FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: CHR/H/PENDIF 599.5 SC

Product name(s): Cevino Trio 599.5 SC/ Trivino 599.5 SC

Chemical active substance(s):

Penoxsulam, 37.5 g/L
Diflufenican, 250 g/L
Flufencaet, 312 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Innvigo Sp. z o.o.

Submission date: October 2021

MS Finalisation date: 24/08/2022

Version history

When	What
February 2022	Dossier sent for evaluation
03/2022	Correction of the elements indicated by the evaluator in accordance with the comments.
April 2022	Updates based on feedback from zRMS Poland
April 2022	zRMS evaluation of dRR
August 2022	Final version prepared by zRMS after Commenting period

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zRMS comments:
The text highlighted in grey was provided by the evaluator.

6 Mammalian Toxicology (KCP 7)

In the following document, data for active substances - penoxsulam, diflufenican and flufenacet - was described during its inclusion on Annex 1 process in respectively 2010, 2009 and 2004 . Were reference to active substance data in the current risk assessment has been made, it was based on the data which protection for expired 10 years from date of inclusion of active substances on Annex I.

6.1 Summary

Table 6.1-1: Information on CHR/H/PENDIF 599.5 SC *

Product name and code	CHR/H/PENDIF 599.5 SC
Formulation type	Suspension concentrate [SC]
Active substance(s) (incl. content)	Penoxsulam: 37.5 g/L Diflufenican: 250 g/L Flufenacet 312 g/L
Function	Herbicide
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	No
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of CHR/H/PENDIF 599.5 SC can be found in the confidential dRR Part C.

Justified proposals for classification and labelling

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the following classification and labelling with regard to toxicological data is proposed for the preparation:

Table 6.1-2: Justified proposals for classification and labelling for CHR/H/PENDIF according to Regulation (EC) No 1272/2008

Hazard class(es), categories	H302, H317, H373
Hazard pictograms or Code(s) for hazard pictogram(s)	
Signal word	Warning
Hazard statement(s)	Acute Tox. 4, H302 – Harmful if swallowed. Skin Sens.1, H317 – May cause an allergic skin reaction. STOT RE 2, H373 – May cause damage to organs through prolonged or repeated exposure.
Precautionary statement(s)	P280 – Wear protective gloves/protective clothing/eye protection/face protection. P302 + P352 – IF ON SKIN: Wash with plenty of water with soap. ~~P305 + P351 + P338 – IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.~~ P362 + P364 – Take off contaminated clothing and wash it before reuse. **Other section of the label:** P270: Do not eat, drink or smoke when using this product. P403 + P233: Store in a well-ventilated place. Keep container tightly closed. P501: Dispose of contents/container to… And P280 as follows: " *Stosować rękawice ochronne, ochronę oczu lub twarzy oraz odzież ochronną, zabezpieczająca przed oddziaływaniem środków ochrony roślin w trakcie przygotowywania cieczy użytkowej oraz w trakcie wykonywania zabiegu.*" "*Wear protective gloves/protective clothing/eye protection/face protection/workwear at loading and mixing and during application.*" For polish version: see the label
Additional labelling phrases	To avoid risks to man and the environment, comply with the instructions for use. [EUH401]
	~~EUH208 – Contains 1,2-Benzisothiazolone. May produce an allergic reaction.~~

Comments of zRMS:	**Classification and labelling for CHR/H/PENDIF 599.5 SC according to Regulation (EC) No 1272/2008** Hazard class(es), categories: Acute Tox. 4, Skin Sens. 1, STOT RE 2 Hazard pictograms or Code(s) for hazard pictogram(s): GHS07, GHS08 Signal word: Warning Hazard statement(s): H302, H317, H373 Precautionary statement(s): P260, P280, P302+P352, P333 + P313, P362 + P364 Additional labelling phrases: EUH 401 – To avoid risks to human health and the environment, comply with the instructions for use.

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for CHR/H/PENDIF 599.5 SC

	Result	PPE / Risk mitigation measures
Operators	Acceptable	With gloves and work wear during mix/loading
Workers	Acceptable	~~With PPE~~ Wearing work wear (arms, body and legs covered) during crop inspection
Residents	Acceptable	
Bystanders	Acceptable	

No unacceptable risk for operators, workers, residents and bystanders was identified when the product is used as intended. No specific PPE is necessary.

A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and residents/bystanders is presented in the following table.

Table 6.1-4 Critical uses and overall conclusion of exposure assessment

1	2	3	4	5	6	7	8	9	10			
Use-No.*	**Crops and situation (e.g. growth stage of crop)**	**F, Fn, Fpn G, Gn, Gpn or I ****	**Application**		**Application rate**		**PHI (d)**	**Remarks:** **(e.g. safener/synergist (L/ha))** **critical gap for operator, worker, resident or bystander exposure based on [Exposure model]**	**Acceptability of exposure assessment**			
			Method / Kind **(incl. application technique *****| **Max. number (min. interval between applications)** **a) per use** **b) per crop/ season**	**Max. application rate kg as/ha** **a) a.s. 1** **b) a.s. 2**	**Water L/ha** **min / max**				**Operator**	**Worker**	**Residents**	**Bystander**
	Cereals BBCH 11-25	F	Spray	1:1	a) Penoxsulam 0.015 kg/ha b) Diflufenican 0.1 kg/ha c) Flufenacet 0.1248 kg/ha	200 – ~~400~~ 300						

* 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
*** e.g. LC: low crops, HC: high crop, TM: tractor-mounted, HH: hand-held

Explanation for column 10 "Acceptability of exposure assessment"

A	Exposure acceptable without PPE / risk mitigation measures
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable/ Evaluation not possible

Data gaps

Noticed data gaps are:
None

6.2 Toxicological Information on Active Substance(s)

Information regarding classification of the active substances and on EU endpoints and critical areas of concern identified during the EU review are given in Table 6.2-1.

Table 6.2-1: Information on active substance(s)

	Penoxsulam	**Diflufenican**	**Flufenacet**
Common Name	Penoxsulam	Diflufenican	Flufenacet
CAS-No.	111991-09-4	79277-27-3	142459-58-3
Classification and proposed labelling			
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	**Hazard classes (s), categories**: Aquatic Acute 1 Aquatic Chronic 1 **Code(s) for hazard pictogram(s):** GHS09 **Signal word:** Warning H400 – Very toxic to aquatic life. H410 – Very toxic to aquatic life with long lasting effects **Precautionary statement(s):** P391 – Collect spillage. P273 – Avoid release to the environment	**Hazard classes (s), categories:** Aquatic Acute 1 Aquatic Chronic 1 **Code(s) for hazard pictogram(s):** GHS09 **Signal word**: Warning **Hazard statement(s):** H400 – Very toxic to aquatic life. H410 – Very toxic to aquatic life with long lasting effects. **Precautionary statement(s):** P391 – Collect spillage. P273 – Avoid release to the environment.	**Hazard classes (s), categories**: Acute Tox. 4 STOT RE 2 Skin Sens. 1 **Code(s) for hazard pictogram(s):** GHS08, GHS07 Signal word: Warning **Hazard statement(s):** H302 – Harmful if swallowed. H373 – May cause damage to organs through prolonged or repeated exposure. H317 – May cause an allergic skin reaction. **Precautionary statement(s):** P280 - Wear protective gloves/ P260 - Do not breathe spray. P264 – Wash hands thoroughly after handling P270 – Do no eat, drink or smoke when using this product P272 - Contaminated work clothing should not be allowed out of the workplace. P301 + P312 – IF SWALLOWED: Call a POISON CENTER or doctor/physician if you feel unwell. P330 - Rinse mouth. P302 + P352 – IF ON SKIN: Wash with plenty of soap and water.

<table>
<tr><th></th><th>Penoxsulam</th><th>Diflufenican</th><th>Flufenacet</th></tr>
<tr><td></td><td></td><td></td><td>P314 - Get medical advice/attention if you feel unwell.
P333 + P313 – If skin irritation or rash occurs: Get medical advice/attention.
P363 – Wash contaminated clothing before reuse.
P501 - Dispose of contents/container to …</td></tr>
<tr><td>Additional C&L proposal</td><td>Not required</td><td>Not required</td><td>Not required</td></tr>
<tr><td colspan="2">Agreed EU endpoints</td><td></td><td></td></tr>
<tr><td>AOEL systemic</td><td>0.18 mg/kg bw/d</td><td>0.11 mg/kg bw/d</td><td>~~0.05~~ 0.017 mg/kg bw/d</td></tr>
<tr><td>Reference</td><td>EFSA Scientific Report (2009) 343, 14-90</td><td>EFSA Scientific Report (2007) 122, 1-84, Conclusion on the peer review of diflufenican</td><td>Addendum to Annex B.5 mammalian toxicology, January 2001
7469/VI/98-Final 3 July 2003 Review report for the active substance flufenacet</td></tr>
<tr><td colspan="4">Conditions to take into account/critical areas of concern with regard to toxicology</td></tr>
<tr><td></td><td>~~Operator:~~

~~The estimated exposure for GF 657 is below the AOEL even when no PPE is used (application rate 0.04 kg penoxsulam/ha) with tractor mounted equipment:~~
~~German model~~
~~No PPE 2.9 % of AOEL~~
~~UK model~~
~~No PPE 14.4 % of AOEL~~

~~Workers~~
~~In accordance with normal rice agricultural practices, re-entry to the crop prior to harvest is not necessary. Residues of penoxsulam at harvest are negligible and will lead to insignificant worker exposure.~~

~~Bystander~~
~~Recommended uses~~</td><td>~~Operator:~~

~~Application in cereals POEM % of AOEL (tractor, 0.12 kg a.s./ha, without PPE) 19.7%~~
~~(tractor, 0.12 kg a.s./ha, PPE = gloves during mixing/loading) 19.5%~~
~~BBA (tractor, 0.12 kg a.s./ha, without PPE) 3.3%~~
~~(tractor, 0.12 kg a.s./ha, PPE = gloves during mixing/loading) 3.2%~~

~~Worker:~~
~~According to van Hemmen et al, 2002 and using EUROPOEM dislodgeable foliar residue and transfer coefficient values : 3 % of AOEL (no PPE)~~

~~Bystender:~~
~~According to Lloyd and Bell, 1983: 0.1% of AOEL~~

Not required.</td><td>~~Operator exposure~~
~~Rate: 0.6 kg as/ha (corn, soybeen, sunflower)~~
<table>
<tr><td></td><td colspan="2">~~German~~</td><td colspan="2">~~Uk~~</td></tr>
<tr><td></td><td>~~No PPE~~</td><td>~~With PPE~~</td><td>~~No PPE~~</td><td>~~With PPE~~</td></tr>
<tr><td>~~Total absorbes dose (mg/kg bw/d~~</td><td>~~0.0817~~</td><td>~~0.0065~~</td><td>~~0.719~~</td><td>~~0.071~~</td></tr>
<tr><td>~~% AOEL syst~~</td><td>~~480.7~~</td><td>~~38.5~~</td><td>~~4229.4~~</td><td>~~417.6~~</td></tr>
</table>
~~Rate: 0.24 kg as/ha (cereals)~~
<table>
<tr><td></td><td colspan="2">~~German~~</td><td colspan="2">~~Uk~~</td></tr>
<tr><td></td><td>~~No PPE~~</td><td>~~With PPE~~</td><td>~~No PPE~~</td><td>~~With PPE~~</td></tr>
<tr><td>~~Total absorbes dose (mg/kg bw/d~~</td><td>~~0.0327~~</td><td>~~0.0026~~</td><td>~~0.2872~~</td><td>~~0.0282~~</td></tr>
<tr><td>~~% AOEL syst~~</td><td>~~192.4~~</td><td>~~15.5~~</td><td>~~1689.4~~</td><td>~~165.9~~</td></tr>
</table>
should pay particular attention to the protection of operators</td></tr>
</table>

	Penoxsulam	Diflufenican	Flufenacet
	~~of GF-657 may potentially result in incidental, brief exposure of bystanders to a highly diluted water-based spray drift, but the predicted exposure should present a negligible hazard and risk (~ 0.2 % of AOEL)~~ Not required.		

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for CHR/H/PENDIF 599.5 SC is given in the following tables. Full summaries of studies on the product that have not been previously considered within an EU peer review process are described in detail in Appendix 2.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for CHR/H/PENDIF 599.5 SC

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat (calculation method)	1923.82 mg/kg bw	Yes	Acute Tox.4, H302	Please refer to Part C
LD_{50} dermal, rat (calculation method)	> 2000 mg/kg bw	Yes	None	Please refer to Part C
LC_{50} inhalation, rat (calculation method)	> 20 mg/L air	Yes	None	Please refer to Part C
Skin irritation, (calculation method)	Non Irritant	Yes	None	Please refer to Part C
Eye irritation, (calculation method)	Non Irritant	Yes	None	Please refer to Part C
Skin sensitisation, (calculation method)	Sensitizatie	Yes	Skin Sens.1, H317	Please refer to Part C
~~Specific target organ toxicity - single exposure (calculation method)~~	~~May cause damage to organs~~		~~STOT RE 2, H373.~~	-
Supplementary studies for combinations of plant protection products	No data – not required	-	None	-

Table 6.3-2: Additional toxicological information relevant for classification/labelling of CHR/H/PENDIF 599.5 SC

	Substance (concentration in product, % w/w)	**Classification of the substance (acc. to the criteria in Reg. 1272/2008)**	**Reference**	**Classification of product (acc. to the criteria in Reg. 1272/2008)**
Toxicological properties of active substance(s) (relevant for classification of product)	Flufenacet (25.99%)	Acute Tox. 4, H302 (the ATE of the mixture = 1924) Skin Sens. 1, H317 (criteria ≥1%) STOT RE 2, H373 (criteria ≥10%) Aquatic Acute 1, H400 Aquatic Chronic 1, H410*	Reg. 1272/2008	Acute Tox. 4, H302 Skin Sens. 1, H317 STOT RE 2, H373
Toxicological properties of non-active substance(s) (relevant for classification of product)	Detailed information provided in Part C			
Further toxicological information	No data – not required			

* Please use concentration range or concentration limit (e.g. 1-10% or > 1%) as provided in MSDS.
** Material safety data sheet by the applicant

6.4 Toxicological Evaluation of Groundwater Metabolites

The following data on metabolites with the potential to reach the groundwater in concentrations above 0.1 µg/L and requiring relevance assessment were submitted. Note that the relevance assessment of the metabolites is reported in Part B.10; the submitted toxicological studies are summarised in this document.

According to DAR Penoxsulam, Volume 3, Annex B., B6, 2005 a total of 16 metabolites were identified in soil, water, crops and animals. The metabolites have not been tested individually for toxicity potential in mammals as it is considered that they are not toxicologically relevant.

6.4.1 5-OH-penoxsulam

According to DAR Penoxsulam, Volume 3, Annex B., B6, 2005 a total of 16 metabolites were identified in soil, water, crops and animals. The metabolites have not been tested individually for toxicity potential in mammals as it is considered that they are not toxicologically relevant.

Table 6.4-1: Summary of the results of toxicity studies for 5-OH-Penoxsulam

Type of test, species (Guideline)	Result	Acceptability	Reference*
In vitro genotoxicity test (OECD 471)	non-mutagenic	Yes	M.S. Mecchi, Study code: 6736-161*

Type of test, species (Guideline)	Result	Acceptability	Reference*
Mammalian cells in culture gene assay in CHO-K1-BH4 cell (OECD 476)	Non-mutagenic	Yes	M. R. Schisler, K.M. Kleinert, Study ID: 061093*
In vitro mammalian cytogenetics (OECD 473)	Non-genotoxic	Yes	M. R. Schisler, K.M. Kleinert, Study ID: 061092*

*indicates that a study was reviewed at EU level

6.4.1 BST

According to DAR Penoxsulam, Volume 3, Annex B., B6, 2005 a total of 16 metabolites were identified in soil, water, crops and animals. The metabolites have not been tested individually for toxicity potential in mammals as it is considered that they are not toxicologically relevant.

Table 6.4-2: Summary of the results of toxicity studies for BST

Type of test, species (Guideline)	Result	Acceptability	Reference*
(Bacterial system, Salmonella typhimurium; Escherichia coli)/mammalian activation gene mutation assay (OECD 471)	Non-mutagenic	Yes	M.S. Mecchi, Study code: 6736-157*
Mammalian cells in culture gene assay in CHO-K1-BH4 cells (OECD 476)	Non-mutagenic	Yes	S.D. Seidel, M. R. Schisler, K.M. Kleinert, Study ID: 061019*
In vitro mammalian cytogenetics (OECD 473)	Non-genotoxic	Yes	G. D. Charles, M. R. Schisler, K.M. Kleinert, Study ID: 061018*

*indicates that a study was reviewed at EU level

6.4.1 BSTCA

According to DAR Penoxsulam, Volume 3, Annex B., B6, 2005 a total of 16 metabolites were identified in soil, water, crops and animals. The metabolites have not been tested individually for toxicity potential in mammals as it is considered that they are not toxicologically relevant.

Table 6.4-3: Summary of the results of toxicity studies for BSTCA

Type of test, species (Guideline)	Result	Acceptability	Reference*
(Bacterial system, *Salmonella typhimurium; Escherichia coli*)/mammalian activation gene mutation assay (OECD 471)	Non-mutagenic	Yes	M.S. Mecchi, Study code: 6736-159*
Mammalian cells in culture gene assay in CHO-K1-BH4 cells (OECD 476)	Non-mutagenic	Yes	M. R. Schisler, K.M. Kleinert, Study ID: 061037*
In vitro mammalian cytogenetics (OECD 473)	Non-genotoxic	Yes	M. R. Schisler, K.M. Kleinert, Study ID: 061038*

*indicates that a study was reviewed at EU level

6.4.1 FOE 5043 sulfonic acid

Table 6.4-4: Summary of the results of toxicity studies for FOE 5043 sulfonic acid

Type of test, species (Guideline)	Result	Acceptability	Reference*
~~Bacterial system,~~ Bacterial reverse mutation assay (OECD 471)	Non-mutagenic	Yes	Herbold, 2000 * M-019064-01-1
In vitro evaluation of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid, Trifluoroacetic acid and Flufenacet methylsulfone genotoxicity using the micronucleus assay (MNA) (OECD 487)	Non-mutagenic	Yes	J.Antonik, 2016.;. Study Number: K81/JA/01.
In vitro Mammalian Cell Gene Mutation test (OECD 490)	Non-genotoxic	Yes	J.Antonik; Study number: K82/JA/01
Rat, Acute Oral	LD50> 2000 mg/kg	Yes	1998, M-004749-01-1*
Rat, Plasma kinetics and excretion	Low oral absorption (<10%) rapid renal clearance (i.v: t1/2 □ 30 min)	Yes	2000 M-042251-01-1*

* indicates that a study was reviewed at EU level

~~FOE 5043 sulfonic acid was initially investigated using the salmonella/microsome plate incorporation test (Salmonella/microsome test with FOE 5043 sulfonic acid. Report Bayer PH 29473. GLP. Unpublished. B. Herbold, 2000.) for point mutagenic effects in doses of up to and including 5000 µg per plate on five Salmonella typhimurium LT2 mutants. These comprised the histidine auxotrophic strains TA 1535, TA 100, TA 1537, TA 98 and TA 102. The independent repeat was performed as preincubation for 20 minutes at 37°C. Other co ditions remained unchanged.~~
~~Doses up to and including 5000µg per plate did not cause any bacteriotoxic effects : total bacteria counts remained unchanged and no inhibition of growth was observed. Evidence of mutagenic ac tivity of FOE 5043 sulfonic acid was not seen. No biologically relevant increase in the mutant co unt, in comparison with the negative controls was observed.~~

~~The positive controls sodium azide, nitrofurantoin, 4 nitro 1,2 phenylene diamine, cumene hydro peroxyde and 2 aminoanthracene had a marked mutagenic effect, as was seen by a biologically relevant increase in mutant colonies compared to the corresponding negative controls.~~

~~Additional two studies were provided by PUH Chemirol:~~

~~- In vitro evaluation of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid, Trifluoroacetic acid and Flufenacet methylsulfone genotoxicity using the micronucleus assay (MNA). J.Antonik, 2016.; SELVITA. Study Number: K81/JA/01.Method: OECD 487~~
~~- In vitro Mammalian Cell Gene Mutation test (OECD 490) - genotoxicity determination of Flufena cet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid by Mo use Lymphoma Assay. J.Antonik; 2016; J.Antonik; Study number: K82/JA/01; SELVITA; OECD 490~~

~~The formation of MN is a consequence of chromosomal breakage and/or spindle fiber dysfunction induced by clastogens and/or aneuploidogens. The present study was performed in accordance with the OECD 487 and under GLP requirements. In order to assess genotoxic potential CHO K1 cells were exposed to test items (Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid, Trifluoroacetic acid and Flufenacet methylsulfone) and appropriate reference items in system with (+S9) and without (S9 short and extended treatment) an exogenous~~

metabolic activation. Stati stical analysis of the MN frequency and binucleate cells with MN was performer using the Chi square test with Yates' correction. To examine the dose response relationship in frequencies of the micronuclei Chi square test for trend was performed.
None of tested concentration of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfo nic acid, Trifluoroacetic acid and Flufenacet methylsulfone exhibit a statistically significant increa se in MN frequency compared with the concurrent negativecontrol (P>0.05, T bles IX XIII, Figure I VII). Chi square test for trend revealed no dose related increase in MN frequency (P>0.05).
Results for positive reference items (mitomycin C and cyclophosphamide) demonstrated reprodu cibility and sensitivity of system.

In summary, the present research has demonstrated that items Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid, Trifluoroacetic acid and Flufenacet methylsulfone did not produce dose dependent genetic toxicity in the CHO K1 cells.

Mutagenic potential of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid was evaluated trough Mouse Lymphoma Assay (MLA) in L5178Y cells. Tested items were analyzed in MLA, in the presence and absence of exogenous metabolic activa tion.Obtained results have shown that tested item did not exceed MF above a value termed as
Global Evaluation Factor 126 ×10−6 in any of the tested doses both in the presence and absence of S9 exogenous activation system.
Obtained results indicate that tested items (Flufenacet oxalate, Flufenacet sulfonic acid, Trifluo roethanesulfonic acid and Trifluoroacetic acid) or their metabolic derivatives were not positive in Mouse Lymphoma Assay under the protocol described and according to the acceptability criteria defined in OECD guideline 490 and SPB 19.

Conclusion:

FOE 5043 sulfonic acid is considered to bee non mutagenic and have no genotoxicity potential in all of these assays.

FOE 5043 sulfonic acid plasmakinetics and excretion in urine in a rat study with single oral vs in travenous administration. Report PH 30052. GLP. Unpublished. XXXXXX, 2000.
A study for the comparison of the plasmakinetics and excretion in urine after the single oral versus intravenous administration of FOE 5043 sulfonic acid, a metabolite of FOE 5043, was conducted in male Wistar rats.
The treatment and observation time of the study has been designed to follow the principles of the following guidelines : OECD Guideline for Testing of Chemicals No 423.

The oral AUC was despite the 10 fold higher dose slightly lower than the intravenous AUC, which also argued in favour of low oral absorption.

The t1/2 after iv administration was short (about 30mn) which suggests the major role of the renal clearance.
FOE 5043 Sulfonsäure : study for acute oral toxicity in rats. Report 27137. GLP. Unpublished. F. Krötinger, 1998.

A study for acute oral toxicity in male and female Wistar rats was conducted with the test substance FOE 5043 Sulfonsäure (soil metabolite of FOE 5043).
The method used complied with the OCDE guideline for Testing of Chemicals; section4: Health effects, No. 401 – "Acute oral Toxicity".
Clinical findings :
Doses of 500 and 2000 mg/kg body weight were tolerated by male and female rats without mortali ties and 500mg/kg b.w. also without clinical signs. At 2000 mg/kg b.w. in both sexes diarrhea oc curred and anuses were moistened. The signs observed started 4 hours and lasted up to 5 hours after administration.
Body weight and body weight gain were not affected by treatment.
The acute oral LD50 of FOE 5043 sulfonic acid is > 2000 mg /kg b.w.

Conclusion on toxicological significance of the metabolite FOE sulfonic acid:

The goal of the additional physico chemical and biological experiments which were requested from the applicant was to demonstrate that the metabolite M2 (FOE sulfonic acid) was poorly absorbed orally, and had a low potential toxicity.

Based firstly on the physical properties that show a high hydrosolubility which suggests a low bio logical

~~absorption,~~
~~The solubility in water is 55g/l at 20°C at pH 4 to 9 ; under the same conditions, its Kow is 0.0019, leading to a log Kow = -2.72 ; the pKa of sulfonic acid is <1~~
~~and secondly on the biological investigations that show poor biological disposition and low toxicity, the metabolite FOE 5043 sulfonic acid is considered of no toxicological relevance.~~

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in CHR/H/PENDIF 599.5 SC are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in CHR/H/PENDIF 599.5 SC

	Penoxsulam		Diflufenican		Flufenacet	
	Value	**Reference**	**Value**	**Reference**	**Value**	**Reference**
Concentrate	50%	Guidance on Dermal Absorption EFSA, EFSA Journal 2017;15(6):4873	10%	Guidance on Dermal Absorption EFSA, EFSA Journal 2017;15(6):4873	10%	Guidance on Dermal Absorption EFSA, EFSA Journal 2017;15(6):4873
Dilution	50%		50%		50%	

6.5.1 Justification for proposed values - penoxsulam

No data on dermal absorption for penoxsulam in CHR/H/PENDIF 599.5 SC is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(6):4873) are presented in the following table.

Table 6.5-2: Default dermal absorption rates for penoxsulam

	Value	Justification for value	Acceptability of justification
Concentrate	50%	A default dermal absorption value of 50% may be applied for concentrated products that are water-based/dispersed or solid-formulated, because nominal content of penoxulam in CHR/H/PENDIF 599.5 SC is 37.5 g/L and therefore this active substance should be treat like dilution.	Yes
Dilution	50%	A default dermal absorption value of 50% may be applied for (in use) dilutions water-based/dispersed or solid-formulated.	Yes

6.5.2 Justification for proposed values – diflufenican

No data on dermal absorption for diflufenican in CHR/H/PENDIF 599.5 SC is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(6):4873) are presented in the following table.

Table 6.5-3: Default dermal absorption rates for diflufenican

	Value	Justification for value	Acceptability of justification
Concentrate	10%	A default dermal absorption value of 10% may be applied for concentrated products that are water-based/dispersed or solid-formulated.	Yes
Dilution	50%	A default dermal absorption value of 50% may be applied for (in use) dilutions water-based/dispersed or solid-formulated.	Yes

6.5.3 Justification for proposed values - flufenacet

No data on dermal absorption for flufenacet in CHR/H/PENDIF 599.5 SC is available. Justifications for default values according to Guidance on Dermal Absorption (EFSA Journal 2017; 15(6):4873) are presented in the following table.

Table 6.5-4: Default dermal absorption rates for flufenacet

	Value	Justification for value	Acceptability of justification
Concentrate	10%	A default dermal absorption value of 10% may be applied for concentrated products that are water-based/dispersed or solid-formulated.	Yes
Dilution	50%	A default dermal absorption value of 50% may be applied for (in use) dilutions water-based/dispersed or solid-formulated.	Yes

6.6 Exposure Assessment of Plant Protection Product (KCP 7.2)

Table 6.6-1: Product information and toxicological reference values used for exposure assessment

Product name and code	CHR/H/PENDIF 599.5 SC
Formulation type	SC
Category	Herbicide

Active substance(s) (incl. content)	**Penoxsulam** 37.5 g/L	**Diflufenican** 250 g/L	**Flufenacet** 312 g/L
AOEL systemic	0.18 mg/kg bw/d	0.11 mg/kg bw/d	0.017 mg/kg bw/d
Inhalation absorption	100%	100%	100%
Oral absorption	100%	100%	100%
Dermal absorption	Concentrate: 50 % Dilution: 50 %	Concentrate: 10 % Dilution: 50 %	Concentrate: 10 % Dilution: 50 %

6.6.1 Selection of critical use(s) and justification

The critical GAP used for the exposure assessment of the plant protection product is shown in Table 6.1-4. A list of all intended uses within the zone is given in Part B, Section 0.

6.6.2 Operator exposure (KCP 7.2.1)

6.6.2.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of CHR/H/PENDIF 599.5 SC according to the critical use(s) is presented in Table 6.6-2. The outcome of the estimation is presented in Table 6.6-3 (acute exposure) and **Błąd! Nie można odnaleźć źródła odwołania.** (longer term exposure). Detailed calculations are in 0.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	CHR/H/PENDIF 599.5 SC (max. 0.4 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

Table 6.6-3: Estimated operator exposure (long term exposure)

		Penoxsulam		**Diflufenican**		**Flufenacet**	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops Application rate: 0.4 L prod./ha							
"EFSA Model" version 30.03.2015	no PPE*	0.0585837	32.55	0.0567433	51.58	0.0675940	397.61
	+ type of PPE (e.g. Gloves + work wear during mixing/loading)	0.0022571	1.25	0.0106982	9.73	0.0133080	78.28
	+ type of PPE	0.0017530	0.97	0.0073374	6.67	0.0091138	53.61

	(work wear during mixing/loading and application + gloves during mixing/loading)						

Comments of zRMS:	Accepted.

6.6.2.2 Measurement of operator exposure

Since the operator exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and consideration of the above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

6.6.3 Worker exposure (KCP 7.2.3)

6.6.3.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with CHR/H/PENDIF 599.5 SC according to the critical use(s). Outcome of the estimation is presented in Table 6.6-5. Detailed calculations are in 0.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	CHR/H/PENDIF 599.5 SC (max. 0.4 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

Table 6.6-5: Estimated worker exposure

		Penoxsulam		Diflufenican		Flufenacet	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Number of applications and application rate:		0.015 kg a.s./ha		0.1 kg a.s./ha		0.1248 kg a.s. / ha	
2 hours/day(1), TC: 12500 cm^2/person/h (2) Body weight: 60 kg	no PPE(3) Potential exposure	0.09375	5.21	0.0625	56.82	0.0780	458.82
~~8~~ 2 hours/day(1), TC: ~~0.25~~ 1400 cm^2/person/h (2) Body weight: 60 kg	~~with PPE(4)~~ Work wear	0.00105	0.58	0.0070	6.36	0.008736	51.39

According to Guidance on Pesticides Exposure Assessment of Operators, Workers, Residents and Bystanders, (EFSA Journal 2014;12(10):3874) to the calculation used the value of ~~2500~~ 1400 transfer coefficient (TC (cm2/h) arms, body and legs covered - workwear; bare hands) and ~~8~~ 2 hours work/day (only crop inspection and irrigation-type). Having regard to the above values, the predicted exposure values for CHR/H/PENDIF without PPP are below ~~above~~ 100% of systemic AOEL and therefore exposure of the worker with using ~~PPP~~ work wear is acceptable.

Comments of zRMS:	Accepted.

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

Not required

6.6.3.3 Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mention PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

6.6.4 Resident and bystander exposure (KCP 7.2.2)

6.6.4.1 Estimation of resident and bystander exposure

Table 6.6.-8 shows the exposure model(s) used for estimation of bystander and resident exposure to penoxsulam, diflufenican and flufenacet. Outcome of the estimation is presented in 9. Detailed calculations are in 0.

.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	CHR/H/PENDIF 599.5 SC (max.0.4L product/ha)
Model	"EFSA Model" version 30.03.2015

Table 6.6-7: Estimated resident exposure (longer term exposure)

	Penoxsulam		Diflufenican		Flufenacet	
Model data	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops Application rate: 0.4 L prod./ha						
Bystanders (adult) Drift rate: 2.77 % (1 m) Body weight: 60 kg	0.0009425	0.52	0.0049802	4.43	0.0061582	36.22
Bystanders (children) Drift rate: 2.77 % (1 m) Body weight: 10 kg	0.0027228	1.51	0.0120885	10.33	0.0148210	87.18
Residents (adult) Drift rate: 2.77 % (1 m) Body weight: 60 kg	0.0009425	0.52	0.0049802	4.43	0.0061582	36.22
Residents (children) Drift rate: 2.77 % (1 m) Body weight: 10 kg	0.0027228	1.51	0.0120885	10.33	0.0148210	87.18

Comments of zRMS:

Accepted.

The summary of new calculation of resident and bystander exposure to diflufenican taking into account 58% oral absorption. Detailed calculations are in point A 2.14.2.

	Penoxsulam		Diflufenican		Flufenacet	
Model data	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops Application rate: 0.4 L prod./ha Buffer zone: 2-3(m)						

Drift reduction technology: no
DT_{50}: 30 days
DFR: 3 µg/cm²/kg a.s./ha

Resident child Body weight: 10 kg	Drift (75th perc.)	0,00100	0,56	0,00671	6,10	0,0083797	49,29
	Vapour (75th perc.)	0,99107	0,59	0,00107	0,97	0,00107	6,29
	Deposits (75th perc.)	0,0001214	0,07	0,000775	0,70	0,001	5,94
	Re-entry (75th perc.)	0,00126	0,7	0,00843	7,67	0,01053	61,94
	Sum (mean)	**0,00272**	**1,51**	**0,01206**	**10,97**	**0,0148**	**87,18**
Resident adult	Drift (75th perc.)	0,000241	0,13	0,0016	1,46	0,002	11,79
	Vapour (75th perc.)	0,00023	0,13	0,00023	0,21	0,00023	1,35
	Deposits (75th perc.)	0,0000511	0,03	0,00034	0,31	0,0004252	2,5
	Re-entry (75th perc.)	0,0007031	0,39	0,004687	4,26	0,00585	34,41
	Sum (mean)	**0,0009425**	**0,52**	**0,00498**	**4,53**	**0,00615**	**36,22**

Risk assessment from combined exposure

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
Resident - child	Penoxsulam	
	Drift	0,0056
	Vapour	0,0059
	Deposits	0,0007
	Re-entry	0,007
	Sum of all pathways	0,0151
	Diflufenican	
	Drift	0,061
	Vapour	0,0097

		Deposits	0,0007
		Re-entry	0,0767
		Sum of all pathways	0,1097
		Flufenacet	
		Drift	0,4929
		Vapour	0,0629
		Deposits	0,0594
		Re-entry	0,6194
		Sum of all pathways	0,8718
		Cumulative risk resident – child (HI)	
		Drift	0,5595
		Vapour	0,0785
		Deposits	0,0608
		Re-entry	0,7031
		Sum of all pathways	**0,744**
	Resident - adult	Penoxsulam	
		Drift	0,0013
		Vapour	0,0013
		Deposits	0,0003
		Re-entry	0,0039
		Sum of all pathways	**0,0052**
		Diflufenican	
		Drift	0,0021
		Vapour	0,0031
		Deposits	0,0426
		Re-entry	0,0453
		Sum of all pathways	0,0021
		Flufenacet	
		Drift	0,1179
		Vapour	0,0135
		Deposits	0,025
		Re-entry	0,3441
		Sum of all pathways	0,3622
		Cumulative risk resident – adult (HI)	
		Drift	0,1213
		Vapour	0,0179
		Deposits	0,0679
		Re-entry	0,3972

	Sum of all pathways	**0,3695**

The Hazard Index is < 1. Thus, combined exposure to all active substances in product is not expected to present a risk for residents and bystanders. No further refinement of the assessment is required.

6.6.4.2 Measurement of resident and/or bystander exposure

Since the resident and/or bystander exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for penoxsulam, diflufenican and flufenacet will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of resident/bystander exposure was not necessary and was therefore not performed.

6.6.5 Combined exposure

The product is a mixture of three active substances.

6.6.5.1 Exposure assessment of penoxsulam, diflufenican and flufenacet in CHR/H/PENDIF 599.5 SC

Note: The combined toxicological effect of these active substances has not been investigated with regard to repeated dose toxicity.

At the first tier, combined exposure is calculated as the sum of the component exposures without regard to the mode of action or mechanism/target of toxicity. Initially, the individual Hazard Quotients (HQ) are calculated for all active substances in the PPP by assessing the exposure according to appropriate models and dividing the individual exposure levels by the respective systemic AOEL. This is equivalent to the predicted exposure as % of systemic AOEL from Table 6.6-3 converted to decimal. The Hazard Index (HI) is the sum of the individual HQs.

Table 6.6-8: Risk assessment from combined exposure

Application scenario	Active ingredient	Estimated exposure / AA-OEL (HQ)
Operators - (work wear during mixing/loading and application + gloves during mixing/loading)	Penoxsulam	0.0097
	Diflufenican	0,0667
	Flufenacet	0,5361
	Cumulative risk operators (HI)	**0,6125**
Operators –with PPE (glove + work wear during mix/loading)	Penoxsulam	0.0125
	Diflufenican	0.0973
	Flufenacet	0.7828
	Cumulative risk operators (HI)	**0.8926**
Workers – ~~with PPE~~ work wear	Penoxsulam	0.0058
	Diflufenican	0.0636
	Flufenacet	0.5139
	Cumulative risk workers (HI)	**0.5833**
Bystander - child	Penoxsulam	0.0151
	Diflufenican	0.1033
	Flufenacet	0.8718
	Cumulative risk bystander – child (HI)	**0.9902**
Bystander - adult	Penoxsulam	0.0052
	Diflufenican	0.0443
	Flufenacet	0.3622
	Cumulative risk bystander – adult (HI)	0.4117
Resident - child	Penoxsulam	0.0151
	Diflufenican	0.1033
	Flufenacet	0.8718
	Cumulative risk bystander – child (HI)	**0.9902**
Resident - adult	Penoxsulam	0.0052
	Diflufenican	0.0443
	Flufenacet	0.3622
	Cumulative risk bystander – adult (HI)	**0.4117**

The Hazard Index is < 1. Thus, combined exposure to all active substances in CHR/H/PENDIF 599.5 SC is not expected to present a risk for operators, workers, residents and bystanders. No further refinement of the assessment is required.

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Verte-brate study Y/N	Owner
KCP 7.1.1 KCP 7.1.2 KCP 7.1.4 KCP 7.1.5 KCP 7.1.6 KCP 7.1.7	K. Żero	2021	Toxicological classification of product CHR/H/PENDIF 599.5 SC based on calculation method taking into consideration health hazards of constituent substances; Chemirol Sp. z o.o. Non GLP Unpublished	N	Chemirol Sp. z o.o.
KCP 7.0/01	J. Antonik	2016	In vitro evaluation of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid, Trifluoroacetic acid and Flufenacet methylsulfone genotoxicity using the micronucleus assay (MNA). Selvita S.A. Park Life Science, Poland Study code: K81/JA/01 GLP Unpublished	N	Chemirol
KCP 7.0/02	J.Antonik	2016	In vitro Mammalian Cell Gene Mutation test (OECD 490) - genotoxicity determination of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid by Mouse Lymphoma Assay Selvita S.A. Park Life Science, Poland Study code: K82/JA/01 GLP Unpublished	N	Chemirol

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

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 7/01	~~XXXXX~~	2000	~~DF~~FOE 5043 sulfonic acid plasmakinetics and excreation in urine in a rat study with single oral vs intravenous PH 30052 GLP Unpublished	Y	Bayer
KCP 7/02	~~XXXXX~~	1998	FOE 5043 Sulfosaure: study for acute oral toxicity in rats 2137 GLP Unpublished	Y	Bayer
KCP 7/03	B. Herbold	2000	Salmonella/microsome test with FOE 5043 sulfonic acid PH 29473 GLP Unpublished	N	Bayer
KCP 7/04	M.S. Mecchi	2006	Salmonella-Escherichia coli/Mammalian-Microsome Reverse Mutation Assay Preincubation Method with a Confirmatory Assay with X689643 (5-OH Metabolite of Penoxsulam). Study code: 6736-161 Covance Laboratories Inc., Vienna, Virginia. GLP Unpublished	N	DOW
KCP 7/05	M.R. Schisler M.K., Kleinert	2006	EVALUATION OF X689643 (5-OH METABOLITE OF PENOXSULAM) IN THE CHINESE HAMSTER OVARY CELL/HYPOXANTHINE-GUANINE-PHOSPHORIBOSYL TRANSFERASE (CHO/HGPRT) FORWARD MUTATION ASSAY. Study code: 061093 Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan,	N	DOW

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		
KCP 7/06	M.R. Schisler M.K., Kleinert	2006	EVALUATION OF X689643 (5-OH METABOLITE OF PENOXSULAM) IN AN IN VITRO CHROMOSOMAL ABERRATION ASSAY UTILIZING RAT LYMPHOCYTES. Study code: 061092 Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan, GLP Unpublished	N	DOW
KCP 7/07	M.S., Mecchi	2006	Salmonella-Escherichia coli/Mammalian-Microsome Reverse Mutation Assay Preincubation Method with a Confirmatory Assay with X768359 (BSTCA Metabolite of Penoxsulam). Study code: 6736-159 Covance Laboratories Inc., Vienna, Virginia. GLP Unpublished	N	DOW
KCP 7/08	S.D. Seidel M. R. Schisler K.M. Kleinert	2006	EVALUATION OF X768359 (BSTCA METABOLITE OF PENOXSULAM) IN THE CHINESE HAMSTER OVARY CELL/HYPOXANTHINE-GUANINE-PHOSPHORIBOSYL TRANSFERASE (CHO/HGPRT) FORWARD MUTATION ASSAY. Study code: 061037 Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan, 48674. GLP Unpublished	N	DOW
KCP 7/09	M.R. Schisler K. M. Kleinert	2006	EVALUATION OF X768359 (BSTCA METABOLITE OF PENOXSULAM) IN AN IN VITRO CHROMOSOMAL ABERRATION ASSAY UTILIZING RAT	N	DOW

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
			LYMPHOCYTES. Study code: 061038 Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan, 48674. GLP Unpublished		
KCP 7/10	M.S., Mecchi	2006	Salmonella-Escherichia coli/Mammalian-Microsome Reverse Mutation Assay Preincubation Method with a Confirmatory Assay with X697134 (BST Metabolite of Penoxsulam). Study code: 6736-157 Covance Laboratories Inc., Vienna, Virginia. GLP Unpublished	N	DOW
KCP 7/11	S.D. Seidel M. R. Schisler K.M. Kleinert	2006	EVALUATION OF X697134 (BST METABOLITE OF PENOXSULAM) IN THE CHINESE HAMSTER OVARY CELL/HYPOXANTHINE-GUANINE-PHOSPHORIBOSYL TRANSFERASE (CHO/HGPRT) FORWARD MUTATION ASSAY. Study code: 061019 Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan, 48674. GLP Unpublished	N	DOW
KCP 7/12	G.D. Charles M.R. Schisler K. M. Kleinert	2006	EVALUATION OF X697134 (BST METABOLITE OF PENOXSULAM) IN AN IN VITRO CHROMOSOMAL ABERRATION ASSAY UTILIZING RAT LYMPHOCYTES. Study code: 061018 Toxicology & Environmental Research and Consulting, The Dow Chemical Company, Midland, Michigan, 48674. GLP	N	DOW

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		

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

Comments of zRMS:	Not applicable

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	The plant protection product CHR/H/PENDIF 599.5 SC was classified by calculation method as described in Regulation (EC) No 1272/2008. The product is classified as **Acute Tox. 4, H302**.

Reference:	7.1.1
Report	Toxicological classification of product CHR/H/PENDIF 599.5 SC based on calculation method taking into consideration health hazards of constituent substances; 2021; according to Part C, appendix 2

According to point 7.1.1 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:
" A test for acute oral toxicity shall be carried out, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, acute oral toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture."

The complete composition of the formulation with the classification of individual ingredients is available in part C.
Due to the fact, that all components of the formulation CHR/H/PENDIF 599.5 SC are known, the acute oral toxicity test is not necessary.

Materials and methods

We use the summation method using the formula:

$$ATE_{mix} = \frac{100}{\sum_{i=1}^{n} \frac{C_i}{ATE_i}}$$

Where:

- Ci - concentration of ingredient i (% w/w or % v/v)
- i – the individual ingredient from 1 to n
- n – the number of ingredients
- ATEi - Acute Toxicity Estimate of ingredient i.

We use the table:
Table 3.1.2
Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for classification for the respective routes of exposure.

Exposure routes	Classification Category or experimentally obtained acute toxicity range estimate	Converted acute toxicity point estimate (see Note 1)

Oral (mg/kg body-weight)	0 < Category 1 ≤ 5 5 < Category 2 ≤ 50 50 < Category 3 ≤ 300 300 < Category 4 ≤ 2 000	0,5 5 100 500
Dermal (mg/kg bod-yweight)	0 < Category 1 ≤ 50 50 < Category 2 ≤ 200 200 < Category 3 ≤ 1 000 1 000 < Category 4 ≤ 2 000	5 50 300 1 100
Gases (ppmV)	0 < Category 1 ≤ 100 100 < Category 2 ≤ 500 500 < Category 3 ≤ 2 500 2 500 < Category 4 ≤ 20 000	10 100 700 4 500
Vapours (mg/l)	0 < Category 1 ≤ 0,5 0,5 < Category 2 ≤ 2,0 2,0 < Category 3 ≤ 10,0 10,0 < Category 4 ≤ 20,0	0,05 0,5 3 11
Dust/mist (mg/l)	0< Category 1 ≤ 0,05 0,05 < Category 2 ≤ 0,5 0,5 < Category 3 ≤ 1,0 1,0 < Category 4 ≤ 5,0	0,005 0,05 0,5 1,5

Note 1
These values are designed to be used in the calculation of the ATE for classification of a mixture based on its components and do not represent test results.

Ingredient A is relevant in this class of hazard.

- A – 25.99 % (Acute Tox. 4, H302)

$$ATE_{mix} = \frac{100}{\sum_{i=1}^{n} \frac{C_i}{ATE_{mix}}} = \frac{100}{\frac{25.99}{500}} = \frac{100}{0.05198} = 1923.82 \frac{mg}{kg\ b.w.}$$

According to the table 3.1.2, a result (1923.82 mg/kg bw < 2 000 mg/kg bw) **classifies** the whole formulation as **Acute Tox. 4, H302.**.

A 2.3 Acute percutaneous (dermal) toxicity (KCP 7.1.2)

Comments of zRMS:	The plant protection product CHR/H/PENDIF 599.5 SC was classified by calculation method. According to Regulation (EC) No 1272/2008, no classification for acute dermal toxicity is required. For details, please refer to Part C.

According to point 7.1.2 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

”A test for dermal toxicity shall be carried out on a case by case basis, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, acute dermal toxicity of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the toxic potential of the total mixture. Findings of severe skin irritation or corrosion in the dermal study may be used instead of performing a specific irritation study.”

The complete composition of the formulation with the classification of individual ingredients is available in part C.

The active substances and the other co-formulants are not classified as acute dermal toxic, it can be assumed that entire formulation is not classified in this class. According to point 7.1.2 of part A of Annex Regulation No 284/2014, it is possible to waive from acute dermal toxicity test. Due to the fact, that all components of the formulation CHR/H/PENDIF 599.5 SC are known, the acute dermal toxicity test is not necessary.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	The plant protection product CHR/H/PENDIF 599.5 SC was classified by calculation method. According to Regulation (EC) No 1272/2008, no classification for acute inhalation toxicity is required. For details, please refer to Part C.

Inhalation study on CHR/H/PENDIF 599.5 SC is not required according to point 7.1.3 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products the inhalation test must be carried out since the preparation is:

- a gas or liquefied gas,
- a smoke generating formulation or fumigant,
- used with fogging equipment,
- a vapor releasing preparation,
- an aerosol,
- a powder containing a significant proportion of particles of diameter <50 µm (> 1% on a weight basis),
- to be applied from aircraft in cases where inhalation exposure is relevant,
- contains an active substance with a vapor pressure > 1x10-2 Pa and is to be used in enclosed spaces such as warehouses or glasshouses,
- to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 µm (> 1% on a weight basis).

The active substances and the other co-formulants are not classified as acute inhalation toxic, it can be assumed that entire formulation is not classified in this class. According to point 7.1.3 of part A of Annex Regulation No 284/2014, it is possible to waive from acute inhalation toxicity test.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	The plant protection product CHR/H/PENDIF 599.5 SC was classified by calculation method. According to Regulation (EC) No 1272/2008, no classification for skin irritation is required. For details, please refer to Part C

Reference:	7.1.4
Report	Toxicological classification of product CHR/H/PENDIF 599.5 SC based on calculation method taking into consideration health hazards of constituent substances; 2021; according to Part C, appendix 2

According to point 7.1.4 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:
" The skin irritancy of the plant protection product shall be reported based on the tiered approach, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture."

The complete composition of the formulation with the classification of individual ingredients is available in part C.
For consideration of corrosive and irritant properties the following table applies:

Table 3.2.3
Generic concentration limits of ingredients classified for skin corrosive/irritant hazard (Category 1 or 2) that trigger classification of the mixture as corrosive/irritant to skin.

Sum of ingredients classified as:	Concentration triggering classification of a mixture as:	
	Skin Corrosive	Skin Irritant
	Category 1 (see note below)	Category 2
Skin Corrosive Categories 1A, 1B, 1C	≥ 5 %	≥ 1 % but < 5 %
Skin irritant Category 2		≥ 10 %
10 × Skin Corrosive Category 1A, 1B, 1C) + Skin irritant Category 2		≥ 10 %

Note
The sum of all ingredients of a mixture classified as Skin Corrosive Category 1A, 1B or 1C respectively, shall each be ≥ 5 % respectively in order to classify the mixture as either Skin Corrosive Category 1A, 1B or 1C. If the sum of the Skin Corrosive Category 1A ingredients is < 5 % but the sum of Category 1A+1B ingredients is ≥ 5 %, the mixture shall be classified as Skin Corrosive Category 1B. Similarly, if the sum of Skin Corrosive Category 1A+1B ingredients is < 5 % but the sum of Category 1A+1B+1C ingredients is ≥ 5 % the mixture shall be classified as Skin Corrosive Category 1C.

Ingredients I_2 and K_2 are classified as corrosive to skin. However, all these ingredients are present in the mixture in concentrations of less than 1%. Therefore, these components will not be relevant for the classification of the mixture for skin corrosion.

Ingredient E_1 is relevant in Skin Irrit. 2, H319 class of hazard:

- E_1 - 4.90 % (Skin Irrit. 2, H315)

The concentration of relevant ingredient (4.9 %) is lower than generic concentration level (10%). Therefore the formulation is not classified as skin irritant.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	The plant protection product CHR/H/PENDIF 599.5 SC was classified by calculation method. According to Regulation (EC) No 1272/2008, no classification for eye

	irritation is required. For details, please refer to Part C.
Reference:	7.1.5
Report	Toxicological classification of product CHR/H/PENDIF 599.5 SC based on calculation method taking into consideration health hazards of constituent substances; 2021; according to Part C, appendix 2

According to point 7.1.5 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:
" Eye irritation tests shall be provided, unless it is likely that severe effects on the eyes may be produced or the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, eye irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture."

Due to the fact, that all components of the formulation CHR/H/PENDIF 599.5 SC are known, eye corrosion test is not necessary.

Ingredients K_2, I_2, F_1, I_1, F_2, H_1 and J_1 are classified as corrosive or irritant to eyes. However, all these ingredients are present in the mixture in concentrations of less than 1%. Therefore, these components will not be relevant for the classification of the mixture for eye corrosion or eye irritant.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	In accordance with the provisions of the Regulation EC 1272/2008, the formulation **requires classification in respect to skin sensitisation as Skin Sens. 1, H317**. For details please see part C of dRR.
Reference:	7.1.6
Report	Toxicological classification of product CHR/H/PENDIF 599.5 SC based on calculation method taking into consideration health hazards of constituent substances; 2021; according to Part C, appendix 2

According to point 7.1.46 of Part A of Annex to the Commission Regulation (EU) No 284/2013 as regards the data requirements for plant protection products:

" The skin sensitisation of the plant protection product shall be reported based on the tiered approach, unless the applicant can justify an alternative approach under Regulation (EC) No 1272/2008. In the latter case, skin irritation properties of all components shall be provided or reliably predicted with a validated method. Consideration shall be given to the possible effects of components on the irritant potential of the total mixture."Due to the fact, that all components of the formulation CHR/H/PENDIF 599.5 SC are known, eye corrosion test is not necessary.

Materials and methods

We use the table:

Table 3.4.5
Generic concentration limits of ingredients of a mixture classified as either skin sensitisers or respiratory sensitisers that trigger classification of the mixture

Ingredient classified as:	Concentration triggering classification of a mixture as:		
	Skin Sensitiser	Respiratory Sensitiser	
	All physical states	Solid/Liquid	Gas
Skin Sensitiser Category 1	≥ 1,0 %	-	-
Skin Sensitiser Category 1A	≥ 0,1 %	-	-
Skin Sensitiser Category 1B	≥ 1,0 %		
Respiratory Sensitiser Category 1	-	≥ 1,0 %	≥ 0,2 %
Respiratory Sensitiser Category 1A	-	≥ 0,1 %	≥ 0,1 %
Respiratory Sensitiser Category 1B		≥ 1,0 %	≥ 0,2 %

Ingredients A, H_1, I_1 and K_2 are classified as skin sensitizers:

- A - 25.99 % (Skin Sens. 1, H317)
- H_1 - 0.01215 % (Skin Sens. 1B, H317)
- I_1 - 0.0163 % (Skin Sens. 1, H317)
- K_2 - 0.000245 % (Skin Sens. 1A, H317)

The concentration of ingredient A classified as Skin Sens. 1, H317 is significantly higher that triggering concentration level. Therefore whole formulation will be **classified as Skin Sens. 1, H317**.

A 2.8 Supplementary studies for combinations of plant protection products (KCP 7.1.7)

Not required

A 2.9 Data on co-formulants (KCP 7.4)

A 2.9.1 Material safety data sheet for each co-formulant

Information regarding material safety data sheets of the co-formulants can be found in the confidential dossier of this submission (Registration Report - Part C).

A 2.9.2 Available toxicological data for each co-formulant

Available toxicological data for each co-formulant can be found in the confidential dossier of this submission (Registration Report - Part C).

A 2.10 Studies on dermal absorption (KCP 7.3)

For the dermal absorption of the active substance the Applicant refers to Guidance on Dermal Absorption1 EFSA, EFSA Journal 2017;15(6):4873.

Based on an evaluation of agreed dermal absorption values for a range of concentrated pesticide formulations and their dilutions, the following default values are recommended (see opinion section 4.1.1.for details).
A default dermal absorption value of 25% may be applied for concentrated products that are organic solvent formulated or in other types of formulations.
A default dermal absorption value of 70% may be applied for (in use) dilutions of organic solvent formulated or in other types of formulation.

A 2.11 Other/Special Studies

A 2.11.1 Specific target organ toxicity

Reference:	7.1.7
Report	Toxicological classification of product CHR/H/PENDIF 599.5 SC based on calculation method taking into consideration health hazards of constituent substances; 2021; according to Part C, appendix 2

According to point 3.8.3 of Regulation (EC) No 1272/2008 as regards the data requirements for plant protection products:
" Mixtures are classified using the same criteria as for substances, or alternatively as described below. As with substances, mixtures shall be classified for specific target organ toxicity following single exposure.
Where there is no reliable evidence or test data for the specific mixture itself, and the bridging principles cannot be used to enable classification, then classification of the mixture is based on the classification of the ingredient substances. In this case, the mixture shall be classified as a specific target organ toxicant (specific organ specified), following single exposure, when at least one ingredient has been classified as a Category 1 or Category 2 specific target organ toxicant and is present at or above the appropriate generic concentration limit as mentioned in Table 3.8.3 for Category 1 and 2 respectively"
Due to the fact, that all components of the formulation CHR/H/PENDIF 599.5 SC are known, eye corrosion test is not necessary.
Materials and methods

For consideration of specific target organ properties the following table applies:
Table 3.8.3
Generic concentration limits of ingredients of a mixture classified as a specific target organ toxicant that trigger classification of the mixture as Category 1 or 2.

Ingredient classified as:	Generic concentration limits triggering classification of the mixture as:	
	Category 1	Category 2
Category 1 Specific Target Organ Toxicant	Concentration ≥ 10 %	1,0 % ≤ concentration < 10 %
Category 2 Specific Target Organ Toxicant		Concentration ≥ 10 % [(Note 1)]

Note 1
If a Category 2 specific target organ toxicant is present in the mixture as an ingredient at a concentration ≥ 1,0 % a SDS shall be available for the mixture upon request.

We also took into account the point 3.8.3.4.5.: "Care shall be exercised when extrapolating toxicity of a mixture that contains Category 3 ingredient(s). A generic concentration limit of 20 % is appropriate; however, it shall be recognised that this concentration limit may be higher or lower depending on the Category 3 ingredient(s) and that some effects such as respiratory tract irritation may not occur below a certain concentration while other effects such

~~as narcotic effects may occur below this 20 % value. Expert judgement shall be exercised."~~

~~Results and discussions~~

~~The ingredient A is classified as STOT RE 2, H373. The concentration of the ingredient (25.99%) is higher than concentration triggering classification 10%. According to table 3.8.3. the formulation is classified as STOT RE 2, H373.~~

-KCP 7.0/01 In vitro evaluation of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoro-ethanesulfonic acid, Trifluoroacetic acid and Flufenacet methylsulfone genotoxicity using the micronucleus assay (MNA). J.Antonik, 2016.; SELVITA. Study Number: K81/JA/01.Method: OECD 487
GLP, Unpublished

The formation of MN is a consequence of chromosomal breakage and/or spindle-fiber dysfunction induced by clastogens and/or aneuploidogens. The present study was performed in accordance with the OECD 487 and under GLP requirements. In order to assess genotoxic potential CHO-K1 cells were exposed to test items (Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesul-fonic acid, Trifluoroacetic acid and Flufenacet methylsulfone) and appropriate reference items in system with (+S9) and without (-S9 short and extended treatment) an exogenous metabolic acti-vation. Stati-stical analysis of the MN frequency and binucleate cells with MN was performer using the Chi-square test with Yates' correction. To examine the dose-response relationship in frequencies of the micronuclei Chi-square test for trend was performed.
None of tested concentration of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfo-nic acid, Trifluoroacetic acid and Flufenacet methylsulfone exhibit a statistically significant in-crea-se in MN frequency compared with the concurrent negativecontrol (P>0.05, T bles IX-XIII, Figure I-VII). Chi-square test for trend revealed no dose-related increase in MN frequency (P>0.05).
Results for positive reference items (mitomycin C and cyclophosphamide) demonstrated reproduc-ibility and sensitivity of system.

In summary, the present research has demonstrated that items Flufenacet oxalate, Flufenacet sul-fonic acid, Trifluoroethanesulfonic acid, Trifluoroacetic acid and Flufenacet methylsulfone did not produce dose-dependent genetic toxicity in the CHO-K1 cells.

~~Mutagenic potential of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid was evaluated trough Mouse Lymphoma Assay (MLA) in L5178Y cells. Tested items were analyzed in MLA, in the presence and absence of exogenous metabolic activa-tion.Obtained results have shown that tested item did not exceed MF above a value termed as~~
~~Global Evaluation Factor 126 ×10−6 in any of the tested doses both in the presence and absence of S9 exogenous activation system.~~
~~Obtained results indicate that tested items (Flufenacet oxalate, Flufenacet sulfonic acid, Trifluo-roethanesulfonic acid and Trifluoroacetic acid) or their metabolic derivatives were not positive in Mouse Lymphoma Assay under the protocol described and according to the acceptability criteria defined in OECD guideline 490 and SPB 19.~~

~~Conclusion:~~
~~FOE 5043 sulfonic acid is considered to bee non-mutagenic and have no genotoxicity potential in all of these assays.~~

Cytotoxicity test results for Flufenacet sulfonic acid.

Flufenacet sulfonic acid - Cytotoxicity test

Test item	CBPI	RI [%]	Cytotoxicity [%]	MN [‰]	P value	Cells with MN [‰]	P value
3h (-S9)							
PBS control	1.88	100.0	0.0	5	**NA**	4.5	**NA**
0.2 µg/mL MMC	1.76	86.3	13.7	34	**<0. 0001 (****)**	32	**<0. 0001 (****)**
0.4 µg/mL MMC	1.69	77.9	22.1	36	**<0.0001 (****)**	34	**<0.0001 (****)**
DMSO control	1.90	100.0	0.0				
0.9 µg/mL Flufenacet sulfonic acid	1.89	98.7	1.3				
2.7 µg/mL Flufenacet sulfonic acid	1.90	100.4	-0.4				
8.2 µg/mL Flufenacet sulfonic acid	1.88	98.6	1.4				
24.7 µg/mL Flufenacet sulfonic acid	1.91	101.4	-1.4				
74.1 µg/mL Flufenacet sulfonic acid	1.88	98.7	1.3				
222.2 µg/mL Flufenacet sulfonic acid	1.91	101.2	-1.2				

666.7 µg/mL Flufenacet sulfonic acid	1.93	103.6	-3.6				
2000.0 µg/mL Flufenacet sulfonic acid	1.91	100.9	-0.9				
27h (-S9)							
PBS control	1.89	100.0	0.0	4	NA	4	NA
0.1 µg/mL MMC	1.81	91.0	9.0	27	<0. 0001 (****)	26	<0.0001 (****)
0.2 µg/mL MMC	1.72	81.3	18.7	31	<0.0001 (****)	28	<0.0001 (****)
DMSO control	1.98	100.0	0.0				
0.9 µg/mL Flufenacet sulfonic acid	1.94	96.8	3.2				
2.7 µg/mL Flufenacet sulfonic acid	1.92	94.1	5.9				
8.2 µg/mL Flufenacet sulfonic acid	1.97	99.6	0.4				
24.7 µg/mL Flufenacet sulfonic acid	1.97	99.5	0.5				
74.1 µg/mL Flufenacet sulfonic acid	1.91	92.9	7.1				
222.2 µg/mL Flufenacet sulfonic acid	1.90	92.2	7.8				
666.7 µg/mL Flufenacet sulfonic acid	1.92	93.7	6.3				
2000.0 µg/mL Flufenacet sulfonic acid	1.84	86.4	13.6				
3h (+S9)							
PBS control	1.81	100.0	0.0	7	NA	6.5	NA
5 µg/mL CP	1.81	99.3	0.7	24	<0.0001 (****)	20	0.0004 (***)
10 µg/mL CP	1.80	98.0	2.0	29	<0.0001 (****)	27	<0.0001 (****)
DMSO control	1.85	100.0	0.0				
0.9 µg/mL Flufenacet sulfonic acid	1.77	90.8	9.2				
2.7 µg/mL Flufenacet sulfonic acid	1.78	92.2	7.8				
8.2 µg/mL Flufenacet sulfonic acid	1.79	92.9	7.1				
24.7 µg/mL Flufenacet sulfonic acid	1.78	92.1	7.9				
74.1 µg/mL Flufenacet sulfonic acid	1.79	93.3	6.7				
222.2 µg/mL Flufenacet sulfonic acid	1.81	95.0	5.0				
666.7 µg/mL Flufenacet sulfonic acid	1.77	90.1	9.9				
2000.0 µg/mL Flufenacet sulfonic acid	1.83	97.3	2.7				

Statistically significant level: ns P>0.05; * P≤0.05; ** P≤0.01; *** P≤0.001, **** P<0.0001.

MNA test results for Flufenacet-sulfonic acid .

Flufenacet-sulfonic acid – Genotoxicity test

Test item	CBPI	RI [%]	Cytotoxicity [%]	MN [‰]	P value	Cells with MN [‰]	P value	Result
3h (-S9)								
PBS control	1.92	100.0	0.0	4	NA	4	NA	NA
0.2 µg/mL MMC	1.78	85.4	14.6	32	<0.0001 (****)	36	<0.0001 (***)	positive
0.4 µg/mL MMC	1.66	72.5	27.5	39	<0.0001 (****)	31	<0.0001 (****)	positive
DMSO control	2.00	100.0	0.0	6	NA	6	NA	NA
250 µg/mL Flufenacet sulfonic acid	2.01	101.2	-1.2	9	0.2868	9	0.2704	negative
500 µg/mL Flufenacet sulfonic acid	2.02	102.4	-2.4	9	0.3674	9	0.3504	negative
1000 µg/mL Flufenacet sulfonic acid	2.03	103.3	-3.3	9	0.3674	9	0.2704	negative
2000 µg/mL Flufenacet sulfonic acid	2.05	105.7	-5.7	11	0.1107	10	0.1335	negative
27h (-S9)								
PBS control	2.05	100.0	0.0		NA		NA	NA
0.1 µg/mL MMC	1.91	86.7	13.3	37	0.0007 (***)	35	0.0008 (***)	positive
0.2 µg/mL MMC	1.80	76.1	23.9	47	<0.0001 (****)	43	<0.0001 (****)	positive
DMSO control	2.03	100.0	0.0	7	NA	6	NA	NA
250 µg/mL Flufenacet sulfonic acid	1.97	93.8	6.2	6	0.9940	6	0.8425	negative
500 µg/mL Flufenacet sulfonic acid	2.04	101.0	-1.0	8	0.7373	8	0.5954	negative
1000 µg/mL Flufenacet sulfonic acid	2.03	99.3	0.7	8	0.8671	8	0.7166	negative
2000 µg/mL Flufenacet sulfonic acid	2.01	97.5	2.5	9	0.4751	9	0.3638	negative
3h (+S9)								
PBS control	1.87	100.0	0.0	8	NA	8	NA	NA
5 µg/mL CP	1.81	92.3	7.7	17	0.0166 (*)	17	0.0201 (**)	positive
10 µg/mL CP	1.81	92.4	7.6	20	0.0031 (**)	19	<0.0001 (****)	positive
DMSO control	1.91	100.0	0.0	8	NA	8	NA	NA
250 µg/mL Flufenacet sulfonic acid	1.80	99.1	0.9	9	0.7245	9	0.7245	negative
500 µg/mL Flufenacet sulfonic acid	1.94	103.6	-3.6	9	0.8613	8	0.8613	negative
1000 µg/mL Flufenacet sulfonic acid	1.91	100.2	-0.2	11	0.3992	10	0.3992	negative
2000 µg/mL Flufenacet sulfonic acid	1.89	98.5	1.5	10	0.5993	9	0.8503	negative

Statistically significant level: ns P>0.05; * P≤0.05; ** P≤0.01; *** P≤0.001, **** P<0.0001.

Comments of zRMS:	The study is considered acceptable. Deviations to OECD 487, 2016 : no historical control data for negative and positive controls. Flufenacet sulfonic acid is negative in the *in vitro* micronucleus test. **MATERIALS** Test material: Flufenacet sulfonic acid Lot/Batch no: EXP-1-5-DFO394 Expiry date: 12/2017 Test system: CHO-K1: Chinese hamster ovary cell line Origin: CLS Cat. No: 603480

	Schedule of the MNA test -S9 short treatment – Treatment for 3h with test items (at 37°C) – Removal the treatment medium – Addition of fresh medium and cytochalasin B (cytoB) – Harvesting 1.5 – 2.0 normal cell cycles later (27h) -S9 extended treatment – Treatment for 1.5 – 2 normal cell cycles (27h) – with test items in the presence of cytoB (at 37°C) – Harvesting at the end of the exposure period +S9 short treatment – Treatment for 3h with test items in the presence of S9 (at 37°C) – Removal the S9 and treatment medium – Addition fresh medium and cytoB – Harvesting 1.5 – 2.0 normal cell cycles later (27h) **Test item concentration** -S9/ +S9: 250, 500, 1000, 2000 µg/mL in DMSO **Results** MN frequency and binucleate cells: Chi-square test with Yates' correction for a=0.05. MN scoring: light microscope using criteria defined by Fenech et al. (2003) Cytotoxicity assessment: cytotoxicity block proliferation index (CBPI) The highest tested concentrations of Flufenacet sulfonic acid at any tested concentration did not reduce CBPI or RI to 45±5% of the concurrent negative control (1% v/v DMSO) in test with and without (-S9 short and extended treatment) metabolic activation. The items tested under condition with and without metabolic activation at analyzed concentrations did not exhibit statistically significant increase in micronucleus frequency per culture compared with the concurrent negative control. A significant concentration-related increase in frequency of MN was not observed in cultures treated with Flufenacet sulfonic acid.

- KCP 7.0/02 *In vitro* Mammalian Cell Gene Mutation test (OECD 490) - genotoxicity determination of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid by Mouse Lymphoma Assay. J.Antonik; 2016; Study number: K82/JA/01; SELVITA; OECD 490, GLP, Unpublished

Mutagenic potential of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid was evaluated trough Mouse Lymphoma Assay (MLA) in L5178Y cells. Tested items were analyzed in MLA, in the presence and absence of exogenous metabolic activation.Obtained results have shown that tested item did not exceed MF above a value

Mouse Lymphoma Assay under the protocol described and according to the acceptability criteria defined in OECD guideline 490 and SPB-19

~~Conclusion on toxicological significance of the metabolite FOE sulfonic acid:~~

~~The goal of the additional physico-chemical and biological experiments which were requested from the applicant was to demonstrate that the metabolite M2 (FOE sulfonic acid) was poorly absorbed orally, and had a low potential toxicity.~~

~~Based firstly on the physical properties that show a high hydrosolubility which suggests a low bio-logical absorption,~~
~~- The solubility in water is 55g/l at 20°C at pH 4 to 9 ; under the same conditions, its Kow is 0.0019, leading to a log Kow = -2.72 ; the pKa of sulfonic acid is <1~~
~~and secondly on the biological investigations that show poor biological disposition and low toxicity, the metabolite FOE 5043 sulfonic acid is considered of no toxicological relevance~~

Evaluation of the potential cytotoxic activity of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid in the Mouse Lymphoma Assay in the presence of S9 fraction – 4h (initial dose range-finding assay).

Cpd.	Conc.	RSG	RTG	RV	RS	Colony counts	% Small colonies	Mutation Frequency [1x10⁻⁶]	Fold increase	Induced MF [1x10⁻⁶]
Flufenacet sulfonic acid	2000.00 µg/mL	0.64	0.38	119%	60%	51	41%	112.34	0.82	-25
Flufenacet sulfonic acid	666.67 µg/mL	0.49	0.22	100%	46%	53	30%	154.37	1.12	17
Flufenacet sulfonic acid	222.22 µg/mL	1.21	0.97	97%	80%	33	45%	93.14	0.68	-44
Flufenacet sulfonic acid	74.07 µg/mL	1.45	1.32	94%	91%	42	36%	125.90	0.92	-12
Flufenacet sulfonic acid	24.69 µg/mL	0.60	0.52	148%	87%	72	36%	151.31	1.10	14
Flufenacet sulfonic acid	8.23 µg/mL	1.20	0.70	89%	58%	38	29%	117.91	0.86	-20
Flufenacet sulfonic acid	2.74 µg/mL	1.02	0.74	98%	72%	43	49%	123.19	0.90	-14
Flufanecet sulfonic acid	0.00 µg/mL*	1.00	1.00	100%	100%	50	46%	137.48	1.00	0.00
Trifluoroethane sulfonic acid	10.00 mM	0.58	0.55	132%	96%	35	46%	88.29	1.32	21
Trifluoroethane sulfonic acid	3.33 mM	0.75	0.67	83%	89%	28	54%	105.74	1.58	39
Trifluoroethane sulfonic acid	1.11 mM	0.60	0.58	102%	97%	35	43%	114.40	1.71	48
Trifluoroethane sulfonic acid	0.37 mM	0.50	0.49	100%	99%	35	60%	112.47	1.68	46
Trifluoroethane sulfonic acid	0.12 mM	0.67	0.66	111%	99%	36	36%	107.59	1.61	41
Trifluoroethane sulfonic acid	0.04 mM	0.51	0.55	115%	107%	40	35%	113.96	1.70	47
Trifluoroethane sulfonic acid	0.01 mM	0.65	0.77	132%	119%	35	46%	88.29	1.32	21
Trifluoroethane sulfonic acid	0.00 mM*	1.00	1.00	100%	100%	21	48%	66.84	1.00	0

Evaluation of the potential cytotoxic activity of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid in the Mouse Lymphoma Assay in the absence of S9 fraction – 4h (initial dose range-finding assay).

Cpd.	Conc.	RSG	RTG	RV	RS	Colony counts	% Small colonies	Mutation Frequency [1x10^{-6}]	Fold increase	Induced MF [1x10^{-6}]
Flufenacet sulfonic acid	2000.00 µg/mL	1.10	1.06	108%	97%	21	57%	59.07	1.16	8
Flufenacet sulfonic acid	666.67 µg/mL	0.71	0.76	135%	107%	23	35%	52.04	1.02	1
Flufenacet sulfonic acid	222.22 µg/mL	0.82	1.09	128%	132%	21	48%	49.92	0.98	-1
Flufenacet sulfonic acid	74.07 µg/mL	0.74	1.00	130%	135%	23	39%	54.00	1.06	3
Flufenacet sulfonic acid	24.69 µg/mL	0.68	0.69	135%	102%	25	64%	56.89	1.11	6
Flufenacet sulfonic acid	8.23 µg/mL	0.56	0.57	112%	102%	19	37%	48.62	0.95	-3
Flufenacet sulfonic acid	2.74 µg/mL	0.64	0.64	138%	100%	22	50%	48.69	0.95	-2
Flufanecet sulfonic acid	0.00 µg/mL*	1.00	1.00	100%	100%	18	56%	51.12	1.00	0

Evaluation of the potential cytotoxic activity of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid in the Mouse Lymphoma Assay in the absence of S9 fraction – 24h (initial dose range-finding assay).

Cpd.	Conc.	RSG	RTG	RV	RS	Colony counts	% Small colonies	Mutation Frequency [1x10^{-6}]	Fold increase	Induced MF [1x10^{-6}]
Flufenacet sulfonic acid	2000.00 µg/mL	1.17	1.23	111%	104%	42	50%	106.39	0.88	-15
Flufenacet sulfonic acid	666.67 µg/mL	1.02	1.01	129%	99%	53	49%	116.63	0.96	-5
Flufenacet sulfonic acid	222.22 µg/mL	1.18	1.16	88%	99%	47	47%	152.45	1.26	31
Flufenacet sulfonic acid	74.07 µg/mL	0.76	1.07	80%	141%	42	38%	146.78	1.21	26
Flufenacet sulfonic acid	24.69 µg/mL	0.46	0.51	161%	109%	37	54%	63.60	0.52	-58
Flufenacet sulfonic acid	8.23 µg/mL	0.80	1.12	141%	139%	44	41%	87.97	0.73	-33
Flufenacet sulfonic acid	2.74 µg/mL	1.00	1.57	107%	156%	46	52%	122.29	1.01	1
Flufanecet sulfonic acid	0.00 µg/mL*	1.00	1.00	100%	100%	43	44%	121.17	1.00	0

Evaluation of the potential mutagenic activity of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid in the Mouse Lymphoma Assay in the presence of S9 - 4h (Definitive Mutagenicity Assay).

Cpd.	Conc.	RSG	RTG	RV	RS	Colony counts	% Small colonies	Mutation Frequency [1x10^{-6}]	Fold increase	Induced MF [1x10^{-6}]
Flufenacet sulfonic acid	2000 µg/mL	1.26	1.55	96%	123%	23	26%	55.98	0.70	-24
Flufenacet sulfonic acid	1000 µg/mL	1.41	1.77	89%	126%	27	33%	72.43	0.91	-7
Flufenacet sulfonic acid	500 µg/mL	0.88	0.84	100%	95%	32	47%	74.53	0.93	-5
Flufenacet sulfonic acid	250 µg/mL	1.35	1.35	98%	100%	35	57%	86.73	1.09	7
Flufanecet sulfonic acid	0.00 µg/mL*	1.00	1.00	100%	100%	35	49%	79.82	1.00	0

Evaluation of the potential mutagenic activity of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid in the Mouse Lymphoma Assay in the absence of S9- 4h (Definitive Mutagenicity Assay).

Cpd.	Conc.	RSG	RTG	RV	RS	Colony counts	% Small colonies	Mutation Frequency [1x10^{-6}]	Fold increase	Induced MF [1x10^{-6}]

Flufenacet sulfonic acid	2000 µg/mL	1.45	1.59	116%	110%	32	56%	106.80	0.93	-8
Flufenacet sulfonic acid	1000 µg/mL	0.75	0.58	135%	78%	34	59%	94.65	0.82	-21
Flufenacet sulfonic acid	500 µg/mL	1.25	1.20	111%	96%	20	60%	67.37	0.58	-48
Flufenacet sulfonic acid	250 µg/mL	1.24	1.01	123%	81%	30	63%	90.29	0.78	-25
Flufanecet sulfonic acid	0.00 µg/mL*	1.00	1.00	100%	100%	31	52%	115.19	1.00	0

Evaluation of the potential mutagenic activity of Flufenacet oxalate, Flufenacet sulfonic acid, Trifluoroethanesulfonic acid and Trifluoroacetic acid in the Mouse Lymphoma Assay in the absence of S9 - 24h (Definitive Mutagenicity Assay).

Cpd.	Conc.	RSG	RTG	RV	RS	Colony counts	% Small colonies	Mutation Frequency [1x10^{-6}]	Fold increase	Induced MF [1x10^{-6}]
Flufenacet sulfonic acid	2000 µg/mL	0.89	0.80	102%	90%	23	57%	57.97	0.94	-4
Flufenacet sulfonic acid	1000 µg/mL	0.89	0.87	75%	98%	17	65%	56.78	0.92	-5
Flufenacet sulfonic acid	500 µg/mL	0.79	0.75	102%	95%	20	70%	49.97	0.81	-12
Flufenacet sulfonic acid	250 µg/mL	0.84	0.89	73%	106%	21	48%	73.05	1.18	11
Flufanecet sulfonic acid	0.00 µg/mL*	1.00	1.00	100%	100%	24	58%	61.71	1.00	0

Comments of zRMS:	The study is considered acceptable. Deviations to OECD 490, 2016 : no historical control data for negative and positive controls. Flufenacet sulfonic acid is negative in the *in vitro m*ammalian cell gene mutation test. **Materials** Test material: Flufenacet sulfonic acid Lot/Batch no: EXP-1-5-DFO394 Expiry date: 12/2017 Test system: Cell line: L5178Y TK+/− clone (3.7.2C) Origin: American type culture collection (ATCC) Cat. No: CRL-9518 Lot No: 607 979 977 **MLA test** +S9 - 4 h -S9 - 4 h -S9 - 24 h **Test item concentration** 250, 500, 1000, 2000 µg/mL in DMSO [1% v/v] **Results**

	None of doses Flufenacet sulfonic acid induced dose-related cytotoxic and mutagenic effects in mouse lymphoma cells under experimental conditions in definitive mutagenicity assays. In the absence and presence of metabolic activation induced mutation frequency level did not exceed 126 $\times 10^{-6}$ in any of the doses tested. MMS and Cp were used in different concentrations as positive controls without or with S9, respectively. Both positive controls yielded MF above 300 $\times 10^{-6}$ in TFT-resistant colonies, therefore indicating the assay sensitivity and responsiveness to mutagens. Negative controls, PBS (for MMS and Cp), DMSO met acceptability criteria defined in OECD 490. Obtained results indicate that the tested item is considered as non-mutagenic under the conditions employed and according to the acceptability criteria defined in OECD guideline 490 and SPB-19.

A 2.12 Operator exposure calculations (KCP 7.2.1.1)

A 2.12.1 Calculations for penoxsulam

Table A 1: Estimation of operator exposure towards penoxsulam using the EFSA Model without PPP

Operator exposure for outdoor spray applications

Application rate of active substance	0.015 kg a.s./ha		*i_AppRate*
Assumed area treated	50 ha/day		*d_AreaTreated*
Amount of active substance applied	0.75 kg a.s./day		*i_AmoutAS*
Dermal absorption of the product	50.00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50.00%		*i_AbsorInuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

Suitable for: soluble concentrates, emulsifiable concentrates, etc. Downward spraying. Vehicle-mounted.

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	3892	14225	AOEM	
	Body	2914	66249	AOEM	
	Head	39	213	AOEM	
	Protected hands (gloves)	29	149	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	18	110	AOEM	
	Protected head (hood and face shield)	1	12	AOEM	
	Inhalation	3	29	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	111	1856	AOEM	
	Body	62	321	AOEM	
	Head	3	9	AOEM	
	Protected hands (gloves)	36	3223	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	2	4	AOEM	
	Inhalation	1	2	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	3.5150247	3.5150247	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0585837	0.0585837	
% of RVNAS	32.55%	32.55%	
Acute			
Total systemic exposure from mixing, loading and application (mg a.s./day)	41.4675725	41.4675725	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.6911262	0.6911262	
% of RVAAS	#DZIEL/0!	#DZIEL/0!	

Table A 2: Estimation of operator exposure towards penoxsulam using the EFSA Model with gloves and protective clothing at mixing/loading

Operator exposure for outdoor spray applications

Application rate of active substance	0.015 kg a.s./ha		*i_AppRate*
Assumed area treated	50 ha/day		*d_AreaTreated*
Amount of active substance applied	0.75 kg a.s./day		*i_AmoutAS*
Dermal absorption of the product	50.00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50.00%		*i_AbsorInuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

Outdoor/Soluble concentrates, emulsifiable concentrate, etc/Downward spraying/Vehicle-mounted

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	3892	14225	AOEM	
	Body	2914	66249	AOEM	
	Head	39	213	AOEM	
	Protected hands (gloves)	29	149	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	18	110	AOEM	
	Protected head (hood and face shield)	1	12	AOEM	
	Inhalation	3	29	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	111	1856	AOEM	
	Body	62	321	AOEM	
	Head	3	9	AOEM	
	Protected hands (gloves)	36	3223	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	2	4	AOEM	
	Inhalation	1	2	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	3.5150247	0.1354264	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0585837	0.0022571	
% of RVNAS	32.55%	1.25%	
Acute			
Total systemic exposure from mixing, loading and application (mg a.s./day)	41.4675725	1.3596960	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.6911262	0.0226616	
% of RVAAS	#DZIEL/0!	#DZIEL/0!	

A 2.12.2 Calculations for Diflufenican

Table A 1: Estimation of operator exposure towards diflufenican using the EFSA Model without PPP

Operator exposure for outdoor spray applications

Application rate of active substance	0.1 kg a.s./ha	*i_AppRate*	
Assumed area treated	50 ha/day	*d_AreaTreated*	
Amount of active substance applied	5 kg a.s./day	*i_AmoutAS*	
Dermal absorption of the product	10.00%	*i_AbsorpProduct*	
Dermal absorption of in-use dilution	50.00%	*i_AbsorInuse*	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

Dispersible concentrate, emulsifiable concentrate, etc. Downward spraying Vehicle-mounted

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	16767	62314	AOEM	
	Body	11058	114960	AOEM	
	Head	259	1423	AOEM	
	Protected hands (gloves)	98	990	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	99	731	AOEM	
	Protected head (hood and face shield)	4	81	AOEM	
	Inhalation	6	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	742	7449	AOEM	
	Body	415	2138	AOEM	
	Head	20	59	AOEM	
	Protected hands (gloves)	102	4021	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	11	28	AOEM	
	Inhalation	2	7	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	3.4045985	3.4045985	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0567433	0.0567433	
% of RVNAS	51.58%	51.58%	
Acute			
Total systemic exposure from mixing, loading and application (mg a.s./day)	22.7296048	22.7296048	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.3788267	0.3788267	
% of RVAAS	#DZIEL/0!	#DZIEL/0!	

Table A 2: Estimation of operator exposure towards diflufenican using the EFSA Model with gloves at mixing/loading

Operator exposure for outdoor spray applications

Application rate of active substance	0.1 kg a.s./ha	*i_AppRate*	
Assumed area treated	50 ha/day	*d_AreaTreated*	
Amount of active substance applied	5 kg a.s./day	*i_AmoutAS*	
Dermal absorption of the product	10.00%	*i_AbsorpProduct*	
Dermal absorption of in-use dilution	50.00%	*i_AbsorInuse*	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

Outdoor;Soluble concentrates, emulsifiable concentrate, etc;Downward spraying;Vehicle-mounted

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	16767	62314	AOEM	
	Body	11058	114960	AOEM	
	Head	259	1423	AOEM	
	Protected hands (gloves)	98	990	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	99	731	AOEM	
	Protected head (hood and face shield)	4	81	AOEM	
	Inhalation	6	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	742	7449	AOEM	
	Body	415	2138	AOEM	
	Head	20	59	AOEM	
	Protected hands (gloves)	102	4021	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	11	28	AOEM	
	Inhalation	2	7	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	3.4045985	0.6418892	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0567433	0.0106982	
% of RVNAS	51.58%	9.73%	
Acute			
Total systemic exposure from mixing, loading and application (mg a.s./day)	22.7296048	5.1743629	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.3788267	0.0862394	
% of RVAAS	#DZIEL/0!	#DZIEL/0!	

A 2.12.3 Calculations for Flufenacet

Table A 1: Estimation of operator exposure towards flufenacet using the EFSA Model without PPP

Operator exposure for outdoor spray applications

Application rate of active substance	0.1248	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	6.24	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	10.00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50.00%		*i_AbsorInuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	19885	74046	AOEM	
	Body	12921	122602	AOEM	
	Head	324	1776	AOEM	
	Protected hands (gloves)	113	1236	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	120	913	AOEM	
	Protected head (hood and face shield)	5	101	AOEM	
	Inhalation	6	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	926	8761	AOEM	
	Body	517	2668	AOEM	
	Head	24	74	AOEM	
	Protected hands (gloves)	115	4126	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	14	35	AOEM	
	Inhalation	3	8	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	4.0556382	4.0556382	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0675940	0.0675940	
% of RVNAS	397.61%	397.61%	
Acute			
Total systemic exposure from mixing, loading and application (mg a.s./day)	25.6320504	25.6320504	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.4272008	0.4272008	
% of RVAAS	#DZIEL/0!	#DZIEL/0!	

Table A 2: Estimation of operator exposure towards flufenacet using the EFSA Model with gloves and protective clothing at mixing/loading

Operator exposure for outdoor spray applications

Application rate of active substance	0.1248	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	6.24	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	10.00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	50.00%		*i_AbsorInuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

	Exposure values	µg exposure/day mixed and loaded 75th centile	95th centile	Reference	Comment
Mixing and loading	Hands	19885	74046	AOEM	
	Body	12921	122602	AOEM	
	Head	324	1776	AOEM	
	Protected hands (gloves)	113	1236	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	120	913	AOEM	
	Protected head (hood and face shield)	5	101	AOEM	
	Inhalation	6	30	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	Yes		Incl. in AOEM model	
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied 75th centile	95th centile	Reference	Comment
Application	Hands	926	8761	AOEM	
	Body	517	2668	AOEM	
	Head	24	74	AOEM	
	Protected hands (gloves)	115	4126	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	14	35	AOEM	
	Inhalation	3	8	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Potential exposure		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	4.0556382	0.7984812	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0675940	0.0133080	
% of RVNAS	397.61%	78.28%	
Acute			
Total systemic exposure from mixing, loading and application (mg a.s./day)	25.6320504	6.1820099	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.4272008	0.1030335	
% of RVAAS	#DZIEL/0!	#DZIEL/0!	

A 2.13 Worker exposure calculations (KCP 7.2.3.1)

A 2.13.1 Calculations for penoxsulam

Worker exposure from residues on foliage for			
Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0.015	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.0		*d_MAF*
Dermal absorption of the product	50.00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	50.00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.045	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	0.5625000	0.0630000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0093750	0.0010500		
% of RVNAS	5.21%	0.58%		

A 2.13.2 Calculations for diflufenican

Worker exposure from residues on foliage for			
Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0.1	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.0		*d_MAF*
Dermal absorption of the product	10.00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	50.00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.3	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	3.7500000	0.4200000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0625000	0.0070000		
% of RVNAS	56.82%	6.36%		

A 2.13.3 Calculations for flufenacet

Worker exposure from residues on foliage for			
Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0.1248	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.0		*d_MAF*
Dermal absorption of the product	10.00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	50.00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.3744	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	4.6800000	0.5241600	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0780000	0.0087360		
% of RVNAS	458.82%	51.39%		

A 2.14 Resident and bystander exposure calculations (KCP 7.2.2.1)

A 2.14.1 Calculations for penoxsulam

Resident exposure for			
Croptype	Cereals		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	0.015	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	0.075	g a.s./l	d_ConcAS
Dermal absorption of product	50.00%		i_AbsorpProduct
Dermal absorption of in-use dilution	50.00%		i_AbsorpInuse
Oral absorption	100.00%		i_AbsorpOralInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.045	µg a.s./cm^2	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Volat
Concentration in air	0.001	mg/m^3	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m^3/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m^3/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm^2/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	d_ReTCCh
Saliva extraction percentage	50.00%		d_SalExt
Surface area of hands mouthed	20	cm^2	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm^2	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) - adı	7500	cm^2/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	d_TcEntryCh

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0100718	0.0107000	0.0012138	0.0126563	0.0272277
Total systemic exposure per kg body weight	0.0010072	0.0010700	0.0001214	0.0012656	0.0027228
% of RVNAS	0.56%	0.59%	0.07%	0.70%	1.51%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0144600	0.0138000	0.0030660	0.0421875	0.0565518
Total systemic exposure per kg body weight	0.0002410	0.0002300	0.0000511	0.0007031	0.0009425
% of RVNAS	0.13%	0.13%	0.03%	0.39%	0.52%

A 2.14.2 Calculations for diflufenican

Resident exposure for				
Croptype	Cereals			
Application method	Downward spraying			
Application equipment	Vehicle-mounted			*i_AppEquip*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.			*i_FormVal*
Buffer strip	2-3	m		*i_Buffer*
Application rate of the product	0.1	kg a.s./ha		*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	0.5	g a.s./l		*d_ConcAS*
Dermal absorption of product	10.00%			*i_AbsorpProduct*
Dermal absorption of in-use dilution	50.00%			*i_AbsorpInuse*
Oral absorption	100.00%			*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.3	µg a.s./cm^2		*d_DFR*
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa		*i_Volat*
Concentration in air	0.001	mg/m^3		*d_AirCon*
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person		
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person		
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person		
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person		
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person		
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person		
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person		
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person		
Exposure duration dermal	2	hours		*d_ReExpDur*
Exposure duration inhalation	24	hours		*d_ReExpDurInhal*
Exposure duration entry into treated crops	0.25	hours		*d_ExpDurTreatCrop*
Light clothing adjustment factor	18.0%			*d_ClothAF*
Breathing rate adult	0.23	m^3/day/kg		*d_BreathRAd*
Breathing rate child (1-3 year old)	1.07	m^3/day/kg		*d_BreathRCh*
Drift percentage on surface (75th percentile)	5.60%			
Drift percentage on surface (mean)	4.10%			
Turf transferable residues percentage	5.00%			*d_Turf*
Transfer coeff. of surface deposits-adult	7300	cm^2/hour		*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour		*d_ReTCCh*
Saliva extraction percentage	50.00%			*d_SalExt*
Surface area of hands mouthed	20	cm^2		*d_AreaHM*
Frequency of hand to mouth activity	9.5	events/hour		*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2		*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20.00%			*d_DRP*
Transfer coefficient for entry into treated crops (75th percentile) - adı	7500	cm^2/h		*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h		*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h		*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h		*d_TcEntryCh*

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0671450	0.0107000	0.0080920	0.0843750	0.1208845
Total systemic exposure per kg body weight	0.0067145	0.0010700	0.0008092	0.0084375	0.0120885
% of RVNAS	6.10%	0.97%	0.74%	7.67%	10.99%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0964000	0.0138000	0.0204400	0.2812500	0.2988119
Total systemic exposure per kg body weight	0.0016067	0.0002300	0.0003407	0.0046875	0.0049802
% of RVNAS	1.46%	0.21%	0.31%	4.26%	4.53%

Resident exposure for		
Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Buffer strip	2-3	m
Application rate of the product	0,1	kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	0,5	g a.s./l
Dermal absorption of product	10,00%	
Dermal absorption of in-use dilution	50,00%	
Oral absorption	58,00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,3	µg a.s./cm^2
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa
Concentration in air	0,001	mg/m^3
Resident dermal spray drift exposure 75th percentile - adult	0,47	ml spray dilution/person
Resident dermal spray drift exposure 75th percentile - child	0,327	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - adult	0,00010	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - child	0,00022	ml spray dilution/person
Resident dermal spray drift exposure mean - adult	0,22318	ml spray dilution/person
Resident dermal spray drift exposure mean - child	0,18	ml spray dilution/person
Resident inhal. spray drift exposure mean - adult	0,00009	ml spray dilution/person
Resident inhal. spray drift exposure mean - child	0,00017	ml spray dilution/person
Exposure duration dermal	2	hours
Exposure duration inhalation	24	hours
Exposure duration entry into treated crops	0,25	hours
Light clothing adjustment factor	18,0%	
Breathing rate adult	0,23	m^3/day/kg
Breathing rate child (1-3 year old)	1,07	m^3/day/kg
Drift percentage on surface (75th percentile)	5,60%	
Drift percentage on surface (mean)	4,10%	
Turf transferable residues percentage	5,00%	
Transfer coeff. of surface deposits-adult	7300	cm^2/hour
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour
Saliva extraction percentage	50,00%	
Surface area of hands mouthed	20	cm^2
Frequency of hand to mouth activity	9,5	events/hour
Ingestion rate for mouthing of grass per day	25	cm^2
Dislodgeable residues percentage transferability for object to mouth	20,00%	
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500	cm^2/h
Transfer coefficient for entry into treated crops (75th percentile) - child	2250	cm^2/h
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)
Total systemic exposure (mg a.s./day)	0,0671450	0,0107000	0,0077510	0,0843750
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0067145	0,0010700	0,0007751	0,0084375
% of RVNAS	6,10%	0,97%	0,70%	7,67%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops
Total systemic exposure (mg a.s./day)	0,0964000	0,0138000	0,0204400	0,2812500
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0016067	0,0002300	0,0003407	0,0046875
% of RVNAS	1,46%	0,21%	0,31%	4,26%

A 2.14.3 Calculations for flufenacet

Resident exposure for			
Croptype	Cereals		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		i_FormVal
Buffer strip	2-3	m	i_Buffer
Application rate of the product	0.1248	kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	0.624	g a.s./l	d_ConcAS
Dermal absorption of product	10.00%		i_AbsorpProduct
Dermal absorption of in-use dilution	50.00%		i_AbsorpInuse
Oral absorption	100.00%		i_AbsorpOralInuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.3744	µg a.s./cm^2	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	i_Volat
Concentration in air	0.001	mg/m^3	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	d_ReExpDur
Exposure duration inhalation	24	hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25	hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%		d_ClothAF
Breathing rate adult	0.23	m^3/day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07	m^3/day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		d_Turf
Transfer coeff. of surface deposits-adult	7300	cm^2/hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	d_ReTCCh
Saliva extraction percentage	50.00%		d_SalExt
Surface area of hands mouthed	20	cm^2	d_AreaHM
Frequency of hand to mouth activity	9.5	events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25	cm^2	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%		d_DRP
Transfer coefficient for entry into treated crops (75th percentile) - ad	7500	cm^2/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	d_TcEntryCh

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0837970	0.0107000	0.0100988	0.1053000	0.1482103
Total systemic exposure per kg body weight	0.0083797	0.0010700	0.0010099	0.0105300	0.0148210
% of RVNAS	49.29%	6.29%	5.94%	61.94%	87.18%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.1203072	0.0138000	0.0255091	0.3510000	0.3694949
Total systemic exposure per kg body weight	0.0020051	0.0002300	0.0004252	0.0058500	0.0061582
% of RVNAS	11.79%	1.35%	2.50%	34.41%	36.22%

A 2.15 Combined exposure calculations for penoxsulam, diflufenican and flufenacet

Application scenario	Active ingredient	Estimated exposure / AAOEL (HQ)
Operators –with PPE (glove + work wear during mix/loading)	Penoxsulam	0.0125
	Diflufenican	0.0973

Application scenario	Active ingredient	Estimated exposure / AA-OEL (HQ)
	Flufenacet	0.7828
	Cumulative risk operators (HI)	**0.8926**
Workers – with PPE	Penoxsulam	0.0058
	Diflufenican	0.0636
	Flufenacet	0.5139
	Cumulative risk workers (HI)	**0.5833**
Bystander - child	Penoxsulam	0.0151
	Diflufenican	0.1033
	Flufenacet	0.8718
	Cumulative risk bystander – child (HI)	**0.9902**
Bystander - adult	Penoxsulam	0.0052
	Diflufenican	0.0443
	Flufenacet	0.3622
	Cumulative risk bystander – adult (HI)	0.4117
Resident - child	Penoxsulam	0.0151
	Diflufenican	0.1033
	Flufenacet	0.8718
	Cumulative risk bystander – child (HI)	**0.9902**
Resident - adult	Penoxsulam	0.0052
	Diflufenican	0.0443
	Flufenacet	0.3622
	Cumulative risk bystander – adult (HI)	**0.4117**

Appendix 3 Detailed evaluation of exposure and/or DFR studies relied upon (KCP 7.2, KCP 7.2.1.1, KCP 7.2.2.1, KCP 7.2.3.1)