FINAL REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: CHR/H/ETO 500 SC

Product name(s): BITT 500 SC, BETRON 500 SC, ETONAL 500 SC

Chemical active substance(s):

Ethofumesate, 500 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Innvigo Sp. z o.o.

Submission date: June 2021

MS Finalisation date: 14/01/2022

Version history

When	What
06/2021	Dossier sent for evaluation to Merit Mark (PL)
11/2021	zRMS finalised evaluation
01/2022	Final version prepared by zRMS after Commenting period

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zRMS comments:
This report has been completed by the applicant.
The text highlighted in grey was provided by the evaluator.

7 Metabolism and residue data (KCA section 6)

In the following document, data for active substance ethofumesate was described during its renewal process in 2016. Were reference to active substance data in the current risk assessment has been made, it was based on the data presented by Bayer.
In June 14th, 2018r Kemiron Koncentrat 500SC product has been renewed in Poland thus according to the art. 59 reg. 1107/2009, data protection for mentioned data expired 30 months from date of first renewal of authorisation of product containing that active substance (in this case December, 14th 2020).
Considering analogous arguments (art. 59 reg 1107/2009) – data protection of studies presented by UPL for renewal of product Bettix Combi 500 SC (renewal of authorisation granted in Poland 14.02.2019 r.) expires August 14th, 2021.
Taking into account that some data was presented by others Notyfiers, Applicant would like to emphasise that unprotected Bayer's endpoints and input parameters accepted during renewal of active substance, should be treated as an equivalent matching data in cases where any of endpoints might be protected.

7.1 Summary and zRMS Conclusion

GAPs proposed for CHR/H/ETO 500 SC on sugar beets (max. 1 kg a.s./ha every three years):
1) 2 appl., BBCH 11-18, max application rate per treatment: 0.5 kg a.s/ha, PHI- not applicable
2) 3 appl., BBCH 11-18, max application rate per treatment: 0.3 kg a.s/ha, PHI- not applicable
EU GAPs on sugar beets (EFSA Journal 2016;14(1):4374):
For data presented by UPL: pre-emergence, 1 appl., max appl. rate 1 kg a.s./ha; Splitting application with a maximum total rate of 1 kg a.s./ha per season. Post-emergence until BBCH 18. *The maximum application rate per treatment is 0.33 kg a.s./ha. The critical GAP therefore is 3 applications of 0.33 kg a.s./ha. More applications (max.6) at a lower application rate are possible, but they do not represent the critical GAP. PHI covered by the vegetation period, max. 1 kg a.s./ha every three years.*
For data presented by Task Force ethofumesate: post-emergence BBCH 16-18, 1-3 appl., interval between appl. 5 days, appl. rate per treatment 0,2-1 kg a.s./ha. The maximum amount of active substance must not exceed 1.0 kg/ha every 3 years. PHI is covered by the normal vegetation period between last application and harvest.
GAP accepted by the Polish Authority for Bettix Combi 500 SC on sugar beets (the Applicant is referring to the study for this product): 3 appl. (interval between appl. 5-10 days), BBCH 11-31, max appl. per treatment 0.3 kg a.s./ha.
The Applicant did not provide any new studies. The dossier is based on studies assessed at Community level during the renewal of approval for ethofumesate as an active substance. The Applicant has informed that it has the right to use the studies assessed at the renewal stage. Authorities competent for authorization should verify whether the explanations provided by the Applicant in this regard are correct and sufficient.
Stability
According to the EFSA Journal 2016;14(1):4374 ethofumesate is stable under frozen storage conditions for at least 12 months in sugar beetroots (high starch content matrix) and sugar beet leaves (high water content matrix). In addition, data showing stability of the metabolite NC 20645 and conjugated NC 20645, analysed as NC 9607 for at least 24 month in sugar beet (roots and leaves) for not less than 24 months. In animal products, ethofumesate and its metabolites NC 9607, NC8493 and NC 20645 were found to be stable under frozen storage for up to 6 months.
Nature of residues in plants
According to the EFSA Journal 2016;14(1):4374:
Primary crop metabolism of 14C ethofumesate was investigated following pre-emergence application and post-emergence foliar application to sugar beet, post-emergence foliar application to ryegrass and tobacco (non GLP), and pre-emergence application to onions (non GLP). In addition, rotational crop metabolism was studied in radish, carrots, cabbage, spinach, wheat, ryegrass, and French beans, investigating different plant-back intervals upon soil application of 14C ethofumesate. Metabolic patterns in the different studies were similar, metabolism of ethofumesate leading to the metabolites ethofumesate-

2-hydroxy (NC 8493), ethofumesate lactone (NC 9607) and ethofumesate carboxylic acid (NC 20645), recovered also in their conjugated form. NC 20645 is the open ring form of NC9607. Intra-molecular ring closure appeared to be conditioned by the pH i.e. primarily when acidic conditions are applied to release the aglycon of conjugated residues. The proportions observed of parent and metabolites and their conjugates varied depending on the time, mode and rate of application as well as on the crop studied. Commonly, until harvest of the mature primary crop, parent had been degraded to a significant extent, if not completely, into its metabolites, majorly present as conjugated compounds. The pertinent residue was identified as NC 20645, free and conjugated.

In a confined rotational crop study, parent ethofumesate was recovered in almost all commodities tested. Upon hydrolysis significant portions of conjugated residues were identified as NC9607 in most of the commodities, and in root crops also of NC 8493. The observation of residues of unchanged ethofumesate in rotational crops was presumably caused by the high persistence and low leaching potential of ethofumesate in some soils and likely increased availability in the root zone upon breaking up of the soil at planting of the following crop.

In view of the metabolic pathway in mammals EFSA considered that the plant metabolites NC 20645, NC 9607 and NC 8493 are covered by the toxicological endpoints of parent compound (see last paragraph in section 2).

In residue trials in the primary crop and in rotational crops residues of ethofumesate and by turns of free NC 9607, free and conjugated NC 20645 and NC 8493 were determined. When the occurrence of residues in the primary or rotational crop (food and feed items) at harvesting stage is considered, ***the residue definition for risk assessment is appropriately defined as the sum of ethofumesate, NC 9607, NC20645 and its conjugate, expressed as ethofumesate. The same residue definition was proposed for monitoring purposes and MRL setting.*** *The proposal took into account the fact that a reliable determination of the relevant ethofumesate residues is only possible if NC 9607 is included in the residue definition as common moiety which comprises the determination of the metabolite NC 20645 (free and conjugated) plus metabolite NC 9607 itself due to occurring intra-molecular rearrangements. Therefore the previously proposed residue definition in the review under Directive 91/414/EEC as sum of ethofumesate and NC9607 was considered as not sufficiently precise and was amended accordingly. It is acknowledged that multi-component definitions for monitoring may not comply with the suggested marker compound concept, however in the specific case of ethofumesate the inclusion of NC9607 appears to be inseparable from NC 20645. Given the presence of parent ethofumesate above LOQ in rotational crop field trials at early plant-back intervals only, the exclusion of ethofumesate itself might be considered an option in case risk managers wish to simplify the proposed monitoring residue definition.*

Hydrolysis products were detected in a range between 0.7 and 2.1%. They were not further investigated, due to their low amount in the test solutions.

Metabolism in livestock

According to the EFSA Journal 2016;14(1):4374:

Metabolism in poultry and lactating ruminants was sufficiently investigated with 14C ethofumesate. ***The relevant residue definition for both enforcement and risk assessment in livestock was derived as the sum of ethofumesate, NC 9607, NC 20645, expressed as ethofumesate. Based on the metabolism studies, it is also concluded that significant residues in animal commodities are not expected, considering livestock exposure linked to the representative uses.***

Magnitude of residues

Residue data have been evaluated at Community level. The Applicant did not provide any additional data. Considering that the GAP proposed for CHR/H/ETO 500 SC on sugar beet is not more critical than accepted at Community level, the presented data should be considered sufficient. No exceedance of the MRL will occur.

Taking into account that the level of residues in sugar beet roots does not exceed 0.1 mg/kg and TMDI is below 10 % of the ADI (no ARfD derived), there is no need to investigate the effect of processing.

Residues in succeeding studies have been evaluated at Community level. In these studies after application of 1 kg a.s./ha on sugar beet residues of ethofumesate were detected in the crops of the first rotation (PBI 25-33 days). Replanting of root and leafy crops could lead to measurable residues in edible plant parts. Therefore it is proposed to set risk mitigation measures to avoid residues in succeeding crops in the case of crop failure. In the label, the Applicant proposed the following entry:

If it is necessary to liquidate a plantation treated with CHR/H/ETO 500 SC, as a result of damage to

plants by frosts, diseases, pests (or for any other reason), in this field after 30 days and carrying out deep plowing (20 cm), beet can be grown. Winter cereals can be sown after at least 5 months. Other plants can be grown approximately 3 months after the last treatment.
None, apart from those specified by the Applicant, additional mitigation measures are required.
According to the Appendix II to SANTE/11956/2016 rev. 9 sugar beet should not be considered a melliferous crop unless it is grown for seed. The proposed use is not for seed production and therefore no residue studies in honey are required.
The consumer risk assessment (chronic) was calculated using EFSA PRIMo rev. 3.1 for all MRLs in force (Reg.(EU) 2017/1016) (overestimated). Results indicated the highest estimate of chronic dietary intake is 0.5 % of the ADI (NL toddler). As ARfD was not deemed necessary, acute risk assessment is not relevant.
The proposed uses of ethofumesate in the formulation CHR/H/ETO 500 SC do not represent unacceptable acute and chronic risks for the consumer.
Conclusion
Authorization can be granted.
For sugar beet, additional data are required in post-registration to confirm that a "no-residue" situation occurs in the worst case application: 2 application of 0.5 g ethofumesate/ha at growth stage BBCH 11-18.

The dossier is based on studies assessed at Community level during the renewal of approval for ethofumesate as an active substance. The Applicant has informed that it has the right to use the studies assessed at the renewal stage. Authorities competent for authorization should verify whether the explanations provided by the Applicant in this regard are correct and sufficient.

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification

The critical GAPs with respect to consumer intake and risk assessment for the preparation CHR/H/ETO 500 SC are presented in Table 7.1-1. They have been selected from the individual GAPs in the central zone for sugar beet. A list of all intended uses within the central zone is given in Part B, Section 0.

Overall conclusion

The data available are considered sufficient for risk assessment. An exceedance of the current MRL of 0.2 mg/kg (sugar beet roots) and 0.3 mg/kg (sugar beets leaves) for ethofumesate as laid down in Reg. (EU) 396/2005 is not expected.
The chronic and the short-term intakes of ethofumesate residues are unlikely to present a public health concern.
As far as consumer health protection is concerned, authority, zRMS agrees with the authorization of the intended use(s).

~~According to available data, no specific mitigation measures should apply.~~

Data gaps

None

Table 7.1-1: Acceptability of critical GAPs (and respective fall-back GAPs, if applicable)

1	2	3	4	5	6	7	8	9	10	11	12	13	14
Use-No.	Member state(s)	Crop and/or situation (crop destination / purpose of crop) (a)	F, Fn, Fpn G, Gn, Gpn or I (b)	Pests or Group of pests controlled (additionally: developmental stages of the pest or pest group) (c)	**Application**				**Application rate**			PHI (days) (l)	Remarks: e.g. g safener/ synergist per ha (m)
					Method / Kind (f-h)	Timing / Growth stage of crop & season (j)	Max. number a) per use b) per crop/ season (k)	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		
	North and South EU	Sugar beet, Fodder beet, red beet	F	Annual dicot weeds and annual grasses	Overall spray	Postemergence BBCH16 to BBCH18	1-3	5	a) 0.4 b) 2.0	a) 0.2 b) 1.0	100-400	*	The maximum amount of active substance must not exceed 1.0 kg/ha every 3 years.
	Northern, central, southern EU	Sugar beet, fodder beet	F	Annual weeds	Overall spray	Preemergence	1	-	-	1	300-400	-	PHI covered by the vegetation period, max. 1 kg a.s./ha every three years
	Northern, central, southern EU	Sugar beet, fodder beet	F	Annual weeds	Overall spray	Postemergence until BBCH 18	6**	5	-	0.16**	200-300	-	PHI covered by the vegetation period, max. 1 kg a.s./ha every three years

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

** Use also code numbers according to Annex I of Regulation (EU) No 396/2005

*** 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

7.1.2 Summary of the evaluation

The preparation CHR/H/ETO 500 SC is composed of ethofumesate.

Table 7.1-2: Toxicological reference values for the dietary risk assessment of ethofumesate

Reference value	Source	Year	Value	Study relied upon	Safety factor
ethofumesate - Parent compound (if applicable)					
ADI	EFSA Journal 2016;14(1):4374	2016	1	Rat, 2 year	100
ARfD	EFSA Journal 2016;14(1):4374	2016	Not applicable	-	-

7.1.2.1 Summary for ethofumesate

Table 7.1-3: Summary for ethofumesate

Use-No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
	Sugar beet	Yes	Yes	Yes	Yes	Yes	~~Yes~~ No	~~Yes/~~ No

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

For sugar beet, additional data are required in post-registration to confirm that a "no-residue" situation occurs in the worst case application: 2 application of 0.5 g ethofumesate/ha at growth stage BBCH 11-18.

The effects of processing on the nature of ethofumesate residues have been investigated. Data on effects of processing on the amount of residue have been submitted.
These data were considered for risk assessment.

Residues in succeeding crops have been sufficiently investigated taking into account the specific circumstances of the cGAP uses being considered here. It is very unlikely that residues will be present in succeeding crops.

7.1.2.2 Summary for CHR/H/ETO 500 SC

Table 7.1-4: Information on CHR/H/ETO 500 SC (KCA 6.8)

Crop	PHI for CHR/H/ETO 500 SC proposed by applicant	PHI/ Withholding period* sufficiently supported for	PHI for CHR/H/ETO 500 SC proposed by zRMS	zRMS Comments (if different PHI proposed)
		Ethofumesate		
Sugarbeet	PHI covered by the vegetation period, max. 1 kg a.s./ha every three years	PHI covered by the vegetation period, max. 1 kg a.s./ha every three years	NR	

NR: not relevant
* Purpose of withholding period to be specified
** F: PHI is defined by the application stage at last treatment (time elapsing between last treatment and harvest of the crop).

Table 7.1-5: Waiting periods before planting succeeding crops

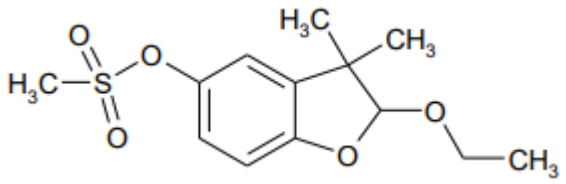
Waiting period before planting succeeding crops			**Overall waiting period proposed by zRMS for product code**
Crop group	**Led by active substance 1**	**Led by active substance 2**	
Leafy vegetables	NR	NR	Do not grow leafy vegetables in the treated field less than 120 days after application of <Product code>. If it is necessary to liquidate a plantation treated with CHR/H/ETO 500 SC, as a result of damage to plants by frosts, diseases, pests (or for any other reason), in this field after 30 days and carrying out deep plowing (20 cm), beet can be grown. Winter cereals can be sown after at least 5 months. Other plants can be grown approximately 3 months after the last treatment.
Root vegetables	NR	NR	
Cereals	NR	NR	

NR: not relevan

7.2 Ethofumesate

General data on Ethofumesate are summarized in the table below (last updated 2021/03/18)

Table 7.2-1: General information on ethofumesate

Active substance (ISO Common Name)	Ethofumesate
IUPAC	(RS)-2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl methanesulfonate
Chemical structure	
Molecular formula	C13H18O5S
Molar mass	286.3
Chemical group	~~Sulfonate~~ Benzofuran
Mode of action (if available)	Selective, systemic, absorbed through emerging shoots and roots. Inhibition of lipid synthesis
Systemic	Yes~~/No~~
Company (ies)	UPL EUROP, TASK Force (Bayer CropScience and ADAMA)
Rapporteur Member State (RMS)	AT
Approval status	Approved COMMISSION IMPLEMENTING REGULATION (EU) 2016/1426 of 25 August 2016.
Restriction (e.g. is restricted to use as "...")	SANTE/10119/2016 Rev. 3 12 July 2016 Reg. (EU) 2016/1426
Review Report	SANTE/10119/2016 Rev. 3 12 July 2016
Current MRL regulation	Regulation (EU) 2017/1016
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Yes
EFSA Journal : Conclusion on the peer review	EFSA Journal 2016;14(1):4374
EFSA Journal: conclusion on article 12	EFSA Journal 2012;10(11):2959
Current MRL applications on intended uses	EFSA Journal 2016;14(1):4374

* Notifier in the EU process to whom the a.s. belong(s)
** If yes: EFSA, YYYY - see list of references

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

No new data submitted in the framework of this application.

Table 7.2-2: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Sugarbeet (leaves)	High water content	1 year for ethofumesate 2 years for NC 20645 and NC 9607	EFSA Journal 2016;14(1):4374
Sugarbeet (roots)	High starch content	1 year for ethofumesate 2 years for NC 20645 and NC 9607	EFSA Journal 2016;14(1):4374
Oilseed rape	High lipid content	2 months for NC 20645 and NC 9607	EFSA Journal 2016;14(1):4374
Orange	High acid content	2 months for NC 20645 and NC 9607	EFSA Journal 2016;14(1):4374
Bean	High protein content	2 months for NC 20645 and NC 9607	EFSA Journal 2016;14(1):4374
Grass, forage	High water content	ETO: 18 months NC 9607: 18 months NC 8493: 18 months	Cole, M. G., 1995, M-134863-01-1, A54281, DRAR, Austria 2015
Spinach leaf	High water	ETO: 35 months NC 9607: 36 months NC 8493: 36 months	Cole, M. G., 2000, M-238461-01-2, B002728,
Carror root	High starch	ETO: 24 months NC 9607: 24 months NC 8493: 24 months	Cole, M. G., 2000, M-238461-01-2, B002728,
Barley grain	High starch	ETO: 24 months NC 9607: 24 months NC 8493: 24 months	Cole, M. G., 2000, M-238461-01-2, B002728,
Sorgum straw	High starch and dry	ETO: 35 months NC 9607: 36 months NC 8493: 36 months	Cole, M. G., 2000, M-238461-01-2, B002728,
Animal Products			
Ruminant	Liver	6 months for ethofumesate, NC 9607, NC 20645, NC 8493	EFSA Journal 2016;14(1):4374
Ruminant	Kidney	6 months for ethofumesate, NC 9607, NC 20645 and 3 months for NC 8493	EFSA Journal 2016;14(1):4374
Ruminant	Muscles	6 months for ethofumesate, NC 9607, NC 8493 and 1 months NC 20645	EFSA Journal 2016;14(1):4374
Ruminant	Fat	6 months for ethofumesate, NC 9607, NC 8493 and <1 months NC 20645	EFSA Journal 2016;14(1):4374
Ruminant	Milk	6 months for ethofumesate, NC 9607, NC 20645, NC 8493	EFSA Journal 2016;14(1):4374

Conclusion on stability of residues during storage

Storage stability of ethofumesate and its metabolites, NC 20645 and its conjugates, NC 9607, and NC 8493 has been demonstrated in high water and high starch content matrices it thus sufficiently covers the longest period of time for which samples from field residue trials of the intended uses presented in this assessment were stored before analysis. Hence, the results of the storage stability studies validate the residue values obtained from these

7.2.1.2 ~~trials~~Stability of residues in sample extracts (KCA 6.1)

~~Not relevant. According to EFSA Journal 2016;14(1):4374 all samples were analyzed less then 24 hours from extractions.~~

zRMS comments:

Stability of residues in sample extracts was evaluated at EU level. Additional studies are not required.

7.2.2 Nature of residues in plants, livestock and processed commodities

7.2.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data

No new data submitted in the framework of this application.

Table 7.2-3: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
EU data								
Leafy vegetables	Tobacco	[14C-benzene]	Soil, G	2.00	1	7, 15, 30, 60, 90 and 120		Study NC 8438/M35 1977
			Foliar, G	2 mg/plant				
Root and tuber vegetables	Sugarbeets	[14C-benzene]	Foliar, G	1.27 or 6.37	1	0+, 10, 30 and 81 and at maturity		Chapleo, 1992
		[14C-benzene]	Foliar, G	1.50 or 7.5	1	0, 7, 28 and at maturity		Caley, C. Y.; Chapleo, S.; Haswell, A.; 1994;
		[14C-benzene]	Foliar, F	1.5	1	1, 10, 50, 90, 137		Hennecke, D. 2003
		[14C-benzene]	Soil, G	2.0	1	10, 20, 30, 40 and 50		Lines, D.S. Adcock, J.W., 1978
			Foliar, G					
		[14C-mesyl]	Soil, F	2.0	1	50, 75, 125 and 175		Lines, D. S.; Adcock, J. W.; 1979; M-155242-01
			Foliar, F			50, 75 and 125		
	Onion	Not	Soil	2.0	1	22, 30, 40,		Study NC

		reported				50, 60, 70, 80, 90, 100, 110, 120 and 162		8438/M30 1976
Cereals	ryegrass	[^{14}Cbenzene]	Foliar, G	2.09 or ~10.451		0-112		Chapleo, 1992

Summary of plant metabolism studies reported in the EU

Metabolism of ethofumesate was investigated in root and tuber vegetables (sugar beet and onions), cereals (ryegrass) and leafy crops (tobacco) following application of [14C-benzene]- or [14C-methylsulfonyl]-ethofumesate. Application was conducted either as a pre-emergent or a post-emergent spray. The application rate in the sugar beet studies ranged between approx. 1.3-2.0 kg a.s./ha and between 2.0 and 2.1 kg a.s./ha in the other crops. Comparison of pre-and post-emergent treatment revealed that ethofumesate is taken-up via roots and leaves. The metabolism in the plants is independent from the route of uptake. The most recent studies on sugar beet (Chapleo, S.; 1992; M-155247-01, Caley, C. Y.; Chapleo, S.; Haswell, A.; 1994; M-161455-01 and Hennecke, D., 2003, GAB-002/7-08) and on ryegrass (Chapleo, S.; 1992; M-155248- 01) show a conclusive picture on the metabolic behaviour of ethofumesate. Two additional studies on sugar beet and the studies on onion and tobacco were conducted before the implementation of GLP certificates and are therefore considered as supportive data only. However, these studies are in very good agreement with the GLP studies and confirm the results of these studies. Nevertheless, the metabolism study which should cover the cereal group was conducted on ryegrass and therefore no information on cereal grains is available from this study.
The major metabolic pathway for ethofumesate in plants was identified as follows:

- cleavage of the ethoxy side chain, with hydroxylation at the 2 position to give metabolite NC 8493 (ethofumesate-2-hydroxy = 2,3-dihydro-2-hydroxy-3,3-dimethylbenzofuran-5-yl methanesulfonate).
- This metabolite can either undergo conjugation to give polar metabolites or oxidation to the lactone NC 9607 (ethofumesate-lactone = 2,3-dihydro-3,3-dimethyl-2-oxobenzofluran-5-yl methanesulfonate).
- The lactone ring opens to the carboxylic acid NC 20645 (ethofumesate-carboxylic acid = 2-(2-hydroxy-5-methanesulfoxyphenyl)-2-methyl propionic acid) which can also undergo conjugation to give polarmetabolites.

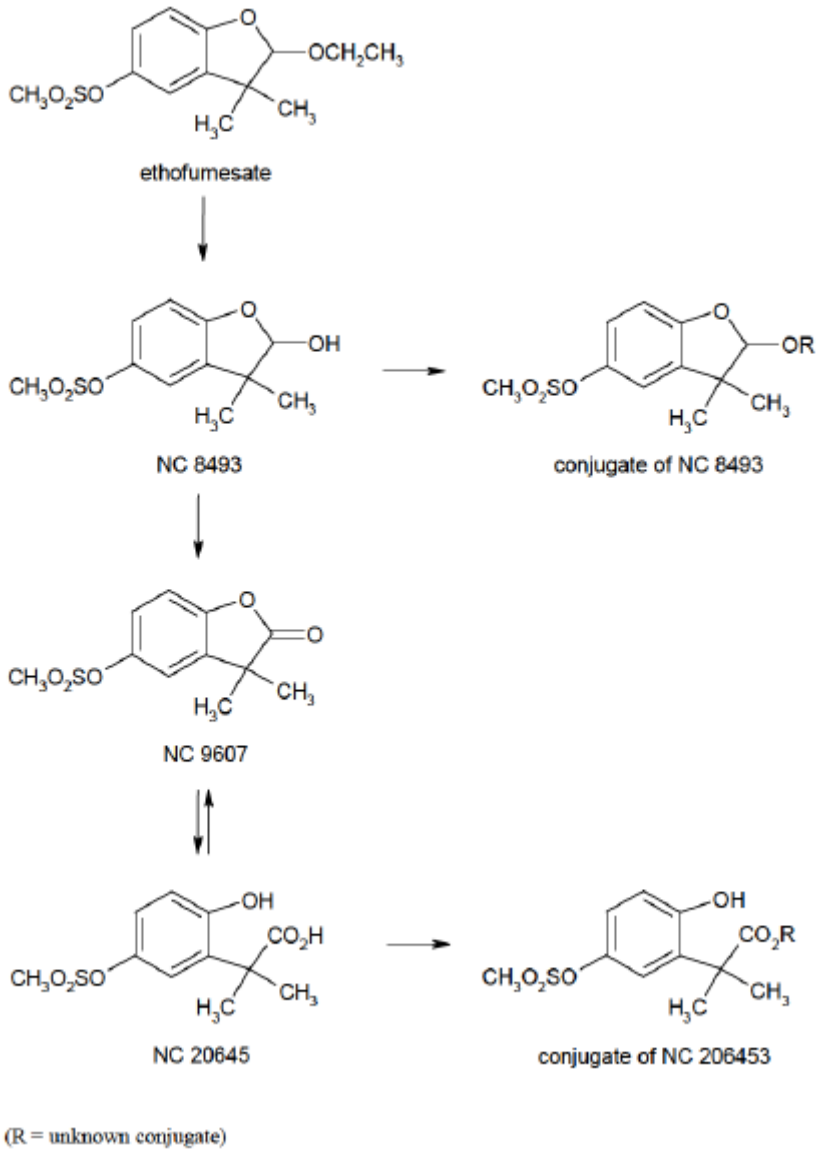
The lactone NC 9607 and the carboxy analogue NC 20645 are inter-convertible and depending on the ambient conditions, either one or the other metabolite will predominate. Under acidic conditions, metabolite NC 20645 is converted to metabolite NC 9607 by an intramolecular ring closure. Cleavage of the molecule under release of methansufphonic acid was excluded in two sugar beet studies using two different chromatographic systems (TLC and TLE). The extraction and analysis processes were validated beforehand with a radiolabelled reference compound (14C-MSA). Recoveries of MSA were above 97% and confirmed that the compound would be detected, if present. According to the GLP studies, the extractability of radioactive residues was high in sugar beet shoots and ryegrass; surface wash and conventional solvent extraction released between 86.4-99.9% of the total radioactive residue. If an additional exhaustive extraction step with hydrochloric acid was applied, the extraction efficiency was always >90%. Exhaustive extraction released generally the known moieties NC 8493 and NC 9607. The extractability in roots was generally lower due to the high sugar and starch content of the tissue. Nevertheless, in the most recent sugar beet study (Caley, C. Y.; Chapleo, S.; Haswell, A.; 1994; M-161455-01), 75.8-93.7% of the radioactivity was released by conventional solvent extraction. Identification rates were always high in samples collected early after the treatment with parent ethofumesate being the predominant residue. However, ethofumesate metabolised rather quickly and an increasing amount of polar components (a polar fraction that was eluted with the solvent front in reversed phase chromatographic systems or was not resolved from the origin in normal phase TLC) was detected with time, besides metabolites NC 8493 and NC 20645. Minor amounts of metabolite NC 9607 were also detected in several samples. The amount of metabolite NC 8493 decreased with time, indicating a further degradation/conjugation. Vigorous acidic treatment (3 M or 6 M HCl) of the extracts or the polar fraction

itself showed that the polar compounds were acid-labile and were transformed to discrete known moieties (NC 8493 and NC 9607). Thus, the polar fraction was assigned to conjugates of the metabolites NC20645 (the carboxy analogue to metabolite NC 9607) and NC 8493. Under the acidic conditions of the hydrolysis, metabolite NC 20645 is immediately converted to metabolite NC 9607. Overall, the plant metabolism studies showed that all crops under investigation followed the same metabolic path. Final residues were always dominated by a polar fraction. The polar fraction was acid labile and could be converted to the common moiety NC 9607 (major amount) and metabolite NC 8493 by vigorous treatment with hydrochloric acid. Since ethofumesate itself is also acid-labile under these vigorous conditions (decomposition to NC 8493 is possible), parent compound should be separated (e.g. by partitioning with dichloromethane) before the acidic treatment. Since major amounts of metabolite NC 8493 were only detected in intermediate growth stages it is not necessary to include this metabolite in the residue definition for mature crops, as well as its conjugate which was always a minor metabolite. Thus with parent compound ethofumesate and the common moiety NC 9607 form the relevant residue for ethofumesate in mature crops. Since the common moiety NC 9607 and NC 20645 are interconvertible, the pH value in the final extract determines which of the compounds the analytical target is.

Conclusion on metabolism in primary crops

Plant metabolism was investigated in two crop groups have shown that there is extensive metabolism of ethofumesate in plants from both pre- and post-emergence uses. No significant quantities of uncharacterised or unidentified metabolites have been found. Although the route of metabolism of ethofumesate in all crops investigated is very similar it has to be pointed out that the definition of residue can be established for root crops only as the metabolism conducted on ryegrass gives no information on the metabolism in cereal grains. The metabolism of ethofumesate in plants is also very similar to that observed in livestock and rats.

Figure 1 Proposed metabolic pathway of ethofumesate in primary crops



(R = unknown conjugate)

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data submitted in the framework of this application.

Table 7.2-4: Summary of metabolism studies in rotational crops

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Leafy vegetables	Cabbage	[^{14}C-benzene]	G	4.6 kg a.s/ha	3,9 and 12 months	At maturnity		Carlton, R.; Cordell, P. 1993

	Spinach			1 kg a.s/ha	30,	77, 98		Chapleo, S., 2003
Root and tuber vegetables	Radish	[^{14}C-benzene]-	G	4.6 kg a.s/ha	3,9 and 12 months	At maturnity		Carlton, R.; Cordell, P. 1993
	Carrots			1 kg a.s/ha	30	95, 133		Chapleo, S., 2003
Pulses and oilseeds	French beans	[^{14}C-benzene]-	G	1 kg as/ha	30	77, 109		Chapleo, S., 2003
Cereals	Wheat	[^{14}C-benzene]-	G	4.6 kg a.s/ha	5,9 and 12 months	At maturnity		Carlton, R.; Cordell, P. 1993
	ryegrass			1 kg a.s/ha	30	84, 132		Chapleo, S., 2003

* Outdoor/field application (F) or glasshouse/protected/indoor application (G)

Summary of plant metabolism studies reported in the EU

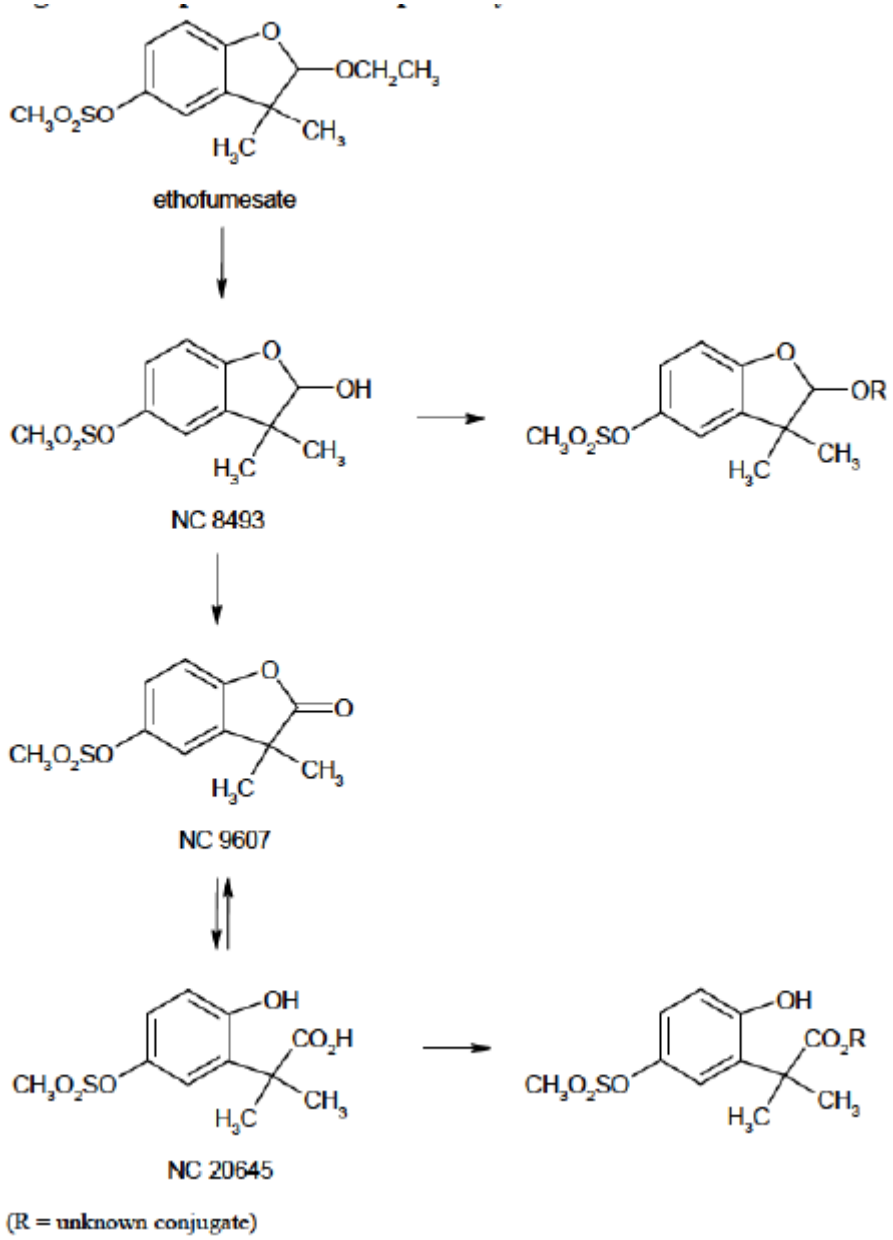
Based on the results of rotational study it can be concluded that the nature of residues in rotational crops is similar to that in primary crops.
Based on the metabolites indentified in following crops , the following metabolic routes were deduced:

- Cleavage oft he ethocy side chaing, with hydroxylation at the 2 postition to give NC 8493
- NC 8493 can either undergo conjugation to give polar metabolites or oxidation tot he lactone NC 9607
- The lactone ring of NC 9607 opens tot he carboxy analogne NC 20645 which can also undergo conjugation to give polar metabolites

The metabolic routes detected are in line with those observed in primary crops. On the basis of these results it can be concluded that the metabolism of (14C]-ethofumesate in confined rotational crops followst he same metabolic path as primary crops.

Conclusion on metabolism in rotational crops

The metabolic routes detected are in line with those observed in primary crops. On the basis of these results it can be concluded that the metabolism of (14C]-ethofumesate in confined rotational crops follows the same metabolic path as primary crops.



7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

No new data submitted in the framework of this application.

Table 7.2-5: Nature of the residues in processed commodities

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
EU data		
Pasteurisation (20 minutes, 90°C, pH 4)	98.6% ethofumesate	Miebach, D.; Bongartz, R.;2010
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	99.3% ethofumesate	Miebach, D.; Bongartz, R.;2010

Conditions (Duration, Temperature, pH)		Identified compound(s) (%)	Reference
Sterilisation (20 minutes, 120°C, pH 6)		100% ethofumesate	Miebach, D.; Bongartz, R.;2010
Other conditions	**Identified compound(s) (%)**		
industrial process of sugar production	97.6% etofumesate		Miebach, D.; Bongartz, R.;2010

Conclusion on nature of residues in processed commodities

The test compound ethofumesate was stable under all conditions of high temperature hydrolysis for simulation of food processing. No significant hydrolysis products of ethofumesate (≤ 2.1%) were detected above an estimated LOD of 0.7% of the total radioactivity

zRMS comments:
Hydrolysis products were detected in a range between 0.7 and 2.1%. They were not further investigated, due to their low amount in the test solutions (EFSA Journal 2016;14(1):4374).

7.2.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.2-6: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Root and tuber vegetables (sugarbeet, oinion) Cereals (ryegrass) Leafy crops (tobacco)
Rotational crops covered	Root/tuber crops (radish, carrots) Leafy crops (cabbage, spinach) Cereals (wheat, ryegrass) Pulses (French beans)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	a.s. is stable under standard hydrolysis conditions
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes
Plant residue definition for monitoring	Sum of ethofumesate, ethofumesate-lactone (NC 9607), ethofumesate-carboxylic acid (NC 20645) and its conjugate, expressed as ethofumesate (EFSA Journal 2016;14(1):4374_
Plant residue definition for risk assessment	Sum of ethofumesate, ethofumesate-lactone (NC 9607), ethofumesate-carboxylic acid (NC 20645) and its conjugate, expressed as ethofumesate (EFSA Journal 2016;14(1):4374)
Conversion factor from enforcement to RA	1 (EFSA Journal 2016;14(1):4374)

* If residue pattern in processed commodities is not similar to that in raw commodities
** A more recent proposal by EFSA may be provided as additional information (EFSA RO XXXX).
*** If no EFSA proposal is available, a proposal should be made by the applicant/zRMS.

7.2.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data

No new data submitted in the framework of this application.

Table 7.2-7: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data								
Lactating ruminants	Cow	[14C-benzene]	1	0.3-0.36	7	Milk	twice daily	EFSA Journal 2016;14(1):4374
						Urine and faeces	Day 1 and 7	
						Tissues	at sacrifice	
				5	4	Milk	twice daily	
						Urine and faeces	daily	
						Tissues	at sacrifice	
	Sheep	[14C-benzene]	1	0.2	1	Milk	Not analysed	
						Urine and faeces	daily	
						Tissues	at sacrifice (4 days after dosing)	
Laying poultry	Hens	[14C-benzene]	6	0.6	14	Eggs	Daily	EFSA Journal 2016;14(1):4374
						Excreta	Daily	
						Tissues	At sacrifice	
			13	0.78	10	Eggs	Twice daily	
						Excreta	Daily	
						Tissue	After sacrifice	

Summary of plant metabolism studies reported in the EU

In egg yolks and whites, residue levels of ethofumesate were detectable 24 hours after the initial dose administration, with residue levels in egg yolks continuing to rise to reach a plateau by day

8 of dosing at a concentration of 0.019 ± 0.001 mg/kg. The residue level in egg whites was an order of magnitude lower, with a maximum concentration of 0.002 mg/kg seen on day 5 of dosing. In undeveloped eggs (eggs of ovary and oviduct), the mean concentration of ethofumesate-derived residue was 0.024 ± 0.003 mg/kg. Residue levels of ethofumesate and/or its metabolites in the edible tissues of the hen were low, with the highest concentration seen in the liver (0.095 ± 0.034 mg/kg). Residues in skin and abdominal fat were lower at 0.020 ± 0.006 mg/kg and 0.019 ± 0.003 mg/kg respectively. Subcutaneous fat levels were also low, at 0.016 ± 0.003 mg/kg. Skeletal muscle levels were the lowest of the edible tissues at 0.007 ± 0.005 mg/kg. Thus transfer of radioactivity into edible tissues is very low. Following administration of the first dose of ethofumesate, elimination of the radioactivity was rapid with >80% of the recovered radioactivity excreted within twenty-four hours. Ethofumesate was present in all tissues and was the major residue identified in egg yolk, fat and skin. NC 20645 (the carboxy analogue of NC 9607) was the major residue identified in the muscle and liver and was also present in the skin and egg yolk. NC 9607 (the lactone) was present in all tissues; the hydroxy derivative NC 8493 was present at low levels in the muscle. A polar fraction (probably containing conjugates of the known metabolites) and some unidentified metabolites were also determined at very low levels. Based on the metabolites identified in edible tissues, the following metabolic routes were deduced:

- Cleavage of the ethoxy side chain, with hydroxylation at the 2 position, to give NC 8493.
- NC 8493 can undergo oxidation to the lactone NC 9607.
- The lactone ring of NC 9607 can open to form the carboxy analogue NC 20645

Following dosing of [14C-benzene]-ethofumesate at a dose rate of 2.94 g per day (equivalent to 274 mg/kg in the diet) for four consecutive days, the mean combined daily recovery for urine and faeces was 60.95 ± 20.66%. Elimination occurred predominantly via the urine. The single component identified in the urine was the water soluble carboxylic acid NC 20645. The tissue residues of ethofumesate ranged from 0.033 mg/kg in the muscle to 1.863 mg/kg in the kidney. In most tissues the major component seen was unchanged parent compound with the metabolites NC 20645, NC 8493 and NC 9607 detected in smaller quantities. However in the kidney, the major metabolite seen was the highly water soluble metabolite NC 20645 which was readily excreted. Residue levels in milk reached a maximum of 0.134 mg/kg at 32 hours post-administration of the initial dose. The main compound identified was parent compound followed by NC 20645. The other metabolites identified were NC 8493 and NC 9607 each accounted for less than 10% of the residue. In blood and plasma residues reached a maximum (0.477 and 0.602 mg/kg, respectively) at 32 hours h after the first dosing. Overall, the transfer of ethofumesate related residues in tissues and milk was low. Highest radioactivity concentrations were detected in the metabolising organs kidney and liver. Based on the metabolites indentified in edible tissues and milk, the followin metabolic routes were proposed:

- Cleavage of the ethoxy side chain with hydroxylation at the 2 position to give NC 8493
- NC 8493 cand undergo oxidation tot he lactone NC 9607
- The lactone ring of NC 9607 can open to form the carboxy analogue NC 20645

Conclusion on metabolism in livestock

Figure 2 Proposed metabolic pathway for ethofumesate in poultry

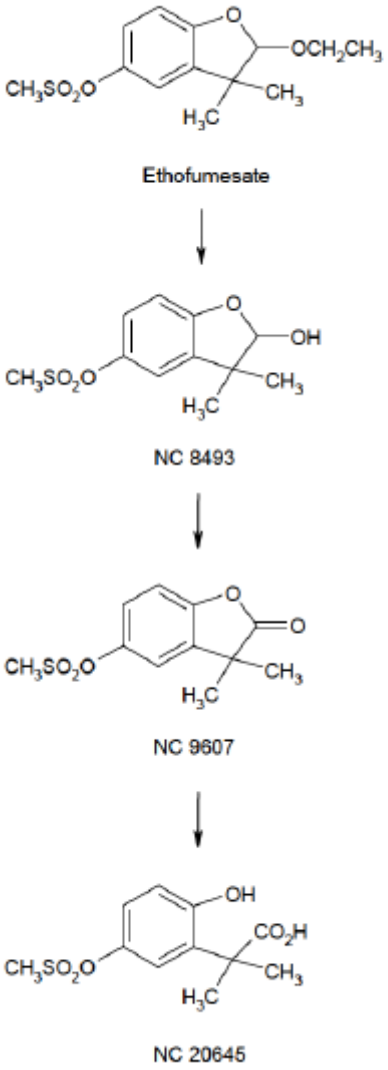
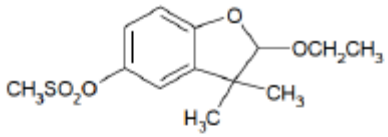
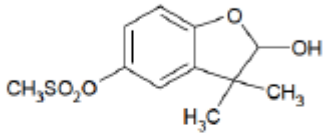


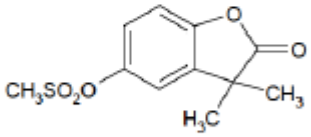
Figure 3 Proposed metabolic pathway for ethofumesate in ruminants



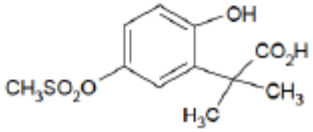
Ethofumesate



NC 8493



NC 9607



NC 20645

7.2.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.2-8: Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	Lactating Cow and ~~sheep~~ goat
	Laying hens
Time needed to reach a plateau concentration	32 hours in milk
	9 days in eggs
Animal residue definition for monitoring	Sum of ethofumesate, ethofumesate-lactone (NC 9607), ethofumesate-carboxylic acid (NC 20645) and its conjugate, expressed as ethofumesate (EFSA Journal 2016;14(1):4374)
Animal residue definition for risk assessment	Sum of ethofumesate, ethofumesate-lactone (NC 9607), ethofumesate-carboxylic acid (NC 20645) and its conjugate, expressed as ethofumesate (EFSA Journal 2016;14(1):4374)

Conversion factor	1 (EFSA Journal 2016;14(1):4374)
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	NO

* A more recent proposal by EFSA may be provided as additional information (EFSA RO XXXX)
** If no EFSA proposal is available, a proposal should be made by the applicant/zRMS.
*** If metabolism in rat and ruminant are not similar

7.2.3 Magnitude of residues in plants (KCA 6.3)

7.2.3.1 Summary of European data and new data supporting the intended uses

No new data are submitted in the framework of this application.

Table 7.2-9: Summary of EU reported and new data supporting the intended uses of CHR/H/ETO 500 SC and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Sugar beet	EFSA Journal 2016;14(1):4374	N-EU	GAP on which MRL/EU a.s. assessment is based: ~~3 x 0.33 kg as/ha, BBCH 0, outdoor~~ 1 x 1000 g a.s./ha, post-emergence, PHI n.a. E/RA: 8x<0.02, 15x<0.06, 0.06, 0.09, 11x<0.1	N/A				
	Overall supporting data for cGAP	N-EU	E/RA: 8x<0.02, 15x<0.06, 0.06, 0.09, 11x<0.1	<0.06	<0.1	0,183	0.2	Yes/No
Sugar beet leaves	EFSA Journal 2016;14(1):4374	N-EU	GAP on which MRL/EU a.s. assessment is based~~: 3 x 0.33 kg as/ha, BBCH 0, outdoor~~ 1 x 1000 g a.s./ha, post-emergence, PHI n.a. E/RA: 8x<0.02, 11x<0.06, 0.06, 0.07, 9x0.1, <0.12, 0.18	N/A				
	Overall supporting data for cGAP	N-EU	E/RA: 8x<0.02, 11x<0.06, 0.06, 0.07, 9x0.1, <0.12, 0.18	<0.06	0.18	0,217	MRL proposed 0.3	Yes/No

* Source of EU MRL: Regulation (EU) 2017/1016

7.2.3.2 Conclusion on the magnitude of residues in plants

According to the available data, the intended uses on sugarbeet are considered acceptable, for both outdoor uses.

The data submitted show that no exceedance of the MRL will occur.

The uses are considered acceptable.

zRMS comments:

Residue data have been evaluated at Community level. The Applicant did not provide any additional data. Considering that the GAP proposed for CHR/H/ETO 500 SC on sugar beet is not more critical than accepted at Community level, the presented in the Table 7.2-9 data should be considered sufficient.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

According to the EFSA Journal 2016;14(1):4374 and RAR Ethofumesate, Volume 3 – B.7 (AS) no new dietary burden calculation are necessary:

Table 7.2-10: Input values for the dietary burden calculation (considering the uses evaluated in Art. 12 procedure and the uses under consideration)

Inputs for animal burden calculations

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
		Representative uses		
Sugar / fodder beet root	0.06		0.1	
Sugar / fodder beet tops	0.06		0.18	
Sugar beet, dried pulp	0.35	value estimated based on the residue in sugar beet root (dry matter (DM) = 15) and the DM of 88 for dried pulp		
Sugar beet, ensiled pulp	**0.06**	**value estimated based on the residue in sugar beet root (dry matter (DM) = 15) and the DM 15 for ensiled pulp**		
molasses	**0.76**	**median processing factor of 12.7 for molasses was applied**		
Cereal, forage	**0.03**	**rotational crops**	**0.03**	**rotational crops**
Root crops, root	**0.04**	**rotational crops**	**0.05**	**rotational crops**

Table 7.2-11: Results of the dietary burden calculation

MRL calculations	**Ruminant**				**Pig/Swine**		**Poultry**		**Fish**	
Highest expected intake (mg/kg bw/d)	Beef cattle	0.012	Ram/Ewe	0.016	Breeding	0.009	Broiler	0.004	Carp	
	Dairy cattle	0.019	Lamb	0.020	Finishing	0.008	Layer	0.006	Trout	
(mg/kg DM for fish)							Turkey	0.004	Fish intake >0.1 mg/kg DM	
Intake >0.004 mg/kg bw	Yes/No		Yes/No		Yes/No		Yes/No		Yes/No	
Feeding study submitted	submitted feeding studies did not fulfil EU requirements; transfer factors were calculated from ruminant metabolism studies; no residues above 0.01 mg/kg are expected in animal tissues						submitted feeding studies did not fulfil EU requirements; transfer factors were calculated from poultry metabolism studies no residues above 0.01 mg/kg are expected in animal tissues		no agreed guidance available; no studies submitted	
Representative feeding level (mg/kg bw/d, mg/kg DM for fish) and **N rates**	Level	Dairy: N	Level	Lamb: N Ewe: N	Level	N rate Breed/Finish	Level	I Layer: N	Level	N rate Carp/Trout
	Estimated HR[a] at 1N	**MRL** proposals	Estimated HR[a] at 1N	**MRL** proposals	Estimated HR[a] at 1N	**MRL** proposals	Estimated HR[a] at 1N	**MRL** proposals	Estimated HR[a] at 1N	**MRL** proposals
Muscle										
Fat										
Meat[b]										
Liver										
Kidney										
Milk[a]										
Eggs										
Method of calculation[c]										

[a]: Estimated HR calculated at 1N level (**estimated mean level for milk**).
[b]: HR in meat calculated for mammalian on the basis of 20% fat + 80% muscle and 10% fat + 90% muscle for poultry
[c]: The OECD guidance document on residues in livestock (series on pesticides 73) recommends three different approaches to derive MRLs for animal products; by applying a transfer factor (Tf), by intrapolation (It) or by linear regression (Ln). Fill in method(s) considered to derive the MRL proposals.

STMR calculations	Ruminant				Pig/Swine		Poultry		Fish	
Median expected intake (mg/kg bw/d)	Beef cattle	0.009	Ram/Ewe	0.011	Breeding	0.007	Broiler	0.003	Carp	
	Dairy cattle	0.013	Lamb	0.014	Finishing	0.007	Layer	0.004	Trout	
(mg/kg DM for fish)							Turkey	0.003		
Representative feeding level (mg/kg bw/d, mg/kg DM for fish) and **N rates**	Level	Beef: N Dairy: N	Level	Lamb : N Ewe: N	Level	N rate Breed/Finish	Level	B or T: N Layer: N	Level	N rate Carp/Trout
	Mean level in feeding level	Estimated **STMR**[b] at 1N	Mean level in feeding level	Estimated **STMR**[b] at 1N	Mean level in feeding level	Estimated **STMR**[b] at 1N	Mean level in feeding level	Estimated **STMR**[b] at 1N	Mean level in feeding level	Estimated **STMR**[b] at 1N
Muscle										
Fat										
Meat[a]										
Liver										
Kidney										
Milk										
Eggs										
Method of calculation[c]										

[a]: STMR in meat calculated for mammalian on the basis of 20% fat + 80% muscle and 10% fat + 90% muscle for poultry
[b]: When the mean level is set at the LOQ, the STMR is set at the LOQ.
[c]: The OECD guidance document on residues in livestock (series on pesticide 73) recommends three different approaches to derive MRLs for animal products; by applying a transfer factor (Tf), by intrapolation (It) or by linear regression (Ln). Fill in method(s) considered to derive the MRL proposals.

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Not required, because no residue above 0.01 mg/kg are expected in animal tissues.

zRMS comments:
According to the EFSA Journal 2016;14(1):4374: *Based on the metabolism studies, it is also concluded that significant residues in animal commodities are not expected, considering livestock exposure linked to the representative uses.* Additional studies/calculations are not required.

7.2.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

7.2.5.1 Available data for all crops under consideration

No new data were submitted in the framework of this application.

Table 7.2-12: Overview of the available processing studies

Processing factors (Regulation (EU) N° 283/2013, Annex Part A, points 6.5.2 and 6.5.3)
OECD Guideline 508 and OECD Guidance, series on testing and assessment No 96

Crop (RAC)/Edible part or Crop (RAC)/Processed product	Number of studies[a]	Processing Factor (PF)		Conversion Factor (CF_P) for RA [b]
		Individual values	Median PF	
Representative uses				
Sugarbeet/Sugar	4	0.1-0.3	0.20	
Sugarbeet/Molasses	4	6-24	12.7	
Sugarbeet/Wet pulp	3	0.2-0.4	0.2	
Sugarbeet/Thick juice	5	4-6.5	4.7	
Sugarbeet/Thin (raw) juice	5	0.5-1.9	1.1	

[a]: Studies with residues in the RAC at or close to the LOQ should be disregarded (unless concentration)
[b]: When the residue definition for risk assessment differs from the residue definition for monitoring

* The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.
** The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

7.2.5.2 Conclusion on processing studies

The total theoretical maximum daily intake (TMDI) of ethofumesate related residues is less than 10% of the ADI when calculating with the STMR values from the supervised field trials. As a conclusion, processing studies are generally not needed for crops treated with ethofumesate according to the intended use pattern. Nevertheless, several processing studies were conducted to support the Annex I inclusion of ethofumesate. These studies demonstrated that ethofumesate related residues were never present in refined sugar indicating that probable residues in the raw agricultural commodity are efficiently eliminated during processing. A concentration of the residue was detected in molasses (maximum and median processing factor was 24 and 12.7, respectively) and in thick juice (maximum and median processing factor was 6.5 and 4.7, respectively). The studies were submitted and evaluated during the Annex I inclusion process and were considered acceptable. Therefore, no additional data was considered necessary.

zRMS comments:
Taking into account that the level of residues in sugar beet roots does not exceed 0.1 mg/kg and TMDI is below 10 % of the ADI (no ARfD derived), there is no need to investigate the effect of processing.

7.2.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation.

Considering available data dealing with nature of residues (see 7.2.2.2), no study dealing with magnitude of residues in succeeding crops is needed.
Data dealing with magnitude of residues in succeeding crops are available/have been submitted and are summarized hereafter.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

Available data

No new data submitted in the framework of this application.

Table 7.2-13: Summary of available studies in field rotational crops

Confined rotational crop study (Quantitative aspect) **OECD Guideline 502**	Additionally to the already evaluated confined rotational crop study on cabbage, radish and wheat; an additional study on carrots, spinach, ryegrass and French bean was submitted (PBI: 30 days). It was concluded that metabolic patterns in primary and succeeding crops are similar, but residues in succeeding crops could not be excluded.
Field rotational crop study **OECD Guideline 504**	Additionally to the already submitted studies, two rotational crop field studies were submitted. The highest total residues of ethofumesate in rotational root crops; detectable residues were only found as ethofumesate; Residues of ethofumesate were only detected in root crops, leafy crops and cereal forage of the first rotation. Highest total residues accounted for - 0.05 mg/kg in root crops - 0.03 mg/kg in leafy crops - 0.03 mg/kg in cereal forage. The only residue detected above the LOQ of 0.01 mg/kg was ethofumesate, the residues of the common moiety NC 9607 were always below the LOQ of 0.01 mg/kg.

zRMS comments:
Residues in succeeding studies have been evaluated at Community level. In these studies after application of 1 kg a.s./ha on sugar beet residues of ethofumesate were detected in the crops of the first rotation (PBI 25-33 days). Replanting of root and leafy crops could lead to measurable residues in edible plant parts. Therefore it is proposed to set risk mitigation measures to avoid residues in succeeding crops in the case of crop failure. In the label, the Applicant proposed the following entry:
If it is necessary to liquidate a plantation treated with CHR/H/ETO 500 SC, as a result of damage to plants by frosts, diseases, pests (or for any other reason), in this field after 30 days and carrying out deep plowing (20 cm), sugar beet can be grown. Winter cereals can be sown after at least 5 months. Other plants can be grown approximately 3 months after the last treatment.
None, apart from those specified by the Applicant, additional mitigation measures are required.

7.2.7 Other / special studies (KCA6.10, 6.10.1)

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of CHR/H/ETO 500 SC. Therefore, other special studies are not needed.

zRMS comments;
According to the Appendix II to SANTE/11956/2016 rev. 9 sugar beet should not be considered a melliferous crop unless it is grown for seed. The proposed use is not for seed production and therefore no residue studies in honey are required.

7.2.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

As ARfD was not deemed necessary, acute risk assessment is not relevant.

7.2.8.1 Input values for the consumer risk assessment

Table 7.2-14: Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue				
Beetroot	0.2	Regulation (EU) 2017/1016	0.2	Regulation (EU) 2017/1016
Sugabeet root	0.2	Regulation (EU) 2017/1016	0.2	Regulation (EU) 2017/1016
Chard/beet leaves	0.3	Regulation (EU) 2017/1016	0.3	Regulation (EU) 2017/1016

7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

Table 7.2-15: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo	0.2 % (based on NL child)
IEDI (% ADI) according to EFSA PRIMo	0.2 % (based on NL child)
IESTI (% ARfD) according to EFSA PRIMo*	N/R

* include raw and processed commodities if both values are required for PRIMo
** if national model is available

The proposed uses of ethofumesate in the formulation CHR/H/ETO 500 SC do not represent unacceptable acute and chronic risks for the consumer.

zRMS comments:
In addition consumer risk assessment (chronic) was calculated using EFSA PRIMo rev. 3.1 for all MRLs in force (Reg.(EU) 2017/1016) (overestimated).

European Food Safety Authority
EFSA PRIMo revision 3.1; 2019/03/19

Ethofumesate

LOQs (mg/kg) range from: 0,03 to: 0,10

Toxicological reference values

ADI (mg/kg bw/day):	1	ARfD (mg/kg bw):	insert valid entry
Source of ADI:	EFSA	Source of ARfD:	
Year of evaluation:	2016	Year of evaluation:	

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment | Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
	0,5%	NL toddler	4,74	0,2%	Milk: Cattle	0,1%	Sugar beet roots	0,0%	Apples	0,4%	
	0,3%	NL child	3,46	0,2%	Sugar beet roots	0,1%	Milk: Cattle	0,0%	Apples	0,2%	
	0,2%	FR child 3 15 yr	2,32	0,1%	Sugar beet roots	0,1%	Milk: Cattle	0,0%	Wheat	0,1%	
	0,2%	DE child	2,29	0,1%	Milk: Cattle	0,0%	Apples	0,0%	Mate/maté	0,2%	
	0,2%	FR toddler 2 3 yr	2,23	0,1%	Milk: Cattle	0,1%	Sugar beet roots	0,0%	Apples	0,2%	
	0,2%	DE women 14-50 yr	2,13	0,1%	Sugar beet roots	0,0%	Milk: Cattle	0,0%	Hybiscus/roselle	0,1%	
	0,2%	UK infant	2,07	0,1%	Milk: Cattle	0,0%	Sugar beet roots	0,0%	Potatoes	0,2%	
	0,2%	DE general	1,97	0,1%	Sugar beet roots	0,0%	Milk: Cattle	0,0%	Hybiscus/roselle	0,1%	
	0,2%	UK toddler	1,89	0,1%	Sugar beet roots	0,1%	Milk: Cattle	0,0%	Wheat	0,1%	
	0,1%	GEMS/Food G06	1,48	0,0%	Sugar beet roots	0,0%	Wheat	0,0%	Tomatoes	0,1%	
	0,1%	NL general	1,41	0,1%	Sugar beet roots	0,0%	Milk: Cattle	0,0%	Potatoes	0,1%	
	0,1%	GEMS/Food G11	1,37	0,0%	Milk: Cattle	0,0%	Potatoes	0,0%	Soyabeans	0,1%	
	0,1%	RO general	1,37	0,0%	Milk: Cattle	0,0%	Sugar beet roots	0,0%	Wheat	0,1%	
	0,1%	GEMS/Food G07	1,35	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	Mate/maté	0,1%	
	0,1%	GEMS/Food G15	1,25	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	Potatoes	0,1%	
	0,1%	GEMS/Food G08	1,23	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	Potatoes	0,1%	
	0,1%	GEMS/Food G10	1,23	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	Soyabeans	0,1%	
	0,1%	DK child	1,23	0,0%	Milk: Cattle	0,0%	Rye	0,0%	Wheat	0,1%	
	0,1%	ES child	1,18	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	Oranges	0,1%	
	0,1%	SE general	1,18	0,0%	Milk: Cattle	0,0%	Bovine: Muscle/meat	0,0%	Potatoes	0,1%	
	0,1%	FR infant	1,18	0,1%	Milk: Cattle	0,0%	Sugar beet roots	0,0%	Potatoes	0,1%	
	0,1%	IE adult	1,09	0,0%	Milk: Cattle	0,0%	Sweet potatoes	0,0%	Wheat	0,1%	
	0,1%	FR adult	0,80	0,0%	Sugar beet roots	0,0%	Milk: Cattle	0,0%	Wine grapes	0,1%	
	0,1%	FI adult	0,78	0,1%	Coffee beans	0,0%	Potatoes	0,0%	Rye	0,1%	
	0,1%	ES adult	0,68	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	Oranges	0,1%	
	0,1%	PT general	0,63	0,0%	Potatoes	0,0%	Wheat	0,0%	Wine grapes	0,0%	
	0,1%	FI 3 yr	0,55	0,0%	Potatoes	0,0%	Bananas	0,0%	Wheat	0,0%	
	0,1%	UK vegetarian	0,54	0,0%	Sugar beet roots	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	
	0,1%	IT toddler	0,53	0,0%	Wheat	0,0%	Other cereals	0,0%	Tomatoes	0,0%	
	0,1%	UK adult	0,51	0,0%	Sugar beet roots	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	
	0,1%	LT adult	0,51	0,0%	Milk: Cattle	0,0%	Potatoes	0,0%	Apples	0,0%	
	0,0%	DK adult	0,50	0,0%	Milk: Cattle	0,0%	Potatoes	0,0%	Wheat	0,0%	
	0,0%	FI 6 yr	0,44	0,0%	Potatoes	0,0%	Wheat	0,0%	Bananas	0,0%	
	0,0%	IT adult	0,42	0,0%	Wheat	0,0%	Tomatoes	0,0%	Apples	0,0%	
	0,0%	PL general	0,33	0,0%	Potatoes	0,0%	Apples	0,0%	Beetroots	0,0%	
	0,0%	IE child	0,24	0,0%	Milk: Cattle	0,0%	Wheat	0,0%	Potatoes	0,0%	

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of Ethofumesate is unlikely to present a public health concern.

Results indicated the highest estimate of chronic dietary intake is 0.5 % of the ADI (NL toddler).

The proposed uses of ethofumesate in the formulation CHR/H/ETO 500 SC do not represent unacceptable acute and chronic risks for the consumer.

7.3 Combined exposure and risk assessment

From a scientific point of view it is regarded necessary to take into account potential combination effects. However, the evaluation of cumulative or synergistic effects as requested by Art. 4 (3b) of Regulation (EC) No. 1107/2009 should only be performed when harmonised "scientific methods accepted by the Authority to assess such effects are available."
Currently, no EU-harmonized guidance is available on the risk assessment of combined exposure to multiple active substances; this approach is not mandatory at EU level.

Not relevant. The product contains only one active substance.

Appendix 1 Lists of data considered in support of the evaluation

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
KCA 6.1/01	Whiteoak, R. J.	1991	Stability of ethofumesate and NC 9607 residues in sugabeet roots and tops during deep freeze storage Report No,: A83111, Reporst includes Trial Nos.: 041/02.001, Edition number: M-155386-01-1 Schering AG, Berlin Germany GLP Unpublished	N	Bayer CropScience
KCA 6.1/02	Cole, M.G.	1995	Ethofumesate: Stability of ethofumesate, NC 9607 and NC 8493 in Grass during frozen storage, usa, 1993 Report No.: A54281, Edition number: M-134863-01-1 Hoechst NOR-AM AgrEvo Inc., USA GLP Unpublished	N	Bayer CropScience
KCA 6.1/03	Schulte, G.	2013	Storage stability of open-ring-2-keto ethofumesate (AE C520645) in plant matrices for 24 month – interim report Report No.: M-13/086, Edition Number: M-459806-01-1 GLP Unpublished	N	Task Force ethofumesate
KCA 6.1/04	Schulte, G.	2015	Storage stability of open-ring-2-keto ethofumesate (AE C520645) in plant matrices for 24 month – interim report Report No.: M-12/058, Bayer CropScience AG, Research & Development -Development - Human Safety – Residue Analysis, Monheim am Rhein, Germany GLP Unpublished	N	Task Force ethofumesate
KCA 6.1/07	Perez, R.; Schmitt, J.L., Patel, D.	2014	Freezer storage stability of ethofumesate in animal matrix samples – interim report Report No.: RAADP031, Edition number: M-467206-02-1 ADPEN Laboratories, INC, Jacksonville, FL, USA Bayer CropScience GLP yes	Y	Task Force Ethofumesate

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
			Unpublished		
KCA 6.2.1/01	Miller, C.	1999	Summary of the metabolism of ethofumesate in plants Ethofumesate AE B049913 Report No.: C003349, Edition Number: M-185979-01-1 AgrEvo UK Crop Protection Ltd., Chesterford Park, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.2.1/02	Adcock, J. W. Warner, P. A. Challis, I. R.	1976	The metabolism of 14C-ethofumesate in the onion Report No.: A82959, Edition Number: M-155236-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.2.1/03	Warner, P. A.; Adcock, J. W.	1977	Metabolism of ethofumesate in tobacco Report No.: A82963, Edition Number: M-155240-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.2.1/04	Lines, D. S. Adcock, J. W.	1979	The metabolism of ethofumesate (98% pure 14C-ethofumesate) by sugar beet under field conditions Report No.: A82965, Edition Number: M-155242-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.2.1/05	Chapleo, S.	1992	The metabolism of [14C]-ethofumesate in sugar beet – a glasshouse study Report No: A82970, Report includes Trail Nos.: 381175, ENVIR 84B, Edition Number: M-155247-01-1 GLP Unpublished	N	Bayer CropScience

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
KCA 6.2.1/06	Caley, C. U.; Chapleo, S.; Haswell, A.	1994	The metabolism of 14-C ethofumesatu in sugar beet Report No.: A87553, Report includes trial Nos.: 382445, Edition Number: M-161455-01-1 Inveresk Research Int. Ltd, Tranent, Scotlant Bayer CropScience GLP Unbpulished	N	Bayer CropScience
KCA 6.2.1/07	Chapleo, S.	1992	The maetabolism of [14C]-ethofumesate in annual ryegrass – a glasshouse study Report No.: A82971, Report includes Trail Nos.: 381169, ENVIR 85B, Edition Number: M-155248-01-1 Inveresk esearch INT. LTD, Tranent, Scotland Bayer CropScience GLP Unpublished	N	Bayer CropScience
KCA 6.2.1/08	Mellet, M.	1993	Determination of the residues of ethofumesate, ethofumesate-2-keto and the conjugates in sugar beets after application of Ethosat 500 SC in France, 1992 Report No.: M-468491-01-1, Report includes Trial Nos.: 92HBEBI01, 92HBEBI06, Edition Number: M-468491-01-1 ANADIAG S.A, Haguenau, Frnce Feinchemie Schebda GLP Unpublished	N	Adama
KCA 6.2.2/01		1992	The metabolism of 14C ethofumesate in laying hens Report No.: A82969, Report includes Trial Nos.: SMS 297/920431, TOX 90542, Edition Number: M-155246-01-1 Bayer CropScience GLP Unpublished	Y	Bayer CropScience
KCA 6.2.2/02		1999	Poultry – Metabolism, Distribution and anture of the residues in eggs and edible tissues Code AE B049913 Report No.: C002998, Report includes Trail Nos.: Tox97227, Edition Number: M-185380-01-1 Bayer CropScience	Y	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			GLP Unpublished		
KCA 6.2.2/03		1976	The metabolism of 14C-ethofumesate in the sheep Report No.: A82958, Edition Number: M-155235-01-1 Bayer CropScience GLP No Unpublished	Y	Bayer CropScience
KCA 6.2.2/04		1992	The metabolism of 14C-ethofumesate in the cow Report No.: A82968, Report includes Trial Nos.: SMS 296/920441, TOX 90541, Edition Number: M-155245-01-1 Huntingdon Research Centre Ltd, Bayer CropScience GLP Unpublished	Y	Bayer CropScience
KCA 6.2.2/05		1999	Metabolism, distribution and nature of the residues in milk and edible tissues ethofumesate ruminant Code: AE B049913 Report No.: C003362, Report includes Trial Nos.: TOX97226, Edition Number: M-185993-01-1 Bayer CropScience GLP no Unpublished	Y	Bayer Crop Science
KCA 6.3/01	Crofts, M.	1976=5	Residues in fodder beet and red beet from 1974 applications of nortron in the UK Report No.: A83007, Edition Number: M-155284-01-1, EPA MRID No.: 41214220 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.3/02	Crofts, M. Whiteoak, R. J.	1976	Residues in mangolds, fodder beet and red beet from 1975 and 1976 applications of nortron in the UK (and 1 red beet trial in sweden) Report No.: A83020, Edition Number: M-155297-01-1, EPA MRID No.: 41214219 Fisons plc, United Kingdom	N	Bayer Crop Science

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
			Bayer CropScience GLP no Unpublished		
KCA 6.3/03	Crofts, M.	1978	Harvest Residues in red beet from nortron trials in the usa (new york, texas and wisconsin) in 1976/77 Report No.: A83036, Edition number: M-155313-01-1, EPA MRID No.: 41214219 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.3/04	Crofts, M.	1978	Harvest residues in red beet from a nortron trial in canada in 1997 Report No.: A83039, Edition Number: M-155316-01-1, EPA MRID No.: 41214233 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.3/05	Wrede, A.	1995	Residues in red beet after application of Betanal progress in France 1993 Report No.: A83118, Report includes Trial Nos.: PF-R 93 098, Edition Number: M-155393-01-1 Hoechst Schering AgrEvo GmbH, Frankfurt am Main, Germany, Bayer CropScience GLP Unpublished	N	Bayer CropScience
KCA 6.3/06	Crofts, M. Whiteoak, R. J.	1973	Harvest residues in sugar beet (roots and leaves) from 1972 trial with nortron in the UK Report No.: A82975, Edition Number: M-155252-01-1, EPA MRID No.: acc.36374 Fisons plc, United Kingdom Bayer CropScience, GLP no Unpublished	N	Bayer CropScience
KCA 6.3/07	Crofts, M. Whiteoak, R. J.	1973	Harvest residues in suger beet (roots and leaves) from french trials with nortron in 1972 Report No.: A82976, Edition Number: M-155253-01-1, EPA MRID No.: 41214219 Fisons plc, United Kingdom	N	Bayer Cropscience

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
			Bayer CropScience, GLP no Unpublished		
KCA 6.3/08	Crofts, M. Whiteoak, R. J.	1973	Harvest residues in suger beet (roots and leaves) from danish trails with nortron in 1972 Report No.: A82977, Edition Number: M-155254-01-1, EPA MRID No.: 41214219 Fisons plc, United Kingdom Bayer CropScience, GLP no Unpublished	N	Bayer CropScience
KCA 6.3/09	Crofts M. Whiteoak, R.J.	1973	Harvest residues in sugar beet (roots and leaves) from austrian trials with nortron in 1972 Report No.: A82978, Edition Number: M-155255-01-1 Fisons plc, United Kingdom Bayer CropScience, GLP no Unpublished	N	Bayer CropScience
KCA 6.3/10	Crofts, M. Whiteoak, R. J.	1973	Harvest residues in sugar beet (roots and leaves) from 1972 trial with nortron in Yugoslavia Report No.: A82979, Edition Number: M-155255-01-1 Fisons plc, United Kingdom Bayer CropScience, GLP no Unpublished	N	Bayer CropScience
KCA 6.3/11	Whiteoak, R., J. Crofts, M.,; Harris, R. J.	1973	Residues in sugar beet (roots and leaves) from 1972 trails with notron in w. Germany (updated) Report No.: A82982, Edition Number: M-155257-01-1, EPA MRID No.: 41214220 Fisons plc., United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.3/12	Whiteoak, R.J.	1973	Residue decline studies in colorado (usa) with sugar beet treated pre-emergence with nortron in 1972 Report No.: A82982, Edition Number: M-155259-01-1, EPA MRID No.: acc. 36365 Fisons plc., United Kingdom	N	Bayer CropScience

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
			Bayer CropScience GLP no Unpublished		
KCA 6.3/13	Whiteoak, R.J. Crofts, M.	1974	Residue decline studies in michigan (usa) withi sugar beet treated pre-emergence with notron in 1972 Report No.: A82983, Edition Number: M-155260-01-1, EPA MRID: acc. 37839 Fisons plc., United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.3/14	Crofts, M. Whiteoak, R.J.	1974	Nortron residue in harvest sugar beet from nine regions of the USA in 1972 Report No.: A82986, Edition Number: M-155263-01-1, EPA MRID No.: acc.36366 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.3/15	Crofts, M. Whiteoak, R. J.	1974	Harvest Residues in sugar beet from 1973 Pre-emergence applications of nortron (tramat) in Italy Report No.: A82990, Edition Number: M-155267-01-1 Fisons plc, United Kingdom, Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.3/16	Crofts, M.; Whiteoak, R.J.	1974	Residue decline study in the UK (1973) with sugar beet treated pre-emergence with nortron Report No.: A82992, Edition Number: M-155269-01-1 Fisons plc, United Kingdom GLP no Unpublished	N	Bayer CropScience
KCA 6.3/17	Crofts, M.; Whiteoak, R.J.	1974	Harvest Residues in fodder beet From 1973 Pre-Emergence Application of nortron (tramat) in W. Germany Report No.: A82993, Edition Number: M-155270-01-1 Fisons plc, United Kingdom GLP no	N	Bayer CropScience

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
			Unpublished		
KCA 6.3/18	Crofts, M.; Whiteoak, R.J.	1974	Harverst residues in fodder beet from 1972 and 1973 post-emergence applications of nortron (tramat) in W. Germany Report No.: A82996, Edition Number: M-155273-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/19	Crofts, M.; Whiteoak, R.J.	1974	Residue decline study in the uk (1973) with sugar beet treated post-emergence with nortron Report No.: A82997, Edition Number: M-155274-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/20	Crofts, M.; Whiteoak, R. J.	1974	Harvest Residues in sugar beet from 1973 pre-emergence applications of nortron (tramat) in w. Germany Report No.: A82998, Edition Number: M-155275-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/21	Crofts, M. Whiteoak, R. J.	1974	Harvest residues in sugar beet and soil from 1973 post-emergence applications of nortron (tramat) in italy Report No.: A83290, Edition Number: M-155559-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/22	Crofts, M.; Whiteoak, R.J	1974	Harvest Residues in sugar beet from 1973 post-emergence applications of nortron in the uk Report No.: A82999, Edition Number: M-155276-01-1 Fisons plc, United Kingdom Bayer CropScience	N	Bayer CropScience

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
			GLP no, Unpublished		
KCA 6.3/23	Crofts, M.	1975	Harvest residues in sugar beet from 1974 pre-emergence applications of nortron in canada Rport No.: A83004, Edition Number: M-155281-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/24	Crofts, M.	1975	Decline in residues in sugar beet treated pre-emergence with nortron (tramat) in italy (1974) Report No.: A83005, Edition Number: M-155282-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/25	Crofts, M.	1975	Deline of residues in sugar beet treated post-emergence with nortron (tramay0 in italy (1974) Report No.: A83006, Edition Number: M-155283-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/26	Crofts, M.	1978	Harvest residues in sugar bet from pre-emergence applications of tramatt (nortron) SC formulation in w. Germany in 1976 Report No.: a83034, Edition Number: M-155311-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/27	Crofts, M.	1978	Harvest residues in sugar beet from 1977 trals with tramat (nortron) SC and EC formulations in w. Germany Report No.: A83035, Edition Number: M0155312-01-1	N	Bayer CropScience

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
			Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished		
KCA 6.3/28	Reary, J. B.	1980	Residues in mature sugar beet following pre and post-emergence application of ethofumesate (20EC) in California 1977 Report No.: A83050 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/29	Browne, P.M; Reary, J.B.	1980	Residues in sugar beet treated pre-emergence with suspension concentrate formulations (50 SC) of ethofumesate in west germany Report No.: A83053, Edition Number: M-155330-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/30	Reary, J.B.	1981	Residues of ethofumesate and metabolites in sugar beet treated pre-emergence with a suspension concentrate formulation (50 SC) of Ethofumesate in West Germany 1980 Report No.: A83059, Edition Number: M-155336-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no, Unpublished	N	Bayer CropScience
KCA 6.3/31	Haldeman, J.K. Ford, J.J.	1982	Antor and nortron herbicide residues in sugar beets from treated plots Report No.: A89134, Edition Number: M-164269-01-1 FBC Limited, Chesterford Park, United Kingdom Bayer CropScience GLP no	N	Bayer CropScience

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
			Unpublished		
KCA 6.3/32	Haldeman, J.K.	1982	Nortron Herbicide Residues in sugar beets treated pre- and post-planting Report No.: A83066, Edition Number: M-155343-01-1 Hercules Inc.; Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.3/33	Cron, J.H.	1982	Residues of Ethofumesate and metaboiltes in sgar/fodder bett treated post-emergence with Ethofumesate (50 SC) in West Germany 1981 Report No.: A83065, Edition Number: M-155342-01-1 FBC Limited, Chesterford Park, United Kingdom Bayer CropScience GLP No Unpublished	N	Bayer CropScience
KCA 6.3/34	Haldeman, J. K.	1982	Ethofumesate residues in sugar beet from two california locations Report No.: A83067, Edition Number: M-155344-01-1 FBC Limited, Chesterford Park, United Kingdom Bayer CropScience GLP No Unpublished	N	Bayer CropScience
KCA 6.3/35	Lee, G.E. Weishedel, B.C.	1984	Ethofumesate (nortron herbicide) residues in sugar beets from quebec and manitoba Report No.: A83069, Edition Number: M-155346-01-1 FBC Limited, Chesterford Park, United Kingdom Bayer CropScience GLP No Unpublished	N	Bayer CropScience
KCA 6.4/01		1975	Investigation of tissue and egg residues from hens following dietary intake of NC 8438 for 21 days Report No.: A83011, Edition Number: M-155288-01-1 Bayer CropScience GLP no Unpublished	Y	Bayer CropScience

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
KCA 6.4/02		1999	Review of animal metabolism data, maximum estimated dietary concentration for poultry and cattle, rebuttal for further animal feeding studies Ethofumesate Code: AE B049913 Report No.: C 003329, Edition Number: M-185950-01-1 Bayer CropScience GLP no Unpublished	Y	Bayer CropScience
KCA 6.4/03		1977	Residues in milk and tissues following a 28-day feeding study with ethofumesate in dairy cows – Part 1 Report No.: A83024, Edition Number: M-155301-01-1, EPA MRID No.: A1214208 Bayer CropScience GLP no Unpublished	Y	Bayer CropScience
KCA 6.4/04		1977	Residues in milk and tissues following a 28-day feeding study with ethofumesate in dairy cows – part 2 Report N0.: A89223, Edition Number: M-164398-01-1 Bayer CropScience GLP no Unpublished	Y	Bayer CropScience
KCA 6.4/05		1994	Ethofumesate-derived residues in the meat and milk of dairy cows: resulting from oral ingestion of ethofumesate Report No.: B002201, Report includes Trial Nos.: B93R04/05, Edition Number: M-237976-01-1, EPA MRID No.: 43458701 Bayer Crop Science GLP no Unpublished	Y	Bayer CropScience
KCA 6.4/06		1999	Review of animal metabolism data, maximum estimated dietary concentration for poultry and cattle, rebuttal for further animal feeding studies Ethofumesate Code: AE B049913 Report No.: C003329, Edition Number: M-185950-01-1 Bayer CropScience GLP no Unpublished	Y	Bayer Cropscience
KCA	Miebach, D.	2010	Nature siedues of ethofumesate in processed commodities – high temperature hydrolysis	N	Bayer

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
6.5/01	Bongartz, R.		Report No.: MEF-10/803, Edition Number: M-397800-01-1 Bayer CropScience GLP Unpublished		CropScience
KCA 6.5/02	Whiteoak, R.J. Crofts, M.	1973	Conjugated residues in fractions processed from sugar beet treated with nortron Report No.: A82973, Edition Number: M-155250-01-1, EPA-MRID No.: acc.36368 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.5/03	Crofts, M. Whiteoak, R.J.	1974	Fate of the metabolite conjugated NC 9607 during production of sugar from nortron treated sugar beet Report No.: A82985, Edition Number: M-155262-01-1, EPA MRID No.: acc.36369 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.5/04	Crofts, M. Whiteoak, R. J.	1975	Fate of the metabolite conjugated NC 9607 durign production of sugar from nortron treated sugar beet – artificially high residues in beet grown and processed in the united kingdom Report No.: 83002, Edition Number: M-155279-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCa 6.5/05	Crofts, M. Whiteoak, R.J.	1975	Faye of the metabolite conjungated NC 9607 during production of sugar from nortron treated sugar beet – artificially high residue in beet grown and processed in w. Germany Report No. A83003, Edition Number: M-155280-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer cropScience

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 6.6/01	Carlton, R. Cordell, P.	1993	The uptake and metabolism of ethofumesate and its soil metabolites in a confined rotational crop study Report No.: A83396, Report includes Trial Nos.: 90B, Edition Nubmer: M-155664-01-1 Schering AG, Berlin, Germany Bayer CropScience GLP Unpublished	N	Bayer CropScience
KCA 6.6/02	Schneider, E.	1994	PR94/025 – ethofumesate – determination of ethofumesate residues in soil of a long time field study after application of Ethosat (FSG031894) to sugar beet plants Report No: M-468487-01-1, Edition Number: M-468487-01-1 DR.G. Krebs Analytik, Koln, Germany GLP yes Unpublished	N	ADAMA
KCA 6.6/04	Castro, L. E.	1994	Ethofumesate emulsifiable concentrate 200 g/L CR 13768. AT-Harvest residues of ethofumesate and metabolites in rotational crops and soil following applications of nortron ec to sugarbeets, usa, 1990 Report No.: A83117, Edition Number: M-155392-01-1, EPA MRID No.: 43298104 Nor-Am Chemical Company, Pikeville, NC, USA Bayer CropScience GLP Unpublished	N	Bayer CropScience
KCA 6.6/05	Crofts, M. Whiteoak, R. J.	1974	Residue analysis of wheat grown in the uk as a following crop after sugar beet treated with nortron (1973) Report No.: A82995, Edition Number: M-155272-01-1 Fisons plc, United Kingdom Bayer CropScience GLP no Unpublished	N	Bayer CropScience
KCA 6.6/07	Crofts, M. Whiteoak, R.J.	1974	Residues analysis of wheat and corn (maize) grown as following crops after sugar beet treated with nortron (1973) Report No.: A82994, Edition Number: M-155271-01-1 Fisons plc, United Kingdom	N	Bayer CropScience

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
			Bayer CropScience GLP no Unpublished		
KCA 6.6/08	Peatman, M. H. Snowdon, P. J.	1991	Residues of soil and emergency crops following application of ethofumesate as a 50 SC formulation in the uk 1990/91 Report No.: A83376, Report includes Trial Nos.: 041/04/057, Edition Number: M-155644-01-1 Schering AG, Berlin, Germny Bayer CropScience GLP yes Unpublished	N	Bayer CropScience
KCA 6.6/09	Schulte, G. Diehl, P.	2013	Amendment No. 1 to Report No.: 10-2501-Determination of the residues of ethofumesate in/on the field rotational crop barley, carrot, lettuce and wheat after spray application of ethofumesate SC 500 on sugar beet and soil in the fiels, in the Netherlands, Italy, Spain and Germany Report no.: 10-2501, Report includes Trial Nos.: 10-2501-02, 10-2501-03, 10-2501-04, 10-2501-05, Edition Number: M-463906-02-1 Bayer CropScience GLP yes Unpublished	N	Task Force Ethofumesate

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 Ethofumesate

Not relevant.

Appendix 3 Pesticide Residue Intake Model (PRIMo)

A 3.1 TMDI calculations

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	1	ARfD (mg/kg bw):	not necessary
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2016	Year of evaluation:	2016

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from: MRLs set at the LOQ (in % of ADI)	Exposure resulting from: commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	0.2%	NL child	1.70	0.2%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	NL toddler	1.08	0.1%	Sugar beet roots	0.0%	Beetroots				
	0.1%	DE women 14-50 yr	0.92	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	DE general	0.85	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	FR child 3 15 yr	0.75	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	UK toddler	0.64	0.1%	Sugar beet roots	0.0%	Beetroots				
	0.1%	NL general	0.59	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	FR toddler 2 3 yr	0.58	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.0%	GEMS/Food G06	0.31	0.0%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.0%	UK infant	0.28	0.0%	Sugar beet roots		Grapefruits				
	0.0%	FR infant	0.28	0.0%	Sugar beet roots	0.0%	Chards/beet leaves	0.0%	Beetroots		
	0.0%	RO general	0.27	0.0%	Sugar beet roots	0.0%	Beetroots				
	0.0%	FR adult	0.17	0.0%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.0%	UK adult	0.11	0.0%	Sugar beet roots	0.0%	Beetroots				
	0.0%	UK vegetarian	0.11	0.0%	Sugar beet roots	0.0%	Beetroots				
	0.0%	GEMS/Food G11	0.06	0.0%	Beetroots		Grapefruits				
	0.0%	ES child	0.06	0.0%	Sugar beet roots	0.0%	Chards/beet leaves	0.0%	Beetroots		
	0.0%	ES adult	0.05	0.0%	Sugar beet roots	0.0%	Chards/beet leaves	0.0%	Beetroots		
	0.0%	PL general	0.04	0.0%	Beetroots	0.0%	Chards/beet leaves				
	0.0%	GEMS/Food G07	0.03	0.0%	Beetroots	0.0%	Sugar beet roots				
	0.0%	GEMS/Food G10	0.03	0.0%	Beetroots	0.0%	Sugar beet roots				
	0.0%	GEMS/Food G15	0.03	0.0%	Beetroots		Grapefruits				
	0.0%	LT adult	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	IE adult	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	SE general	0.02	0.0%	Beetroots	0.0%	Chards/beet leaves				
	0.0%	FI 6 yr	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	GEMS/Food G08	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	IT adult	0.02	0.0%	Chards/beet leaves	0.0%	Beetroots				
	0.0%	FI 3 yr	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	IT toddler	0.02	0.0%	Chards/beet leaves		Grapefruits				
	0.0%	FI adult	0.01	0.0%	Beetroots		Grapefruits				
	0.0%	DE child	0.01	0.0%	Beetroots	0.0%	Chards/beet leaves				
	0.0%	DK child	0.00	0.0%	Beetroots		Grapefruits				
	0.0%	IE child	0.00	0.0%	Beetroots		Grapefruits				
		DK adult			Grapefruits		Grapefruits				
		DK adult			Grapefruits		Grapefruits				

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of is unlikely to present a public health concern.

A 3.2 IEDI calculations

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	1	ARfD (mg/kg bw):	not necessary
Source of ADI:	EFSA	Source of ARfD:	EFSA
Year of evaluation:	2016	Year of evaluation:	2016

Input values

Details - chronic risk assessment | Supplementary results - chronic risk assessment

Details - acute risk assessment/children | Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	0.2%	NL child	1.70	0.2%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	NL toddler	1.08	0.1%	Sugar beet roots	0.0%	Beetroots				
	0.1%	DE women 14-50 yr	0.92	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	DE general	0.85	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	FR child 3 15 yr	0.75	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	UK toddler	0.64	0.1%	Sugar beet roots	0.0%	Beetroots				
	0.1%	NL general	0.59	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.1%	FR toddler 2 3 yr	0.58	0.1%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.0%	GEMS/Food G06	0.31	0.0%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.0%	UK infant	0.28	0.0%	Sugar beet roots		Grapefruits				
	0.0%	FR infant	0.28	0.0%	Sugar beet roots	0.0%	Chards/beet leaves	0.0%	Beetroots		
	0.0%	RO general	0.27	0.0%	Sugar beet roots	0.0%	Beetroots				
	0.0%	FR adult	0.17	0.0%	Sugar beet roots	0.0%	Beetroots	0.0%	Chards/beet leaves		
	0.0%	UK adult	0.11	0.0%	Sugar beet roots	0.0%	Beetroots				
	0.0%	UK vegetarian	0.11	0.0%	Sugar beet roots	0.0%	Beetroots				
	0.0%	GEMS/Food G11	0.06	0.0%	Beetroots		Grapefruits				
	0.0%	ES child	0.06	0.0%	Sugar beet roots	0.0%	Chards/beet leaves	0.0%	Beetroots		
	0.0%	ES adult	0.05	0.0%	Sugar beet roots	0.0%	Chards/beet leaves	0.0%	Beetroots		
	0.0%	PL general	0.04	0.0%	Beetroots	0.0%	Chards/beet leaves				
	0.0%	GEMS/Food G07	0.03	0.0%	Beetroots	0.0%	Sugar beet roots				
	0.0%	GEMS/Food G10	0.03	0.0%	Beetroots	0.0%	Sugar beet roots				
	0.0%	GEMS/Food G15	0.03	0.0%	Beetroots		Grapefruits				
	0.0%	LT adult	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	IE adult	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	SE general	0.02	0.0%	Beetroots	0.0%	Chards/beet leaves				
	0.0%	FI 6 yr	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	GEMS/Food G08	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	IT adult	0.02	0.0%	Chards/beet leaves	0.0%	Beetroots				
	0.0%	FI 3 yr	0.02	0.0%	Beetroots		Grapefruits				
	0.0%	IT toddler	0.02	0.0%	Chards/beet leaves		Grapefruits				
	0.0%	FI adult	0.01	0.0%	Beetroots		Grapefruits				
	0.0%	DE child	0.01	0.0%	Beetroots	0.0%	Chards/beet leaves				
	0.0%	DK child	0.00	0.0%	Beetroots		Grapefruits				
	0.0%	IE child	0.00	0.0%	Beetroots		Grapefruits				
		DK adult			Grapefruits		Grapefruits				
		DK adult			Grapefruits		Grapefruits				

Conclusion:
The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.
The long-term intake of residues of is unlikely to present a public health concern.

A 3.3 IESTI calculations - Raw commodities

Not relevant

A 3.4 IESTI calculations - Processed commodities

Not relevant

Appendix 4 Additional information provided by the applicant