.04	-	21.12	263	1924	7
	Seppl	m	12.04	-	16.11	218	1976	11
	Egon	m	12.04	-	27.07	106	1721	11
Ottenheim	Petra *	f	17.04	-	02.11	199	1014	19
	Hoho *	f	19.04	-	02.11	197	1142	20
Allmannsweier	Rustica	f	17.04	-	02.05	15	-	-
	Mübke	m	03.05	-	07.06	35	-	12
Herbolzheim	Speranza	f	17.04	-	06.05	19	-	-
	Reißer*	m	19.04	-	27.11	222	946	16
overall	21 field hares	11 bucks 10 does				2874 ($\bar{x}$=137)	23879 ($\bar{x}$=1837)	18.8 (n=17)

The areas preferred for plant cover were described on the basis of the combination of all field observations, in particular the observation of the 21 tracked hares.

The dominant character of the area concerned was used to assign the fields to the categories of "grazing" and "plant cover". For example, a high-grown clover field provides cover for the field hare, but it is primarily used for feeding. Conversely, the field hare finds some food on a newly ploughed field, but the protection and coverage aspect of a trough for a simultaneous overview of the terrain is more important. Over the course of the year, different fields are sought out for cover depending on the condition of the plant cover.

The table below summarises the proportion of habitat in the home range for each hare monitored. The use of these areas for grazing was confirmed by observation, as described above.

Landscape structure and land use within the home ranges of radio-tracked field hares is presented in table below.

The area proportions of individual field crop types are specified as a percentage of the area of the home range for the respective time period

Name of the field hare	***Willi***				***Seppl***				***Annie***				***Dollie***				***Egon***	
Time period: (months)	*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*
Winter grain	*9*	*2*	*-*	*-*	*15*	*2*	*-*	*12*	*31*	*19*	*-*	*16*	*14*	*37*	*6*	*16*	*26*	*18*
Summer grain	*13*	*20*	*-*	*-*	*53*	*81*	*2*	*-*	*10*	*15*	*6*	*-*	*19*	*24*	*-*	*-*	*30*	*39*
Maize	***-***	***51***	***31***	***-***	***-***	***2***	***2***	***-***	***-***	***6***	***8***	***-***	***-***	***6***	***7***	***-***	***-***	***4***
Grain stubble	*-*	*-*	*20*	*-*	*-*	*-*	*40*	*18*	*-*	*-*	*20*	*-*	*-*	*-*	*10*	*-*	*-*	*-*
Volunteer grain	*-*	*-*	*12*	*18*	*-*	*-*	*40*	*30*	*-*	*-*	*35*	*22*	*-*	*-*	*4*	*11*	*-*	*-*
Catch crop	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*19*	*-*	*-*	*34*	*15*	*-*	*-*
Maize stubble	*-*	*-*	*-*	*25*	*-*	*-*	*-*	*3*	*-*	*-*	*-*	*12*	*-*	*-*	*-*	*25*	*-*	*-*
Bare field	*49*	*-*	*-*	*29*	*3*	*-*	*-*	*5*	*29*	*-*	*-*	*-*	*46*	*-*	*9*	*19*	*16*	*-*
Meadow	*24*	*20*	*32*	*21*	*24*	*6*	*7*	*23*	*28*	*45*	*21*	*18*	*13*	*16*	*12*	*7*	*26*	*32*
Root crops	*1*	*2*	*2*	*2*	*-*	*3*	*1*	*4*	*-*	*12*	*10*	*5*	*-*	*15*	*14*	*5*	*-*	*3*
Fallow land/groves	*4*	*5*	*3*	*5*	*5*	*6*	*8*	*4*	*2*	*4*	*-*	*8*	*8*	*2*	*2*	*2*	*2*	*4*
Average parcel size	*.40*	*.22*	*.24*	*.34*	*.29*	*.34*	*.36*	*.23*	*.16*	*.16*	*.13*	*.16*	*.24*	*.11*	*.12*	*.18*	*.62*	*.40*

Name of the field hare	***Iwan***				***Petra***				***Hoho***				***Reißer***					
Time period:	*3-5*	*5-7*	*7-8*		*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*	*7-8*		*3-5*	*5-7*	*7-8*	*9-12*		
Winter grain	*40*	*37*	*-*		*6*	*9*	*-*	*-*	*22*	*8*	*-*		*19*	*21*	*-*	*12*		
Summer grain	*26*	*16*	*19*		*15*	*11*	*2*	*-*	*24*	*25*	*10*		*12*	*23*	*5*	*-*		
Maize	***-***	***24***	***-***		***-***	***12***	***13***	***-***	***-***	***35***	***17***		***-***	***7***	***16***	***-***		
Grain stubble	*-*	*-*	*15*		*-*	*-*	*12*	*-*	*-*	*-*	*6*		*-*	*-*	*5*	*-*		
Volunteer grain	*-*	*-*	*-*		*-*	*-*	*-*	*8*	*-*	*-*	*10*		*-*	*-*	*14*	*8*		
Catch crop	*-*	*-*	*-*		*-*	*-*	*6*	*27*	*-*	*-*	*20*		*-*	*-*	*17*	*33*		
Maize stubble	*-*	*-*	*-*		*-*	*-*	*-*	*21*	*-*	*-*	*-*		*-*	*-*	*-*	*14*		
Bare field	*15*	*-*	*-*		*21*	*-*	*-*	*-*	*17*	*-*	*8*		*20*	*-*	*5*	*8*		
Meadows (= strawberries)*	*24**	*20**	*64**		*38*	*59*	*47*	*29*	*5*	*2*	*4*		*35*	*14*	*19*	*12*		
Clover/clover grass meadows	*-*	*-*	*-*		*6*	*8*	*10*	*5*	*15*	*30*	*25*		*-*	*-*	*-*	*-*		
Root crops (= beans)*	*-*	*-*	*-*		*7**	*2**	*1**	*5**	*15**	*-*	*-*		*2**	*3**	*-*	*-*		
Fallow land/groves (= wild fields)*	*7*	*3*	*3*		*7*	*-*	*11*	*5*	*2*	*-*	*-*		*12**	*32**	*21**	*13**		

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Average parcel size	*1.88*	*1.31*	*1.47*		*.58*	*.47*	*.71*	*.46*	*.46*	*.43*	*.50*		*.71*	*.31*	*.48*	*.47*

*(note – to ease review, the values highlighted in **bold** in the table below are the values that have been used to calculate the overall PT)*

Grazing preferences of radio-tracked hares in the study areas (B values)

The average value is provided for the respective crop type in the time periods considered																		
Name of the field hare	***Willi***				***Seppl***				***Annie***				***Dollie***				***Egon***	
Time period: (months)	*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*
Winter grain	*3.1*	*0.0*	*-*	*-*	*2.4*	*2.8*	*-*	*1.7*	*1.7*	*0.0*	*-*	*1.8*	*3.1*	*0.4*	*2.7*	*2.4*	*1.1*	*1.0*
Summer grain	*3.8*	*1.1*	*-*	*-*	*0.8*	*0.4*	*3.3*	*-*	*3.4*	*2.0*	*6.7*	*-*	*3.0*	*0.7*	*-*	*-*	*1.4*	*1.2*
Maize	*-*	*0.4*	*0.3*	*-*	*-*	*0.0*	*0.0*	*-*	*-*	*4.2*	*0.0*	*-*	*-*	*3.0*	*0.0*	*-*	*-*	*7.1*
Grain stubble	*-*	*-*	*1.9*	*-*	*-*	*-*	*0.8*	*0.8*	*-*	*-*	*2.6*	*-*	*-*	*-*	*3.3*	*-*	*-*	*-*
Volunteer grain	*-*	*-*	*3.3*	*2.0*	*-*	*-*	*1.0*	*1.2*	*-*	*-*	*1.6*	*2.2*	*-*	*-*	*6.7*	*1.0*	*-*	*-*
Catch crop	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*1.7*	*-*	*-*	*0.8*	*2.3*	*-*	*-*
Maize stubble	*-*	*-*	*-*	*1.5*	*-*	*-*	*-*	*3.3*	*-*	*-*	*-*	*1.4*	*-*	*-*	*-*	*0.3*	*-*	*-*
Meadow	*1.3*	*0.5*	*0.8*	*1.0*	*0.7*	*2.1*	*1.2*	*1.2*	*1.1*	*0.7*	*1.5*	*2.0*	*3.1*	*1.7*	*0.9*	*7.0*	*1.3*	*0.7*
Root crops	*12*	*7.0*	*5.3*	*0.0*	*-*	*5.1*	*9.6*	*2.9*	*-*	*1.6*	*0.0*	*0.0*	*-*	*2.9*	*0.0*	*1.0*	*-*	*4.2*
Fallow land/groves	*5.6*	*60*	*7.9*	*3.8*	*1.2*	*6.2*	*3.7*	*3.0*	*6.0*	*2.8*	*-*	*2.0*	*5.0*	*7.5*	*4.0*	*2.5*	*0.0*	*2.2*
Name of the field hare	***Iwan***				***Petra***				***Hoho***				***Reißer***					
Time period:	*3-5*	*5-7*	*7-8*		*3-5*	*5-7*	*7-8*	*9-12*	*3-5*	*5-7*	*7-8*		*3-5*	*5-7*	*7-8*	*9-12*		
Winter grain	*1.5*	*0.3*	*-*	*-*	*0.0*	*0.0*	*-*	*-*	*0.7*	*0.9*	*-*	*-*	*0.7*	*0.6*	*-*	*3.9*		
Summer grain	*2.2*	*2.4*	*1.1*	*-*	*2.8*	*3.1*	*5.0*	*-*	*1.4*	*1.9*	*3.8*	*-*	*6.4*	*0.9*	*5.6*	*-*		
Maize	*-*	*1.0*	*-*	*-*	*-*	*2.2*	*0.0*	*-*	*-*	*0.7*	*- 0.0*	*-*	*-*	*4.5*	*0.0*	*-*		
Grain stubble	*-*	*-*	*0.5*	*-*	*-*	*-*	*1.0*	*-*	*-*	*-*	*6.2*	*-*	*-*	*-*	*3.6*	*-*		
Volunteer grain	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*0.0*	*-*	*-*	*5.2*	*-*	*-*	*-*	*2.5*	*2.5*		
Catch crop	*-*	*-*	*-*	*-*	*-*	*-*	*7.0*	*1.2*	*-*	*-*	*1.3*	*-*	*-*	*-*	*1.9*	*1.7*		
Maize stubble	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*1.7*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*0.0*		
Meadows (= strawberries)*	*1.2**	*0.8**	*0.4**	*-*	*1.0*	*0.8*	*1.2*	*2.1*	*4.0*	*8.0*	*0.7*	*-*	*0.3*	*1.7*	*1.3*	*1.8*		
Root crops (= beans)*	*-*	*-*	*-*	*-*	*2.5*	*2.0*	*0.0*	*0.0*	*1.0*	*-*	*-*	*-*	*0.0*	*0.0*	*-*	*-*		
Wild fields/clover grass	*1.1*	*9.0*	*14*	*-*	*4.2*	*0.0*	*2.4*	*0.0*	*2.4*	*0.0*	*-*	*-*	*1.3*	*0.9*	*1.2*	*0.8*		

The popularity of the types of grains initially falls sharply in the summer and rises above the spring value again with winter grains in autumn/winter. The summer grains reach higher values than the winter grains in comparable periods. High B values were calculated for the grain harvest period. Maize only serves the hare as a grazing plant in a narrow period of time, from about mid-May to the end of June; it only reaches moderate preference values.

In the second half of the year (after the grain harvest), the grain stubble, the volunteer grain and the catch crops are sought for grazing. The maize stubble is only slightly preferred during short periods of time.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

The meadows are among the preferred grazing areas for the entire observation period.

The permanent cover areas (wild fields, fallow land, groves) are highly popular throughout the entire observation period. Preference for root crops is from May to July.

The B values for maize are in the range of >1 in May and June. The young maize plant is gladly accepted for grazing up to a height of about 30 – 50 cm. Before herbicides are sprayed, the sprouting grasses and herbs have additional importance as food vegetation. From about mid-July, the use of maize as a grazing area is almost completely ceased; the calculated B value is close to 0 (aversion).

With the harvesting of grain maize, the maize fields again gain in importance for the field hares. The maize stubble is attractive as a grazing area for a period of up to four weeks.

Grazing preferences of field hares observed during spotlighting

1. *Between 40 and 80% of the hare population can be found on grain and maize fields during the course of year. The highest proportions are measured during the winter half-year from November to April.*
2. *Over the course of the year, a fixed chronological sequence in grazing activity can be observed between the fields cultivated with grains and maize. The sequence from January to December is: Winter grain... Summer grain... Maize... Grain stubble... Volunteer grain... Catch crops... Maize stubble... Winter grain.*
3. *Between 20 and 60% of the hare population can be found on grassland and fields with legumes and root crops during the course of year. The highest proportion can be observed in the summer half-year from May to October.*
4. *During the course of the year, a certain chronological sequence can be recognised in the hare's use of the above-mentioned areas, which are also largely characterised by wild plants. The sequence from January to December is: Meadows, ryegrass... Grass paths, turnips, peas, beans... Clover, clover grass, wild fields... Meadow, grass paths, ryegrass.*

Based on presented above results, the following PT values were calculated by the Applicant in Alvarez (2019):

Animal No	***Time period***	***Percentage maize in home range [%]***
1	*May-July*	*51*
2		*2*
3		*6*
4		*6*
5		*4*
6		*24*
7		*12*
8		*35*
9		*7*
Mean (n=9)		***16.3***
90th percentile		***38***

Comments of zRMS:	*During the commenting period additional information regarding potential refinement of the mean RUD value in maize has been submitted by the Applicant. The summary is presented below for information of the concerned Member States.* *It is noted that very limited information was provided by the Applicant and for this reason the summary was supplemented with more extent information available from the poster presented by the authors during the SETAC Europe 25th Annual Meeting 2015 in Barcelona.* *From the available information it seems that derivation of the RUD values in maize followed approach taken to derive the default RUD values for grass+cerals in EFSA (2009). Based on obtained results, the mean RUD of 46.8 mg/kg was derived for maize and may potentially be used for purposes of the risk assessment, especially it actually originates from the*

	sufficient dataset derived from residue trials in maize and is more relevant than RUD derived for grass+cereals, excluding residue trials in maize. *Nevertheless, it is noted that very limited information on the study by Murfitt et al. (2015) is available and no background documents were presented. Taking this into account the zRMS could not confirm validity of the provided RUD value and this refinement option must be further considered at the national level.*

Reference:	*KCP 10.1.2.2/13*
Report	*Murfitt R., Foudoulakis M., Ebeling M., Guth K., Brugger K. (2015) 'Measured residues on maize foliage for use in bird and mammal risk assessment'* *Syngenta, Bracknell, UK; and others.* *Not GLP* *Poster presented at SETAC Barcelona, 2015*
Guideline(s):	*Not applicable*
Deviations:	*Not applicable*
GLP:	*No*
Acceptability:	*In opinion of the zRMS the study provides useful information on RUD values derived specifically for maize and which could supersede the default RUD values indicated in EFSA (2009) for grass+cereals (with no maize included in this dataset). However, due to very limited information available, validation of the RUD by the zRMS was not possible and should be thus addressed by particular cMS at the product authorisation, if necessary.*
Duplication (if vertebrate study)	*No*

Introduction

In mammal risk assessment for plant protection products in the EU according to Tier 1 of the EFSA Guidance Document on Risk Assessment for birds and mammals (EFSA, 2009) small herbivorous mammals are considered to consume maize leaves at early growth stages (BBCH 10-29). However, the initial residue for maize leaves in this assessment is based upon Residue per Unit Dose (RUD) values for "grasses and cereals". These are in turn are derived from industry field residue data on grasses and cereals, excluding any maize trials (Appendix 18, PPR Panel Scientific Opinion on the Science behind the Guidance Document on Risk Assessment for birds and mammals, 2008).
Since maize has quite a different growth habit from grasses and small-grain cereals like wheat and barley, it is appropriate to consider residues on this crop separately in order to determine whether they are significantly different.

Methods

A large dataset of industry dietary residue trials (436 trials: 255 EU-N; 181 EU-S) has been collated which give initial (0 days after application) foliar residue values for spray applications of pesticides to maize plants in growth stage range BBCH 10-19. Since in the BBCH monograph (Meier,2001), BBCH 20-29 (principal growth stage 2) does not exist for maize, these data will cover the BBCH 10-29 range. These initial residues were converted to RUD values using the application rate. Mean and 90th percentile RUD values were calculated across all European trials and subsets covering the Northern and Southern residue regions (Anon,2008), in order to check for any potential effect of region on RUD outcome.

Trials have been analysed from 15 European countries: Austria, Belgium, Denmark, France, Germany, Greece, Hungary, Italy, Netherlands, Poland, Portugal, Spain, Sweden, Switzerland, UnitedKingdom

Results

Table below shows mean and 90th percentile RUD values for maize foliage alongside the currently used EFSA values for grasses and cereals.

Summary of measured maize foliage RUD values compared to EFSA values for grasses and cereals

Crop	Residue region	No. of field trials	90th %ile RUD (mg a.s/kg fw)	Mean RUD (mg a.s/kg fw)
Maize	Europe	436	80.3	46.8
	North	255	80.4	46.1
	South	181	79.1	47.6
Grasses and cereals (EFSA, 2009)	Europe	132	102.3	54.2

The measured maize RUD's were lower than the values for grasses and cereals for both 90th percentile (21% lower) and mean (14% lower). It is clear that there is very little difference between the RUDs from Southern residue region and those from Northern residue region field trials, and hence it is reasonable to use the data from all European trials to set a standard RUD for European risk assessment.

Conclusions

- *Measured RUD values for maize in Northern and Southern European residue regions are virtually the same and hence can be combined*
- *The measured RUD values for maize for Europe of 80.3 (90th %ile) and 46.8 (mean) should be used to more accurately estimate exposure in mammal risk assessment under the EFSA Guidance for the early growth stages in maize i.e.BBCH 10-29*

****

Comments of zRMS:	*During the commenting period the new population modelling based on modified parameters agreed with The Netherlands has been submitted by the Applicant (Kleinmann, 2020). This new modelling was performed using the same concept as in Kleinmann (2019a), but it addressed concerns of The Netherlands principally on: the implementation of toxicity dose-response curves which they suggested should be implemented as threshold levels rather than extrapolated; on the worst-case nature of the landscape assessed; and on the extremely high EMFs required to demonstrate effects. There were also a number of clarifications on the parameterisation data.* *This new report was indicated as an updated Kleinmann (2019a), but due to the modified parameters it would require completely new evaluation which was not possible within the given timeframes, which could be adjusted in case the zRMS was informed about the ongoing discussion with The Netherlands or about intention to perform additional population modelling.* *As no such information was provided by the Applicant, at this stage the zRMS may only indicate that there is such a new modelling, which may be potentially less uncertain. Nevertheless, its acceptability and applicability must be decided at the national level, similarly as in case of Kleinmann (2019a), since in absence of the common agreement on evaluation of population modelling at the EU level and within the Central Zone, no final conclusion may be taken at the zonal level based on such data. The detailed summary of Kleinmann (2020) is provided below to aid preliminary review by the cMS.*

Reference:	*KCP 10.1.2.2/14*
Report	*Kleinmann J. (2020) Mesotrione - Population-level risk assessment for the brown hare: use in maize. Report Number 18014-SYN-4. WSC Scientific GmbH, Dossenheimer Landstrasse 9/1 69121 Heidelberg Germany.* *Syngenta File No. VV-847099*
Guideline(s):	*European Food Safety Authority (EFSA) 2009. Guidance Document on Risk Assessment for*

	Birds and Mammals on request from EFSA. EFSA J. 7: 1438. *European Food Safety Authority (EFSA) 2014. Scientific Opinion on good modelling practice in the context of mechanistic effect models for risk assessment of plant protection products. EFSA J. 12: 3589.*
Deviations:	*Not applicable*
GLP:	*Not applicable*
Acceptability:	*Due to the given timeframes the zRMS was not able to evaluate the new population modelling, superseding Kleinmann (2019a).* *Acceptability and applicability of the modelling has to be thus dealt with by particular cMS at the product authorisation.*
Duplication (if vertebrate study)	*No*

Summary

This report details a population-level risk assessment which was conducted for mesotrione applied in maize at 1 x 150 g /ha, to address the chronic risk to populations of the brown hare (Lepus europaeus). Simulations were conducted with the population model for the brown hare implemented in the commercial software POLARIS. This population model was developed in line with a recent EFSA opinion on good modelling practice (EFSA, 2014). The model, which has recently been published (Kleinmann and Wang, 2017[1]), is validated and documented in detail, including parameterisation, model verification, calibration, sensitivity analysis and validation.

The entities of the model are the landscape and the individual hares. The landscape consists of multiple habitats, each characterised by habitat type (e.g. grassland) and amount of food resources. Individuals are characterised by the state variables: age, gender, developmental stage (lactating offspring, subadult, adult), reproductive status (breeding or non-breeding), fertility (fertile, infertile; applies to females only), pregnancy. Exposure is simulated for each individual according to its daily movement. Most processes defined in the model are updated in daily time steps for each individual. However, movement is simulated on a smaller time step, depending on the individual daily walking distance.

Based on Kleinmann and Wang (2017), a worst-case landscape was selected for application in maize characterised by a high proportion of maize fields (30% of the landscape consisted of maize) in a mixed agricultural landscape. Since brown hare densities are low compared to other small mammals (<10 hares per 100 ha) a relatively large simulation landscape (>1000ha) is necessary for the evaluation in order to obtain robust population sizes. The suitability of the landscape for use in risk assessment was confirmed by applying a hypothetical 'toxic standard' i.e. by applying e.g. 25% mortality, 25% reduced pup production or 5% reduced body weight per day for all hares in maize fields. Results showed that this landscape was sufficiently sensitive to detect effects. Additionally, a comparison of PT values from model simulations and PT values from a field study (Grimm & Katzschner 2019) demonstrated that the simulations produced realistic, but slightly worst-case PT values.

The parameterisation of adverse effects due to application of mesotrione was based on the findings from a multi-generation study in rat (Milburn, 1997). For the simulations the endpoints decreased body weight, reduced litter size and reduced pup survival were considered. Since this study covered only a limited range of doses, a threshold value has been implemented in order to be conservative: thus 100% effect has been assumed for any dose higher than the tested doses.

Exposure of each hare was calculated using the default value from the EFSA Bird and Mammal Guidance (2009), including the default DT_{50} value of 10 days for ground vegetation including maize (conservative as the measured DT_{50} values were 0.8-2.05 days for maize and dicots, respectively). Simulations were run for

[1] Kleinmann, J. and Wang, M. 2017. Modeling individual movement decisions of brown hare (*Lepus europaeus*) as a key concept for realistic spatial behavior and exposure: A population model for landscape-level risk assessment. Environ. Toxicol. Chem. 36:2299-2307

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

20 years during which applications were simulated annually for 10 years in years 6 to 15. Population level effects were assessed based on a comparison of the exposed population density to the untreated control density at the end of each of the 10 years with treatment.

*Simulations with the population model showed that for an **E**xposure **M**ultiplication **F**actor (EMF) up to 5x the maximum intended application rate of mesotrione of 150 g/ha, no effects (above the limit of detection of 5%) were observed.*

The results from this risk assessment can be considered worst case for the following reasons: First, in the two-generation study by Milburn (1996), animals were continuously exposed over several months (> 28 weeks) while exposure in the field is much shorter because residues decline quickly and the application window for the proposed uses is very short. Second, dissipation was simulated using the default DT_{50} from EFSA (2009) which is much longer than the measured substance-specific values ($DT_{50} \leq 2.05$ d). Third, a landscape with a high proportion of maize fields (30%) was considered; the worst-case character of this landscape had previously been confirmed. Fourth, a closed population with no immigration was considered in modelling, hence there was no possibility of recovery by immigration.

Based in the highest EMF at which no effects were detected and the described conservative assumptions regarding exposure and effect simulation, the risk assessment includes a quantifiable margin of safety of >20.9. Based on these results no unacceptable effects are expected for real populations at the maximum intended application rate under worst-case field conditions, and hence an acceptable risk can be concluded. Results are summarized in the table below.

Summary of results

Endpoint	***Comment***
No detectable effects (effects <5%) found at up to 5x the maximal intended application rate (EMF ≤ 5)	*This margin of safety can be compared to the assessment factor of five in the deterministic assessment (i.e. the margin of safety is 5)*
Quantifiable margin of safety is >20.9x derived as follows: • *Use of default instead of measured residue decline in the 21d TWA DDD: >3.8* • *Maximum EMF without an effect: 5 x* • *Use of default monocot RUD (54.2) instead of the realistic measured geomean RUD=48 in maize: >1.1 (if a mixed diet of monocots and dicots would be assumed, there would be an additional margin of safety of up to 1.89)*	*Estimated from the conservatism in the inputs to the modelling, principally driven by using default rather than measured values for residue levels and residue declines. Calculated based on quantified worst-case assumptions and the EMF of 5*

To demonstrate that the effect model could detect effects if the exposure was high enough, EMFs were increased stepwise until population level effects were visible. Small first population level effects (up to 6.26% reduction of population density) started to be detected at an EMF of 1000x the maximum intended application rate. The predicted population-level effects on an annual basis could be considered to be surprisingly low considering the high exposure. However, all relevant effects affected reproductive success (pup survival and litter size reduction). These effects result in a decreased population density directly after application. However, at the end of the year the population has already recovered to a large extent. This occurs because of the very short exposure window compared to the entire reproductive season.

To evaluate the sensitivity of the outcome of this risk assessment to changes in model parameter values and the considered exposure and toxicity scenario, further simulations were run with different parameterisations for the most relevant parameters, and unrealistically worst-case exposure and toxicity scenarios. These simulations indicated a low sensitivity of the outcome of this risk assessment to parameter variations. Regarding the different exposure and toxicity scenarios, simulations resulted in similar population level effects. Hence, results of this risk assessment may be considered robust regarding the considered variations.

Overall it can be concluded that no unacceptable risk to brown hare populations is expected following application of mesotrione at 150 g a.s./ha in maize.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Materials and methods

Population model

Simulations were conducted with the population model for the brown hare (Lepus europaeus) implemented in the commercial software POLARIS (software version 3.1, brown hare model version 1.0, WSC Scientific GmbH). This model has recently been published (Kleinmann and Wang, 2017) and is described in Kleinmann and Wang (2019[2]) following the ODD (Overview, Design concepts, and Details) protocol, together with a detailed description on the calibration, validation and sensitivity analyses.

The entities of the model are the landscape and the individuals. The model is a spatially explicit two-dimensional landscape with fields and other habitats included. For each habitat, food resources and vegetation cover is simulated for a given calendar date (food resources are only considered to simulate realistic home range sizes). Individuals are characterised by the state variables: age, gender, developmental stage (lactating offspring, subadult, adult), reproductive status (breeding or non-breeding), fertility (fertile, infertile; applies to females only), pregnancy, and the home range occupied.

The main processes defined in the model are updated in daily time steps for each individual: survival, update developmental stage, update of reproductive state (fertility, giving birth), update home range (ranges result from the daily movement of individuals), disperse (if no home range), mating. It was assumed that if a female encountered a male and mated, that the mating was successful i.e. it always led to a pregnancy. This is acknowledged to be unlikely to be realistic for a variety of reasons. The 'diestrous period' used in the modelling includes all sources of potential infertility including unsuccessful matings, rather than just strictly a post-partum infertile diestrous period. This parameter was calibrated in order to produce the realistic numbers of litters per female and per season that are available in published literature sources.

Toxicity parameterisation

In parametrisation of the model three toxicity studies evaluated at the EU level were originally considered:

1. *28-day dynamic exposure study in rat by Lees, 2000.*
2. *Acute oral toxicity study with rat by Robinson, 1984.*
3. *Multigenerational study with rat by Milburn, 1997 (from this study the NOAEL of 0.3 mg a.s./kg bw/d was derived and used in the risk assessment). From this study crucial parameters related to the bodyweight reduction, litter size reduction and reduced pup survival were considered.*

However since studies 1 and 2 relate to acute effects at levels which far exceed the levels potentially causing chronic effects and well beyond the threshold values implemented, these studies were not included in the modelling.

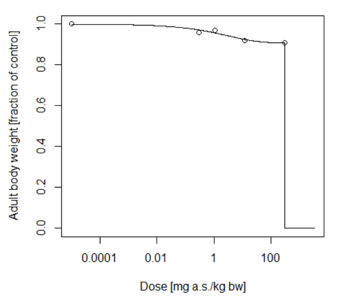
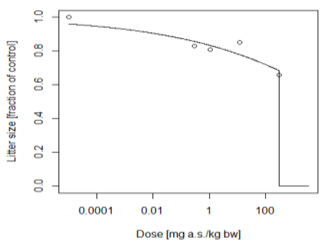
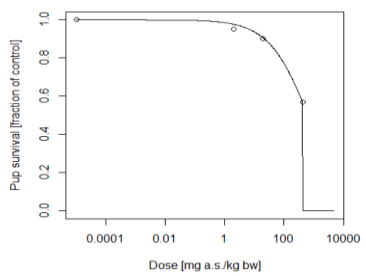
For this risk assessment, only effects which affect individual survival or reproduction are considered relevant, since only such effects may influence the population development. Other effects such as histological changes are not considered relevant for the purpose of this risk assessment as it is not clear how these changes, if at all, translate to individual effects. Changes of feed consumption or body weight changes are also unlikely to be relevant for the current risk assessment as if such effects had indirectly affected individual survival or reproduction, then such effects would already be covered. However, as a worst-case, effects on body-weight were also considered in the modelling, together with reduced litter size and reduced pup survival.
In all cases the data used to estimate the dose response curve does not cover very high dose ranges (above c. 290 mg a.s./kg bw/d). Hence the upper part of the dose response remains uncertain. To address this

[2] Kleinmann, J. and Wang, M. 2019. POLARIS – Brown hare population model description, model version 1.0. Unpublished report 19045-WSC. WSC Scientific GmbH, Heidelberg, Germany. Report available directly from WSC.

uncertainty, a conservative threshold level was implemented such that for any dose above the highest tested dose, 100% effect occurs.

While for most effect endpoints 100% effect would represent a worst-possible case, this is impractical regarding modelling the effects on body weight since a 100% body weight reduction would result in a body weight of zero grams. Therefore, for the purposes of modelling it has been (unrealistically) assumed that the body weight of individuals exposed to a higher dose than the highest tested dose, is reduced to the birth weight. This reduction to birth weight has no impact on reproductive performance as such effects are simulated separately. The alternative would be to assume death of the individual concerned when the threshold is exceeded, however this would be extremely conservative since mortalities were not recorded at the highest tested dose in the reproduction study, the LD50 is >5000mg a.s./kg (EU endpoint). A reduction of body weight to birth weight is therefore considered an unrealistically strong effect for adults that clearly represents a worst-case threshold that enables modelling to be carried out.

Dose-response curves are illustrated below:

<table>
<tr><th>Adult body weight</th><th>Litter size</th><th>Pup survival</th></tr>
<tr><td>
</td><td>
</td><td>
</td></tr>
<tr><td colspan="3">Curve used:</td></tr>
<tr><td>$\text{Body weight rel. to control } [0.. = a \cdot \left[\left(c-(c-1)\right)\cdot e^{-b\cdot dose^{d}}\right]$
with:
a: top of the dose-response curve
b: slope parameter
c: bottom of the dose-response curve
d: form parameter</td><td>$\text{Litter size rel. to control } [0.. = a \cdot e^{-b\cdot dose^{d}}$
with:
a: top of the dose-response curve
b: slope parameter
d: form parameter</td><td>$\text{Pup survival rel. to control } [0.. = a \cdot \left[1-\frac{dose^{d}}{b^{d}+dose^{d}}\right]$
with:
a: top of the dose-response curve
b: EC_{50}
d: form parameter</td></tr>
<tr><td colspan="3">Dose response curve fit:</td></tr>
<tr><td><table><tr><th></th><th>Exponential 5</th></tr><tr><td>Fitted parameters:</td><td>3</td></tr><tr><td>AIC</td><td>-31.99</td></tr><tr><td>R^2</td><td>0.93</td></tr></table></td><td><table><tr><th></th><th>Exponential 3</th></tr><tr><td>Fitted parameters:</td><td>2</td></tr><tr><td>AIC</td><td>-18.98</td></tr><tr><td>R^2</td><td>0.88</td></tr></table></td><td><table><tr><th></th><th>Hill 3</th></tr><tr><td>Fitted parameters:</td><td>2</td></tr><tr><td>AIC</td><td>-19.93</td></tr><tr><td>R^2</td><td>0.96</td></tr></table></td></tr>
<tr><td colspan="3">Parameters used:</td></tr>
<tr><td><table><tr><th>Parameter</th><th>Value (95% confidence interval)</th></tr><tr><td>a (top) [0..1]:</td><td>1.000 (natural limit)</td></tr><tr><td>b:</td><td>0.618 (0.232 – 1.568)</td></tr><tr><td>c:</td><td>0.908 (0.877 – 0.940)</td></tr><tr><td>d:</td><td>0.409 (0.077 – 3.924)</td></tr></table></td><td><table><tr><th>Parameter</th><th>Value (95% confidence interval)</th></tr><tr><td>a [0..1]:</td><td>1.000 (natural limit)</td></tr><tr><td>b:</td><td>0.181 (0.093 – 0.282)</td></tr><tr><td>d:</td><td>0.130 (0.000 – 0.239)</td></tr></table></td><td><table><tr><th>Parameter</th><th>Value (95% confidence interval)</th></tr><tr><td>a [0..1]:</td><td>1.000 (natural limit)</td></tr><tr><td>b:</td><td>648.9 (233.7–2171.2)</td></tr><tr><td>d:</td><td>0.646 (0.356 – 2.197)</td></tr></table></td></tr>
</table>

Data from Milburn, 1997; the first circle always indicates the control group

Exposure

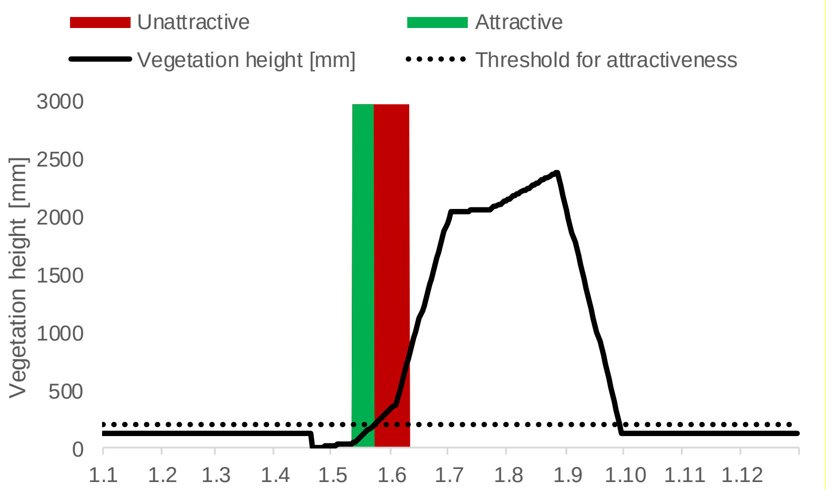
The exposure was calculated with consideration of the application rate of 1x150, 2x150 and 5x150 g a.s./ha. Higher rates of 10 x, 20 x 100 x and 1000 x 150g/ha were considered in establishing the EMF that would *demonstrate effects. Default values as indicated in EFSA (2009) were used for FIR/bw, RUD and foliar DT_{50}. Deposition factor of 1 was considered. A default 21 day time weighted average (moving time window) was used.*

The application dates were determined using the AppDate tool with consideration of the groundwater scenarios.

Application dates for maize for the FOCUS scenarios from the central zone according to AppDate version 3.06.

BBCH	*FOCUS Scenario*	*Maize*
12	*Hamburg*	*12.05.*
	Kremsmunster	*12.05.*
	Okehampton	*29.05.*
18	*Hamburg*	*29.05.*
	Kremsmunster	*29.05.*
	Okehampton	*08.06.*

Hence varying application dates between the 12th May and the 08th June may be considered. However, to simulate a worst-case application period for exposure to hares (rather than a worst-case for exposure to groundwater, which is the raison d'etre for the FOCUS scenarios), the attractiveness of maize for brown hares also needs to be considered. Since brown hares start to avoid crops above a vegetation height of 20-25 cm for feeding, in order to address a worst-case, maize plants should not be higher than 20 cm when applications are simulated. For higher vegetation heights, PT values for brown hares would decrease, which reduces the individual and population level risk. The figure below illustrates the seasonal vegetation height in maize fields and the part of the application period in which maize fields are an attractive habitat for hares.



Seasonal vegetation height of maize plants as simulated in the present risk assessment. The part of the application period in which maize fields are attractive for brown hares is marked in green, the part of the application period in which maize fields are not attractive is marked in red

Thus maize fields start to become unattractive for brown hares on the 24th of May. To simulate applications only during a worst-case period, a reduced application window was assumed to cover the range of possible *application dates in which maize fields are attractive for hares. This approach is worst case as the simulated application window was shortened from BBCH 12 to 18, to BBCH 12 to 16.*

Calculation of Effects

Body weight reductions were calculated using the 21d TWA exposure and the dose-response curve calculated on the basis of results of the study by Milburn (1997). Body weight reductions alone may have no influence on population density or structure. However, as described above, individuals with a body weight of 2884g or less on 31st of October may not survive winter. Therefore, in all simulations these animals were assumed to die immediately. This natural threshold could also include unexposed young individuals which were not old enough to have a body weight above this threshold.
The reduction of litter size was simulated at the time of birth. This was done by calculating the 21 d TWA concentration for each individual hare using the default EFSA (2009) values. Then, based on this concentration and on the respective dose response curves derived on the basis of results of the study by Milburn (1997), the proportion was calculated by which litter size is reduced. Regarding the increased pup mortality, this effect was also simulated as a reduced litter size at birth. Hence, when birth was simulated, litter size was reduced twice: (1) according to the dose-response of the effect reduction of litter size; and (2) according to the dose-response of the effect increased pup mortality (based on Milburn, 1997). This means, increased pup mortality was assumed to occur at birth for simplicity. This assumption had no influence on the model results, since brown hares do not stop reproduction during lactation.

Landscape scenario

The worst-case character of various landscapes for population level risk assessments of brown hares has previously been evaluated in Kleinmann and Wang (2017). In this publication it has been found that PT values of brown hares in maize are higher when the treated habitat is distributed equally over the entire landscape (compared to a landscape with clusters of treated habitat). The worst landscape in Kleinmann and Wang (2017), resulting in the highest PT values, was a landscape from Lincolnshire (UK), in which hares spent a large proportion of their time foraging in fields since they were surrounded by suitable off-crop habitat in which they could rest. This landscape has been adapted for a risk assessment in maize.
For the risk assessment it was assumed conservatively that 30% of the landscape area is composed of maize. Other habitats were winter wheat, winter, barley, woodland, pastures, oilseed rape, field margins, hedgerows and roads (see figure below). All habitats have been parameterised using measured data.

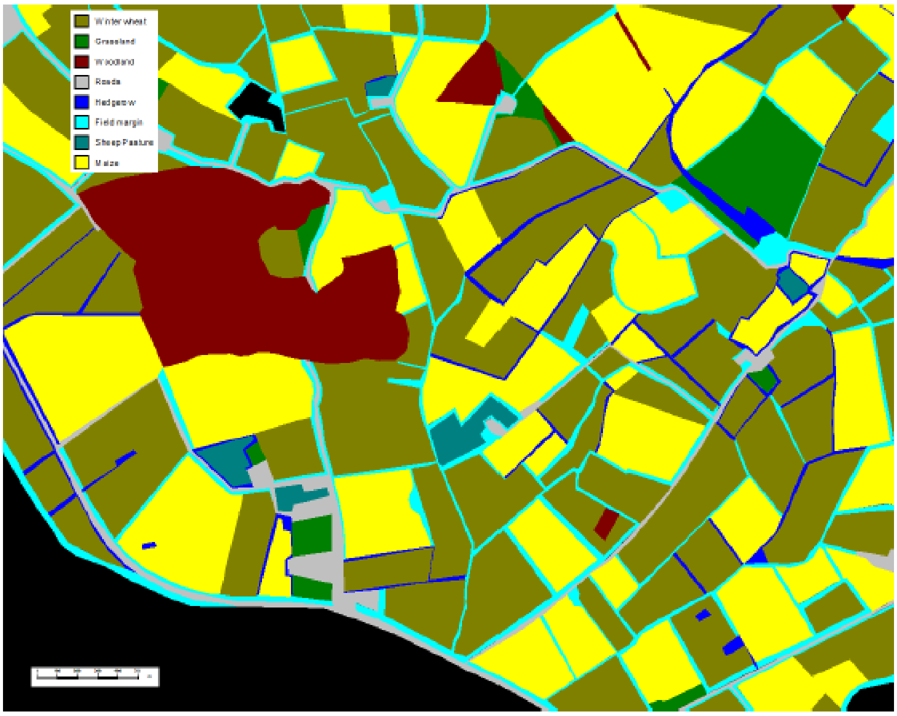


Figure 5. Habitat composition of the landscape from Lincolnshire, which has been used for the risk assessment.

For validation of the PT values derived by the model, results of the study by Grimm & Katzschner (2019, KCP 10.1.2.2/07) were used. It is, however, noted that due to the small size of locations in Germany, only part of the study performed in Hungary was taken into account with only 2 out of 3 test sites. The locations in Germany were rather small (<200 ha) which was not sufficient to simulate stable hare populations and therefore these landscapes could not be used for validation. However, the landscapes Szany and Bösarkany in Hungary were large enough for analysis. It is noted by the zRMS that part of the study performed in Germany resulted with higher 90th percentile PT comparing to part performed in Hungary and for this reason it is questioned if consideration of only two sites from Hungary was sufficient for proper validation of the model. Nevertheless, PT values simulated by the model were above 0.9 for about 30% of all hares, which clearly represents worst case as in the study by Grimm & Katzschner (2019) only one of all monitored hares had PT >0.9 and one had PT of 0.89 (both in Germany). For remaining hares the PT values ranged from 0.02 to 0.63.

Selection of a worst-case landscape for the risk assessment

To evaluate the worst-case character of the landscape considered for the present risk assessment ('Lincolnshire'), the mean daily dose and mean effect resulting from the following considered landscapes were compared: Lincolnshire; Szany and Bösarkany. For this comparison, simulated PT values of adult hares during the application period were used to calculate individual daily doses and individual daily effects in all three landscapes. Daily doses were calculated including the simulated individual PT value in maize and the individual body-weight. It has been shown that the effect on litter size is predominantly driving the risk assessment (please see details in the full study report), so only this effect was calculated. This approach allowed a comparison of the distribution of daily doses and effect strengths resulting from the different landscapes. The landscape with the highest mean daily dose and the strongest mean effect was considered worst-case in the context of the present risk assessment.
Simulations

Simulations were performed over a period of 20 years. Applications were considered to take place from year 6 to year 15. This approach ensures that populations stabilise during the first five years and potentially allows populations to stabilise again for five years after the last application. The number of simulations was based on a parametric power analysis (conducted in R), with the aim to be able to reveal effects of 5%

magnitude with a confidence of 95%. For this analysis, the typical variation of population density after one year was measured based on 50 one-year simulations. Notably, the 5% threshold refers to the desired statistical power or limit of detection only. This does not mean that an effect size of 5% is biologically relevant. Effects in the range of the limit of detection are considered negligible. This assumption is considered worst-case since natural fluctuations of population density of hares are usually much larger. For the 1500 ha landscape, the mean density over the whole landscape (4.9 N/100 ha) had a standard deviation (coefficient of variation) of 9% of the mean (delta = 0.554). The power analysis revealed that for detecting effects of 5% with a confidence of 95%, 85.7 simulations are necessary. Therefore, 90 simulations were conducted in the present risk assessment. As a simulation endpoint, population density on 31st December was used to compare control populations and treatment populations.

Sensitivity of the risk assessment to variations of model parameters

Additional simulations were run to address potential uncertainty regarding the most relevant model parameters which have the strongest influence on the simulated population density and how uncertain and variable these parameters are. The parameters density dependent mortality, litter size and the breeding season end of females were found to be the most relevant ones. Further parameters were considered relevant in the sensitivity analysis (e.g. gestation length), but the uncertainty of these parameters was considered low, since e.g. gestation length can easily be measured in laboratory and field studies with a high level of certainty. Other parameters were not relevant for population density but e.g. only for home range size (e.g. step size).

To evaluate if the results of the present risk assessment depend on the exact values of sensitive and less certain parameters, risk assessment simulations were repeated (EMF of 5x and 10x the maximum intended application rate) with:

- *30% lower and 30% higher litter size,*
- *30% lower and 30% higher density dependent mortality*
- *30% earlier and 30% later female breeding season end.*

A range of ±30% has been chosen since such differences in the parameterisations are large enough to show whether a parameter has an influence on the outcome of the risk assessment but does not result in biologically completely unrealistic values. In this way the sensitivity of the outcome of the risk assessment to variations of the most important parameter values could be demonstrated. For these six scenarios, 90 iterations were conducted.

Changes of the landscape or application scenario needed to trigger strong population-level effects

To assess how the landscape composition or application scenario would need to be changed to produce considerable population-level effects, additional simulations were run. This helps to understand whether a population could potentially reach a point at which small changes of the landscape, or of the application scenario, may at some point trigger very strong population level effects. For the risk assessment, simulated exposure and toxicity scenarios have been based on realistic worst-case assumptions. These were:
A landscape covered by 30% of maize fields
Assuming threshold toxicities, i.e. 100% effect if the highest dose for which measured data was available is surpassed

- *Single application during a worst-case application period*
- *Use of the default worst-case DT_{50} from EFSA (2009), although measured DT_{50}s are lower*
- *Use of the default worst-case RUD from EFSA (2009), although a lower RUD has been measured*

To evaluate if the results of the present risk assessment may change if assumptions of this risk assessment were different (just like tipping points), simulations with the following changes were additionally run:

- *All agricultural fields in the landscape were covered by maize fields*
- *Two applications at the maximum proposed rate were conducted with an interval of seven days in the worst-case application period*
- *The threshold dose above which 100% effects are assumed was 50% of the dose measured in laboratory study*

For these scenarios, again simulations with increasing EMFs (1 to 10x the maximum intended application rate) were conducted and 90 iterations were run. These additional simulations are expected to produce strong population level effects.

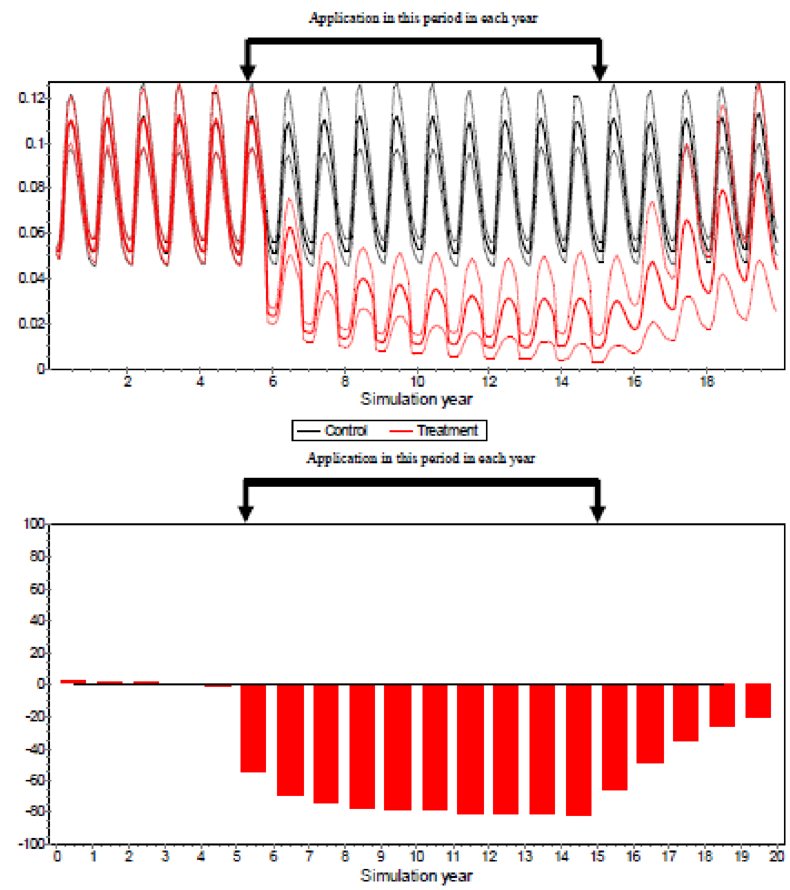
Results

Selection of worst-case landscapes and validation of maize PT values

The measured PT values could be sampled from the simulated distribution of PT values. Since the simulated PT-values were also worst-case compared to the measured PT values, the simulation model provides a worst-case result for the exposure of brown hares in a landscape.
To investigate the worst-case character of the risk assessment landscape, the distribution of simulated PT values were compared for all three landscapes (Szany, Bösarkany, and Lincolnshire). In the Lincolnshire landscape, about 30% of all hares have a PT larger than 0.9. This value is by far the largest of all investigated landscapes, which suggests this may be worst-case. However this landscape also had the most PT<0.1 and there is clearly a range of PT distributions in the different landscapes, and it remains unclear which landscape will be overall worst-case. To confirm the worst-case character of the risk assessment landscape (Lincolnshire), all individual PT values of adult hares during the application period were used to calculate individual doses for mesotrione. These distributions of simulated doses were compared for all three landscapes (Szany, Bösarkany, and Lincolnshire). Additionally for each calculated individual dose, the corresponding effect has been calculated to compare mean effects for all landscapes. Since the effect on litter size following mesotrione exposure was found to be the dominant effect driving the risk assessment, only this effect has been calculated. In the risk assessment landscape (Lincolnshire), the mean daily dietary dose and the mean effect on litter size was higher than in the two other landscapes (Szany and Bösarkany). This indicates that the Lincolnshire landscape is a worst-case landscape in the context of this risk assessment. Additionally, the fraction of hares with the highest DDDs was highest in the Lincolnshire landscape; and the fraction of hares with the lowest DDDs was lowest again in the Lincolnshire landscape compared to the other landscapes. It can therefore be concluded that the landscape 'Lincolnshire' used for the risk assessment represents a worst-case in the context of the present risk assessment.

'Toxic reference'

In order to demonstrate that the model is able to detect effects, additional 90 simulations for 20-years were performed for a toxic reference substance with assumption of 25% mortality and 25% reduced litter size for 21 days. Effects were applied in the entire landscape (all habitats). Additionally, the body weight of all individuals in maize fields was reduced by 5% per day for 21 d starting at 1st of October. This corresponds to an overall weight reduction of about 65%. Clear effects at the population level could be observed. As an *example the graph presenting population density over 20 years assuming 5% bodyweight reduction for individual in maize for 21 days is presented below:*



Maximal and minimal differences of densities of treatment vs. control simulations at the end of the year (31st Dec) for years in which the toxic reference was applied are presented in the table below.

Toxic reference	Max. difference to control	Min. difference to control[1]	Recovery after years
25% additional mortality	-39.63	-20.86	3
25% reduced litter size for 21 d	-18.56	-7.19	2
5% body weight reduction per day in maize for 21 d (overall ~65% reduction)	-82.64	-55.51	>5

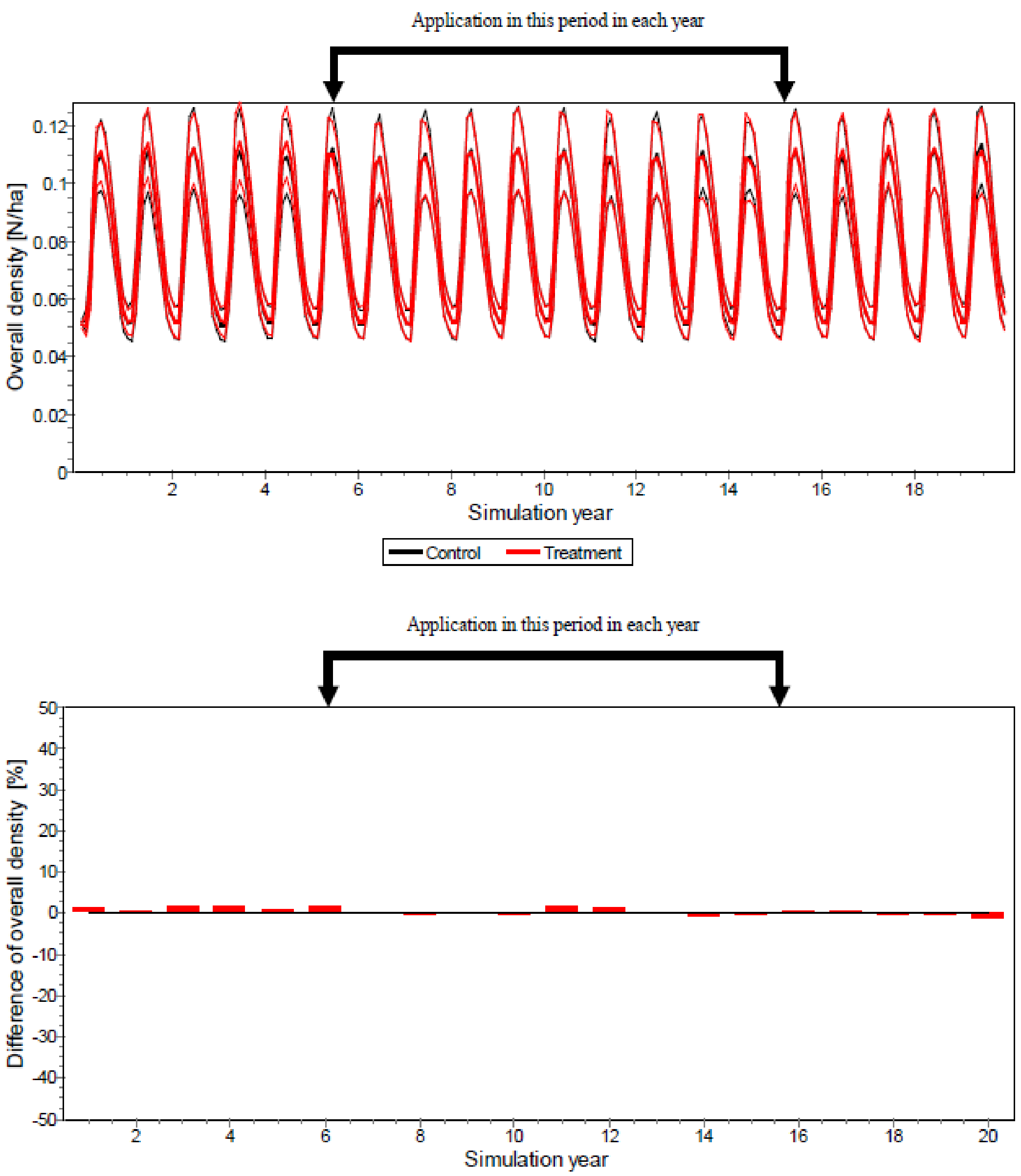
[1] Values >0 indicate that density in the treatment was higher than in the control.

Results obtained for simulations performed for mesotrione

The population densities over 20 years assuming 1x, 2x and 5x the maximum intended application rate of Callisto are copied from the modelling report below. Dashed lines indicate standard deviations.

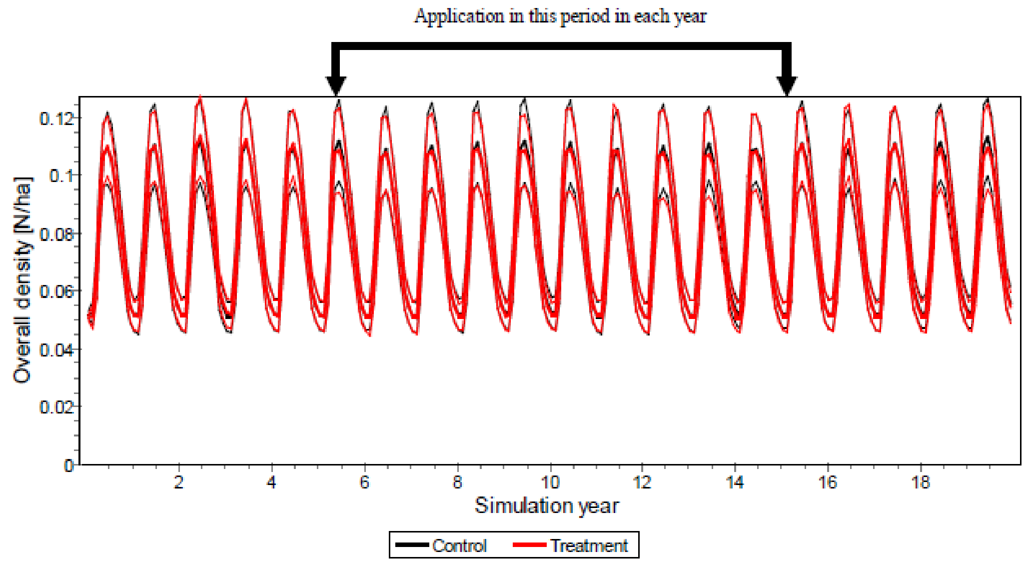
Population density over 20 years assuming 1x 150g/ha

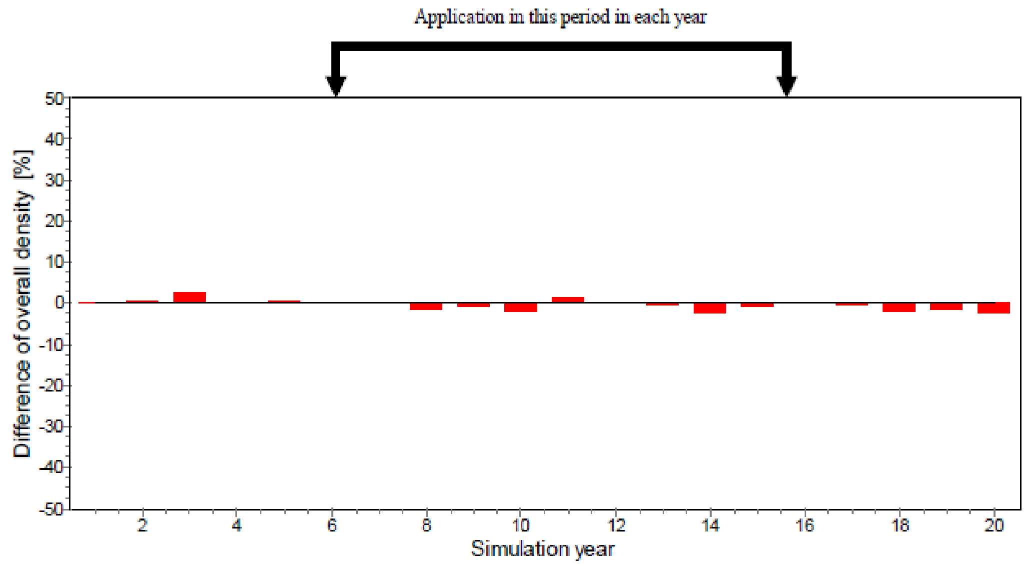
Top: Control (black) and treatment simulations (red). Dashed lines indicate standard deviations. Bottom: Difference of density in treatment compared to the control:



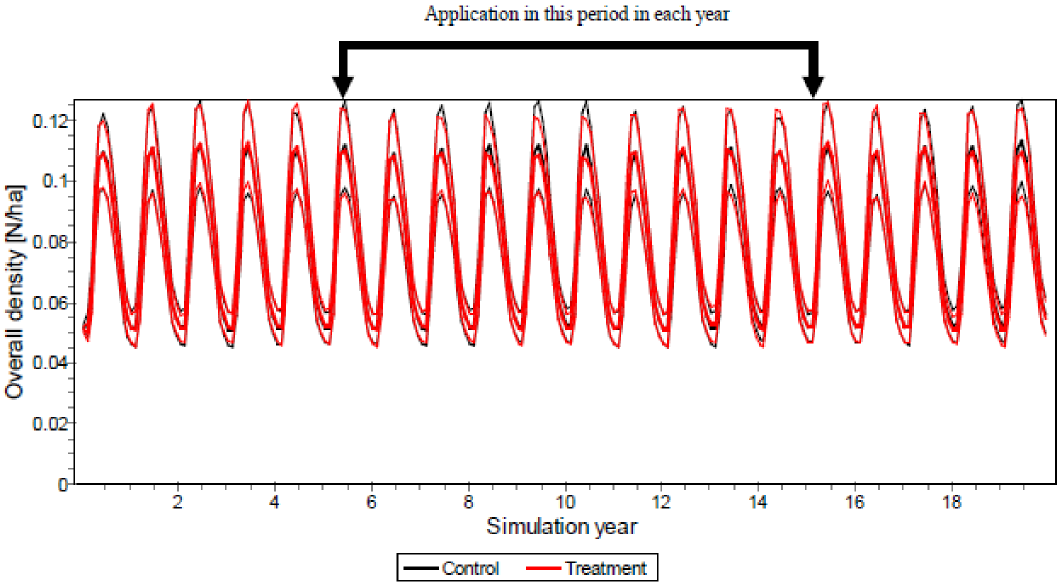
Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

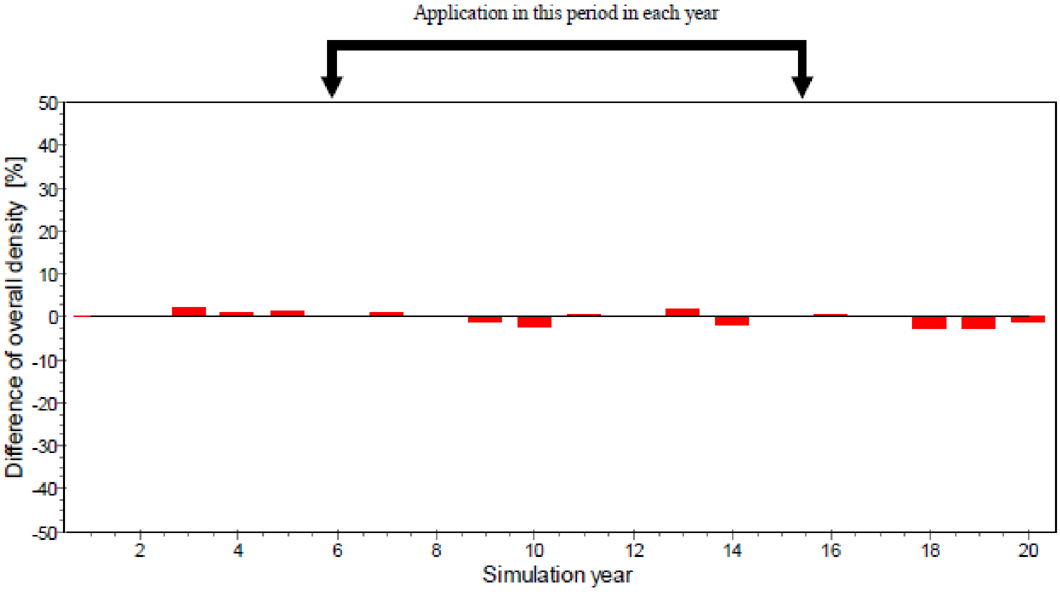
Population density over 20 years assuming 2x 150g/ha:





Population density over 20 years assuming 5x 150g/ha:





Maximal and minimal differences of densities of treatment vs. control simulations at the end of the year (31st Dec) for years in which the mesotrione was applied are presented in the table below.

	Max. difference to control	*Min. difference to control* [1]	*Recovery after years*
1x AR	*-1.18*	*1.66*	*0 (no effect)*
2x AR	*-2.67*	*1.27*	*0 (no effect)*
5x AR	*-2.47*	*1.82*	*0 (no effect)*

[1] Values >0 indicate that density in the treatment was higher than in the control.

Overall, performed population modelling demonstrates that application of Callisto at 150 g a.s./ha (or even 5 times this rate) is not expected to have adverse effects to the brown hare at the population level.

EMF needed to cause population level effects

Since no population level effects from application of mesotrione could be found in the present risk assessment even when considering an EMF of 5, EMFs were further increased until population level effects

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

could be detected. This has been done to show that the population model could detect population level effects after application of mesotrione, if exposure were high enough to cause effects. Results of these simulations are summarized below.

Maximum and minimum differences of population density in treatment vs. control simulations at the end of the year (31st Dec) for years in which application occurred. The limit of detection is +/-5%

	Max. difference to control	***Min. difference to control*** [1]	***Recovery after years***
10x AR	*-2.02*	*1.60*	*0 (no effect)*
20x AR	*-3.44*	*0.48*	*0 (no effect)*
100x AR	*-4.27*	*0.29*	*0 (no effect)*
1000x AR	*-6.26*	*-2.31*	*1*

[1] Values >0 indicate that density in the treatment was higher than in the control

These simulations resulted in a maximum difference between treatment and control populations of -6.26% for 1000 x 150g/ha which would be considered 'significant' as they are higher than the limit of detection. Consistent but not significant effects can be seen at rates above 20 x 150g/ha during the application years.

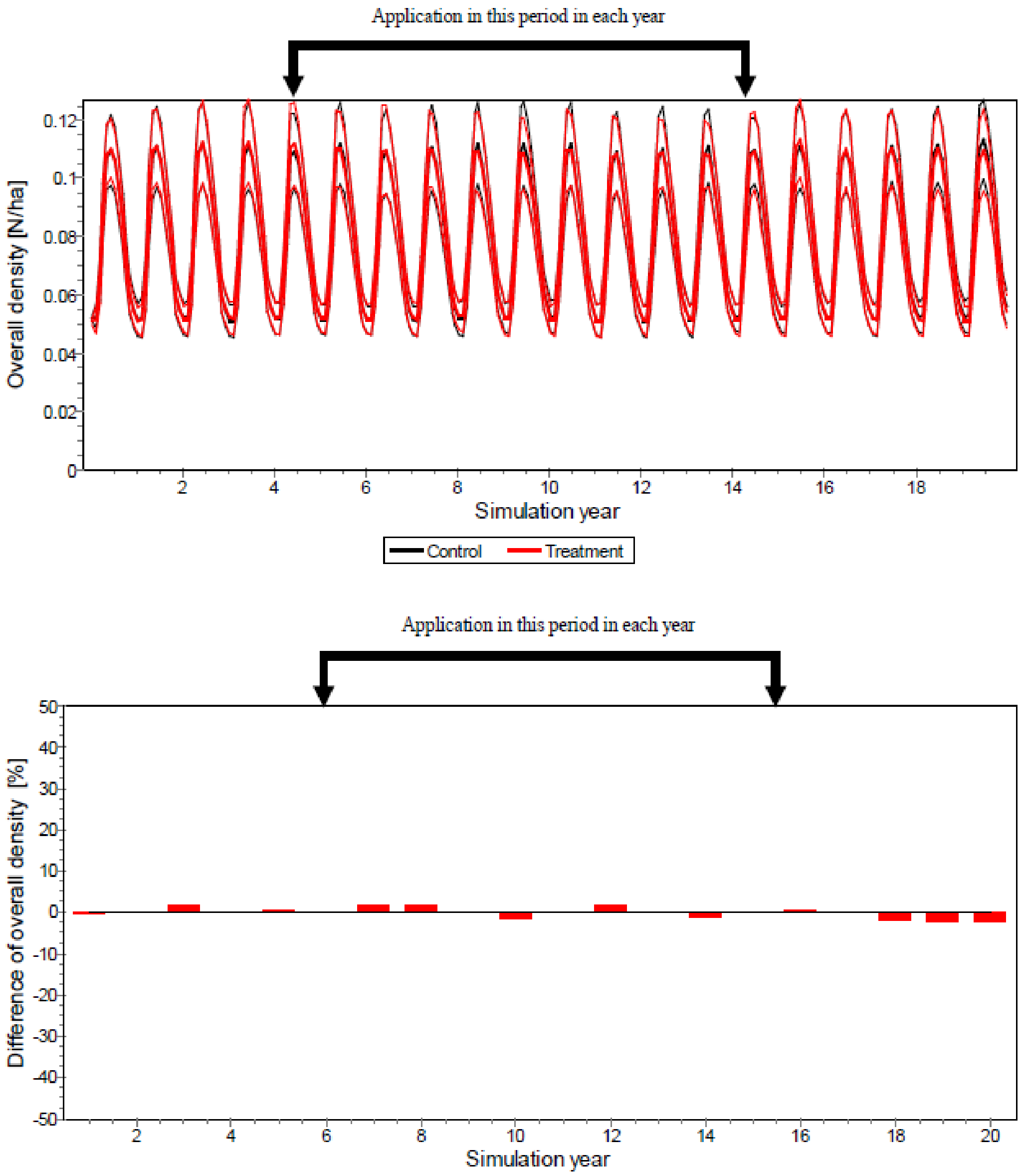
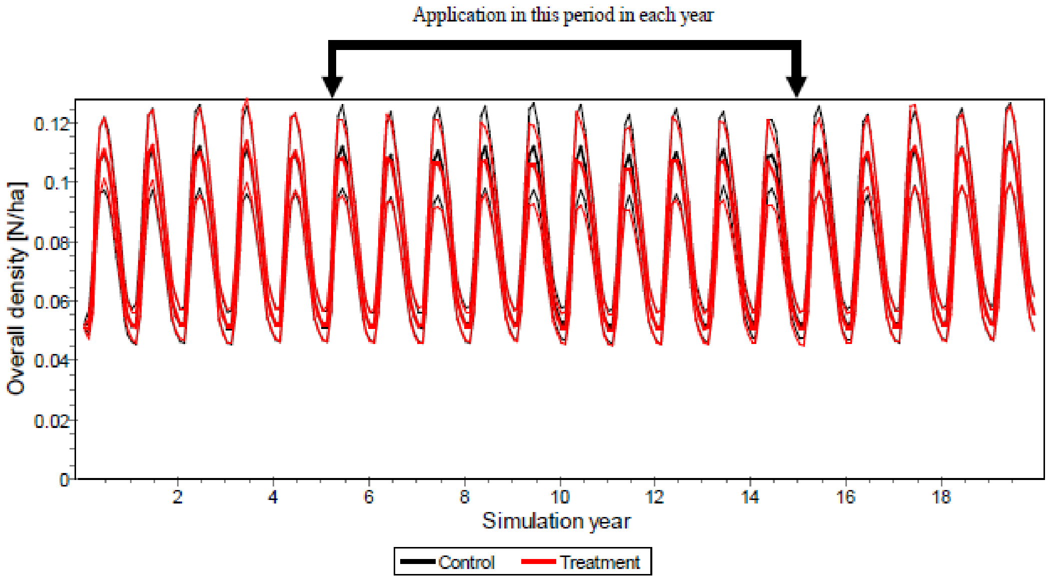


Figure 33. Population density over 20 years assuming 10x the maximum intended application rate. Difference of density in treatment compared to the control



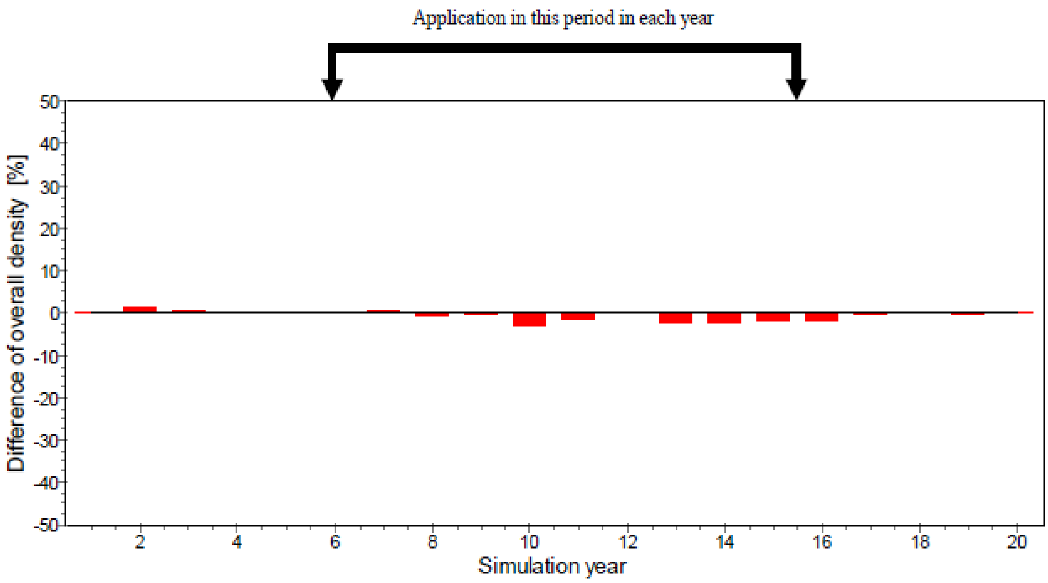
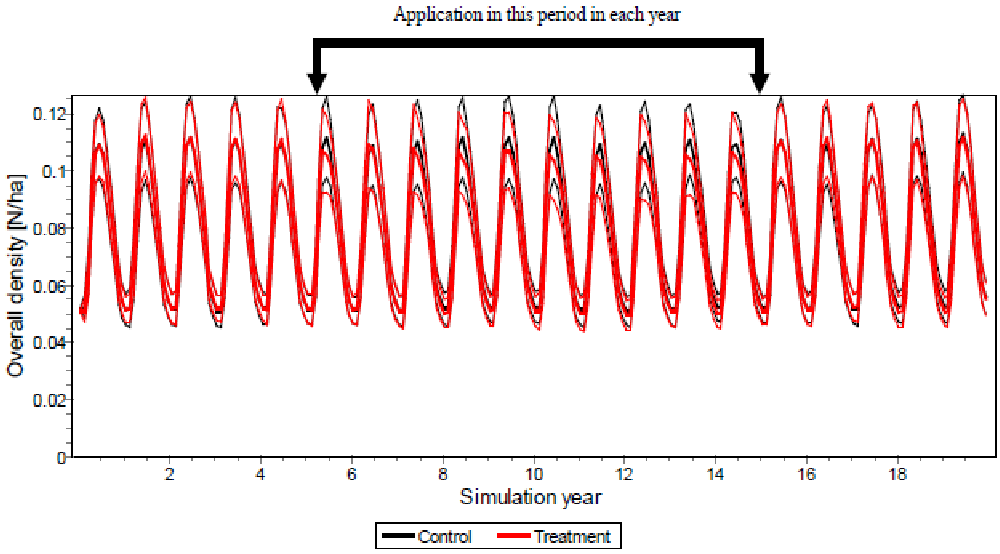


Figure 34. **Population density over 20 years assuming <u>20x</u> the maximum intended application rate. Difference of density in treatment compared to the control**



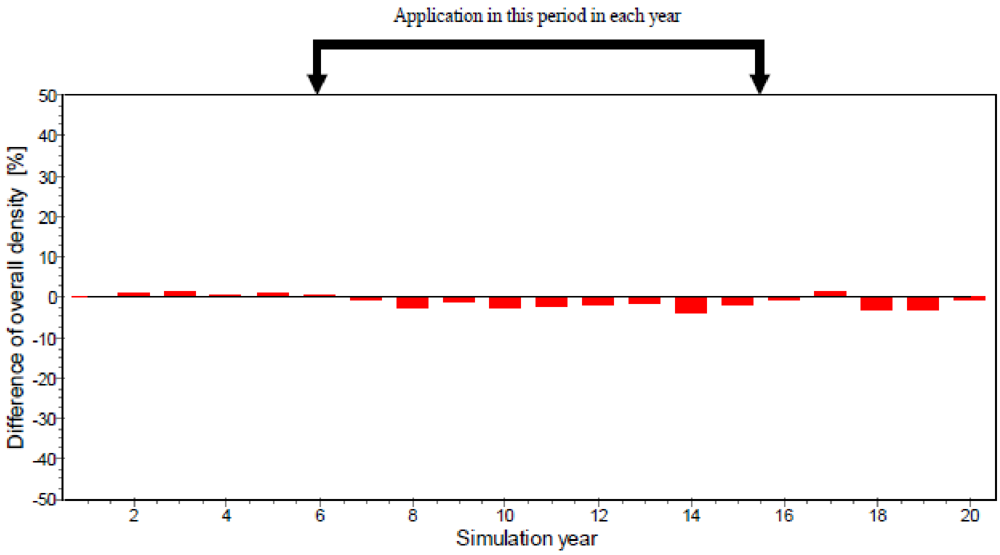
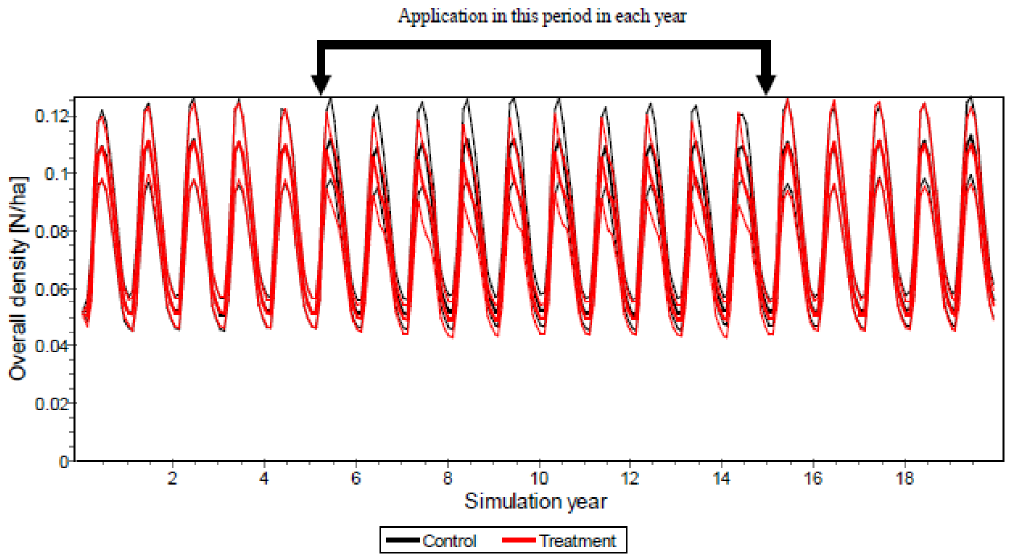


Figure 35. **Population density over 20 years assuming 100x the maximum intended application rate. Difference of density in treatment compared to the control**

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020



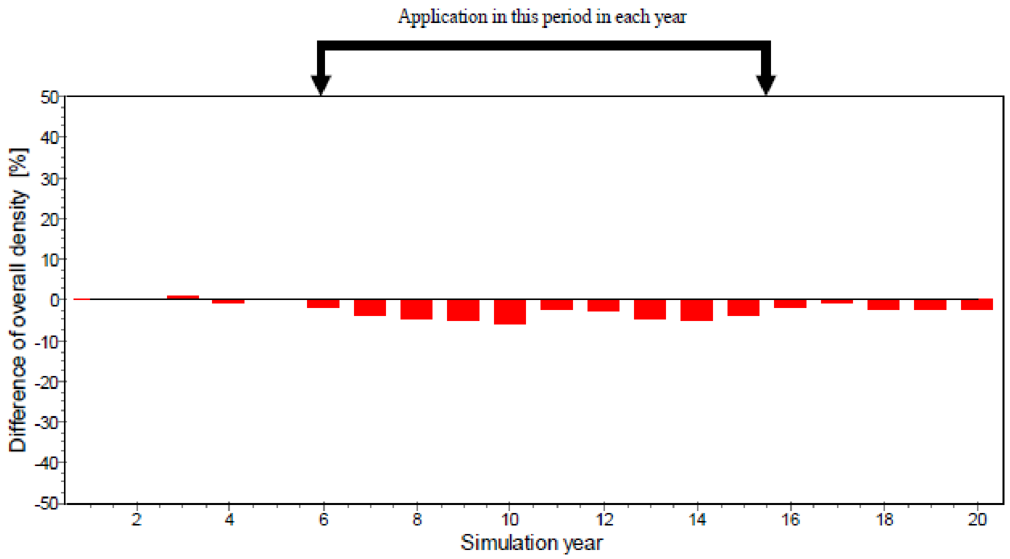


Figure 36. Population density over 20 years assuming <u>1000x</u> the maximum intended application rate. Difference of density in treatment compared to the control

The population densities in the treatments were significantly lower after applications started (year 6) and EMFs follow a dose-response indicating that population-level effects could be reliably detected at these higher EMFs. However these differences were still small and below 10. The reasons why a high EMF is necessary to result in marked population level effects can be explained as:

1. *Effects on adult body weight: because of the long period between application of mesotrione (May/June) and the date at which the mortality because of a low winter bodyweight is evaluated (end of October), individuals have time to recover from body weight effects. Therefore, body weight effects are not relevant at the population level if applications are early in the year. However, body weight effects can have a strong impact on the population level if applications are closer to winter, as seen for the 'toxic reference'.*
2. *Effects on reproduction (litter size, pup survival): it has been shown that almost exclusively the effect on litter size is relevant. This effect results in a complete inhibition of reproduction if the threshold dose is surpassed. The threshold dose which results in 100% effect on litter size can be reached at an EMF*

of 217.3 if individuals feed entirely in treated habitats (PT=1). Individuals with a lower PT correspondingly need higher EMF values until the threshold dose is reached. This describes the increase of the population level effect with increasing EMF and means that increasing EMF values above an EMF of 218 does not result in stronger individual effects, but in more individuals with maximum effects. If this maximum possible effect (complete cessation of reproduction) is not strong enough to cause very strong population level effects (e.g. extinction of populations), a further increase of the EMF cannot further increase the magnitude of effects.

3. *Breeding season: The breeding season for the European brown hare lasts from January to September. Thus when considering an exposure period of 21days, less than 10% of the total breeding season is affected (3 weeks out of 8 months). Additionally, more than half of the reproductive period is already over when applications are simulated in May. Hence, the influence of a 21d period in which reproduction may be reduced is limited.*

For these reasons, the results of the present population level risk assessment can be considered to represent a realistic worst-case of the situation for brown hare populations

Sensitivity of the outcome of the risk assessment to changes of the most relevant model parameters

Additional simulations were run to address potential uncertainty regarding the most relevant model parameters. Simulations were conducted assuming 5x and 10x the maximum intended application rate for different parameterisations of the most relevant model parameters.

Maximum and minimum differences of population density in treatment vs. control simulations at the end of the year (31st Dec) for years in which application occurred. An EMF of 5 was used. Effects were below or very close to the limit of detection of 5%.

Parameter	***Variation***	***Max. difference to control***	***Min. difference to control [1]***	***Recovery after years***
Litter size	*-30%*	*-4.55*	*0.17*	*0 (no effect)*
	+30%	*-2.83*	*-0.04*	*0 (no effect)*
Density dependent mortality	*-30%*	*-2.63*	*0.29*	*0 (no effect)*
	+30%	*-3.37*	*0.35*	*0 (no effect)*
Female breeding season end	*-30%*	*-2.54*	*-0.22*	*0 (no effect)*
	+30%	*-1.06*	*0.98*	*0 (no effect)*

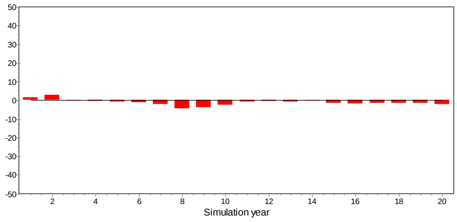
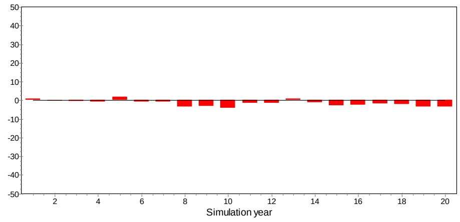
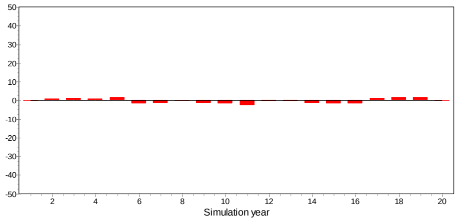
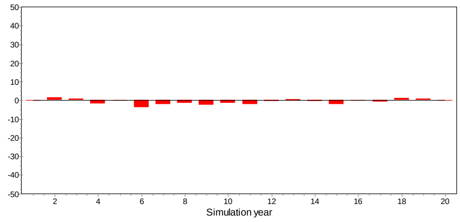
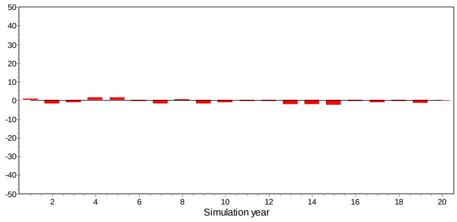
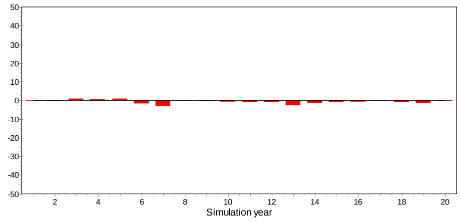
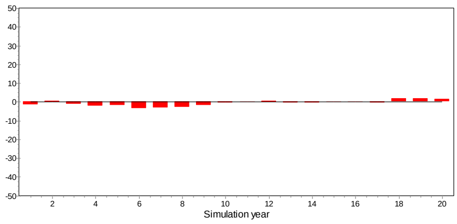
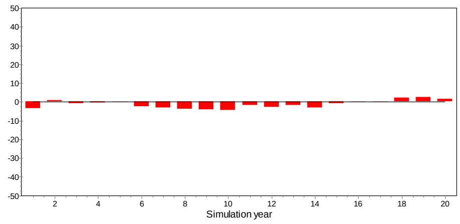
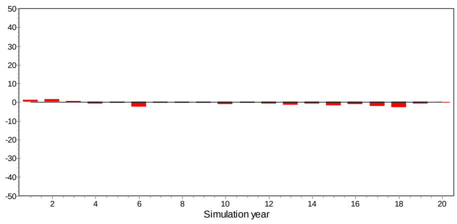
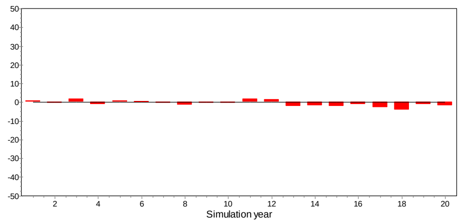
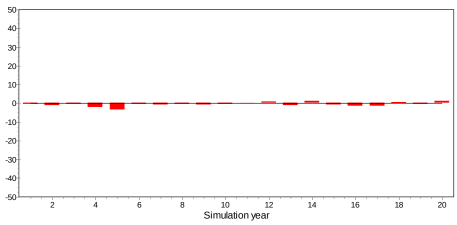
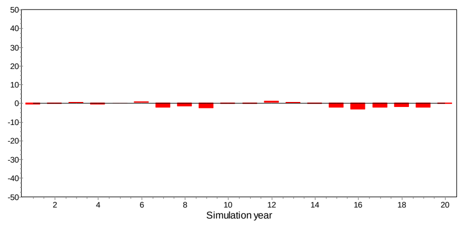
[1] Values >0 indicate that density in the treatment was higher than in the control.

Maximum and minimum differences of population density in treatment vs. control simulations at the end of the year (31st Dec) for years in which application occurred. An EMF of 10 was used.

Parameter	***Variation***	***Max. difference to control***	***Min. difference to control [1]***	***Recovery after years***
Litter size	*-30%*	*-4.22*	*0.87*	*0 (no effect)*
	+30%	*-3.85*	*0.57*	*0 (no effect)*
Density dependent mortality	*-30%*	*-3.02*	*0.04*	*0 (no effect)*
	+30%	*-4.50*	*-0.90*	*0 (no effect)*
Female breeding season end	*-30%*	*-2.18*	*1.65*	*0 (no effect)*
	+30%	*-2.76*	*1.14*	*0 (no effect)*

[1] Values >0 indicate that density in the treatment was higher than in the control.

Difference of density in treatment compared to the control over 20 years assuming 5x and 10x the maximum intended application rate for all simulated parameter variations:

	EMF 5x	*EMF 10x*
Litter size -30%		
Litter size +30%		
Density dependent mortality -30%		
Density dependent mortality +30%		
Female breeding season end -30%		
Female breeding season end +30%		

Results revealed that variations of the parameterisation of parameters with the highest influence on the population density had no influence on the outcome of the present risk assessment, indicating the assessment is robust.

Conclusion and discussion

The potential population-level effects on the brown hare after application of mesotrione in maize were assessed using a population model which was developed in line with the recent EFSA 2014 opinion on good modelling practice. To provide further evidence that the simulation model provides a realistic worst-case exposure for brown hare populations in maize, additional validation was provided considering PT values

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

from Grimm & Katzschner (2019). In this validation it has been shown that simulated PT values were realistic but slightly worst-case compared to measured PT values.

Simulations were conducted in a closed (1500 ha) landscape, for which the worst-case character has been shown in Kleinmann and Wang (2017) and during a further validation experiment in the present report. The hare populations in this landscape were considered to represent closed populations (no immigration considered), which adds to the worst-case character of the landscape. The worst-case character of the landscape has been shown by simulating 'toxic references' with effects on litter size, mortality and body weight.

Long-term toxicity was considered based on findings in Milburn (1996) which showed a reduction of litter size, pup survival, and adult body weight. These effects were implemented with dose response curves with a threshold level that assumes 100% effects for all doses above the highest measured dose. A detailed evaluation of the endpoints of all effects revealed that the effect on litter size following exposure to mesotrione is the most relevant effect. This effect had the lowest threshold dose resulting in 100% reduction of litter size. Hence, above this threshold dose, all other effects on pups (pup survival) can have no further impact, because no pups are available to affect. Effects on adult body weight were found to occur too early in the year to cause an increased winter mortality because affected individuals have plenty of time to recover from early body weight reductions.

Exposure was calculated using default values from EFSA (2009). To add further margins of safety, exposure multiplication factors of up to 5x the maximum intended application rate were applied in simulations.

For up to 5x the maximum intended application rate, no effects were observed in treatment compared to control simulations in maize. This finding is plausible because relevant effects only cause a reduction of reproductive success during the exposure period. Since this period covers only less than 10% of the reproductive season and a maximum of one out of four litters per female, a strong population level effect at the end of the year would be unrealistic. When the EMF was further increased up to a value of 1000x the maximum intended application rate, clearly detectable population level effects were seen. This relatively small effect (for the unrealistically high EMF) is explained by the fact that only 10% of the reproductive season is affected: if no offspring can be produced during the application period, then further increasing the application rate does not increase effects further.

Where there was uncertainty in a number of the parameters available, worst-case assumptions or worst-case refined parameters were considered in the risk assessment in order to conservatively address the overall uncertainty compared to the first tier assessment. These are summarised in the table below. To evaluate to what extent the simulated results depend on the parameterisation of the population model (in particular of the ones to which the model is most sensitive) and the exposure and toxicity scenarios, further simulations have been run with different parameterisations for the most relevant parameters and different landscape and toxicity scenarios. These results revealed that the parametrisation of the most relevant model parameters had no impact on the outcome of this risk assessment. The overall uncertainty of this population model-based risk assessment can therefore be considered as much smaller when compared to the first-tier risk assessment. A complete uncertainty analysis as proposed by EFSA (2008) is shown in the table below.

Comparison of uncertainties of first tier risk assessment with those of the present population level risk assessment

Input assumption or omission from each row were taken from EFSA (2009; appendix C, table 8). The extent to which the 'true worst' case for each element could decrease (-) or increase (+) the risk of causing an effect is indicated by the number of symbols (e.g. +++ indicates a factor that would increase the risk by an amount equivalent to reducing the TER by about a factor of about 10). For factors which could vary for different substances or which are uncertain, ranges are given (e.g. + /+++).

	First tier risk assessment (EFSA 2009)			*Population level risk assessment*		
	Potential for true risk to be		*Explanation*	*Potential for true risk to be*		*Explanation*
	lower	*higher*		*lower*	*higher*	
Relevance of reproduction toxicity study	*-/--*	*0*	*The ecological relevance of some of the endpoints to the goal of preventing reproductive effects is difficult to determine. This may lead to possible overprotection.*	*--*	*0*	*Worst-case effects on all endpoints on reproduction and body weight from all generations of all available reproductive toxicity studies have been used. Above the range of measured doses, 100% effect is assumed for each effect. An overprotection is very likely.*
Screening assessment indicator species and type of food	*-*	*0*	*Realistic worst case – relatively small species eating only the most contaminated food type. Real worst case could be lower in some scenarios.*	*-*	*0*	*Focal species according to first tier risk assessment were used.*
Tier 1 generic focal species and type of food	*0*	*+*	*Mixed diet based on average of available data on dietary composition. Some individual mammals will eat more than average proportion of most contaminated food on individual days.*	*-*	*0*	*Worst-case diet has been considered. Individuals feed only on grasses and cereals including maize, which is the realistic food item resulting in the highest exposure for brown hares. An overprotection is likely.*
Body weight (impact on exposure)	*-*	*0*	*In some scenarios such small species may not occur. However, this has only a limited impact on risk due to scaling of food intake with body weight.*	*0*	*0*	*Exposure is calculated based on simulated individual body weights. Hence, the true risk (or a close approximation) is simulated.*
Body weight (impact on toxicity)	*0*	*0*	*Less effect than for birds. Scaling of toxicity with body weight is close to 1 (0.94, Sample and Arenal, 1999).*	*0*	*0*	*Same approach as in first tier risk assessment is used.*
Daily food intake	*0*	*+*	*According to the raw data for non-marine, non desert, eutherian mammals, 72% of records make no mention of breeding status or season., 22% of records indicate winter or non-breeding status and only 6% make a definite mention of animal in engaged in breeding (e.g. pregnant or lactating). On the basis of this information, it is likely that the daily food intake for an individual during breeding could be greater than used.*	*0*	*+*	*The same approach as in first tier risk assessment is used. Hence also the uncertainty is the same.*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

	First tier risk assessment (EFSA 2009)			*Population level risk assessment*		
	Potential for true risk to be		*Explanation*	*Potential for true risk to be*		*Explanation*
	lower	*higher*		*lower*	*higher*	
Percent of diet taken by individual in treated area	*-*	*0*	*Likely only a few scenarios where true worst case individual is less than 0.5 (i.e. factor of 2 reduction). The factor cannot be higher (PT>1 is not possible)*	*-*	*+*	*The percent of diet taken from an area is simulated as the percent of time (PT) an individual spends in that area. Simulated PT values were validated using independent data from field studies. It has been shown that simulated PT values were slightly worst-case compared to field data. Hence some overprotection is likely.*
Residue per unit dose	*0*	*++*	*True distribution for pesticide under assessment could be higher than average RUD used in assessment, so true worst case could be higher than average RUD. Also, RUD values may underestimate peak concentration on highly-exposed food items. Any underprotection would be more pronounced where long term effects are the result of short-term exposure.*	*-*	*+*	*The default RUD from the worst-case food item has been used, although the true measured RUDs were lower. For a population level risk assessment, the geometric mean value is a realistic estimate, because although in reality individual mammals might feed on food which is exposed above average, there are also individuals which feed on food exposed below average. Therefore, no underprotection may be expected.*
Half-life on food (DT_{50})	*--*	*+*	*Default value of 10 days for the various TWA measurements is conservative: most pesticides have DT_{50}s below 10. However, some pesticides have DT_{50}s longer than 10 days (e.g. 19% of pesticides registered in Canada in 2005). Also dissipation in first few days is often faster than implied by assumption of first order kinetics.*	*--*	*0*	*The default value of 10 days has been used although measured DT_{50}s are much lower. Hence exposure is very likely to be overpredicted by at least a factor of 3.6.*
Interception factors	*0*	*0*	*Interception factors are based on those used in FOCUS Step 2, which were derived from field measurements and are considered to be conservative for spray reaching ground. Within each growth stage a conservative (early) value is used.*	*-*	*0*	*An interception factor of 1 has been used, i.e. no interception. Since this is an absolute worst-case, no uncertainty is introduced here. Because of the early BBCH stage and the in-row cultivation of maize, it is very likely that sprayed substances will partly settle on bare soil instead of maize plants or weeds.*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

	First tier risk assessment (EFSA 2009)			*Population level risk assessment*		
	Potential for true risk to be		*Explanation*	*Potential for true risk to be*		*Explanation*
	lower	*higher*		*lower*	*higher*	
Non-dietary exposure	*0*	*+/++*	*This parameter is ignored, however, the true contribution uncertain, but could, in short term, increase risk by up to two times or more although this is very uncertain as based on bird studies*	*0*	*+/++*	*As in first-tier risk assessment, this factor is ignored. Skin contact by direct spraying is unlikely because brown hares try to escape from agricultural machinery.*
Variation of toxicity between species and/or stages within species	*---*	*+++*	*There is very little data on toxicity in mammalian species other than the standard species used for human toxicology. There is in principle no reason to believe variation in sensitivity between tested mammals and wild mammal species will be different to that for birds.*	*---*	*+++*	*The same approach as in first-tier risk assessment has been used. However, the risk from different toxicity in different live stages is low, because toxic effects were parameterised for all stages separately.*
Variation of toxicity between individuals	*0*	*+/++*	*Most sensitive individuals could be more sensitive (most NOAELs used are based on tests of significance between treatment group averages and not individual effects).*	*-*	*0*	*Effect models were parameterised according to mean values of groups, not from worst-case individuals. However, for a population level risk assessment, this is a realistic approach: in the model, variation between individuals is considered, because effects are simulated as probabilities using Monte Carlo. This means effects of the same dose can be different for different individuals. Since effects were parameterised according to data from worst-case generations, a realistic worst-case estimate has been used. Hence effects are likely to be overpredicted.*
Uncertainty factor	*--*	*0*	*TER is compared with trigger value of 5.*	*--*	*0*	*No effect could be observed when up to 5 times the maximum intended application rate was used in simulations.*
Avoidance of contaminated food or of treated area as a whole	*--*	*0*	*Parameter is ignored, which would be realistic for non-avoided pesticides. Potential effect of avoidance less for sublethal effects which occur at doses closer to avoidance threshold and thus less likely to be prevented. Longer time scales increase potential for learned avoidance for pesticides without ARfDs, but effects may occur at intakes below avoidance threshold.*	*-*	*0*	*No direct information on avoidance of treated food is available. Indirectly, food consumption in the reproductive toxicity study decreased in a dose-response manner, so it is possible that there may be some avoidance. Hence ignoring avoidance of treated food or areas provides a realistic worst-case and is likely to over-estimate the risk.*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

	First tier risk assessment (EFSA 2009)			***Population level risk assessment***		
	Potential for true risk to be		***Explanation***	***Potential for true risk to be***		***Explanation***
	lower	***higher***		***lower***	***higher***	
Effect of metabolism	*0*	*0*	*Effect of metabolism is incorporated in non-acute toxicity studies.*	*0*	*0*	*Effect of metabolism is incorporated in non-acute toxicity studies.*
Proportion of the population exposed	*0*	*0*	*The surrogate protection goal relates to a realistic worst case individual, which would be exposed.*	*-*	*0*	*Instead of the surrogate protection goal (individual), the actual protection goal (no long-term repercussions on abundance and diversity) has been addressed. This relates to a worst-case population which would be exposed. Since a worst-case landscape was been used, the proportion of population exposed is very likely to be overpredicted.*
Timing of applications	*-*	*+*	*Assessment assumes worst case exposure in all phases for same individual, whereas in practice exposure is likely to peak in different phases for different individuals. However, it is likely at least some individuals will be exposed in most sensitive phase, so not over-conservative for surrogate protection goal.*	*-*	*+*	*As a worst-case, the application window has been shortened to the period in which maize is attractive for hares for foraging. Exposure is likely to realistically peak in different phases for different individuals. Hence a realistic worst-case approach is used for a population level risk assessment.*
Recovery from effects	*---*	*0*	*Affected individuals may be able to recover and successfully reproduce at a later date.*	*0*	*0*	*Affected individuals may be able to recover and successfully reproduce at a later date. However this is taken into account because the population level risk assessment takes the time after exposure into account (simulations were conducted throughout the year)*
Landscape	*0*	*0*	*Not addressed in first-tier risk assessment.*	*-*	*0*	*A realistic worst-case landscape has been used. The worst-case character of this landscape has been confirmed.*
Overall	*There are uncertainties in both directions. Because of the potential for wide variation in toxicity between species, some individuals in sensitive species may experience reproductive effects at TER>5, potentially breaching the surrogate protection goal. The assessment procedure is more likely to fulfil the actual protection goal of preventing long-term repercussions on abundance and diversity, due to variation in exposure between individuals and over space and time, and the potential for replacement through recovery and immigration.*			*As in first-tier risk assessment, there are uncertainties in both directions. However, the uncertainty factor of 5 (which is the same factor as in first tier risk assessment) needs to cover much less uncertainty compared to first-tier.* *Compared to first-tier risk assessment, many uncertainties which could result in a higher true risk could be reduced (e.g. RUD, toxicity variation between individuals) by doing the risk assessment based on a worst-case population instead of a worst-case individual. Also, the comparison of default data from first-tier with true measured data (e.g. RUD, DT_{50}) decreases the uncertainty. Hence by using a population model, uncertainties could be largely decreased compared to first-tier risk assessment.*		

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

In particular, measured dose-response curves were used in the range of measured doses. For doses above this range, 100% effect was conservatively assumed. Furthermore, demonstrably worst-case assumptions have been used with regard to the following:

- *Effects from a study with much longer exposure (continuous exposure over 28 weeks) than exposure under field conditions were considered. In reality only a short exposure period is expected under field conditions because of the low substance-specific DT_{50} values (DT_{50} ≤ 2.05 d.*
- *Residue decline according to the default DT_{50} from EFSA (2009) of 10 days has been used instead of the much lower measured substance-specific DT_{50}.*
- *Exposure has been calculated using the default RUD from EFSA (2009) instead of the lower measured substance-specific RUD (mesotrione: 48.0 mg/kg in maize measured in the DT_{50} studies).*
- *A worst-case landscape was considered. The worst-case character of this landscape has previously been confirmed: a proportion of 30% treated maize fields in the landscape was assumed, which is a reasonable worst-case for Central Europe; and an additional validation regarding PT in maize has confirmed that PT values resulting from simulations in this landscape are worst-case compared to field data.*
- *A closed population with no immigration was considered in modelling, hence there was no possibility of recovery by immigration.*

This large number of worst-case assumptions allows us to quantify the margin of safety included in this risk assessment for each part of the risk assessment separately:

List of parameters or assumptions and their margin of safety used in the population level risk assessment.

Parameter/assumption	***Margin of safety***	***Uncertainty***
RUD in the exposure calculation (without residue decline)	*>1.1 (54.2 is the default value from EFSA;the realistic measured geomean for mesotrione RUD = 48.0 in maize North, 2016) PD=1 assumed* *Up to x1.89 from the use of the default monocot RUD (54.2) instead of dicot RUD (28.7), but both are likely to be food items for the hare*	*Very small (true risk probably lower)*
Residue decline	*>3.8x (21d TWA DDD is 1.36 when the default value is used, compared to a 21d TWA DDD of 0.36 when the realistic worst-case DT_{50} of 2.05d from dicots is used)*	*None (default DT_{50} of 10 d was used while the measured DT_{50} for mesotrione in maize is 0.8 d and in a representative dicot it is 2.05 d)*
Dose response modelling	*1x (realistic dose response curves have been used in the range of measured doses, worst-case effects were assumed as a threshold for higher doses).*	*Very small (true risk probably lower)*
Worst-case landscapes	*1x (realistic worst-case)*	*Small (realistic worst-case)*
Assumption that all fields are treated simultaneously	*1x (realistic worst-case)*	*None (worst-case)*
No effects at 5x the maximum intended application rate	*5x*	*Small (worst-case landscape used, closed population, default DT_{50} and dose response)*
Overall margin of safety:	***>20.9x***	

Hence, overall it can be concluded that negligible effects to brown hare populations are expected following application of mesotrione in maize at 150g/ha. This risk assessment includes a quantifiable margin of safety of >20.9x in the inputs for modelling.

A 2.1.3 KCP 10.1.3 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

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

Comments of zRMS:	*The study was performed in line with OECD 221 with no deviations.* *The doubling time was 1.6 days, so the validity criteria were met.* *The measured concentrations were analysed in fresh and aged medium at each renewal. Measured concentrations were within 80-120% of nominal, so the endpoints may be based on nominal concentrations.* *The recovery phase was not summarised by the Applicant below and was also not presented by the zRMS as not relevant for the risk assessment purposes.* *Overall, the study is considered acceptable with following endpoints relevant for the risk assessment:* *lowest 7-d E_rC_{50} = 0.028 mg test item ~~a.s.~~/L* *lowest 7-d E_yC_{50} = 0.0052 mg test item ~~a.s.~~/L* *During the commenting period it was pointed out that endpoints from the study were not corrected for content of the pure active substance in the test item (86.1%, analysed). Following corrected endpoints are relevant for the risk assessment:* *lowest 7-d E_rC_{50} = 0.0241 mg a.s./L* *lowest 7-d E_yC_{50} = 0.0045 mg a.s./L* *Respective information has been added to the study summary below.*

Reference:	*KCP 10.2.1/01*
Report	*Hengsberger A. & Wydra V. (2015), Mesotrione Wet Paste (ZA1296) - Toxicity to the Aquatic Plant Lemna gibba in a Semi-Static Growth Inhibition Test with a Subsequent Recovery Period. Report Number 105732240. ibacon GmbH Arheilger Weg 17 64380 Rossdorf Germany. Syngenta file no ZA1296_10438).*
Guideline(s):	*OECD Guidelines 221: Lemna sp. Growth Inhibition Test (2006)* *US EPA Ecological Effects Test Guidelines, OPPTS 850.4400: Aquatic Plant Toxicity using Lemna spp., Tiers I and II, (1996)*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Acceptable*
Duplication (if vertebrate study)	*-*

Materials

Test Material *ZA1296*
Mesotrione Wet Paste
Actual content of active ingredients: *631795 (SMO7F333)*
Purity: *86.1% (wt/wt)*
Description: *Brown solid*
Stability of test compound: *Stable under standard conditions*
Reanalysis/expiry date: *End of February 2016*
Density: *n/a*

Treatments

Test concentrations: *Dilution water control; nominal concentration of 64, 32, 16, 8, 4 and 2 µg test item/L*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Solvent:	*None*
Vehicle and/or positive control:	*Potassium dichromate is used as a positive control at least twice a year.*
Analysis of test concentrations:	*Yes, analysis of fresh and aged medium at each renewal ~~on days 0 and 7~~*
Test organisms	
Species:	*Lemna gibba*
Source:	*In-house cultures*
Test design	
Test vessels:	*250 mL glass flasks filled with 200 mL test medium covered with glass dishes*
Test medium:	*20X AAP-Growth Medium*
Replication:	*Three vessels for the control and each test concentration*
Initial frond number:	*4 fronds per plant, total 12 fronds per replicate*
Exposure regime:	*Semi-static (renewal at days 3 and 5)*
Duration:	*7 days*
Environmental conditions	
Temperature:	*23 - 24 °C*
pH:	*Fresh media:7.5 – 7.9* *Aged media: 8.5 – 9.0*
Lighting:	*Continuous illumination, 7300 - 7770 Lux (mean 7467 Lux).*

Study Design and Methods

Experimental dates: 21 August to 28 October 2015

Before test start and before the test medium renewal a concentrated stock solution was prepared by dissolving 10.2, 10.0 and 10.3 mg test item in 1020, 1000 and 1030 mL test water, respectively. The stock solution was intensively stirred for 40 minutes and short ultrasonic treatment was used for 15 minutes. Then, adequate volumes were mixed into test water to obtain the desired test concentrations. Appropriate volumes of the stock solution were diluted to give the test concentration series. The control consisted of culture medium only.

200 mL of the test solutions were transferred into 250 mL glass flasks and inoculated with Lemna plants. Cultures were then transferred to a temperature-controlled room where they were maintained under the conditions indicated above.

Assessments of frond number were made on days 0, 3, 5 and 7. Fronds were harvested for measurement of dry weight after 7 days, and the initial dry weight was determined using a sample of 12 fronds identical to that used to inoculate the test.

Temperature was measured continuously, light intensity was recorded once at test start and pH was recorded on days 0, 3, 5 and 7 days.

The test concentrations were verified by chemical analysis of ZA1296 at days 0 and 7, using high performance liquid chromatography with ultra violet-visible detection.

Results and Discussion

At the start of the test, the concentrations of the test item were found to be in the range 93 to 107 % of the nominal values and at the end of the test were in the range 87 to 122 % (see table below). Nominal concentrations were used for the calculation and reporting of results.

Table A 6: Analytical results

Nominal concentrations (µg test item ~~a.s.~~/L)	*% of nominal measured at 0 days*	*% of nominal measured at 3 days (aged)*	*% of nominal measured at 3 days (fresh)*	*% of nominal measured at 5 days (aged)*	*% of nominal measured at 5 days (fresh)*	*% of nominal measured at 7 days*
2	*107*	*100*	*110*	*101*	*110*	*103*
4	*119*	*108*	*110*	*109*	*113*	*122*
8	*97*	*97*	*113*	*108*	*102*	*103*
16	*97*	*92*	*99*	*94*	*100*	*87*
32	*93*	*88*	*97*	*93*	*95*	*94*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

64	*101*	*91*	*102*	*95*	*98*	*91*

Data for frond number and dry weight was used to calculate growth rates and yield for the control and each exposure concentration. Non-linear regression was used to calculate the 7-day ErC_{50} and EyC_{50}, based on percent inhibition relative to the control. For the No Observed Effect Concentration and Lowest Observed Effect Concentration, a Williams test was used to determine values significantly different to the control.

Mean frond numbers are presented below along with the growth rate, yield and respective inhibition values, alongside estimated EC_{50} values:

Table A 7: Effect of ZA1296 on growth rate and yield (frond number) of Lemna gibba

Nominal concentration (µg/L) [1)]	*Mean No. fronds/replicate (day 7)*	*Based on Frond Number (0-7 days)*			
		Growth Rate	*Inhibition of Growth Rate (%)*	*Yield*	*Inhibition of Yield (%)*
Control	*250.0*	*0.434*	*-*	*238.0*	*-*
2	*246.3*	*0.431*	*0.6*	*234.3*	*1.5*
4	*138.7*	*0.349**	*19.6*	*126.7**	*46.8*
8	*107.0*	*0.312**	*27.9*	*95.0**	*60.1*
16	*66.0*	*0.243**	*43.9*	*54.0**	*77.3*
32	*49.0*	*0.200**	*53.8*	*37.0**	*84.5*
64	*43.7*	*0.184**	*57.7*	*31.7**	*86.7*
EC_{50} µg/L		*28*		*6.0*	
95% confidence limits		*20 - 37*		*4.3 – 8.4*	
NOEC		*2.0*		*2.0*	
LOEC		*4.0*		*4.0*	

Inoculum = 12 fronds
[1)] Given as the test item not corrected for purity
** mean value significantly different from the control (tested with Williams Test, α = 0.05, one-sided)*

Mean dry weights are presented below along with the growth rate, yield and respective inhibition values, alongside estimated EC_{50} values:

Table A 8: Effect of ZA1296 on growth rate and yield (dry weight) of Lemna gibba

Nominal concentration (µg/L) [1)]	*Dry Weight (mg) (day 7)*	*Based on Dry Weight (0-7 days)*			
		Growth Rate	*Inhibition of Growth Rate (%)*	*Yield*	*Inhibition of Yield (%)*
Control	*32.8*	*0.440*	*-*	*31.3*	*-*
2	*32.5*	*0.439*	*0.3*	*31.0*	*0.7*
4	*16.9*	*0.345**	*21.7*	*15.4**	*50.9*
8	*11.2*	*0.287**	*34.8*	*9.7**	*69.0*
16	*8.0*	*0.238**	*45.9*	*6.5**	*79.2*
32	*7.5*	*0.230**	*47.8*	*6.0**	*80.8*
64	*5.6*	*0.188**	*57.3*	*4.1**	*86.9*
EC_{50} µg/L		*28*		*5.2*	
95% confidence limits		*19 - 42*		*3.5 – 7.7*	
NOEC		*2.0*		*2.0*	
LOEC		*4.0*		*4.0*	

Inoculum = 1.5 mg dry weight per vessel
[1)] Given as the test item not corrected for purity
** mean value significantly different from the control (tested with Williams Test, α = 0.05, one-sided)*

Conclusions

For frond number, the 7-day EC_{50} for yield (EyC_{50}) and growth rate (ErC_{50}) for ZA1296 to Lemna gibba were 6.0 and 28 µg test item ~~a.s.~~/L respectively, based on nominal concentrations.
For dry weight, the 7-day EC_{50} for yield (EyC_{50}) and growth rate (ErC_{50}) for ZA1296 were 5.2 and 28 µg test item ~~a.s.~~/L respectively, based on nominal concentrations.
The 7-day NOEC was determined to be 2.0 µg/L and the 7-day LOEC was determined to be 4.0 µg test item/L

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Comments of zRMS:	*It should be noted that most of the Central Zone Member States has concerns regarding reliability of the modified exposure studies due to uncertainties related to the exposure profiles modelled using FOCUS. Extensive discussion regarding this issue took place during the Central Zone harmonisation meetings and it was concluded that results of Tier 2C studies should be considered only when no acceptable risk may be demonstrated using standard approach (i.e. standard toxicity endpoints and exposure calculated with consideration of the risk mitigation measures).* *For mesotrione applied as Callisto acceptable risk to aquatic organisms could be concluded using the endpoint required by EFSA, 2013 (i.e. E_rC_{50}) and applying standard risk mitigation measures. Taking this into account, the summarised below Tier 2C study was not necessary to finalise the risk assessment at the zonal level and in consequence was not evaluated by the zRMS.*

Reference:	*KCP 10.2.1/02*
Report	*Hengsberger A. & Wydra V. (2015a), Mesotrione Wet Paste (ZA1296) - Toxicity to the Aquatic Plant Lemna gibba in a Reciprocal Growth Inhibition Test. Report Number 105731240. ibacon GmbH Arheilger Weg 17 64380 Rossdorf Germany. (Syngenta file no ZA1296_10436).*
Guideline(s):	*OECD Guidelines 221: Lemna sp. Growth Inhibition Test (2006)* *US EPA Ecological Effects Test Guidelines, OPPTS 850.4400: Aquatic Plant Toxicity using Lemna spp., Tiers I and II, (1996)*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Not evaluated, not required for finalisation of risk assessment performed in line with EFSA (2013)*
Duplication (if vertebrate study)	*No*

Comments of zRMS:	*Pulsed-exposure part* *It should be noted that most of the Central Zone Member States has concerns regarding reliability the modified exposure studies due to uncertainties related to the exposure profiles modelled using FOCUS. Extensive discussion regarding this issue took place during the Central Zone harmonisation meetings and it was concluded that results of Tier 2C studies should be considered only when no acceptable risk may be demonstrated using standard approach (i.e. standard toxicity endpoints and exposure calculated with consideration of the risk mitigation measures).* *For mesotrione applied as Callisto acceptable risk to aquatic organisms could be concluded using the endpoint required by EFSA, 2013 (i.e. E_rC_{50}) and applying standard risk mitigation measures. Taking this into account, the pulsed-exposure part of the summarised below was not necessary to finalise the risk assessment at the zonal level and in consequence was not evaluated by the zRMS.* *Standard toxicity part* *With regard to the standard toxicity part, the design of the study in terms of test conditions and experimental treatment was in line with recommendations of OECD 239. No deviations regarding environmental conditions were observed.* *It was, however, noted that the number of shoots tested in control and test item groups was not in line with recommendations of OECD 239. According to the test guideline, 6 replicates per control and 4 replicates per test item group with 3 shoots each are recommended, resulting with 18 and 12 plants per control and test item group, respectively.* *In this study one shoot per replicate was used with 10 replicates per control and 5 replicates per test item group, resulting with 10 and 5 plants per control and test item group, respectively.* *In general, this deviation could reduce the statistical power of the study.*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

	Nevertheless, as clear dose-response relationship could be seen on all parameters measured, it was concluded by the zRMS that results of this study should not be rejected due to deviation mentioned, especially all validity criteria were met. *The measured concentrations were analysed in fresh and aged medium at each renewal. Measured concentrations were within 80-120% of nominal, so the endpoints may be based on nominal concentrations.* *In the course of the commenting period it was pointed out by DE that the derived E_rC_{50} value may not be reliable due to the wide confidence intervals. It was proposed to consider the lower limit CI as the relevant endpoint for the risk assessment. It should be, however noted that the EC_{50} values for both, growth rate and yield, were at expected level, i.e. above the concentration resulting with <50% effect but below the next concentration resulting with >50% effect. For this reason, in opinion of the zRMS, they accurately reflect the observed dose-response.* *Additional explanation of this issue has been provided by the Applicant and the zRMS fully agrees with this statement:* *In general, three parameter non-linear regression models typically result in wider confidence intervals than simpler two parameter models. This does not mean that the ErC50 estimate is inaccurate as the fitted model should always be checked to ensure it correctly models the actual dose response. For example, a quick examination of the Myriophyllum spicatum data clearly shows that the E_rC_{50} would be expected to be between 15.3 µg /L and 48.8 µg /L based on 37.6% and 63.2% reduction in growth rate respectively compared to the control. As the E_rC_{50} was estimated to be 33.3 µg /L and the graphical output of the model generally reflects the dose response, the endpoint can be considered an accurate estimate of the 50% effect level and should be used in the risk assessment. It should also be noted that the current risk assessments are calibrated for use of the EC_{50} and not the EC_{50} lower limit. Use of a lower limit EC_{50} would require the safety factors to be re-calibrated due to use of a more conservative endpoint.* *It is possible to calculate tighter confidence intervals. For Myriophyllum, for example, based on the Weibull 3 parameter non-linear regression model, the results are: ErC50 = 32.942; 95%-CL lower 10.866; upper 56.250.* *Overall, despite deviation indicated above, the study is considered acceptable with following endpoints relevant for the risk assessment:* *lowest 14-d E_rC_{50} = 0.0339 mg test item ~~a.s.~~/L* *lowest 14-d E_yC_{50} = 0.00301 mg test item ~~a.s.~~/L* *During the commenting period it was pointed out that endpoints from the study were not corrected for content of the pure active substance in the test item (84.6%, analysed). Following corrected endpoints are relevant for the risk assessment:* *lowest 14-d E_rC_{50} = 0.0287 mg a.s./L* *lowest 14-d E_yC_{50} = 0.00255 mg a.s./L*

Reference:	*KCP 10.2.1/03*
Report	*Gonsior G, (2017), Mesotrione – Growth Inhibition of Myriophyllum spicatum in a Water/Sediment System. Report Number S16-06273. Eurofins Agroscience Services EcoChem GmbH / Eurofins, Agroscience Services Ecotox GmbH, Eutinger Strasse 24, 75223 Niefern-Öschelbronn, Germany. (Syngenta file no ZA1296_10504)*
Guideline(s):	*OECD Guidelines for Testing of Chemicals, Section 2 - Effects on Biotic Systems, Method 239: Water-Sediment Myriophyllum spicatum Toxicity Test (2014)*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Standard part of the test: acceptable*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

	Pulsed-exposure part: not evaluated as not required for finalisation of risk assessment performed in line with EFSA (2013)
Duplication (if vertebrate study)	*No*

Materials and methods

Test Material	*Mesotrione Technical*
	ZA1296
Lot/Batch #:	*765385*
	SMO0H028
Purity:	*84.6 % wt/wt*
Description:	*Brown powder*
Stability of test compound:	*Stable under standard conditions*
Reanalysis/expiry date:	*28 February 2019*
Density:	*Not applicable*
Treatments	
Test concentrations:	*Toxicity test: Dilution water control; nominal concentration of 4.77, 15.3, 48.8, 156 and 500 µg mesotrione tech./L*
Solvent:	*None*
Analysis of test concentrations:	*Yes, analysis of mesotrione in overlying water at the start, day 4 (aged and fresh), day 8 (aged and fresh), day 11 (aged and fresh) and at day 14 (aged) in the toxicity test, using HPLC-MS/MS*
Test organisms	
Species:	*Myriophyllum spicatum L.*
Source:	*In-house cultures, originally obtained from the Federal Environment Agency Berlin, Germany*
Test design	
Test vessels:	*300 mL glass vessels (9 cm diameter, 5 cm height) placed in 2 L glass-beakers (12 cm diameter, 24 cm height) containing approximately 350 g moist sediment and 1.5 L growth medium*
Test medium:	*SMART AND BARKO growth medium*
Replication:	*Toxicity test: five replicates for each test concentration and ten for the control*
Number of shoots per vessel:	*1 rooted apical shoot*
Exposure regime:	*Semi-static*
Duration:	*14 days*
Environmental conditions	
Temperature:	*Toxicity test: 19.2 ± 1.0 °C (18.0 – 21.7 °C)*
pH:	*Toxicity test: 7.93 ± 0.47 (7.48 – 9.84)*
Dissolved oxygen:	*Toxicity test: 100 ± 14 % (78 – 156 %)*
Lighting:	*16 hour day length, approximately 120 – 160 µE m^{-2} s^{-1}*

Study Design and Methods

Experimental dates: 03 November 2016 to 02 December 2016

A semi-static toxicity test were performed. A stock solution with a nominal concentration of 500 µg mesotrione tech./L was prepared by adding the required amount of the test item to a volumetric flask and adding test medium up to the benchmark. The solution was homogenised by shaking and ultrasonication for 4 hours. Appropriate volumes of the stock solution and preceding test solutions were diluted to give the test concentrations. The control consisted of test medium only.

Three days before the start of the test, approximately 350 g of moist sediment was transferred to the test vessels. The surface was overlaid with moist sediment without ammonium chloride and sodium phosphate and a thin layer of washed quartz sand to minimise displacement of the sediment when the medium was added. The test vessels were placed in 2 L glass beakers and filled carefully with 1.5 L of growth medium to a depth of 14 cm. On the day of the test, one rooted apical shoot per vessel was planted carefully, ensuring the plant was rooted into the sediment. Only plants of the same size (e.g. ± 10 – 20 % of mean shoot length) were used for the test. The test item solution was then added and mixed in with gentle stirring. The test

solution renewal was performed at day 4, 8 and 11 in the toxicity test ~~and at day 1 and 4 in the pulse dose tests~~. The test vessels were maintained in a controlled environment under the conditions indicated above. Assessments of plant growth were made on days 0, 7 and 14. Plants were harvested for measurement of biomass (plant fresh weight and plant dry weight), shoot length and number and length of side shoots on day 14, and observations on shoot and root development (e.g. necrosis, deformation) were documented. The initial biomass (plant fresh weight and plant dry weight) and shoot length were determined using a sample of 15 additional plants, representative of those used in the test.
Water temperature, pH and dissolved oxygen saturation were recorded on days 0, 4 (aged and fresh), 8 (aged and fresh), 11 (aged and fresh) and 14 (aged) in the toxicity test and on days 0, 1 (aged and fresh), 4 (aged and fresh), 8 (aged and fresh), 11 (aged and fresh) and 14 (aged) in the pulse dose tests. Light intensity on the water surface was measured at test start.
The test concentrations were verified by analyses of mesotrione at all concentration levels by analysing the overlaying water at test start, day 4 (aged and fresh), 8 (aged and fresh), 11 (aged and fresh) and 14 (aged) in the toxicity test, using high performance liquid chromatography with tandem mass spectrometry.

Results and Discussion

The concentrations of the test item in the freshly prepared solutions were found to be in the range 83 to 110 % of the nominal values and in the aged solutions in the range 87 to 108 %.

The limit of quantification in this study was 0.4 µg mesotrione/L (in water) corresponding to 0.473 µg mesotrione tech./L. Since all concentrations were within 20% of nominal, the latter were used for the calculation and reporting of all results.

Table A 9: Analytical results

Test	**Nominal concentrations**		**% of nominal mesotrione concentration measured in overlaying water**									
	(µg mesotrione tech./L)	**(µg mesotrione/L)**	**Day 0**	**Day 1**		**Day 4**		**Day 8**		**Day 11**		**Day 14**
			fresh	**aged**	**fresh**	**aged**	**fresh**	**aged**	**fresh**	**aged**	**fresh**	**aged**
Toxicity test	Control	0	-	n.a.	n.a.	-	-	-	-	-	-	-
	4.77	4.04	102	n.a.	n.a.	108	91	101	83	87	84	91
	15.3	12.9	97	n.a.	n.a.	102	95	98	84	87	95	95
	48.8	41.3	99	n.a.	n.a.	100	93	95	86	88	94	96
	156	132	105	n.a.	n.a.	98	94	96	90	92	98	102
	500	423	108	n.a.	n.a.	101	96	100	98	99	110	105

- Not detectable
n.a. – not analysed

Biological Results 'Toxicity Test'

Data for total shoot length and biomass was used to calculate growth rates and yield for the control and each exposure concentration. Non-linear analysis was used to calculate the 14-day $E_rC_{10, 20, 50}$ and $E_yC_{10, 20, 50}$. For the No Observed Effect Concentration and Lowest Observed Effect Concentration, all data were subjected to ANOVA. Normality was tested using Shapiro-Wilk's test and homogeneity of variances across treatment groups were tested using a Bartlett's or Levene's test. Normally distributed and homogeneous data were analysed using a Dunnett's test and a Bonferroni-U Exact Test was used to analyse non-normal distribution data to determine significant differences from controls.

Mean total shoot length are presented below along with the growth rate, yield and respective inhibition values, alongside calculated $EC_{10, 20, 50}$ values:

Table A 10: Effect of mesotrione technical on growth rate and yield (mean total shoot length) of Myriophyllum spicatum in the 'toxicity test'

Test type	Nominal concentration (µg mesotrione tech./L)	Mean total shoot length (cm)		Based on mean total shoot length (0-14 days)			
		Day 0[1]	Day 14	Growth Rate (1/day)	Reduction of Growth Rate (%)	Yield (cm)	Reduction of Yield (%)
Toxicity test	Control	5.6	44.0	0.1466	-	38.44	-
	4.77	5.6	23.2	0.1013*	30.9*	17.6*	54.2*
	15.3	5.6	20.5	0.0915*	37.6*	14.9*	61.2*
	48.8	5.6	12.5	0.0562*	61.7*	6.9*	82.0*
	156	5.6	12.1	0.0540*	63.2*	6.5*	83.1*
	500	5.6	10.4	0.0429*	70.7*	4.8*	87.5*
EC_{10} µg mesotrione tech./L[2]				0.149		(-)	
95 % confidence limits				0.024 – 0.930		(-)	
EC_{20} µg mesotrione tech./L[2]				0.958		(-)	
95 % confidence limits				0.164 – 5.78		(-)	
EC_{50} µg mesotrione tech./L[2]				33.9		3.01	
95 % confidence limits				3.69 – 294		0.117 – 90.3	
NOEC				n.d.		n.d.	
LOEC				4.77		4.77	

[1] Based on 15 additional plants, representative of those used in the test
[2] Calculation based on 3-param. Normal CDF (cumulative distribution function)
(-) Values not reliable, control CV exceeded the effect level
** Significantly different reduction compared to the control*
n.d.- not detectable; no NOEC could be determined

Mean fresh weights are presented below along with the growth rate, yield and respective inhibition values, alongside calculated $EC_{10, 20, 50}$ values:

Table A 11: Effect of mesotrione technical on growth rate and yield (mean fresh weight) of Myriophyllum spicatum in the 'toxicity test'

Test	Nominal concentration (µg mesotrione tech./L)	Mean fresh weight (g)		Based on mean fresh weight (0-14 days)			
		Day 0[1]	Day 14	Growth Rate (1/day)	Reduction of Growth Rate (%)	Yield (g)	Reduction of Yield (%)
Toxicity test	Control	0.1069	1.1573	0.1685	-	1.0504	-
	4.77	0.1069	0.7195	0.1357	19.5*	0.6126*	41.7*
	15.3	0.1069	0.5317	0.1140	32.3*	0.4248*	59.6*
	48.8	0.1069	0.3545	0.0847*	49.7*	0.2476*	76.4*
	156	0.1069	0.3261	0.0769*	54.4*	0.2192*	79.1*
	500	0.1069	0.2896	0.0709*	57.9*	0.1827*	82.6*
EC_{10} µg mesotrione tech./L[2]				0.300		(-)	
95 % confidence limits				0.044 – 2.03		(-)	
EC_{20} µg mesotrione tech./L[2]				2.26		(-)	
95 % confidence limits				0.341 – 15.3		(-)	
EC_{50} µg mesotrione tech./L[2]				108		6.90	
95 % confidence limits				8.97 - 1174		0.267 - 200	
NOEC				n.d.		n.d.	
LOEC				4.77		4.77	

[1] Based on 15 additional plants, representative of those used in the test
[2] Calculation based on 3-param. Normal CDF (cumulative distribution function)
(-) Values not reliable, control CV exceeded the effect level
** Significantly different reduction compared to the control*
n.d.- not detectable; no NOEC could be determined

Mean dry weights are presented below along with the growth rate, yield and respective inhibition values, alongside calculated $EC_{10, 20, 50}$ values:

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Table A 12: Effect of mesotrione technical on growth rate and yield (dry weight) of Myriophyllum spicatum in the toxicity test

Test	**Nominal concentration (µg mesotrione tech./L)**	**Mean dry weight (g)**		**Based on mean dry weight (0-14 days)**			
		Day 0[1]	**Day 14**	**Growth Rate (1/day)**	**Reduction of Growth Rate (%)**	**Yield (g)**	**Reduction of Yield (%)**
Toxicity test	*Control*	*0.0116*	*0.0740*	*0.1311*	*-*	*0.0624**	*-*
	4.77	*0.0116*	*0.439*	*0.0943**	*28.1**	*0.0323**	*48.2**
	15.3	*0.0116*	*0.0415*	*0.0900**	*31.4**	*0.0299**	*52.1**
	48.8	*0.0116*	*0.0243*	*0.0509**	*61.2**	*0.0127**	*79.6**
	156	*0.0116*	*0.0278*	*0.0595**	*54.6**	*0.0162**	*74.0**
	500	*0.0116*	*0.0208*	*0.0412**	*68.6**	*0.0092**	*85.3**
EC_{10} µg mesotrione tech./L[2]				*(-)*		*(-)*	
95 % confidence limits				*(-)*		*(-)*	
EC_{20} µg mesotrione tech./L[2]				*1.42*		*(-)*	
95 % confidence limits				*0.124 – 17.1*		*(-)*	
EC_{50} µg mesotrione tech./L[2]				*53.3*		*5.81*	
95 % confidence limits				*2.37 - 1087*		*0.067 - 533*	
NOEC				*n.d.*		*n.d.*	
LOEC				*4.77*		*4.77*	

[1] Based on 15 additional plants, representative of those used in the test
[2] Calculation based on 3-param. Normal CDF (cumulative distribution function)
(-) Values not reliable, control CV exceeded the effect level
** Significantly different reduction compared to the control*
n.d - no NOEC could be determined

In the toxicity test, visible effects of the test material on shoot development were observed after 7 days at 48.8 µg mesotrione tech./L and 14 days at 15.3 µg mesotrione tech./L and above.

Validity

Control plants had no visual symptoms of chlorosis and were visibly free from contamination by other organisms such as algae and/or bacterial films on the plants, at the surface of the sediment and in the aqueous growth medium. Since the coefficient of variations (CV) for fresh weight and shoot length yield were below 35 % (actual: 24.3 and 16.0 %, respectively, in the toxicity test and 15.5 and 14.1 %, respectively, in the pulse dose tests) and a doubling of shoot biomass and length was reached within the test duration (actual: > 6-fold), the mean control growth rates and variability were considered acceptable.

Conclusions

Based on nominal concentrations, the 14-day EC_{50} values for growth rate (E_rC_{50}) and yield (E_yC_{50}) for mesotrione technical to Myriophyllum spicatum were 33.9 and 3.01 µg mesotrione tech./L, respectively, based on total shoot length. The E_rC_{50} and E_yC_{50} values based on biomass (fresh weight) were 108 and 6.90 µg mesotrione tech./L, respectively, and were 53.3 and 5.81 µg mesotrione tech./L, respectively, based on biomass (dry weight). The 14-day NOEC for growth rate and yield based on total shoot length and biomass could not be determined. The 14-day LOEC for growth rate and yield was 4.77 µg mesotrione tech./L, based on total shoot length and biomass (fresh weight and dry weight).

A 2.2.2 KCP 10.2.2 Additional long-term and chronic toxicity studies on fish, aquatic invertebrates and sediment dwelling organisms

A 2.2.3 KCP 10.2.3 Further testing on aquatic organisms

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 2.3.1.1.2 KCP 10.3.1.1.2 Acute contact toxicity to bees

A 2.3.1.2 KCP 10.3.1.2. Chronic toxicity to bees

Comments of zRMS:	*It is noted that data regarding chronic toxicity to adult bees obtained in studies performed with the representative formulation (Callisto) were deemed sufficient at the EU level and no data gap in this area was identified in EFSA Journal 2016;14(3):4419. Taking this into account it may be concluded that data requirements as set by the Commission Regulation (EU) No 284/2013 are fulfilled and no additional studies are deemed necessary. Additional studies performed with the active substance were thus not evaluated by the zRMS as sufficient data package is already available from the EU review.*

Reference:	*KCP 10.3.1.2/01*
Report	*Wendling, K., (2018), Mesotrione - Honey Bee (Apis mellifera L.) Chronic Oral Toxicity Test 10 Day Feeding Test in the Laboratory. Report Number S18-03658. Eurofins Agroscience Services Ecotox GmbH, Eutinger Str. 24, 75223 Niefern-Öschelbronn, Germany. (Syngenta file no ZA1296_10608)*
Guideline(s):	*OECD Guideline No. 245 (2017)*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Not evaluated*
Duplication (if vertebrate study)	*No*

A 2.3.1.3 KCP 10.3.1.3 Effects on honey bee development and other honey bee life stages

Comments of zRMS:	*It is noted that data regarding toxicity to bee larvae obtained in studies performed with the representative formulation (Callisto) were deemed sufficient at the EU level and no data gap in this area was identified in EFSA Journal 2016;14(3):4419. Taking this into account it may be concluded that data requirements as set by the Commission Regulation (EU) No 284/2013 are fulfilled and no additional studies are deemed necessary. Additional studies performed with the active substance were thus not evaluated by the zRMS as sufficient data package is already available from the EU review*

Reference:	*KCP 10.3.1.3/01*
Report	*Eckert (2016), Mesotrione - Honey bee (Apis mellifera L.) Larval Toxicity Test (Repeated Exposure through to Adult Emergence), Report Number S16-00332. Eurofins Agroscience Services Ecotox GmbH, Eutinger Str. 24 75223 Niefern-Öschelbronn, Germany (Syngenta file No. ZA1296_10465).*
Guideline(s):	*OECD DRAFT Guidance Document on Honey bee (Apis mellifera) larval toxicity test, repeated exposure (version dated 20 July 2015)*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Not evaluated*
Duplication (if vertebrate study)	*No*

A 2.3.1.4 KCP 10.3.1.4 Sub-lethal effects

A 2.3.1.5 KCP 10.3.1.5 Cage and tunnel tests

A 2.3.1.6 KCP 10.3.1.6 Field tests with honeybees

A 2.3.2 KCP 10.3.2 Effects on non-target arthropods other than bees

A 2.3.2.1 KCP 10.3.2.1 Standard laboratory testing for non-target arthropods

A 2.3.2.2 KCP 10.3.2.2 Extended laboratory testing, aged residue studies with non-target arthropods

A 2.3.2.3 KCP 10.3.2.3 Semi-field studies with non-target arthropods

A 2.3.2.4 KCP 10.3.2.4 Field studies with non-target arthropods

A 2.3.2.5 KCP 10.3.2.5 Other routes of exposure for non-target arthropods

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 10.4.1.1 Earthworms - sub-lethal effects

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

Folsomia candida

Comments of zRMS:	*The study was performed in line with recommendations of OECD 232 (2007) and was checked against criteria of the most recent versions of the guideline adopted in 2016.* *It is noted that the temperature during the study deviated from the recommended 20±1°C with minimum temperature of 16.4°C. However, according to the test report, the temperature dropped below 18°C for 12 hours only and the mean temperature during the test was 19.8°C, so it was within the required range.* *It is also noted that the CV value for the number of juveniles was 30%, while it should be less than 30%. Nevertheless, in opinion of the zRMS, CV calculated to be exactly the required limit should not invalidate the study, which is considered acceptable.* *It is noted that up to 180 mg pm/kg dw soil, no clear dose-response relationship could be observed on reproduction and for this reason the lower confidence interval for EC_{10} could not be determined. This was also noted by AT during the commenting period and it was pointed out that there is some uncertainty over the EC_{10} derived from this study as the lower CI limits of EC_{10} and EC_{20} could not be calculated and in addition the lower limit of EC_{50} (133 mg pm/kg dws) was slightly lower than the median EC_{10} (134 mg pm/kg dws). Furthermore, at the concentration set as NOEC (180 mg pm/kg dws), 18% effect on reproduction was observed and the CV among replicates was 55.2% which along with the CV of 30 % in the control could prevent resulting in a statistically significant difference. Therefore AT proposed to set the NOEC to 100 mg pm/kg dws, where no effect on reproduction was observed, and use this value in the risk assessment for precautionary reasons. The zRMS agrees with AT comment and suggestion and for this reason the following endpoint is considered relevant for the risk assessment:* *NOEC = 100 mg pm/kg dws* *In the course of the commenting period it was pointed out by DE that the Abbott correction for mortality in control was applied which is not appropriate for quantile data (see OECD GD No 54). Taking this into account the corrected mortality has been struck through in the Table A 23 below. Consideration of not corrected mortality has no impact on the test results, as according to OECD 232, the reproductive output is the main endpoint for F. candida.*

Reference:	*KCP 10.4.2.1/01*
Report	*Dickinson RA, (2015) R169649 - Collembola (Folsomia candida) Reproduction Test in Soil, Report Number ENV-14-015. Agrochemex Ltd., Aldhams research station, Manningtree, Essex, CO11 2NF, United Kingdom. (Syngenta File No. CA3511_10011)*
Guideline(s):	*OECD Guideline for Testing of Chemicals, Method 232 (adopted 7 September 2009): Collembolan reproduction test in soil.*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Acceptable with minor deviations*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Duplication (if vertebrate study)	*No*

Materials and methods

Test Material	*R169649 (MNBA; CA3511)*
Lot/Batch #:	*454319*
Actual content of active ingredients:	*99.9%*
Description:	*Off-white powder*
Stability of test compound:	*Stable under standard conditions*
Reanalysis/Expiry date:	*30 June 2017*
Treatments	
Test rates:	*17.2, 30.9, 55.6, 100, 180, 324, 583 and 1050 mg R169649/kg soil dry weight*
Control:	*Oven dried sand*
Toxic standard:	*Boric acid (Separate study – No.: ENV-13-051, date: February 2014)*
Application method:	*R169649 mixed in oven dried sand was mixed into artificial soil prior to introduction of collembolans*
Test organisms	
Species:	*Collembolans Folsomia candida (Willem)*
Age:	*9 to 12 days old*
Source:	*Bias Labs Ltd., UK*
Feeding:	*Approximately 10 mg ground baker's yeast at the start of the test and after 7, 14 and 21 days*
Test design	
Arenas:	*Glass test vessels (60 mL capacity) with lids*
Substrate	*Artificial soil comprising 5 % sphagnum peat, 20 % kaolinite clay, 69.77 % quartz sand (> 50 % of the particles between 0.05 mm and 0.2 mm) and 0.23 % calcium carbonate. 30 g wet weight of artificial soil was added to each test vessel.*
Replication:	*Treated groups 4, control group 8, plus an additional vessel per treatment for measurement purposes*
No./arena:	*10**
Duration of test:	*28 days*
Environmental test conditions	
Temperature:	*16.4 to 21.6 °C*
pH of soil:	*Test start: 5.96 to 6.50* *Test end: 5.63 to 6.21*
Water content of soil:	*Test start: 15.86 to 16.37 % soil moisture content* *Test end: 13.86 to 15.05 % soil moisture content*
Photoperiod:	*16 hours light and 8 hours dark at 715 to 720 Lux*

**During the extraction process it was noted that some of the test vessels contained more than 10 organisms. This was considered most likely due to an addition error on Day 0, and was not considered significant or to have affected the integrity of the study.*

Study Design and Methods

Experimental dates: 24 November 2014 to 22 December 2014

The highest test concentration was prepared by weighing 630.2 mg of the test item and making up to 30.0597 g with oven dried sand. This was mixed thoroughly and serially diluted with oven dried sand to prepare the lower test concentrations. Aliquots of the respective treated sand were thoroughly mixed with artificial soil at 25 % of the WHC, and distilled water was added to achieve a final nominal water content of 50 % of WHC. The control was treated with oven dried sand only.

Nominally ten juvenile collembolans were transferred after the application to the substrate surface of each test vessel using a pooter. Four and eight replicates were used for each test item treatment and control group, respectively (+ one replicate per treatment not loaded with collembolans for measurement purposes). The test organisms were fed four times during the experiment (at the start of the test and after

7, 14 and 21 days) with approximately 10 mg of ground baker's yeast per test vessel. Four weeks after introducing the test organisms, the surviving parental collembolans and offspring (juveniles) were counted.

All values presented throughout this report were calculated using the original raw data and were not based on rounded values.
The percentage mortality of the springtails was calculated for each treatment, both before and after correction for any control treatment losses using Abbott's formula (1925), modified by Schneider-Orelli (1947). The 28-day mortality data for the individual test-item treatments were compared to those for the control using Fisher Exact /Bonferroni-Holm Test (α = 0.05). The LC_{50} was determined by nonlinear regression analysis. The percentage reduction in reproductive performance in the test item treatment groups, compared to the control group, was calculated.

For the fecundity assessment, the data from the test-item treatments were compared to the control data using Wilcoxon/Bonferroni Adjustment Test (α = 0.05). The results were used to determine the NOEC with respect to reproduction. The median effect concentration (EC_{50}) and also values for the EC_{20} and EC_{10} were determined by nonlinear regression analysis.

Results and Discussion

Mortality and fecundity are summarised in the table below.

Table A 13: Effects of residues of R169649 on mortality and reproduction of Folsomia candida

Endpoint	**Treatment group (mg R169649/kg soil d.w.)**								
	Control	**17.2**	**30.9**	**55.6**	**100**	**180**	**324**	**583**	**1050**
% Mortality of parental collembolans after 4 weeks[a]	11	3	3	0	0	18	23	33*	40*
Mean number of juveniles after 4 weeks[c]	323	267	400	505	466	264	86*	88*	59*
Standard deviation	96.8	54.3	189.1	61.9	117.7	145.9	9.1	24.8	18.5
CV (%)	30.0	20.4	47.3	12.3	25.2	55.2	10.7	28.1	31.2
% reduction compared to control[d]	-	17	-24	-56	-44	18	74	73	82
NOEC (mortality)	324								
NOEC (reproduction)	180								
LOEC (mortality)	583								
LOEC (reproduction)	324								
LC_{50}	> 1050								
EC_{10}	134 (95 % confidence limits: n.d. and 225)								
EC_{20}	163 (95 % confidence limits: n.d. and 274)								
EC_{50}	237 (95 % confidence limits: 133 and 423)								

[a] Mortality amongst springtails originally introduced. Individual treatments compared to the control data using Fisher Exact/Bonferroni-Holm Test (α = 0.05), and an asterisk indicates where there was a significant difference.
[c] Fecundity data were compared to the control data using Wilcoxon/Bonferroni Adjustment Test (α = 0.05). Treatments marked with an asterisk (*) differed significantly from the control.
[d] A negative value indicates an increase in reproduction relative to the control and a positive value indicates a decrease
d.w.: dry weight
n.d.: could not be determined

Validity Criteria

The validity criteria for the control group were met:

- *Control treatment mortality was 11 % (must be < 20 %)*
- *The mean number of juveniles recorded in the control treatment was 323 (must be > 100 per replicate)*

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

- *The coefficient of variation of reproduction in the control was 30 % (must not be > 30 %)*

Conclusion

The toxicity of R169649 to the reproduction and the parental mortality of collembola species Folsomia candida were determined. The NOECs for survival and reproduction were determined to be 324 and 180 mg R169649/kg soil dry weight, respectively. The EC_{50} for number of juvenile collembolans was determined to be 237 mg R169649/kg soil dry weight.

Hypoaspis aculeifer

Comments of zRMS:	*The study was performed in line with recommendations of OECD 226 (2008) and was checked against criteria of the most recent versions of the guideline adopted in 2016.* *It is noted that the temperature during the study deviated from the recommended 20±2°C with minimum temperature of 17.4°C. However, according to the test report, the temperature dropped below 18°C for one brief occasion only and the mean temperature during the test was 19.1°C, so it was within the required range.* *Nevertheless, all test validity criteria were met and for this reason this deviation is considered to have no impact on the obtained results. The study is considered acceptable.* *No dose-response relationship could be observed on mortality and reproduction and the NOEC from the study was determined to be 1050 mg pm/kg dw soil. This value is recommended for the risk assessment purposes.* *EC_{10} could not be calculated.* *In the course of the commenting period it was pointed out by DE that the Abbott correction for mortality in control was applied which is not appropriate for quantile data (see OECD GD No 54). Taking this into account the corrected mortality has been struck through in the Table A 23 below. Consideration of not corrected mortality has no impact on the test results, as according to OECD 226, the reproductive output is the main endpoint for H. aculeifer.*

Reference:	*KCP 10.4.2.1/02*
Report	*Ramsden C, (2015), R169649 – Predatory Mite (Hypoaspis (Geolaelaps) aculeifer) Reproduction Test in Soil, Report Number ENV-14-012. AgroChemex Environmental Ltd., Aldhams Farm Research Station, Dead Lane, Manningtree, Essex, CO11 2NF, United Kingdom. (Syngenta file No. CA3511_10010)*
Guideline(s):	*OECD (2008). OECD Guideline for Testing of Chemicals, Section 2 – Effects on Biotic Systems, Method 226 (adopted 3 October 2008): Predatory mite (Hypoaspis (Geolaelaps) aculeifer) reproduction test in soil.*
Deviations:	*No*
GLP:	*Yes*
Acceptability:	*Acceptable with minor deviations*
Duplication (if vertebrate study)	*No*

Materials and methods

Test Material	*R169649* *NMSBA (= MNBA)*
Lot/Batch #:	*454319*
Purity:	*99.9 % ± 0.5 % w/w*
Description:	*Off white powder*
Stability of test compound:	*Stable under test conditions*
Reanalysis/Expiry date:	*30 June 2017*
Density:	*Not applicable*

Treatments

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Test rates:	*17.2, 30.9, 55.6, 100, 180, 324, 583 and 1050 mg R169649/kg soil dry weight*
Control:	*Oven dried sand*
Toxic standard:	*Boric acid (separate study ENV-14-017; November 2014)*
Test organisms	
Species	*Hypoaspis aculeifer*
Source:	*Obtained from Bias Labs Ltd., UK*
Food:	*Cheese mites, Tyrophagus putrescentiae , three times per week, ad libitum*
Age at test start:	*28 – 35 days*
Test design	
Vessels:	*Glass test vessels (volume: 60 mL; inner diameter: 38 mm) fitted with a 53 µm plastic mesh, and screw tops with a hole approximately 10 mm in diameter. Each vessel was filled with approximately 20 g soil d.w.*
Substrate:	*Artificial soil comprising 5% sphagnum peat, 20 % kaolinite clay, 74.77% quartz sand (with > 50% of particles between 50 – 200 µm) and 0.23% calcium carbonate*
Replication:	*Control group: 8 (+3 temperature surrogates)* *Treated group: 4 (+1 surrogate per concentration)*
No. of mites/arena :	*10*
Duration of test:	*14 days*
Environmental test conditions	
Temperature:	*17 to 21 °C (mean: 19 °C)**
pH:	*Test start: 5.20 to 5.94* *Test end: 5.40 to 6.03*
Water content of soil:	*Test start: 16.11 to 16.59 % wet weight of soil* *Test end: 13.51 to 15.54 % wet weight of soil*
Photoperiod:	*16 h light : 8 h dark, 480 lux*

** The temperature briefly dropped below the intended minimum (i.e. the guideline range of 18 – 22 °C) but there was no apparent effect on control mites and no impact was identified on the outcome or validity of the study.*

Study Design and Methods

Experimental dates: 12 November 2014 to 29 November 2014

Adult females of the soil mite Hypoaspis aculeifer were exposed to concentrations of R169649 incorporated into the test soil. A 30 g aliquot of the highest test concentration was prepared using exactly weighed amounts of the test item and oven-dried sand in a 60-mL glass jar, which was shaken and inverted repeatedly until well mixed. The lower test item concentrations were prepared by serial dilution with sand, starting with an appropriate volume from the aliquot of the highest concentration. Appropriate amounts of the test concentrations were then mixed with pre-moistened soil, and distilled water added such that a final moisture content value of 50 % WHC was achieved. Adult females were transferred to the test vessels which contained untreated (control) or test item treated artificial soil. Ten adult females were introduced to each test vessel. As a source of food, cheese mites (Tyrophagus putrescentiae) were added throughout the test. The test was carried out under controlled light-dark cycle. Fourteen days after introducing the test organisms, the surviving mites and the juveniles of Hypoaspis aculeifer were extracted by heat/light extraction. From these data the mortality of the adult females and the reproductive output were calculated.

The mean number of dead adult female mites for each treatment, the mean number of juvenile mites for each treatment, the NOEC, the LOEC, and the EC_{50} at day 14 were determined.
Mortality data were corrected for control mortality according to Abbott (1925) modified by Schneider-Orelli (1947), and statistically analysed using Fisher's Exact/Bonferroni-Holm test ($p = 0.05$). Reproduction data was statistically analysed using a Dunnett Multiple Comparison Test ($p = 0.05$).
The determination of the NOEC and LOEC values was based on the results of the statistical evaluation. The software used to perform the statistical analysis was CETIS™, Version 1.8.7.14. The LC_{50} and EC_{50} were not able to be determined by statistical analysis due to the outcome of the study.

Results and Discussion

Mortality and fecundity are summarised in the table below.

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

Table A 14: Effects of residues of R169649 on mortality and reproduction of Hypoaspis aculeifer

Endpoint	**Treatment group (mg R169649/kg soil d.w.)**								
	Control	**17.2**	**30.9**	**55.6**	**100**	**180**	**324**	**583**	**1050**
	Mortality of adult mites after 14 days								
% mortality[a]	*5.0*	*10.0*	*17.5*	*17.5*	*2.5*	*15.0*	*5.0*	*7.5*	*15.0*
	Number of juveniles after 14 days								
Mean no. progeny per replicate[c]	*115*	*93*	*102*	*103*	*117*	*91*	*109*	*95*	*108*
standard deviation	*16.7*	*15.4*	*12.2*	*14.5*	*5.7*	*21.5*	*20.4*	*6.4*	*32.8*
% reduction compared to control[d]	*n.a.*	*19.2*	*11.2*	*10.3*	*-1.8*	*21.4*	*5.8*	*17.7*	*6.0*

The results represent rounded values calculated from the exact raw data
[a] There were no statistically significant differences compared to the control for mortality (Fisher's Exact/Bonferroni Holm test)
[c] There were no statistically significant differences compared to the control for reproduction (Dunnett Multiple Comparison Test)
[d] A positive value indicates a decrease and a negative an increase in reproduction, relative to the control
d.w.: dry weight

Validity Criteria

The validity criteria for the control group were met:

- *Mean mortality of adult females: ≤ 20 % (observed: 5.0 %)*
- *Mean number of juveniles per replicate: ≥ 50 (calculated: 115)*
- *Coefficient of variation (mean number of juveniles per replicate): ≤ 30 % (calculated: 14.5 %)*

Conclusion

The effects of R169649 on the mortality and reproductive output of the soil mite species Hypoaspis aculeifer were determined during a 14-day test.

The NOEC for mortality and reproduction was determined to be 1050 mg R169649/kg soil dry weight, and the 14-day EC_{50} and LC_{50} could not be determined but were considered to be > 1050 mg R169649/kg soil dry weight, the highest concentration tested.

A 2.4.2.2 KCP 10.4.2.2 Higher tier testing

Data written in italics, highlighted in yellow origins from RR of Callisto 100 SC of 21.09.2020

A 2.5 KCP 10.5 Effects on soil nitrogen transformation

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

A 2.6.2 KCP 10.6.2 Testing on non-target plants

A 2.6.3 KCP 10.6.3 Extended laboratory studies on non-target plants

A 2.6.4 KCP 10.6.4 Semi-field and field tests on non-target plants

A 2.7 KCP 10.7 Effects on other terrestrial organisms (flora and fauna)

A 2.8 KCP 10.8 Monitoring data