FINAL REGISTRATION REPORT

Part B

Section 9

Ecotoxicology

Detailed summary of the risk assessment

Product code: M-100SC-OR2-C

Product name(s): Juzan Extra 100 SC

Chemical active substance:

mesotrione, 100 g/L

Central Zone

Zonal Rapporteur Member State: Poland

NATIONAL ADDENDUM

Poland

(authorization)

Applicant: CIECH Sarzyna S.A.

Submission date: 04/2023

MS Finalisation date: 05/2023

Version history

When	What
May 2023	National Addendum was prepared after commenting period

Table of Contents

9 Ecotoxicology (KCP 10)

This National Addendum has been prepared to support a national decision on a possible authorisation of the product Juzan Extra 100 SC in Poland for the uses listed below.

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	PL	Maize (ZEAMX)	F	Monotyledonous weeds (TTDMS); Dicotyledonous weeds (TTDSS)	spraying	BBCH 12 - 18	a) 1 b) 1	n.a.	~~a) 1,5 L/ha~~ a) 1,0 L/ha ~~b) 1,5 L/ha~~ b) 1,0 L/ha	~~a) 150 g as/ha~~ a) 100 g as/ha ~~b) 150 g as/ha~~ b) 100 g as/ha	200 / 400	n.a.	Dose range: 0,75 ~~-1,5~~ 1.0 L/ha		**A**					
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)																				
2	PL	sugar maize (ZEAMS); Popcorn (ZEAME);	F	Monotyledonous weeds (TTDMS); Dicotyledonous weeds (TTDSS)	spraying	BBCH 12 - 18	a) 1 b) 1	n.a.	~~a) 1,5 L/ha~~ a) 1,0 L/ha ~~b) 1,5 L/ha~~ b) 1,0 L/ha	~~a) 150 g as/ha~~ a) 100 g as/ha ~~b) 150 g as/ha~~ b) 100 g as/ha	200 / 400	n.a.	Dose range: 0,75 ~~-1,5~~ 1.0 L/ha		A					
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/m^3 in case of fumigation of empty rooms. See also EPPO-Guideline PP 1/239 Dose expression for plant protection products
(11) The dimension (g, kg) must be clearly specified. (Maximum) dose of a.s. per treatment (usually g, kg or L product / ha).
(12) If water volume range depends on application equipments (e.g. ULVA or LVA) it should be mentioned under "application: method/kind".
(13) PHI - minimum pre-harvest interval
(14) Remarks may include: Extent of use/economic importance/restrictions

9.1.1 Overall conclusions

9.1.1.1 Effects on birds (KCP 10.1.1),

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

The risk assessment performed for birds in the Core dossier indicates acceptable acute and long-term risk to birds exposed to mesotrione following application of Juzan Extra 100 SC acc. to intended GAP. Regarding effects on other terrestrial vertebrate wildlife (reptiles and amphibians), no data/information available.

The risk assessment on mammals organisms has been re-calculated. It has been concluded that Juzan Extra 100 SC poses low risk to mammals when the following refinements are implemented as indicated in the present Addendum to the Core Assesment.

9.1.1.3 Please refer to the Core Assessment.

9.1.1.4 Effects on aquatic organisms (KCP 10.2)

Please refer to the Core Assessment.

9.1.1.5 Effects on bees (KCP 10.3.1)

Please refer to the Core Assessment.

9.1.1.6 Effects on arthropods other than bees (KCP 10.3.2)

Please refer to the Core Assessment.

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

Please refer to the Core Assessment.

9.1.1.8 Effects on non-target terrestrial plants (KCP 10.6).

Please refer to the Core Assessment.

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

Please refer to the Core Assessment.

9.1.2 Grouping of intended uses for risk assessment

Please refer to the Core Assessment.

9.1.3 Consideration of metabolites

Please refer to the Core Assessment.

9.2 Effects on birds (KCP 10.1.1)

Please refer to the Core Assessment.

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

9.3.1 Toxicity data

Mammalian toxicity studies have been carried out with mesotrione. Full details of these studies are provided in the respective EU RAR and related documents.

Effects on mammals of Juzan Extra 100SC were not 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 9.3-1: Endpoints and effect values relevant for the risk assessment for mammals

Species	Substance	Exposure System	Results	Reference
Rat	mesotrione	Acute	LD_{50}>5000 mg a.s./kg bw	EFSA Journal 2016;14(3):4419
Rat	mesotrione	Longterm	NOEL=0.3 mg a.s./kg bw/d NOEL=1.2 mg a.s./kg bw/d*	EFSA Journal 2016;14(3):4419

*For details, please see the consideration below.

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)

In the screening step for the risk assessment for mammals the TER_A values for mesotrione are exceed the trigger value for acceptability for effects. Further refinement for acute risk assessment is not required. Nevertheless, TER_{LT} values are below the trigger value for acceptability and further refinement is required.

9.3.2.2 Higher-tier risk assessment

In the Core Dossier, due to unacceptable reproductive risk to mammals in post-emergence use as the risk refinement new residue decline study to determine DT_{50} of mesotrione in maize (Peda T., 2021, SGS study code: 21SGS76) were presented. However, refinement of DT_{50} was not accepted by RMS, due to the uncertainties related to the kinetic analysis of the data of the residue trials.
In order to respond to the evaluators' requirements, the refined kinetic evaluation is presented below.

1. Kinetic analysis to derive the rate of residue decline (DT_{50}) for mesotrione applied on maize plants

1.1 Executive summary

A kinetic analysis was performed for the derivation of the rate of residue decline (DT_{50}) for mesotrione applied on maize plants. Crop residue data are available from field studies performed at four locations in Europe: Poland (two sites), Hungary and France (Peda T., 2021; Final report for study 21SGS76).

The study was conducted as crop field trials for the determination of the magnitude of the pesticide residue in or on raw agricultural commodities according to OECD 509. Mesotrione was applied on maize at BBCH 12 (leaf development) at a nominal rate of 150 g a.i./ha. During the 0 to 5 day period after application, samples of plant material (excluding roots) were removed for analysis according to a 10-point time-course series.

Approximately 95% of applied mesotrione was dissipated during the study period and the measured quantity of mesotrione in all samples in the study were greater than the limit of quantification (0.01 mg/kg). The kinetic analysis for mesotrione was performed according to the general principles described in "FOCUS Generic guidelines for estimating persistence and degradation kinetics from environmental fate studies" (FOCUS, 2014).

Kinetic modelling was performed using CAKE version 3.5 (Hybrid Engineering and Syngenta, 2021), using the IRLS (iteratively reweighted least squares) optimisation algorithm. Three kinetic models: single first order (SFO), first order multi-compartment (FOMC) and double first order in parallel (DFOP) were fitted to the datasets. The best model was selected based on visual and statistical goodness of fit.

The single first order (SFO) model is the preferred model for deriving endpoints for modelling calculations and was found appropriate for describing degradation of mesotrione on maize at the field sites in Poland, Hungary and France.

The derived endpoints are listed in Table 9-2. The derived model parameters were considered acceptable in all cases, based on visual and statistical goodness of fit and passing of the t-test ($p<0.05$).

Table 9-2: Summary residue decline endpoints, mesotrione

Location	Model	Model parameter, *k*	χ^2-error	DT_{50} (d)	t-test p-value
Poland 01	SFO	0.4813	9.34	1.44	$p < 0.05$
Hungary	SFO	0.5078	7.74	1.37	$p < 0.05$
Poland 05	SFO	0.4921	4.04	1.41	$p < 0.05$
France	SFO	0.5625	7.89	1.23	$p < 0.05$

1.2 Introduction

Crop field trials for the determination of the magnitude of the pesticide residue in or on raw agricultural commodities were conducted with the herbicide mesotrione (Table 9-3), which is used to control broad-leaf weeds.

Mesotrione was applied by spray application onto maize plants at BBCH 12 (leaf development) at field sites in Poland, Hungary and France. Samples of whole plants excluding roots were collected over time and analysed for mesotrione. The field study was performed according to OECD 509.

The following consideration relates to the kinetic analysis of the reported residue data for the determination of the rate of decline of mesotrione residue on maize shoot material for the purpose of refining the ecotoxicology risk assessment for mammals.

Table 9-3: **Mesotrione**

Substance	Chemical name	Molecular mass (g/mol)
Mesotrione	2-(4-mesyl-2-nitrobenzoyl)cyclohexane-1,3-dione	339.32

1.3 Crop field trial study data

1.3.1 Crop field trial study with mesotrione

Mesotrione was applied by spray application onto maize plants at BBCH 12 (leaf development) at field sites in Poland, Hungary and France (Peda, 2021). Soil properties and other site characteristics at the four locations are shown in Table 9-4. A range of soil textures are represented, and the test sites are typical of areas used for maize production under central and southern EU conditions.

Two other trials were not able to provide reliable data: the trial in Germany (21SGS76-02) was cancelled because in the period between sample collection and analysis the freezer in which the samples were stored malfunctioned and sample integrity was compromised. Trial 21SGS76-04 (France) was also cancelled because owing to extensive bird damage it was not possible to collect at least 100 g of plant material for analysis. The second trial in Poland (21SGS76-05), ~100 km north and under different edaphic conditions from 21SGS76-01, was established in place of the German trial; and a replacement trial was established at the site in France (21SGS76-06).

The test substance was applied as a single application in May and June 2021 (Table 9-5). Spray equipment was used to apply the chemical to young maize plants at a nominal rate of 150 g a.s./ha.

Table 9-4: Soil properties and site characteristics at the field sites

Trial ID	Location	Soil texture (USDA)	Soil organic matter (%)	pH-H_2O	Slope (%)	Air temp. (°C) Min. – max.	Rainfall (mm)
21SGS76-01	Wenecja, Poland	Sand	<0.5	7.0*	0	13.5 – 27.9	20.8 (June)
21SGS76-03	Nyírtel, Hungary	Clay loam	2.44	6.0	1	8.4 – 20.6	84.1 (May)
21SGS76-05	Zamarte, Poland	Sandy clay loam	1.5	8.7*	0	10.6 – 26.3	32.4 (June)
21SGS76-06	Auménancourt, France	Loam	2.5	8.5	0	13.0 – 24.0	114.2 (June)

*converted from reported pH-$CaCl_2$ using the German input decision tool 3.3

Table 9-5: Application dates at the field sites

Trial ID	Location	Plot area (m^2)	Nominal crop density (Plants/ha)	Sowing date	Application date
21SGS76-01	Wenecja, Poland	1008	80,000	19 May 2021	07 June 2021
21SGS76-03	Nyírtel, Hungary	1125	77,000	09 May 2021	25 May 2021
21SGS76-05	Zamarte, Poland	1008	95,000	04 June 2021	15 June 2021
21SGS76-06	Auménancourt, France	552	75,000	08 June 2021	24 June 2021

1.3.2 Residue data

Single composite samples of 12 plants (without roots), of about 100 g mass, were collected on designated sampling times and dates (Table 1-5) and analysed for mesotrione. There were no residue detections < LOD (0.002 mg/kg) or < LOQ (0.01 mg/kg) in any sample, at any time.

Table 9-6: Sampling times and dates

Sampling time point No.	Hours after application	Days after application	Time (DAA)
S1	0 - 1	-	0.02
S2	2	-	0.08
S3	4	-	0.17
S4	6	-	0.25
S5	20	-	0.83
S6	24	-	1
S7	-	2	2
S8	-	3	3
S9	-	4	4
S10	-	5	5

1.4 Kinetic analysis

The kinetic analysis for mesotrione was performed according to the general principles described in "FOCUS Generic guidelines for estimating persistence and degradation kinetics from environmental fate studies" (FOCUS, 2014).

1.4.1 Software and kinetic models

Kinetic modelling for the mesotrione → sink transformation was performed using CAKE version 3.5 (Hybrid Engineering and Syngenta, 2021), which is a tool for Computer Assisted Kinetic Evaluation. The software fulfils the requirements by FOCUS (2014), as it provides the kinetic models recommended by the FOCUS group and provides the standard statistical information needed to assess the quality of the curve fitting (χ^2-error and t-test).

All optimisation settings were kept at the defaults set in the software. The iteratively reweighted least squares (IRLS) optimisation algorithm was used in agreement with FOCUS (2014, p.74). It has been argued that this approach yields more realistic estimates of confidence intervals for model parameters than nonlinear least squares (NLLS, OLS) as it is not limited by the assumption of equal error variances, nor does it rely upon assigning arbitrary weighting to the data (Gao *et al*. 2011).

Four primary models, simple first-order (SFO), first order-multi-compartment (FOMC), double-first order in parallel (DFOP) and hockey-stick (HS), are accepted to derived degradation endpoint values for environmental risk assessments within the EU (FOCUS, 2014). The differential equations associated with the first three models are listed below (the hockey stick model is not considered in this report).

[1] SFO: $$\frac{dM}{dt} = -k\,M$$

[2] FOMC: $$\frac{dM}{dt} = -\frac{\propto}{\beta} M\left(\frac{t}{\beta} + 1\right)^{-1}$$

[3] DFOP: $$\frac{dM}{dt} = -\frac{k_1 g e^{-k_1 t} + k_2 (1-g) e^{-k_2 t}}{g e^{-k_1 t} + (1-g) e^{-k_2 t}} M$$

Where:
M = total amount of chemical present at time t
t = time since the beginning of the experiment (days)
k = rate constant (d^{-1})
k_1 = rate constant in compartment 1 of DFOP model (d^{-1})
k_2 = rate constant in compartment 2 of DFOP model (d^{-1})
α = shape parameter
β = location parameter
g = fraction of parent compound applied into compartment 1

In the integrated form of the above equations, an additional variable is needed: M_0 is the amount of chemical present at time 0.

Simple first order kinetics is described by an exponential equation with only two parameters (M_0 and k). The rate of change in pesticide concentration is at any time proportional to the actual concentration remaining in the system. The SFO equation is the default degradation model for all EU kinetic assessments and is the starting point for the derivation of all degradation end-points. However, there are a number of reasons why the degradation rate of a chemical might change over time resulting in 'biphasic' degradation, as described by the FOMC and DFOP models.

In the FOMC model it is assumed that the rate of residue decline changes with time and can be described by a gamma distribution and expressed by a simple analytical equation with only 3 parameters (M_0, α and β). Dissipation is faster for larger values of α and for smaller values for β. The DFOP model assumes that the chemical residue is split into 2 unconnected compartments, each with its own rate constant.

The parameter g is required to describe the proportion of residue in the 'fast' and 'slow' compartments, and each compartment requires a rate constant (k_1 and k_2) along with the initial concentration (M_0).

1.4.2 Modelling strategy

The aim of the kinetic analysis was to determine the rate of decline of mesotrione residue on the raw agricultural commodity of interest (maize shoot material) for the purpose of refining the ecotoxicology risk assessment for mammals.

Single first-order (SFO) kinetics is the preferred option for deriving degradation endpoints, as the first-order DT_{50} can be used directly as input in the environmental fate modelling tools (FOCUS, 2014). Alternative models are considered if no satisfactory fit can be obtained by the SFO model. When the data shows biphasic pattern then the FOMC, or DFOP models are tested. According to the FOCUS flow diagram (Figure 7-2 in FOCUS, 2014) the FOMC model should be used when 10% of the initially measured concentration is reached within the experimental period.

1.4.3 Statistical assessment

For each model fit, the goodness of fit is assessed, both visually and statistically. The overall pattern was assessed visually by plotting measured data points against the fitted line of predicted concentrations and by plotting the residuals (observed minus calculated values).

The statistical goodness of fit is expressed as the χ^2 error which is calculated in CAKE according to FOCUS (2014):

$$err = 100 * \sqrt{\frac{1}{\chi^2_{tabulated}} * \sum \frac{(C-O)^2}{\bar{O}^2}}$$

Where:

C = calculated value
O = observed value
Ō = mean of all observed values
err = measurement error percentage (χ^2 error)
χ^2 tabulated = tabulated χ^2 value (depending on degrees of freedom)

A significance test, known as the ‘t-test’ (FOCUS, 2014), is applied to test the probability that the optimised degradation rate parameter is different from zero. CAKE presents the probability (p value), whereby a value smaller than 0.05 indicates that the t-test is passed, *i.e.,* the degradation rate is significantly different from zero.

$$t = \frac{\hat{a}_i}{\sigma_i}$$

Where:
$\hat{a}_i$= estimate of degradation rate
σ_i= standard error of degradation rate

Note that the t-test cannot be applied to the FOMC model, as the parameters alpha (α) and beta (β) are shape parameters rather than representing kinetic rates. An alpha or beta value close to zero does not mean that degradation is slow. On the contrary, smaller values of beta indicate more rapid degradation, and alpha only indicates the shape of the curve and has nothing to do with the rate of degradation (FOCUS, 2014; p.97).

The 90% probability interval is reported because in kinetic analysis the t-test is single-sided.

1.5 Residue data

Plant residues at each sampling time were reported as concentrations expressed as mg/kg plant material and are summarized in Table 9-7.

Table 9-7: Total residues on maize plants (mg/kg)

Sampling time point	DAA [a)]	Mesotrione (mg/kg)			
		Poland 01	**Hungary**	**Poland 05**	**France**
S1	0.02	8.53	14.16	15.06	16.55
S2	0.08	7.73	14.08	14.50	15.22
S3	0.17	8.34	12.29	14.45	13.34
S4	0.25	6.76	12.16	13.95	13.35
S5	0.83	6.07	10.06	10.11	11.45
S6	1	6.24	10.03	10.51	10.13
S7	2	2.63	3.91	5.27	5.14
S8	3	2.5	3.38	3.73	2.76
S9	4	0.64	2.15	2.02	0.41
S10	5	0.34	0.10	0.79	0.19
Residue remaining [b)] (%)		4.00	0.71	5.25	1.15

a) DAA = days after application
b) Calculated as % remaining on day 5 relative to the concentrations measured at the first sampling timepoint (0-1 h)

1.6 Modelling results mesotrione

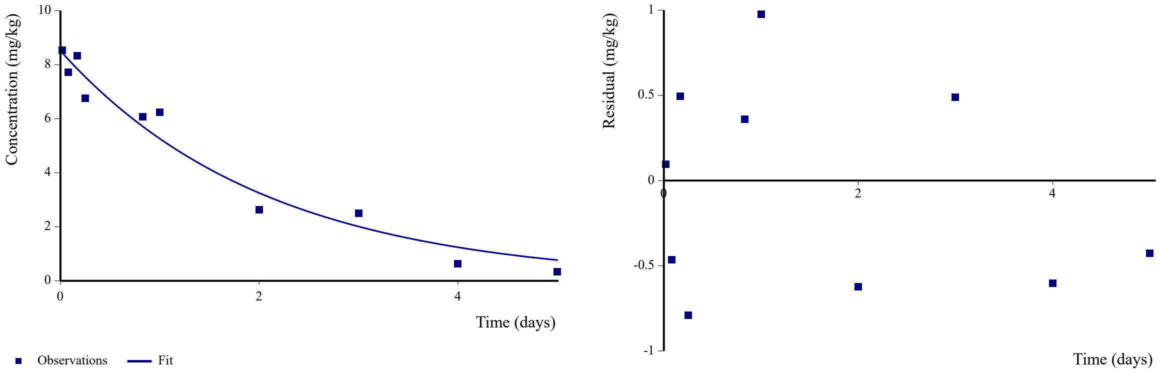
Despite mesotrione residue concentrations reaching 10 % of the initially measured concentration in all four trials (Table 9-7), in order to achieve the best model description for the degradation of mesotrione all three kinetic models were fitted and evaluated. The results are presented in the graphs and tables below.

1.6.1 Poland 01 (21SGS76-01)

Degradation of mesotrione at the first site in Poland was described well by all models, which gave good statistical goodness of fit (χ^2-error <15.0) and acceptable visual fit with no systematic error. The calculated DT_{50} values for all models was 1.44 days. Overall, the statistical goodness of fit (χ^2-error = 9.34) for the SFO model was marginally better than for the other models (FOMC χ^2-error = 9.81; DFOP χ^2-error = 10.4). The SFO model was selected for deriving the DT_{50}.

Poland 01 (21SGS76-01)

SFO model: **χ^2-error = 9.34**

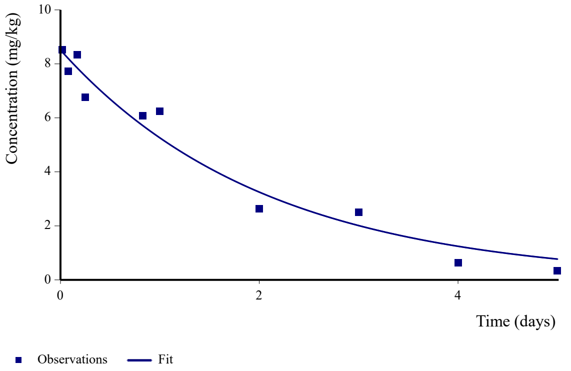


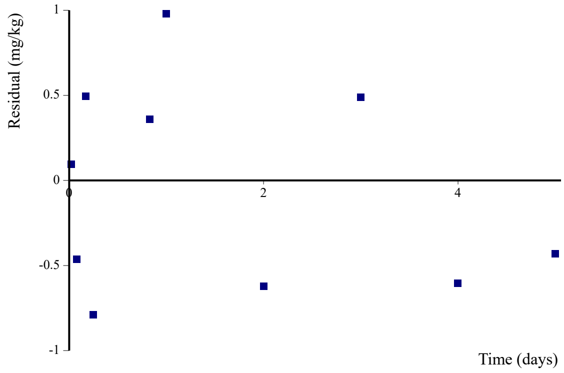
Poland 01 (21SGS76-01) - SFO model

	Model	χ^2-error	DT_{50} (d)	DT_{90} (d)
21SGS76-01				
Mesotrione	SFO	9.34	1.44	4.78

Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	8.515	0.3566	-	7.852	9.178
k_Parent	0.4813	0.058	1.68E-05	0.3734	0.5891

FOMC model: χ^2 **-error = 9.81**





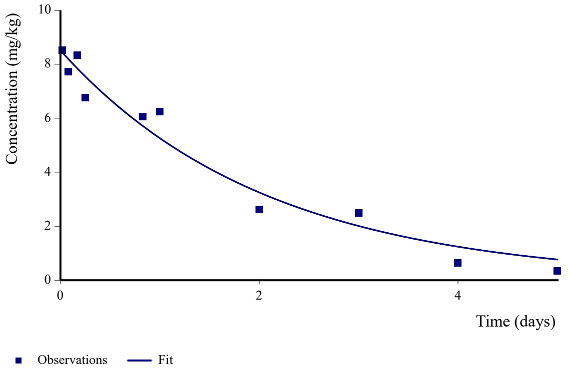
Poland 01 (21SGS76-01) - FOMC model

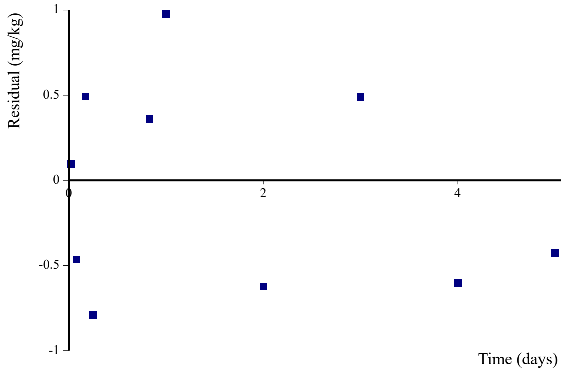
21SGS76-01
Mesotrione

Model	χ^2 -error	DT_{50} (d)	DT_{90} (d)
FOMC	9.81	1.44	4.79

Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	8.517	0.3764	-	7.803	9.23
alpha	415.5	695.8	-	-	-
beta	861.9	1440	-	-	-

DFOP model: χ^2 **-error = 10.4**





Poland 01 (21SGS76-01) - DFOP model

21SGS76-01
Mesotrione

Model	χ^2 -error	DT_{50} (d)	DT_{90} (d)
DFOP	10.4	1.44	4.79

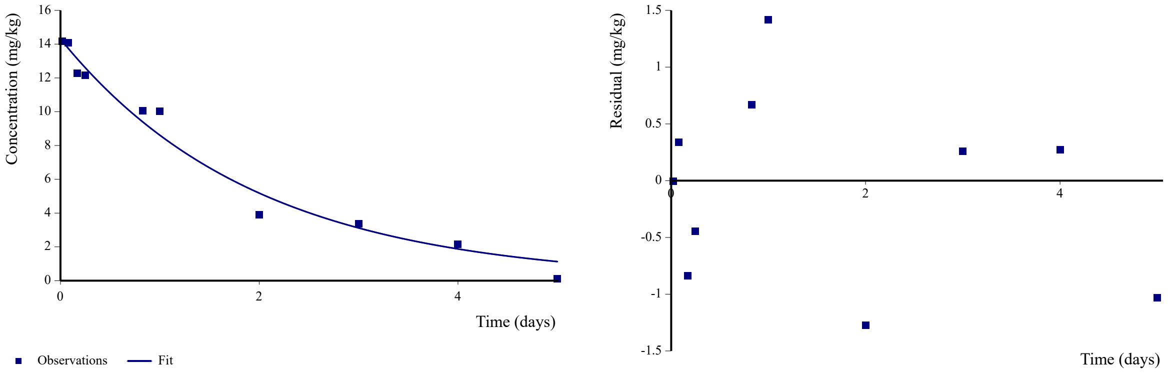
Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	8.515	0.4061	-	7.726	9.304
k1_Parent	0.4813	0.06369	0.00014	0.3575	0.605
k2_Parent	0.01252	nd	nd	nd	nd
g	1	nd	-	nd	nd

1.6.2 Hungary (21SGS76-03)

Degradation of mesotrione at the site in Hungary was described well by all models, which gave good statistical goodness of fit (χ^2-error <15.0) and acceptable visual fit with no systematic error. The calculated DT_{50} values ranged between 1.36 and 1.37 days. Overall, the statistical goodness of fit (χ^2-error = 7.74) for the SFO model was marginally better than for the other models (FOMC χ^2-error = 8.13; DFOP χ^2-error = 8.59). The SFO model was selected for deriving the DT_{50}.

Hungary (21SGS76-03)

SFO model: χ^2**-error = 7.74**

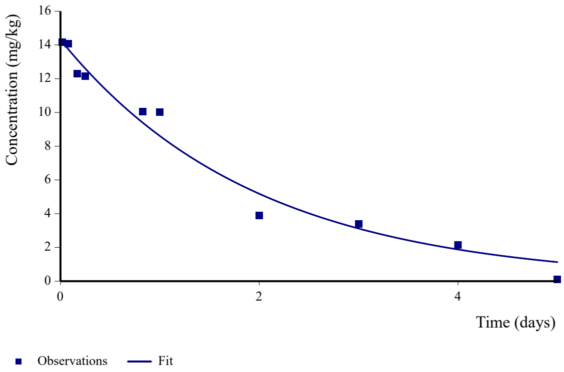


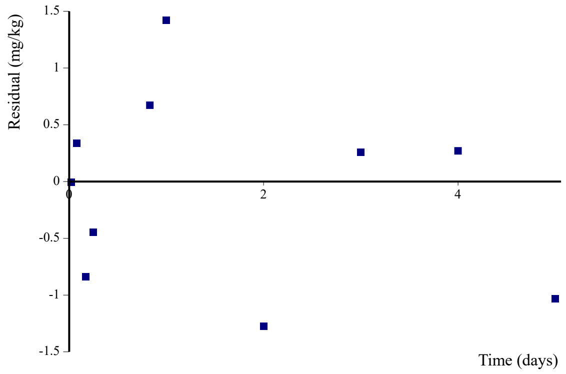
Hungary (21SGS76-03) - SFO model

21SGS76-03	**Model**	**χ^2-error**	**DT_{50} (d)**	**DT_{90} (d)**
Mesotrione	SFO	7.74	1.37	4.53

Parameter	**value**	**st.dev**	**t-test p-value**	**90% probability interval**	
M_0	14.31	0.4942	-	13.39	15.23
k_Parent	0.5078	0.05037	3.99E-06	0.4141	0.6015

FOMC model: χ^2-error = 8.13





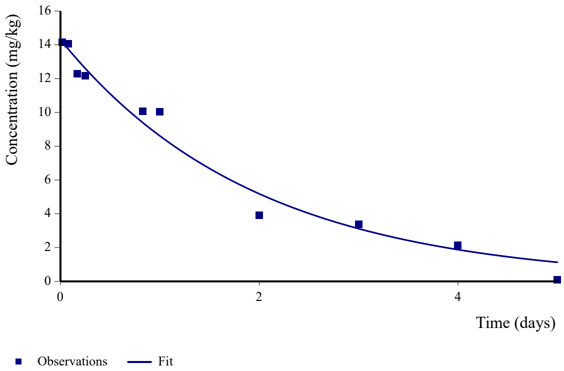
Hungary (21SGS76-03) - FOMC model

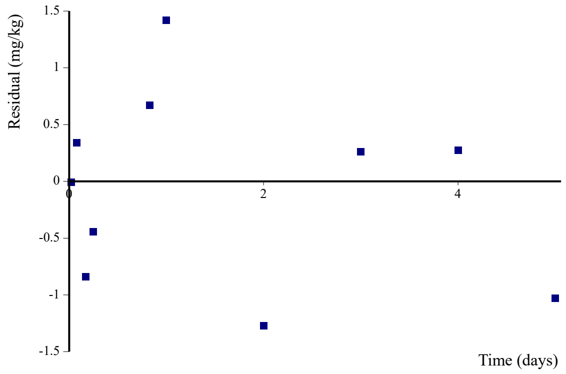
21SGS76-03
Mesotrione

Model	χ^2-error	DT_{50} (d)	DT_{90} (d)
FOMC	8.13	1.36	4.54

Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	14.31	0.5233	-	13.32	15.3
alpha	651.7	1.32E+03	-	-	-
beta	1.28E+03	2.59E+03	-	-	-

DFOP model: χ^2-error = 8.59





Hungary (21SGS76-03) - DFOP model

21SGS76-03
Mesotrione

Model	χ^2-error	DT_{50} (d)	DT_{90} (d)
DFOP	8.59	1.37	4.53

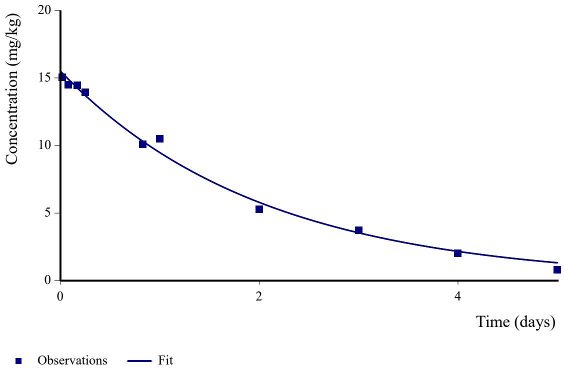
Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	14.31	0.5647	-	13.21	15.41
k1_Parent	0.5078	0.05603	5.06E-05	0.3989	0.6167
k2_Parent	0.01453	nd	nd	nd	nd
g	1	nd	-	nd	nd

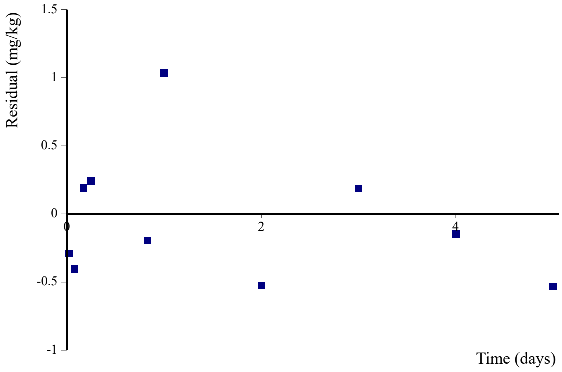
1.6.3 Poland 05 (21SGS76-05)

Degradation of mesotrione at the second site in Poland was described very well by all models, which gave good statistical goodness of fit (χ^2-error <15.0) and acceptable visual fit with no systematic error. The calculated DT_{50} values for all models was 1.41 days. Overall, the statistical goodness of fit (χ^2-error = 4.04) for the SFO model was marginally better than for the other models (FOMC χ^2-error = 4.24; DFOP χ^2-error = 4.48). The SFO model was selected for deriving the DT_{50}.

Poland 05 (21SGS76-05)

SFO model: χ^2-error = 4.04



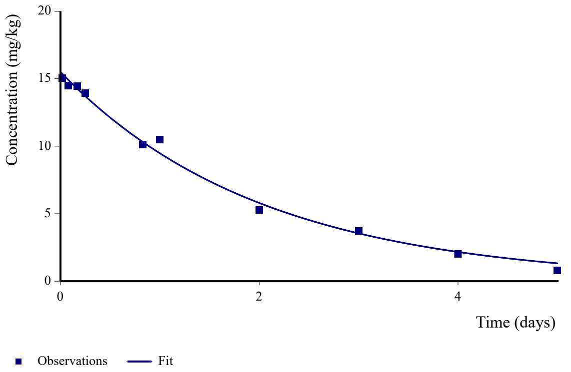


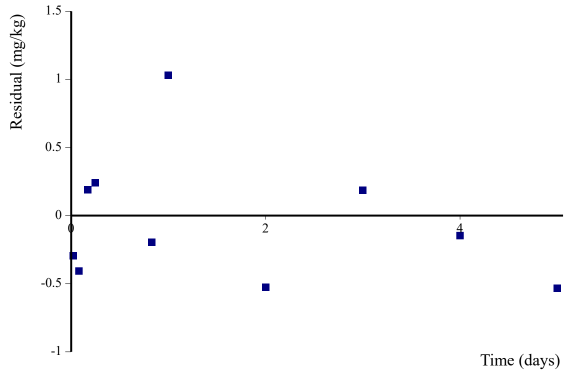
Poland 05 (21SGS76-05) - SFO model

	Model	χ^2-error	DT_{50} (d)	DT_{90} (d)
21SGS76-05 Mesotrione	SFO	4.04	1.41	4.68

Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	15.5	0.2811	-	14.98	16.02
k_Parent	0.4921	0.02566	2.83E-08	0.4444	0.5398

FOMC model: χ^2**-error = 4.24**





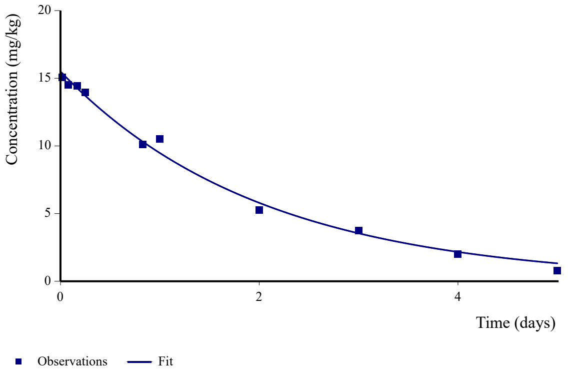
Poland 05 (21SGS76-05) - FOMC model

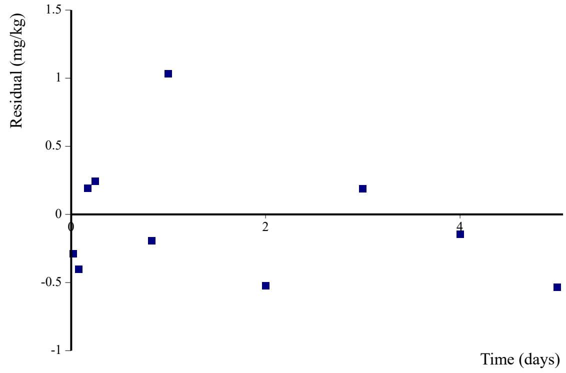
21SGS76-05
Mesotrione

Model	χ^2-error	DT_{50} (d)	DT_{90} (d)
FOMC	4.24	1.41	4.68

Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	15.5	0.337	-	14.87	16.14
alpha	5.71E+07	8.01E+06	-	-	-
beta	1.16E+08	1.31E+07	-	-	-

DFOP model: χ^2**-error = 4.48**





Poland 05 (21SGS76-05) - DFOP model

21SGS76-05
Mesotrione

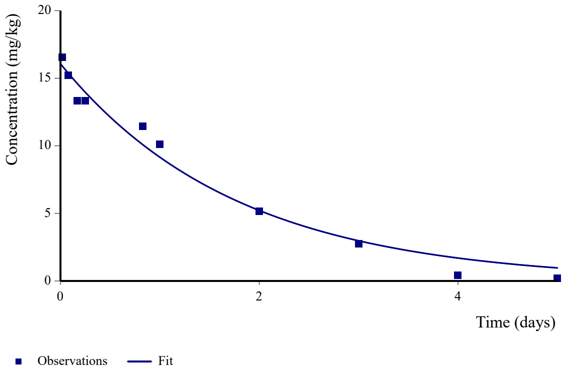
Model	χ^2-error	DT_{50} (d)	DT_{90} (d)
DFOP	4.48	1.41	4.68

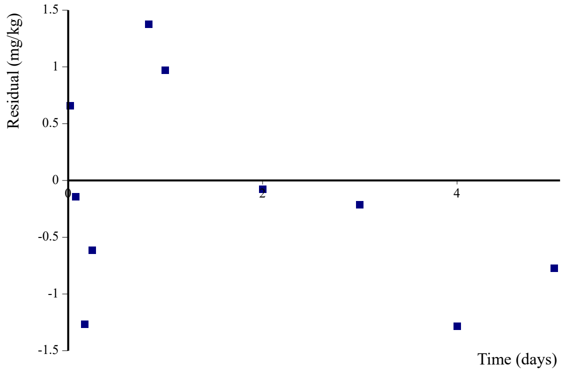
Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	15.5	0.3223	-	14.88	16.13
k1_Parent	0.4921	0.02889	1.31E-06	0.436	0.5482
k2_Parent	0.01078	nd	nd	nd	nd
g	1	nd	-	nd	nd

1.6.4 France (21SGS76-06)

Degradation of mesotrione at the site in France was described reasonably well by all models, which gave good statistical goodness of fit (χ^2-error <15.0). The visual fit was acceptable, but there was systematic over-estimation by all models between day 2 and day 5. The calculated DT_{50} values for all models was 1.23 days. Overall, the statistical goodness of fit (χ^2-error = 7.89) for the SFO model was marginally better than for the other models (FOMC χ^2-error = 8.28; DFOP χ^2-error = 8.76). The SFO model was selected for deriving the DT_{50}.

SFO model: **χ^2 -error = 7.89**



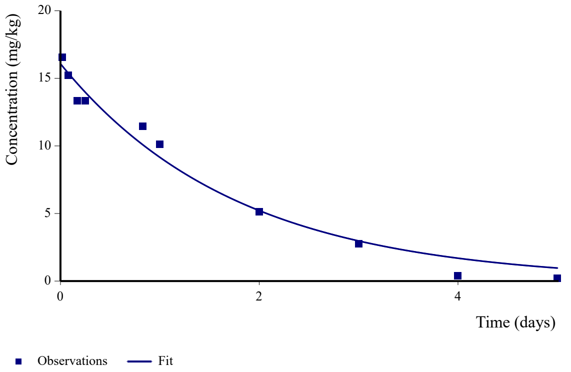


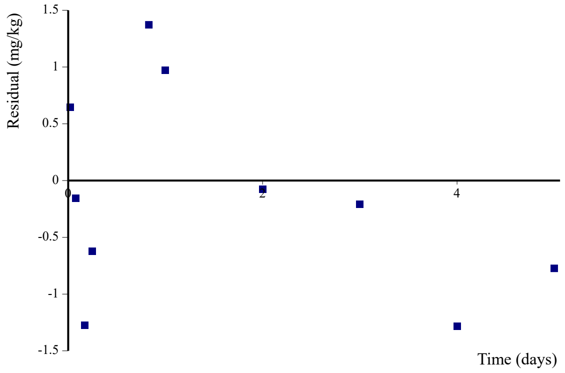
France (21SGS76-06) - SFO model

21SGS76-06	**Model**	**χ^2 -error**	**DT_{50} (d)**	**DT_{90} (d)**
Mesotrione	SFO	7.89	1.23	4.09

Parameter	**value**	**st.dev**	**t-test p-value**	**90% probability interval**	
M_0	16.07	0.5534	-	15.04	17.1
k_Parent	0.5625	0.05554	3.86E-06	0.4592	0.6658

FOMC model: χ^2 **-error = 8.28**





France (21SGS76-06) - FOMC model

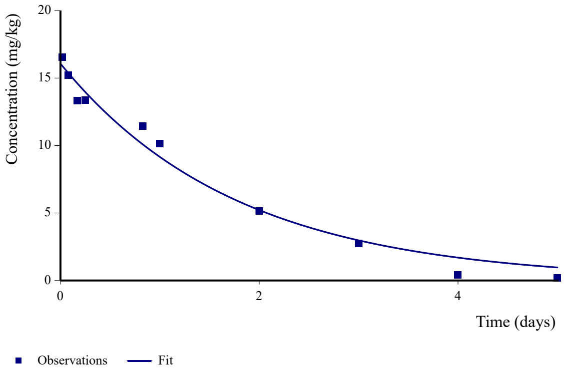
21SGS76-06

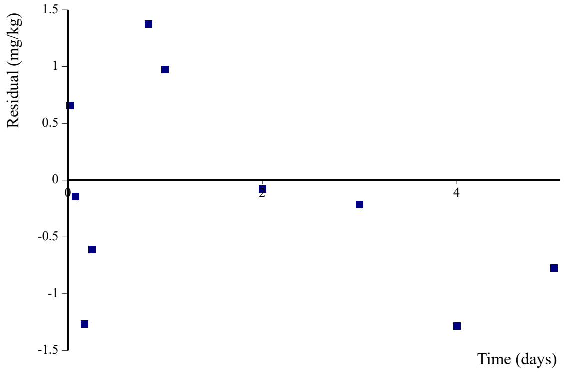
Mesotrione

Model	χ^2 -error	DT_{50} (d)	DT_{90} (d)
FOMC	8.28	1.23	4.09

Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	16.08	0.7348	-	14.69	17.47
alpha	3.26E+07	1.48E+07	-	-	-
beta	5.78E+07	2.39E+07	-	-	-

DFOP model: χ^2 **-error = 8.76**





France (21SGS76-06) - DFOP model

21SGS76-06

Mesotrione

Model	χ^2 -error	DT_{50} (d)	DT_{90} (d)
DFOP	8.76	1.23	4.09

Parameter	value	st.dev	t-test p-value	90% probability interval	
M_0	16.07	0.6275	-	14.85	17.29
k1_Parent	0.5625	0.06002	4.19E-05	0.4459	0.6791
k2_Parent	0.01724	nd	nd	nd	nd
g	1	nd	-	nd	nd

1.7 Conclusions of the kinetic analysis

Table 9-8 shows the residue decline endpoints derived for mesotrione on maize. Mesotrione decline was consistently rapid in all four field trials and was best described by single first-order (SFO) kinetics. Based on visual and statistical assessment, each of the selected model descriptions and derived parameters were considered acceptable.

Table 9-8: Summary residue decline endpoints, mesotrione

Location	Model	Model parameter, *k*	χ^2-error	DT_{50} (d)	t-test p-value
Poland 01	SFO	0.4813	9.34	1.44*	$p < 0.05$
Hungary	SFO	0.5078	7.74	1.37	$p < 0.05$
Poland 05	SFO	0.4921	4.04	1.41	$p < 0.05$
France	SFO	0.5625	7.89	1.23	$p < 0.05$
*the worst case			Geomean	1.36	

RMS comment: In the Core Dossier, due to unacceptable reproductive risk to mammals in post-emergence use as the risk refinement new residue decline study to determine DT_{50} of mesotrione in maize (Peda T., 2021, SGS study code: 21SGS76) were presented. In the Core refinement of DT_{50} was not accepted by RMS, due to the uncertainties related to the kinetic analysis of the data of the residue trials. In order to respond to the evaluators' requirements, the refined kinetic evaluation was performed by Applicant. The kinetic analysis was accepted by RMS. The DT_{50} 1.36 as geometric mean was proposed by Applicant. However, according to the harmonization arrangements for Poland, when the tests include 4 - 9 locations - maximum values can be used DT_{50}. The worst case is DT_{50} = 1.44 d and this value should be used in risk assessment. Estimated new f_{TWA} based on residue decline study will be used as a risk refinement for reproductive risk to mammals in post-emergence use.

The presented by the Applicant refinement risk assessment for the vertebrates was evaluated by the RMS. The DT_{50} value of 1.44 days was considered adequate and taken into account in the risk assessment for mammals.

Another refinement presented in the core dossier was to propose relevant focal species such as wood mouse and brown hare. It was also suggested to use PT=0.139 in risk assessment for wood mouse. These proposals were accepted. However, the long-term risk assessment was still not acceptable.
In addition, the use of a refinement of toxicity endpoint (NOAEL= 1.2 mg/kg bw/d) has been proposed.

Here justifications for using the refined endpoint for a NOAEL based on F1 data are provided, as well as the refined risk assessment for wood mouse and brown hare.

2 Mesotrione selection of endpoint for wild mammals assessment

2.1 EFSA long-term mammal endpoint for mesotrione

The long-term endpoint for mammals for mesotrione was discussed at the Pesticides Peer Review Experts Meeting 136 in December 2015 (EFSA, 2016). The experts agreed on a NOAEL of 0.3 mg/kg bw per day based on the effects on litter size of the F2 generation in the 3-generation study (1997) submitted with the original DAR in 1999. The original study is not accessible, data and information reported here were taken from the 2015 Renewal Assessment Report (RAR). The multigeneration study was conducted between 1995-1996 and it is considered to be compliant with OECD 416 (2001) by RMS. Rats (26/sex/dose level) were fed diet containing 0, 2.5, 10, 100 or 2500 ppm mesotrione. Animals were mated after 10 weeks and allowed to rear litters (F1) to weaning. Selected F1 animals were similarly bred to produce F2 litters after a 10-week pre-mating period. F2 animals were fed experimental diets until Week 14, after which approximately half of the animals continued with the same treatment (F2CT) while the remainder were assigned to a recovery sub-group (F2R) and fed control diet. At Week 18, F2 sub-groups were mated to produce F3 litters (F3CT and F3R). Test diets were fed continuously throughout the study with the exception of the recovery sub-groups (RAR, 2015). The mammal reproductive endpoint is based from the litter size dose-response results reported in Table 9-9. Results indicated that F1 litter sizes were decreased at concentration ≥10 ppm, although values attained statistical significance only at 2500 ppm. F2 litter size was decreased in all treated groups, however no clear dose-response was seen and values attained statistical significance only at 2500 ppm. The magnitude of the reduction in F2 pup number at 2500 ppm was greater than that seen in F1 litters. Reductions in litter size were seen at ≥10 ppm in F3CT and F3R litters. F3R litter size at 2.5 ppm was reduced compared to the concurrent control value but was similar to F3CT controls.

Table 9-9: Mesotrione effects on the litter size from the multigeneration study in rats (RAR (2015))

Parameter	Generation	Dose Level (ppm)				
		0	2.5	10	100	2500
Litter size (no. pups)	F1	11.7	12.4	10.9	10.3	9.2**
	F2	11.8	9.8	9.5	10	7.8**
	F3CT	10.6	10.8	8.4	8.5	5.5**
	F3R	11.7	10.5	9.6	9.2*	8.2*

* significantly different to control (p<0.05), ** (p<0.01)

The NOAEL for reproductive performance was determined to be 2.5 ppm (equivalent to 0.3 mg/kg bw/day) based on reduced litter sizes in the F2 generation at ≥10 ppm. Values did not attain statistical significance; however, effects were consistent in all generations and are therefore considered to be of significance.
The concentrations in diet (ppm) were converted into mg/kg bw/d dose levels using the standard factor of 0.12 for two-generation study in rats from the birds and mammals guidance document (EFSA 2009).

2.2 Selection of Endpoint for Wild Mammals Assessment

The long-term endpoint for mammals for mesotrione is based on the effects on litter size of the F2 generation from the multigeneration rat study (EFSA, 2016). Here is presented a discussion to propose the use of a NOAEL specific for the F1 generation, as more relevant the ecotoxicology risk assessment in contrast with the mammalian toxicology assessment.

In mammalian toxicology, the aim of protection is the individual, whereas in ecotoxicology the goal is to protect animal populations. This means that, although the same tests are considered in both mammalian toxicology and ecotoxicology, each effect and endpoint must be considered from a different perspective.

Developmental data for the F1 generation from the RAR for mesotrione (2015) are presented in the Table 9-10 below. F1 results indicate a clear effect at dose levels of 2500 ppm, with all results being significantly different to the control. A reduction in litter size by 6.8% is seen in animals treated at 10 ppm and by 11.1% for those treated at 100 ppm when compared to the control group. Litter weight is similarly reduced at these doses, but this effect is a consequence of the reduced litter size. A significant reduction in pup survival is seen at 10 ppm but this is not dose-related and is therefore not considered to be of toxicological concern. Based on F1 developmental data, a NOAEL of 10 ppm (1.2 mg/kg bw/d) is therefore proposed.

Table 9-10: Mesotrione effects on F1 generation from the multigeneration study in rats (RAR (2015))

Parameter	Generation	Dose Level (ppm)				
		0	**2.5**	**10**	**100**	**2500**
Gestation length (d)	F1	22.3	22.3	22.4	22.8**	22.9**
Litter size (no. pups)	F1	11.7	12.4	10.9	10.3	9.2**
Litter weight (g) Day 0	F1	70.4	72.2	65.9	63.4	57.1**
Pup survival (%)	F1	92.4	89.9	85.2**	89.7	77.6**

* significantly different to control (p<0.05), ** (p<0.01)

As it can be observed in Table 9-10, the reduction in pup survival observed at 10ppm cannot be incidental because the trend in pup survival reduction is carried on in the higher doses. Pup survival in tested animals shows a 2.7, 7.8, 2.9 and 16% of reduction from untested animals at 2.5, 10, 100 and 2500 ppm, respectively. A similar trend is observed in all the other tested endpoints:

- Gestation length: increase of gestation duration of 0.4, 2.2 and 2.7 % compared to control for 10, 100 and 2500 ppm respectively.
- Litter size: reduction in litter size of 6.8, 12.0 and 21.4 % compared to the control for 10, 100 and 2500 ppm respectively.
- Litter weight: reduction in litter weight of 6.4, 9.9 and 18.9 % compared to the control for 10, 100 and 2500 ppm respectively.

This demonstrates that the effects observed at the 10 ppm treatment are clearly not incidental as all tested endpoints at 100ppm show a damaging effect compared to control (although not significant).

The use of the NOAEL of 10 ppm (1.2 mg/kg bw/d) was proposed by the applicant in the mesotrione RAR (2015), and the RMS commented that “the ecotoxicity assessment will need to consider whether exposure of to F2 generation needs to be considered and if not whether the reduction in litter size of 6.8% which is seen in the F1 generation is acceptable for wild populations.”

The effects in the second generation of multigeneration reproductive tests could potentially be the result of exposure during a critical developmental phase and, this being the case, it should be considered relevant in deriving a risk assessment endpoint. The NOAEL value currently considered in the risk assessment (2.5 ppm) results in a reduction in litter size of the F2 generation of 16.9%; however, at the same concentration pup survival is not affected and actually shows a survival increase of 5.7%. Also, the gestation length is similar across generations (

An additional reason for why data from F2 generation are not relevant in the risk assessment concerns the use pattern of mesotrione. Mesotrione is a selective herbicide applied to maize BBCH 12-18 once per season, which means the F2 generation are unlikely to be exposed in the wild situation and therefore effects seen in this generation are not applicable to the ecotoxicology risk assessment.

The litter size effects on which the EFSA NOAEL is based on are from a repeated exposure for several weeks to rats from F0 through mature F1 animals, corresponding to more than 20 weeks of exposure to the test substance. According to OECD 416 test protocol, the test substance should be administered via diet or drinking water preferably on a 7-days-a-week basis, dosing shall be continued for at least 10 weeks before the mating period and also during the 2-week mating period. In the laboratory experiment, F2 litter size is thus an effect of 12 weeks of exposure of the parent animals and 12 weeks of exposure of F1 adult animals. The total exposure in the multigenerational laboratory experiment is thus much higher than the possible real exposure in a treated field, as mesotrione should be applied just once per season. Consequently, developmental data from the F1 generation are considered to be more appropriate to calculate the long-term mammals endpoint for environmental risk assessment and a NOAEL of 10 ppm (1.2 mg/kg bw/d) is proposed.

Table 9-11), and adults from the F2 generation that continued with the same dosing treatment (F2CT) did not show any effect at the two higher doses, similarly to adults from F2 generation that were assigned to a recovery sub-group (F2R) and fed the control diet. These results indicate that mesotrione effects were not the result of exposure during a critical developmental phase and data from F2 generation might not be relevant in the risk assessment.

An additional reason for why data from F2 generation are not relevant in the risk assessment concerns the use pattern of mesotrione. Mesotrione is a selective herbicide applied to maize BBCH 12-18 once per season, which means the F2 generation are unlikely to be exposed in the wild situation and therefore effects seen in this generation are not applicable to the ecotoxicology risk assessment.
The litter size effects on which the EFSA NOAEL is based on are from a repeated exposure for several weeks to rats from F0 through mature F1 animals, corresponding to more than 20 weeks of exposure to the test substance. According to OECD 416 test protocol, the test substance should be administered via diet or drinking water preferably on a 7-days-a-week basis, dosing shall be continued for at least 10 weeks before the mating period and also during the 2-week mating period. In the laboratory experiment, F2 litter size is thus an effect of 12 weeks of exposure of the parent animals and 12 weeks of exposure of F1 adult animals. The total exposure in the multigenerational laboratory experiment is thus much higher than the possible real exposure in a treated field, as mesotrione should be applied just once per season. Consequently, developmental data from the F1 generation are considered to be more appropriate to calculate the long-term mammals endpoint for environmental risk assessment and a NOAEL of 10 ppm (1.2 mg/kg bw/d) is proposed.

Table 9-11: Mesotrione effects on gestation length from the multigeneration study in rats in the RAR (2015)

Parameter	Generation	Dose Level (ppm)				
		0	2.5	10	100	2500
Gestation length (d)	F0	22.7	22.4*	22.6	22.7	22.9
	F1	22.3	22.3	22.4	22.8**	22.9**
	F2CT	23	22.9	22.5*	22.9	23.1
	F2R	22.4	22.4	22.7	22.8	22.7

2.3 Conclusions of the toxicity endpoint

It is here proposed to use the NOAEL of 10 ppm (corresponding to 1.2 mg/kg bw/d) from the F1 generation data, being in more relevant in the ecotoxicology risk assessment because of the use pattern of mesotrione (it is applied once per season, thus results from the single generation are more appropriate than results from a second generation after more than 20 weeks of exposure) and results from different generations indicate that mesotrione effects were not the result of exposure during a critical developmental phase.

RMS comment: In the light of the new justification provided by the Applicant the use of a refinement of toxicity endpoint (NOAEL=1.2 mg/kg bw/d) in risk assessment has been accepted.

3 Higher-Tier risk assessment for mammals exposed to mesotrione following application on maize

According to EFSA (2009), the omnivorous wood mouse (*Apodemus sylvaticus*) and the herbivorous European brown hare (*Lepus europaeus*) are considered as appropriate focal species for maize at the early stages after germination (BBCH 10-16).

Refinement of mammals reproductive risk assessment was performed using the relevant focal species in early maize (BBCH 12-18), with consideration of the refined PT (proportion of time spent on foraging in the crop) ~~and PD (the assumed proportion of food items in the diet) values, Food Intake Rate and residue decline data.~~ The NOAEL for reproductive performance of 1.2 mg/kg bw/d is also used as additional refinement.

Comment RMS: The new RUD values were not taken into account in the present risk assessment by RMS.

3.1 Refined risk assessment for the wood mouse (*Apodemus sylvaticus*)

Determination of PT for focal species

The agreed PT value of 0.139 from mesotrione EFSA conclusion (2016) is used for the wood mouse.

PD values

~~For purposes of the risk refinement assumption, the standard diet of the wood mouse consisting of 25% weeds, 50% weed seeds and 25% of ground arthropods as indicated in EFSA (2009) is used in the risk assessment.~~

~~**Food Intake Rate**~~

~~FIR/bw of 0.27 is used for the wood mouse based on calculation performed in line with indications of Appendix G of EFSA (2009) with consideration of the bodyweight of 21.7 g and the mixed diet indicated in EFSA guidance (Table 3-1).~~

~~**Table 9-12: Food intake rate calculations for the wood mouse**~~

~~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* (kJ/g fresh weight)~~	~~5.76~~		
~~bw~~ [e]	~~(g)~~	~~21.7~~		
~~FIR/bw~~	~~(g fresh weight/bw/day)~~	~~0.27~~		

~~[a] PD for wood mouse Tier I 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 EFSA (2009)~~
~~[f] Plant material is assumed to be equal in maize shoot (using the default value for grasses and cereal shoots)~~

Refined RUD values

Default RUD values for maize indicated in the EFSA birds and mammals' guidance document (2009) originate from the residue trials performed on grass + cereals with no maize trials included in derivation of the RUD. The lack of residue decline data for maize was addressed also by Lahr et al. (2018) in the EFSA external scientific report "Data collection for the estimation of ecological data (specific focal species, time spent in treated areas collecting food, composition of diet), residue level and residue decline on food items to be used in the risk assessment for birds and mammals", which reported a large number of data available for maize and calculated a RUD value for maize of 29.7 mg/kg. This refined value has been also included in the new Birds and Mammals guidance document (2023) as the default RUD value for maize. Therefore, for the refinements presented here, the RUD value of **29.7** mg/kg from Lahr et al. (2018) was used.

Comment RMS: The new RUD values were not taken into account in the present risk assessment by RMS.

Residue decline and fTWA

In order to determine the DT_{50} value in maize, a residue decline study by Peda (2021, Final report for study 21SGS76) was submitted. The residue decline field trails on maize were conducted in Poland (at two sites), Hungary and France. Mesotrione was applied at a nominal rate of 150 g a.i./ha to maize BBCH 12. These data were fitted using the single first order model to derive the DT_{50} values of 1.44 and 1.41 for Poland, 1.37 for Hungary and 1.23 for France. Here the geomean DT_{50} value of **1.36** for all four locations was used for fTWA refinement.

Higher-tier assessment including the refinements presented above demonstrates an unacceptable risk to the wood mouse following an application of mesotrione at 150 g a.i./ha (Table 3-2) when using the EFSA agreed long-term endpoint for mesotrione of 0.3 mg/kg bw/d.

However, when these calculations were performed with the more relevant long-term mammal endpoint of 1.2 mg/kg bw/d, an acceptable risk is concluded (Table 3-3).

RMS comment: The kinetic analysis has been accepted by RMS. However, according to the harmonization arrangements for Poland, when the tests include 4 - 9 locations - maximum values can be used $DT_{50.}$ The worst case is DT_{50} = 1.44 d and this value should be used in risk assessment. Estimated new f_{TWA} based on residue decline study will be used as a risk refinement for reproductive risk to mammals in post-emergence use. MAFm * TWA (refined DT_{50}) = 0.099 should be used in risk assessment.

Table 9-13: Higher-tier assessment using the long-term/reproductive risk of 0.3 mg/kg/bw/d

Intended use	Maize						
Active substance/product	Mesotrione						
Application rate (g/ha)	1 x 150						
Reprod. toxicity (mg/kg bw/d)	0.3						
TER criterion	5						
Focal species	**Food category, % in diet**	**FIR/bw**	**RUD_{90} × DF (mg/kg food)**	**MAF_m x TWA**	**PT**	**DDD_{90} (mg/kg bw/d)**	**TER_a**
Wood mouse	Maize, 0.25	0.27	29.7	0.093	0.139	0.0039	
	Seeds, 0.5	0.27	40.2	0.53	0.139	0.0600	
	Arthropods, 0.25	0.27	3.5	0.53	0.139	0.0026	
	Whole diet					0.0665	**4.51**

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.

Table 9-14: Higher-tier assessment using the refined long-term/reproductive endpoint of 1.2 mg/kg/bw/d

Intended use	Maize						
Active substance/product	Mesotrione						
Application rate (g/ha)	1 x 150						
Reprod. toxicity (mg/kg bw/d)	1.2						
TER criterion	5						
Focal species	**Food category, % in diet**	**FIR/bw**	**RUD_{90} × DF (mg/kg food)**	**MAF_m x TWA**	**PT**	**DDD_{90} (mg/kg bw/d)**	**TER_a**
Wood mouse	Maize, 0.25	0.27	29.7	0.093	0.139	0.0039	
	Seeds, 0.5	0.27	40.2	0.53	0.139	0.0600	
	Arthropods, 0.25	0.27	3.5	0.53	0.139	0.0026	
	Whole diet					0.0665	18.05

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.

3.2 Refined risk assessment for the European brown hare (*Lepus europaeus*)

Determination of PT for focal species

As the only agreed PT value from the mesotrione EFSA conclusion (2016) is for brown hare, the PT value used was **1** as a worst-case scenario.

PD values

Brown hare diet relevant for maize in spring indicated in the Northern Zone Guidance Document is used here (i.e., 84% maize and 16% dicotyledons weeds). The derived PD values were based on published data from studies carried out in Sweden (Frylestam 1980), England (Tapper and Barnes 1986), France (Chapuis 1990) and Denmark (Olesen & Asferg 2006; Hansen 1990).

Food Intake Rate

FIR/bw of **0.328** is used for the brown hare based on calculation performed in line with indications of Appendix G of EFSA (2009) with consideration of the bodyweight of 3800 g and the mixed diet indicated in EFSA guidance (Table 3-4).

Table 9-15: Food intake rate calculations for the brown hare

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)	2363.40	
Food intake rate of total mixed diet [d]	FIR*total,fresh* (kJ/g fresh weight)	1245.61	
bw [e]	(g)	3800	
FIR/bw	(g fresh weight/bw/day)	0.328	

[a] PD for hare according to the Northern Zone Guidance Document
[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 EFSA (2009)
[f] Plant material is assumed to be equal in maize shoot (using the default value for grasses and cereal shoots)

Refined RUD values

Same RUD refinements presented above for the wood mouse.

Residue decline and fTWA

The same residue decline study and calculated DT_{50} and fTWA values presented above for the wood mouse are used for the brown hare.

The risk assessment based on refined parameters, including the refined toxicity endpoint, demonstrated acceptable risk to the brown hare from exposure to mesotrione applied at 150 g a.i./ha (Table 3-6).

Table 9-16: Higher-tier assessment using the long-term/reproductive endpoint of 0.3 mg/kg/bw/d

Intended use	Maize						
Active substance/product	Mesotrione						
Application rate (g/ha)	1 x 150						
Reprod. toxicity (mg/kg bw/d)	0.3						
TER criterion	5						
Focal species	**Food category, % in diet**	**FIR/bw**	**RUD_{90} × DF (mg/kg food)**	**MAF_m x TWA**	**PT**	**DDD_{90} (mg/kg bw/d)**	**TER_a**
Brown hare	Maize, 0.84	0.328	29.7	0.093	1	0.114	
	Dicots weeds, 0.16	0.328	28.7	0.53	1	0.120	
	Whole diet					0.234	**1.28**

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.

~~**Table 9-17: Higher-tier assessment using the long-term/reproductive endpoint of 1.2 mg/kg/bw/d**~~

~~**Intended use**~~	~~Maize~~						
~~**Active substance/product**~~	~~Mesotrione~~						
~~**Application rate (g/ha)**~~	~~1 x 150~~						
~~**Reprod. toxicity (mg/kg bw/d)**~~	~~1.2~~						
~~**TER criterion**~~	~~5~~						
~~**Focal species**~~	~~**Food category, % in diet**~~	~~**FIR/bw**~~	~~**RUD_{90} × DF (mg/kg food)**~~	~~**MAF_m x TWA**~~	~~**PT**~~	~~**DDD_{90} (mg/kg bw/d)**~~	~~**TER_a**~~
~~Brown hare~~	~~Maize, 0.84~~	~~0.328~~	~~29.7~~	~~0.093~~	~~1~~	~~0.114~~	
	~~Dicots weeds, 0.16~~	~~0.328~~	~~28.7~~	~~0.53~~	~~1~~	~~0.120~~	
	~~Whole diet~~					~~0.234~~	~~5.13~~

~~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.~~

Refinement risk assessment for mammals provided by RMS for Poland:

Tier-1 step assessment of the long-term risk for mammals due to the use of Juzan Extra 100 SC in maize

Intended use	Maize (***also minor uses i e: sugar maize, popcorn***);				
Active substance/product	mesotrione				
Application rate (g/ha)	150				
Reprod. toxicity (mg/kg bw/d)	1.2				
TER criterion	5				
Crop scenario Growth stage	**Indicator/generic focal species**	**SV_m**	**MAF_m × TWA**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
Maize BBCH 10-19	Small insectivorous mammal – “shrew”	4.2	0.099	0.06	20
Maize BBCH 10-29	Small herbivorous mammal – “vole”	72.3	0.099	1.07	**1.12**
Maize BBCH 10-29	Small omnivorous mammal – “mouse”	7.8	0.099	0.1158	10.36

*In grey verified by RMS based on DT_{50} of 1.44 d as worst case.

Comment RMS: Based on the new f_{TWA}, application for vole is still unacceptable. However, based on EFSA Conclusion 2016 voles are not representative species in maize. The focal species for maize at early BBCH growth stages such as wood mouse and brown hare were accepted by zRMS.

Higher-tier assessment of the long term risk for mammals due to the mesotrione use of Juzan Extra 100 EC in maize

\Intended use	maize						
Active substance/product	mesotrione						
Application rate (g/ha)	1 × 150						
Reprod. toxicity (mg/kg bw/d)	1.2						
TER criterion	5						
Crop scenario Growth stage	**Indicator/generic focal species**	**Fir/bw**	**RUD**	**SV_m**	**MAF_m × TWA**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**

Maize	Rabit (100 % plant material)"	0.334	54.2	-	0.099	0.2688	**4.46**
	Apodemus sylvaticus	-	-	7.8	0.099	0.1158	10.36

*In grey verified by RMS based on DT_{50} of 1.44d.

Based on the new f_{TWA}, application for rabbit is still unacceptable. The RMS proposes to reduce the dose to 0.100 kg s.a./ha. New calculation was provided by RMS based on reduced dose (0.100 kg s.a./ha).

Higher-tier assessment of the long term risk for mammals due to the mesotrione use of Juzan Extra 100 EC in maize based on reduced dose

\Intended use	maize						
Active substance/product	mesotrione						
Application rate (g/ha)	1 × 100						
Reprod. toxicity (mg/kg bw/d)	1.2						
TER criterion	5						
Crop scenario Growth stage	**Indicator/generic focal species**	**Fir/bw**	**RUD**	**SV_m**	**MAF_m × TWA**	**DDD_m (mg/kg bw/d)**	**TER_{lt}**
Maize	Rabbit (100 % plant material)"	0.334	54.2	-	0.099	0.179	6.7

*In grey verified by RMS based on DT_{50} of 1.44d.

The trigger value for rabbit and *Apodemus sylvaticus* are above the trigger of 5.
Therefore, further refinement is not required for this species as the TER_{LT} is above the trigger of 5 **indicating acceptable risk to mammals.**

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 (Koc < 500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥ 500 L/kg).

Effective application rate (g/ha)* =	150		
Acute toxicity (mg/kg bw) =	5000	quotient =	0.03
Reprod. toxicity (mg/kg bw/d) =	0.3	quotient =	**500**

With a K(f)oc of 14 (as a worst case), mesotrione belongs to the group of less sorptive substances. Since the ratio of effective application rate (150 g/ha) to relevant endpoint (0.3 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:

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

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)

There was unacceptable chronic risk to mammals from drinking water from puddles (Table 3-7). However, when the risk assessment was completed using refined parameters, it demonstrated acceptable risk to mammals from exposure to mesotrione applied at 150 g a.i./ha (Table 3-8).

Table 9-18: Puddle drinking water exposure route from mesotrione using the long-term/reproductive endpoint of 0.3 mg/kg/bw/d

Intended use		Maize			
Active substance		Mesotrione			
Application rate (g/ha)		1 x 150			
Reprod. toxicity (mg/kg bw/d)		0.3			
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)**	**TER_a TER_{lt}**
150	50	0.1579	0.24	0.03789	7.92
150	14	0.3659	0.24	0.08780	**3.42**

Table 9-19: Puddle drinking water exposure route from mesotrione using the revised long-term/reproductive risk of 1.2 mg/kg/bw/d

Intended use		Maize			
Active substance		Mesotrione			
Application rate (g/ha)		1 x 150			
Reprod. toxicity (mg/kg bw/d)		1.2			
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)**	**TER_a TER_{lt}**
150	50	0.1579	0.24	0.03789	31.67
150	14	0.3659	0.24	0.08780	13.67

RMS comment: Agreed. In the light of the new justification provided by the Applicant the use of a refinement of toxicity endpoint (NOAEL=1.2 mg/kg bw/d) in risk assessment has been accepted. The refinement assessment of the risk for mammals due to exposure to mesotrione via contaminated drinking water in puddles was accepted by RMS.

9.3.2.4 Effects of secondary poisoning

Please refer to the Core Assessment.

9.3.2.5 Biomagnification in terrestrial food chains

Please refer to the Core Assessment.

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

Please refer to the Core Assessment.

9.3.1 Overall conclusions

An acceptable mammalian risk is concluded for the relevant focal species exposed to mesotrione applied on early maize (BBCH 12-18) using PT, PD and residue decline DT_{50} higher-tier refinements in conjunction with the NOAEL for reproductive endpoint of 1.2 mg/kg bw/d.

9.4 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians) (KCP 10.1.3)

Please refer to the Core Assessment.

9.5 Effects on aquatic organisms (KCP 10.2)

9.5.1 Toxicity data

Please refer to the Core Assessment.

9.5.1.1 Justification for new endpoints

Please refer to the Core Assessment.

9.5.2 Risk assessment

Please refer to the Core Assessment.

9.5.3 Overall conclusions

Please refer to the Core Assessment.

9.6 Effects on bees (KCP 10.3.1)

9.6.1 Toxicity data

Please refer to the Core Assessment.

9.6.1.1 Justification for new endpoints

Please refer to the Core Assessment.

9.6.2 Risk assessment

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

Please refer to the Core Assessment.

9.6.3 Effects on bumble bees

Please refer to the Core Assessment.

9.6.4 Effects on solitary bees

Please refer to the Core Assessment.

9.6.5 Overall conclusions

Please refer to the Core Assessment.

9.7 Effects on arthropods other than bees (KCP 10.3.2)

9.7.1 Toxicity data

Please refer to the Core Assessment.

9.7.1.1 Justification for new endpoints

Please refer to the Core Assessment.

9.7.2 Risk assessment

Please refer to the Core Assessment.

9.7.2.1 Risk assessment for in-field exposure

Please refer to the Core Assessment.

9.7.2.2 Risk assessment for off-field exposure

Please refer to the Core Assessment.

9.7.2.3 Additional higher-tier risk assessment

Please refer to the Core Assessment.

9.7.2.4 Risk mitigation measures

Please refer to the Core Assessment.

9.7.3 Overall conclusions

Please refer to the Core Assessment.

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

9.8.1 Toxicity data

Please refer to the Core Assessment.

9.8.1.1 Justification for new endpoints

Please refer to the Core Assessment.

9.8.2 Risk assessment

Please refer to the Core Assessment.

9.8.2.1 First-tier risk assessment

Please refer to the Core Assessment.

9.8.2.2 Higher-tier risk assessment

Not relevant.

9.8.3 Overall conclusions

Please refer to the Core Assessment.

9.9 Effects on soil microbial activity (KCP 10.5)

9.9.1 Toxicity data

Please refer to the Core Assessment.

9.9.1.1 Justification for new endpoints

Please refer to the Core Assessment.

9.9.2 Risk assessment

Please refer to the Core Assessment.

9.9.3 Overall conclusions

Please refer to the Core Assessment.

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

9.10.1 Toxicity data

Please refer to the Core Assessment.

9.10.1.1 Justification for new endpoints

Please refer to the Core Assessment.

9.10.2 Risk assessment

Please refer to the Core Assessment.

9.10.2.1 Higher-tier risk assessment

Please refer to the Core Assessment.

9.10.2.2 Risk mitigation measures

Please refer to the Core Assessment.

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

Please refer to the Core Assessment.

9.12 Monitoring data (KCP 10.8)

Please refer to the Core Assessment.

9.13 Classification and Labelling

Please refer to the Core Assessment.

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
KCP 10.1.2/02	Tilston E.L, Eastabrook Ch.	2023	Mammalian risk assessment higher-tier refinements for mesotrione applications on maize, Enviresearch Limited, UK, Report no. E2023-06 Non-GLP Unpublished	N	CIECH Sarzyna S.A.

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

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

The following tables are to be completed by MS

List of data submitted by the applicant and not relied on

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

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

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

Appendix 2 Detailed evaluation of the new studies

A 2.1 KCP 10.1 Effects on birds and other terrestrial vertebrates

A 2.1.1 KCP 10.1.1 Effects on birds

Please refer to the Core Assessment.

A 2.1.1.1 KCP 10.1.1.1 Acute oral toxicity

Please refer to the Core Assessment.

A 2.1.1.2 KCP 10.1.1.2 Higher tier data on birds

Please refer to the Core Assessment.

A 2.1.2 KCP 10.1.2 Effects on terrestrial vertebrates other than birds

Please refer to the Core Assessment.

A 2.1.2.1 KCP 10.1.2.1 Acute oral toxicity to mammals

Please refer to the Core Assessment.

A 2.1.2.2 KCP 10.1.2.2 Higher tier data on mammals

Please refer to the Core Assessment.

Clarifications on the issues raised by the Evaluators in this point are explained in this National Addendum in point 9.3.2.2.

A 2.1.3 KCP 10.1.3 Effects on other terrestrial vertebrate wildlife (reptiles and amphibians)

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

Please refer to the Core Assessment.

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

Please refer to the Core Assessment.

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

A 2.3.1.3 KCP 10.3.1.3 Effects on honey bee development and other honey bee life stages

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 arthropods other than bees

Please refer to the Core Assessment.

A 2.3.2.1 KCP 10.3.2.1 Standard laboratory testing

Please refer to the Core Assessment.

A 2.3.2.2 KCP 10.3.2.2 Extended laboratory testing

Please refer to the Core Assessment.

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

Please refer to the Core Assessment.

A 2.4.1.2 KCP 10.4.2.2 Higher tier testing

Please refer to the Core Assessment.

A 2.5 KCP 10.5 Effects on soil nitrogen transformation

Please refer to the Core Assessment.

A 2.6 KCP 10.6 Effects on terrestrial non-target higher plants

A 2.6.1 KCP 10.6.3 Extended laboratory studies on non-target plants

A 2.6.2 KCP 10.6.2 Testing on non-target plants

Please refer to the Core Assessment.

A 2.6.3 KCP 10.6.3 Extended laboratory studies 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