FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: A18385B

Product name: Spandis 54 WG

Chemical active substances:

Dicamba, 400 g/kg
Nicosulfuron, 100 g/kg
Prosulfuron, 40 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(new authorization)

Applicant: Syngenta

Submission date: 26/11/2020

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Version history

When	What
February 2021	Dossier sent for evaluation
April 2022	zRMS evaluation of dRR
July 2022	Updates from the applicant based on the comments from Slovenia (cMS)
July 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)

6.1 Summary

Table 6.1-1: Information on A18385B *

Product name and code	A18385B
Formulation type	Water dispersible granule [WG]
Active substance(s) (incl. content)	Prosulfuron, 40 g/kg Nicosulfuron, 100 g/kg Dicamba, 400 g/kg
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	Yes For a detailed list of authorizations granted by various MS' please refer to Part B, Section 0.

* Information on the detailed composition of A18385B 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 A18385B according to Regulation (EC) No 1272/2008

Hazard class(es), categories:	Eye Irrit. 2
Hazard pictograms or Code(s) for hazard pictogram(s):	GHS07
Signal word:	Warning
Hazard statement(s):	H319 Causes serious eye irritation
Precautionary statement(s):	P264 Wash skin thoroughly after handling, P280 Wear eye protection/face protection; P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing; P337 + P313 If eye irritation persists: Get medical advice/attention.
Additional labelling phrases:	EUH401 To avoid risks to man and the environment, comply with the instructions for use.

Table 6.1-3: Summary of risk assessment for operators, workers, bystanders and residents for A18385B

	Result	PPE / Risk mitigation measures
Operators	Acceptable	None according to the exposure assessment. Due to the classification of the product - Wear eye protection/face protection when handling the product.
Workers	Acceptable	None
Bystanders	Acceptable	None
Residents	Acceptable	None

No unacceptable risk for operators, workers, bystanders and residents 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 bystanders/residents 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, bystander or resident 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) prosulfuron** **b) nicosulfuron** **c) dicamba**	**Water L/ha** **min / max**			**Operator**	**Worker**	**Bystander**	**Residents**
1	Maize (BBCH 12-18)	F	Spraying, LCTM	1 (1 appl. every 3rd year)	a) 0.02 b) 0.05 c) 0.20	200 - 400	-	Operators, workers, residents [EFSA Guidance]; Bystanders, residents (Martin *et al.*) Use with and without adjuvant	A	A	A	A

* 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:

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 substances

	Prosulfuron	**Nicosulfuron**	**Dicamba**
Common Name	Prosulfuron	Nicosulfuron	Dicamba
CAS-No.	94125-34-5	111991-09-4	1918-00-9
Classification and proposed labelling			
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes(s), categories: Acute Tox. 4 Code(s) for hazard pictogram(s): GHS07 Signal word: Warning Hazard statement(s): H302 Precautionary statement(s): P264, P270; P301 + P312, P330; P501	Hazard classes (s), categories: None Code(s) for hazard pictogram(s): None Signal word: None Hazard statement(s): None Precautionary statement(s): None	Hazard classes (s), categories: Acute Tox. 4 Eye Dam. 1 Code(s) for hazard pictogram(s): GHS07, GHS07 Signal word: Danger Hazard statement(s): H302 H318 H332* Precautionary statement(s): P264, P270; P301 + P312, P330; P501 P280; P305 + P351 + P338; P310
Additional C&L proposal	Not applicable	Not applicable	Not applicable
Agreed EU endpoints			
AOEL systemic	0.06 mg/kg bw/d (not corrected for oral absorption)	0.8 mg/kg bw/d (corrected for 40% oral absorption)	0.3 mg/kg bw/d (not corrected for oral absorption)
Reference	EFSA Journal 2014;12(9):3815	EFSA Scientific Report (2007) 120, 1-91	EFSA Journal 2011;9(1):1965
Conditions to take into account/critical areas of concern with regard to toxicology			
EFSA Conclusion for active substance	None	None	None

* While this is not a harmonized classification for Dicamba yet, Syngenta is proactively included that classification here.

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for A18385B 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 A18385B

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat (OECD 425 (2008); EPA OPPTS 870.1100 (2002))	> 2000 mg/kg bw	Yes	None	xxxxxxxx
LD_{50} dermal, rat (OECD 402 (1987); OPPTS 870.1200 (1998); EC 440/2008 (2008))	> 2000 mg/kg bw	Yes	None	xxxxxxxx
LC_{50} inhalation	Not submitted, not necessary. Justification presented in Appendix 2. Justification accepted.			
Skin irritation, rabbit skin (OECD 404 (2002); OPPTS 870.2500 (1998); EC No 440/2008, B.4 (2008))	Non-irritant	Yes	None	xxxxxxxxxxx
Eye irritation, rabbit eye (OECD 405 (2012); EPA OPPTS 870.2400 (1998); EC No 440/2008, B.5 (2008); Directive 2004/73/EC B.5 (L 152 2004 29th April))	Irritant	Yes	Eye Irrit. 2, H319	xxxxxxxxx
Skin sensitisation, mouse (OECD 429 (2010); EC No 440/2008 of 30 May 2008, B.42, LLNA)	Non-sensitising	Yes	None	xxxxxxxxxxx
Supplementary studies for combinations of plant protection products	No data – not required			

Table 6.3-2: Additional toxicological information relevant for classification/labelling of A18385B

	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)	Prosulfuron (4.12% (w/w))	Hazard statement(s) H302 (LD_{50} ~~546~~ 986 mg/kg bw)	Reg. 1272/2008 / EFSA conclusion	Hazard statement(s) Non applicable (acute oral toxicity study on formulation does not warrant classification)
	Dicamba (42.1% (w/w))	Hazard statement(s) H302 (LD_{50} 1581 mg/kg bw) H332 (LC_{50} 4.46 mg/L/4h) H318 (criteria e.g. ≥ 10 %)	Reg. 1272/2008 / EFSA conclusion	~~Non applicable~~ (acute oral toxicity study ~~and eye irritation studies~~ on formulation ~~do~~ does not warrant classification, calculations for inhalation toxicity do not warrant~~ge~~ classification either) Product classified as Eye Irrit. 2, H319
	Nicosulfuron (10.5% (w/w))	Hazard statement(s) None	Reg. 1272/2008 / EFSA conclusion	Non applicable
Toxicological properties of non-active substance(s) (relevant for classification of product)	Not applicable	Not applicable	Not applicable	Not applicable
Further toxicological information	No data – not required			

6.4 Toxicological Evaluation of Groundwater Metabolites

Comments of zRMS:	Details on the evaluation of the groundwater metabolites in line with the SANCO guidance document (221/2000 Rev 10; 25/2/2003) are included in dRR Part B, Section10. Overall, prosulfuron and nicosulfuron groundwater metabolites were determined not to be of concern.

Prosulfuron metabolites

The following data on metabolites (CGA349707, CGA159902, ~~CGA300406,~~ CGA150829~~, CGA325025, SYN542604 and SYN547308~~) 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, Section10. The submitted toxicological studies are summarized in this document.

Nicosulfuron metabolites

The relevance of the metabolites was already assessed for the authorization of the product A18385B for the GAP and groundwater scenarios considered in this dRR. Hence, a new assessment according to Step 1-5 of guidance document SANCO/221/2000 –rev.10 is not required.
The metabolite ADMP is predicted to occur in groundwater <0.001µg/L, the metabolites MU-466 ~~<0.1 µg/L~~ and the metabolite HMUD >0.1 µg/L but <0.75 µg/L. The metabolites AUSN, UCSN and ASDM are predicted to occur in groundwater at concentrations >0.75µg/L but <10µg/L.

HMUD, AUSN, UCSN, ASDM and MU-466 are not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. The relevance assessment of the metabolites is reported in Part B.10.

Dicamba metabolites

All metabolite concentrations are predicted to stay below 0.001µg/L – no groundwater assessment is required.

6.4.1 Metabolite CGA349707

An overview of the results of the accepted genotoxicity studies for groundwater metabolite CGA349707 is given in the following table. The following genotoxicity studies were assessed in the EU review of prosulfuron. The reports are not enclosed with this submission as the studies were deemed to be acceptable during the EU review. Nevertheless, short conclusions of the studies are provided for completeness in Appendix 2 (A 2.11 Other/Special Studies).

Table 6.4-1: Summary of the results of toxicity studies for CGA349707

Type of test, species (Guideline)	Result	Acceptability	Reference*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1997): OPPTS 870.5100 (1998): 2000/32/EEC B.13/B.14 (2000))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Callander, 2005/ CGA349707_0011*
Gene mutation assay (Test OECD 476 (1997): OPPTS 870.5300 (1998): 2000/32/EEC B.17 (2000))	Negative (+/-S9)	Yes, the study was reviewed at EU level	xxxxxxxxx 2005a/ CGA349707_0012*
Chromosome aberration test (OECD 473 (1997); OPPTS 870.5375 (1998); 2000/32/EC B10 (2000); ICH S2A and S2B Genotoxicity (1997))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Fox, 2005a/ CGA349707_0013*

* indicates that a study was reviewed at EU level

CGA349707 is considered not relevant from the perspective of genotoxicity.

The SAR analysis using DEREK showed that this metabolite did not have any novel toxicological alerts in comparison to parent with regards to genotoxicity, reproductive or carcinogenic properties. Therefore, metabolite CGA349707 is considered not relevant in terms of toxicological properties according to Guidance Document SANCO/221/2000.

The potential exposure to CGA349707 is >0.1 µg/L but <0.75 µg/L ~~but <10 µg/L,~~ therefore, no further ~~a~~ refined risk assessment of its potential toxicological significance for consumers was required. ~~The maximum potential exposure of CGA349707 *via* groundwater would only be 0.03% of a conservatively derived ADI.~~

6.4.2 Metabolite CGA159902

An overview of the results of the accepted genotoxicity studies for groundwater metabolite CGA159902 is given in the following table. The following genotoxicity studies were assessed in the EU review of prosulfuron. The reports are not enclosed with this submission as the studies were deemed to be acceptable during the EU review. Nevertheless, short conclusions of the studies are provided for completeness in Appendix 2 (A 2.11 Other/Special Studies).

Table 6.4-2: Summary of the results of toxicity studies for CGA159902

Type of test, species (Guideline)	Result	Acceptability	Reference*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1983): OPPTS 798.5265 (1987): 92/69/EEC B.13/B.14 (1992): Ministry of Health & Welfare, Japan (1984))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Hertner, 1993/ CGA159902_0009*
Gene mutation assay (Test OECD 476 (1997): OPPTS 870.5300 (1998): 2000/32/EEC B.17 (2000))	Negative (-S9) Positive (+S9)	Yes, the study was reviewed at EU level	xxxxxx 2005b/ CGA159902_0014*
Chromosome aberration test (OECD 473 (1997): OPPTS 870.5375 (1998): 2000/32/EC B10 (2000): ICH S2A and S2B Genotoxicity (1997))	Positive (-S9) Negative (+S9)	Yes, the study was reviewed at EU level	Fox, 2005b/ CGA159902_0015*
Rat liver unscheduled DNA synthesis assay (OECD 486 (1997): 2000/32/EEC B.39 (2000): ICH S2A and S2B (1997))	Negative	Yes, the study was reviewed at EU level	xxxxxxxx 2005c/ CGA159902_0016*
Mouse micronucleus assay (OECD 474 (1997): 2000/32/EEC B.12 (2000): US EPA OPPTS 870.5395 (1998): ICH S2A and S2B (1997))	Negative	Yes, the study was reviewed at EU level	xxxxxxxxxx 2005d/ CGA159902_0017*

* indicates that a study was reviewed at EU level

CGA159902 is considered not relevant from the perspective of genotoxicity.

The SAR analysis using DEREK showed that this metabolite did not have any novel toxicological alerts in comparison to parent with regards to genotoxicity, reproductive or carcinogenic properties. Therefore, metabolite CGA159902 is considered not relevant in terms of toxicological properties according to Guidance Document SANCO/221/2000.

Metabolite CGA159902 was predicted to be below the threshold of 0.75 µg/L, therefore, no further refinement of risk assessment was required.

6.4.3 Metabolite CGA300406

An overview of the results of the accepted genotoxicity studies for groundwater metabolite CGA300406 is given in the following table. The following genotoxicity studies were assessed in the EU review of prosulfuron. The reports are not enclosed with this submission as the studies were deemed to be acceptable during the EU review. Nevertheless, short conclusions of the studies are provided for completeness in Appendix 2 (A 2.11 Other/Special Studies).

Table 6.4-3: Summary of the results of toxicity studies for CGA300406

Type of test, species (Guideline)	Result	Acceptability	Reference*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1997); OPPTS 870.5100 (1998); 2008/440/EC B.13/B.14 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Sokolowski, 2015a/ CGA300406_10009*
Gene mutation assay (OECD 476 (1997): OPPTS 870.5300 (1998): EC 440/2008 B17 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Wollny, 2015/ CGA300406_10011*
Chromosome aberration test (OECD 473 (2014); EPA OPPTS 870.5375 (1998); EC 440/2008 B.10 (2008))	Positive (-S9) Negative (+S9)	Yes, the study was reviewed at EU level	Sokolowski, 2015b/ CGA300406_10013*
Mouse micronucleus assay (OECD 474 (1997): OPPTS 870.5395 (1998): 2000/32/EC 440/2008 B.12 (2008))	Negative	Yes, the study was reviewed at EU level	Dunton, 2015/ CGA300406_10015*

* indicates that a study was reviewed at EU level

CGA300406 is considered not relevant from the perspective of genotoxicity.

The SAR analysis using DEREK showed that this metabolite did not have any novel toxicological alerts in comparison to parent with regards to genotoxicity, reproductive or carcinogenic properties. Therefore, metabolite CGA300406 is considered not relevant in terms of toxicological properties according to Guidance Document SANCO/221/2000.

Metabolite CGA300406 was predicted to be below the threshold of 0.75 µg/L, therefore, no further refinement of risk assessment was required.

6.4.4 Metabolite CGA150829

An overview of the results of the accepted genotoxicity studies for groundwater metabolite CGA150829 is given in the following table. The following genotoxicity studies were assessed in the EU review of prosulfuron. The reports are not enclosed with this submission as the studies were deemed to be acceptable during the EU review. Nevertheless, short conclusions of the studies are provided for completeness in Appendix 2 (A 2.11 Other/Special Studies).

Table 6.4-4: Summary of the results of toxicity studies for CGA150829

Type of test, species (Guideline)	Result	Acceptability	Reference*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1997), OPPTS 870.5100 (1998), 2000/32/EEC, B13/14 (2000), JMAFF Notification No. 12-Nousan-8147 Guideline No. 2-1-19-1 (2000 and later revisions))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Wagner, VanDyke, 2009/ CGA150829_10016*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1997), OPPTS 870.5100 (1998), 2000/32/EEC, B13/14 (2000), JMAFF Notification No. 12-Nousan-8147 Guideline No. 2-1-19-1 (2000 and later revisions))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Stammberger, Braun, 1998/ CGA150829_10024*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1983): OPPTS 798.5265 (1987): 92/69/EEC B.13/B.14 (1984): Ministry of Health & Welfare, Japan (1984): Ministry of Labour Japan (1979))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Geleick, 1991/ CGA150829_0002*
Gene mutation assay (OECD 476 (1997): OPPTS 870.5300 (1998): 440/EEC B.17 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Lloyd, 2015/ CGA150829_10077*
Gene mutation assay (OECD 476 (1997): OPPTS 870.5300 (1998): 2000/32/EEC B.17 (2000), JMAFF 59-Nousan-4200 (1985))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Clarke, 2009; CGA150829_10015*
Chromosome aberration test (OECD 473 (1983): EPA 798.5375 (1987): 79/831/EEC B10 (1984))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Meyer, 1991/ CGA150829_0009*
Chromosome aberration test (No regulatory guidelines were specified but the study method was based on Evans HJ and O'Riordan ML, 1975; Basler A, Baumann M and Röhrborn G, 1982, Ames BN, McCann J and Yamasaki E, 1975 and Obe G, Beek B and Vaidya V, 1975.)	Positive (+S9) Negative (-S9)	Yes, the study was reviewed at EU level	Dollenmeier, 1987/ CGA150829_0012*
Chromosome aberration test (OECD 473 (1997), OPPTS 870.5375 (1998): 2000/32/EC B10 (2000), Japanese Ministry of Agriculture, Forestry and Fisheries (JMAFF) (November 24, 2000 and later revisions))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Gudi, 2009/ CGA150829_10014*
Unscheduled DNA synthesis test (OECD 482 (1987))	Negative	Yes, the study was reviewed at EU level	Hertner, 1987~~7~~8/ CGA150829_0011*
Unscheduled DNA synthesis test (OECD 482 (1987))	Negative	Yes, the study was reviewed at EU level	Meyer, 1988/ CGA150829_0010*
Chromosome aberration test (OECD 475 (1983))	Negative	Yes, the study was reviewed at EU level	Strasser, 1988/ CGA150829_0013*

* indicates that a study was reviewed at EU level

CGA150829 is considered not relevant from the perspective of genotoxicity.

The SAR analysis using DEREK showed that this metabolite did not have any novel toxicological alerts in comparison to parent with regards to genotoxicity, reproductive or carcinogenic properties. Therefore, metabolite CGA150829 is considered not relevant in terms of toxicological properties according to Guidance Document SANCO/221/2000.

Metabolite CGA150829 was predicted to be below the threshold of 0.75 µg/L, therefore, no further refinement of risk assessment was required.

6.4.5 Metabolite CGA325025

An overview of the results of the accepted genotoxicity studies for groundwater metabolite CGA325025 is given in the following table. The following genotoxicity studies were assessed in the EU review of prosulfuron. The reports are not enclosed with this submission as the studies were deemed to be acceptable during the EU review. Nevertheless, short conclusions of the studies are provided for completeness in Appendix 2 (A 2.11 Other/Special Studies).

Table 6.4-5: Summary of the results of toxicity studies for CGA325025

Type of test, species (Guideline)	Result	Acceptability	Reference*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1997): OPPTS 870.5100 (1998): EC 440/2008 B.13/14 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Sokolowski, 2013/ CGA325025_10007*
Gene mutation assay (OECD 476 (1997): OPPTS 870.5300 (1998): EC 440/2008 B17 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Wollny, 2013/ CGA325025_10008*
Chromosome aberration test (OECD 473 (1997); OPPTS 870.5375 (1998); EC 440/2008 B10 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Bohnenberger, 2013/ CGA325025_10009*

* indicates that a study was reviewed at EU level

CGA325025 is considered not relevant from the perspective of genotoxicity.

The SAR analysis using DEREK showed that this metabolite did not have any novel toxicological alerts in comparison to parent with regards to genotoxicity, reproductive or carcinogenic properties. Therefore, metabolite CGA325025 is considered not relevant in terms of toxicological properties according to Guidance Document SANCO/221/2000.

Metabolite CGA325025 was predicted to be below the threshold of 0.75 µg/L, therefore, no further refinement of risk assessment was required.

6.4.6 Metabolite SYN542604

An overview of the results of the accepted genotoxicity studies for groundwater metabolite SYN542604 is given in the following table. The following genotoxicity studies were assessed in the EU review of prosulfuron. The reports are not enclosed with this submission as the studies were deemed to be acceptable during the EU review. Nevertheless, short conclusions of the studies are provided for completeness in Appendix 2 (A 2.11 Other/Special Studies).

Table 6.4-6: Summary of the results of toxicity studies for SYN542604

Type of test, species (Guideline)	Result	Acceptability	Reference*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1997); OPPTS 870.5100 (1998); 2008/440/EC B.13/B.14 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Sokolowski, 2010/ SYN542604_10001*
Gene mutation assay (OECD 473 (1997); OPPTS 870.5375 (1998); EC 440/2008 B.10 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Wollny, 2010/ SYN542604_100002*
Chromosome aberration test (OECD 476 (1997): OPPTS 870.5300 (1998): 440/EEC B.17 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Bohnenberger, 2010/ SYN542604_100020*

* indicates that a study was reviewed at EU level

SYN542604 is considered not relevant from the perspective of genotoxicity.

The SAR analysis using DEREK showed that this metabolite did not have any novel toxicological alerts in comparison to parent with regards to genotoxicity, reproductive or carcinogenic properties. Therefore, metabolite SYN542604 is considered not relevant in terms of toxicological properties according to Guidance Document SANCO/221/2000.

Metabolite SYN542604 was predicted to be below the threshold of 0.75 µg/L, therefore, no further refinement of risk assessment was required.

6.4.7 Metabolite SYN547308

An overview of the results of the accepted genotoxicity studies for groundwater metabolite SYN547308 is given in the following table. The following genotoxicity studies were assessed in the EU review of prosulfuron. The reports are not enclosed with this submission as the studies were deemed to be acceptable during the EU review. Nevertheless, short conclusions of the studies are provided for completeness in Appendix 2 (A 2.11 Other/Special Studies).

Table 6.4-7: Summary of the results of toxicity studies for SYN547308

Type of test, species (Guideline)	Result	Acceptability	Reference*
Bacterial reverse mutation assay (Ames test) (OECD 471 (1997): OPPTS 870.5100 (1998): EC 440/2008 B.13/14 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Sokolowski, 2014/ SYN547308_10002*
Gene mutation assay (OECD 476 (1997): OPPTS 870.5300 (1998): EC 440/2008 B17 (2008))	Negative (+/-S9)	Yes, the study was reviewed at EU level	Wollny, 2014/ SYN547308_10000*
Chromosome aberration test (OECD 473 (1997); OPPTS 870.5375 (1998); EC 440/2008 B10 (2008))	Positive (-S9) Negative (+S9)	Yes, the study was reviewed at EU level	Bohnenberger, 2014/ SYN547308_10004*
Mouse micronucleus assay (OECD 474 (1997): OPPTS 870.5395 (1998): 2000/32/EC 440/2008 B.12 (2008))	Negative	Yes, the study was reviewed at EU level	Dunton, 2014/ SYN547308_10006*

* indicates that a study was reviewed at EU level

SYN547308 is considered not relevant from the perspective of genotoxicity.

The SAR analysis using DEREK showed that this metabolite did not have any novel toxicological alerts in comparison to parent with regards to genotoxicity, reproductive or carcinogenic properties. Therefore, metabolite SYN547308 is considered not relevant in terms of toxicological properties according to Guidance Document SANCO/221/2000.

Metabolite SYN547308 was predicted to be below the threshold of 0.75 µg/L, therefore, no further refinement of risk assessment was required.

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in A18385B are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in A18385B

	Prosulfuron		Nicosulfuron		Dicamba	
	Value	**Reference**	**Value**	**Reference**	**Value**	**Reference**
Concentrate	50%	Guidance on Dermal Absorption (EFSA Journal 2017;15(6): 4873). Assessment in Appendix 2.	10%	Guidance on Dermal Absorption (EFSA Journal 2017;15(6): 4873). Assessment in Appendix 2.	10%	Guidance on Dermal Absorption (EFSA Journal 2017;15(6): 4873). Assessment in Appendix 2.
Dilution	50%		~~40%~~ 50%		50%	

6.5.1 Justification for proposed values - prosulfuron

No data on dermal absorption for prosulfuron in A18385B 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 prosulfuron

	Value	Justification for value	Acceptability of justification
Concentrate	50%	<5% (40 g/kg of prosulfuron in A18385B)	Yes
Dilution	50%	<5% (0.05-0.1 g a.s./L in spray dilution)	Yes

6.5.2 Justification for proposed values - nicosulfuron

No data on dermal absorption for nicosulfuron in A18385B 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 nicosulfuron

	Value	Justification for value	Acceptability of justification
Concentrate	10%	>5% (100 g/kg of nicosulfuron in A18385B)	Yes
Dilution	~~40%~~ 50%	~~The oral absorption value for nicosulfuron is established as ~40% (EFSA's Scientific Report (2007) 120, 1-91), which is <50%, therefore, according to the guidance, oral absorption value can be applied as a dermal absorption estimate for the diluted product.~~ Default value for a WG formulation.	Yes

6.5.3 Justification for proposed values - dicamba

No data on dermal absorption for dicamba in A18385B 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 dicamba

	Value	Justification for value	Acceptability of justification
Concentrate	10%	>5% (400 g/kg of dicamba in A18385B)	Yes
Dilution	50%	<5% (0.5-1 g a.s./L in spray dilution)	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	A18385B		
Formulation type	Water dispersible granule [WG]		
Category	Herbicide		
Container size(s), short description	Packaging for for products maketed by Syngenta 50 – 250g and 0.5-10kg HDPE canister Packaging for for products maketed by Cheminova 0.5 – 10kg HDPE, COEX HDPE/PA, fluorinated HDPE, PET bottles		
Active substance(s) (incl. content)	**Prosulfuron** 40 g/L or g/kg	**Nicosulfuron** 100 g/L or g/kg	**Dicamba** 400 g/L or g/kg
AOEL systemic	0.06 mg/kg bw/d	0.8 mg/kg bw/d	0.3 mg/kg bw/d
Inhalation absorption	100%	100%	100%
Oral absorption	100%	40%	100%
Dermal absorption	Concentrate: 50% Dilution: 50% (Default)	Concentrate: 10% Dilution: ~~40%~~ 50% (Default)	Concentrate: 10% Dilution: 50% (Default)

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.

Justification

The critical GAP has been defined following evaluation of the individual GAPs for each crop in each relevant Member State.

6.6.2 Operator exposure (KCP 7.2.1)

Comments of zRMS:	The operator exposure calculations for the proposed uses of Spandis 54 WG conducted by the Applicant using the EFSA calculator and presented in Table 6.6-3 are accepted. The predicted longer term systemic operator exposure for application via tractor mounted boom sprayer is within acceptable limit. The values are calculated as 21.77% of the AOEL for prosulfuron, 0.99% of the AOEL for nicosulfuron and 9.12% of the AOEL for dicamba for an operator wearing work wear (arms, body and legs covered). Taking into consideration the classification of the Spandis 54 WG regarding human health (H19 Causes serious eye irritation), the following operator protection phrase is recommended: Wear eye protection/face protection when handling the product.

6.6.2.1 Estimation of operator exposure

A summary of the exposure model used for estimation of operator exposure to the active substances during application of A18385B according to the critical use is presented in Table 6.6-2. Outcome of the estimation is presented in Table 6.6-3. Detailed calculations are in Appendix 3.

As guidance on the derivation of acute endpoints for non-dietary human exposure has not yet been published, it is not possible to carry out an acute risk assessment for operators at this time.

Table 6.6-2: Exposure models for intended uses

Critical use	Maize (max. 0.5 kg product/ha)
Model	EFSA 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 [55 pp.]

Table 6.6-3: Estimated operator exposure

		Prosulfuron		**Nicosulfuron**		**Dicamba**	
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:		0.02 kg a.s./ha		0.05 kg a.s./ha		0.2 kg a.s./ha	
EFSA model (75th percentile) Application volume: 200 L/ha** Body weight: 60 kg	no PPE*	0.01306	21.77	~~0.00794~~ 0.00858	~~0.99~~ 1.07	0.0274	9.12

[#] Reference Value Non Acutely Toxic Active Substance (RVNAS) for EFSA Guidance
* no PPE: Operator wearing long-sleeved shirt, long trousers ("permeable") but no gloves
** Presents the worst case estimation

Results

Based on the EFSA model predictions for tractor-mounted application techniques, the operator long-term exposure for prosulfuron, nicosulfuron and dicamba are predicted to be within acceptable limits for an operator that applies the product without using PPE.

Thus, according to the EFSA Guidance calculations, a safe use could be demonstrated for operators using A18385B for proposed uses, even if no PPE is worn.

6.6.3 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 considering above mentioned personal protective equipment (PPE), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

6.6.4 Worker exposure (KCP 7.2.3)

Comments of zRMS:	The worker exposure calculations for the proposed uses of Spandis 54 WG conducted by the Applicant using the EFSA calculator and presented in Table 6.6-4 are accepted. The potential worker exposure undertaking crop inspection activity is within acceptable limit assuming workers are wearing workwear (arms, body and legs covered). The values are calculated as 2.33% of the AOEL for prosulfuron, 0.35% of the AOEL for nicosulfuron and 4.67% of the AOEL for dicamba.

6.6.4.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with A18385B according to the critical use. Outcome of the estimation is presented in Table 6.6-5. Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use	Maize (max. 1 x 0.5 kg product/ha)
Model	EFSA 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 [55 pp.]

Table 6.6-5: Estimated worker exposure

		Prosulfuron		Nicosulfuron		Dicamba	
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:		1 x 0.02 kg a.s./ha		1 x 0.05 kg a.s./ha		1 x 0.2 kg a.s./ha	
2 hours/day (1), Body weight: 60 kg DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha	no PPE(3) TC: 1400 cm²/person/h (2)	0.00140	2.33	~~0.00280~~ 0.00350	~~0.35~~ 0.44	0.01400	4.67

Reference Value Non Acutely Toxic Active Substance (RVNAS) for EFSA Guidance
(1) 2 h/day for professional applications for maintenance, inspection or irrigation activities etc.
(2) EFSA 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 [55 pp.]
(3) no PPE: Worker wearing long sleeved shirt, long trousers ("permeable") but no gloves

Results

It is concluded that there is no unacceptable risk anticipated for the worker wearing adequate work clothing when re-entering crops treated with A18385B. As a standard rule, it should be mentioned on the label that treated crops should not be re-entered before spray deposits on leaf surfaces have completely dried.

6.6.4.2 Refinement of generic DFR value (KCP 7.2)

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 mentioned PPE, exposure estimates using dislodgeable residue data are considered to be not necessary.

6.6.4.3 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 mentioned PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

6.6.5 Bystander and resident exposure (KCP 7.2.2)

Comments of zRMS:	The bystander and resident exposure calculations for the proposed uses of Spandis 54 WG conducted by the Applicant using the EFSA calculator presented in Tables 6.6-7 are accepted.

	Resident exposure According to calculations using EFSA calculator the predicted longer term systemic exposure to a child and adult resident from spray drift, vapour, surface deposits, entry into treated crops and sum of all pathways is within acceptable limits. Bystander exposure It is noteworthy that according to EFSA 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): "No bystander risk assessment is required for PPPs that do not have significant acute toxicity or the potential to exert toxic effects after a single exposure. Exposure in this case will be determined by average exposure over a longer duration, and higher exposures on one day will tend to be offset by lower exposures on other days. Therefore, exposure assessment for residents also covers bystander exposure." The Applicant performed additional calculations using German guidance paper (Martin S. et al. (2008) Guidance for Exposure and Risk Evaluation for Bystanders and Residents Exposed to Plant Protection Products During and After Application. However, according to EFSA opinion this approach is not scientifically supported any longer, since the predictions are considered underestimated.

6.6.5.1 Estimation of bystander and resident exposure

Consequently, this evaluation provides a first tier assessment based on the EFSA guidance for longer term exposures to residents only, using 75th percentile data and comparing with the relevant AOEL. This assessment is equally applicable to longer term exposures for bystanders (see **Błąd! Nieprawidłowy odsyłacz do zakładki: wskazuje na nią samą.**).

Additionally, an assessment according to the German guidance paper (see Table 6.6-8) considering bystanders is provided.
Table 6.6-6 shows the exposure models used for estimation of resident exposure to prosulfuron, nicosulfuron and dicamba. Outcome of the estimation is presented in Table 6.6-8. Detailed calculations are in Appendix 3.

According to EC guidance document SANTE-10832-2015, the (*EFSA Guidance*) risk assessment on residents and bystanders cannot be fully considered until a procedure for the derivation of the AAOEL and higher risk assessment schemes, identified as missing by the Standing Committee, are available.

Since no AAOEL has been agreed for the active ingredients, only estimates of resident exposures (using 75th percentile values) which consider the long-term risk are presented according to the EFSA model.

Consequently, this evaluation provides a first tier assessment based on the EFSA guidance for longer term exposures to residents only, using 75th percentile data and comparing with the relevant AOEL. This assessment is equally applicable to longer term exposures for bystanders (see **Błąd! Nieprawidłowy odsyłacz do zakładki: wskazuje na nią samą.**).

Additionally, an assessment according to the German guidance paper (see **Błąd! Nieprawidłowy odsyłacz do zakładki: wskazuje na nią samą.**) considering bystanders is provided.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	Maize (max. 1 x 0.5 kg product/ha)
Models	EFSA 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 [55 pp.] Martin S. *et al.* (2008) [Guidance for Exposure and Risk Evaluation for Bystanders and Residents Exposed to Plant Protection Products During and After Application; J. Verbr. Lebensm. 3 (2008): 272-281 Birkhäuser Verlag Basel] and Bundesanzeiger (BAnz), 06 January 2012, Issue No. 4, pp. 75-76.

Table 6.6-7: Estimated resident exposure (EFSA model)

		Prosulfuron		**Nicosulfuron**	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops Buffer zone: 2-3(m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 3 years					
Number of applications and application rate		1 x 0.02 kg a.s./ha		1 x 0.05 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0013429	2.24	~~0.00276869~~ 0.0033573	~~0.34~~ 0.42
	Vapour (75th perc.)	0.00110700	1.78	~~0.00110700~~ 0.0010700	~~0.13~~ 0.13
	Deposits (75th perc.)	0.00021618	0.27	~~0.0003074~~ 0.0003802	~~0.04~~ 0.05
	Re-entry (75th perc.)	0.00176875	2.81	~~0.00343750~~ 0.0042188	~~0.42~~ 0.53
	Sum (mean)	0.00332737	5.46	~~0.00554663~~ 0.0065614	~~0.68~~ 0.82
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0003213	0.54	~~0.0006428~~ 0.0008033	~~0.08~~ 0.10
	Vapour (75th perc.)	0.0002300	0.38	~~0.0002300~~ 0.0002300	~~0.03~~ 0.03
	Deposits (75th perc.)	0.00010681	0.11	~~0.0001363~~ 0.0001703	~~0.02~~ 0.02
	Re-entry (75th perc.)	0.0009375	1.56	~~0.00198750~~ 0.0023438	~~0.23~~ 0.29
	Sum (mean)	0.00121800	1.97	~~0.0021302~~ 0.0026051	~~0.27~~ 0.33

Dicamba			
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops Buffer zone: 2-3(m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha Interval between treatments: 3 years			
Application rate		1 x 0.2 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0134290	4.48
	Vapour (75th perc.)	0.00110700	0.36
	Deposits (75th perc.)	0.0016184	0.54
	Re-entry (75th perc.)	0.01698750	5.63
	Sum (mean)	0.0231069	7.70
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0032133	1.07
	Vapour (75th perc.)	0.0002300	0.08
	Deposits (75th perc.)	0.00076813	0.23
	Re-entry (75th perc.)	0.00943750	3.13
	Sum (mean)	0.0097304	3.24

Table 6.6-8: Estimated bystander and resident exposure (Martin *et al.*)

	Prosulfuron		Nicosulfuron		Dicamba	
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:	1 x 0.02 kg a.s./ha		1 x 0.05 kg a.s./ha		1 x 0.2 kg a.s./ha	
Vapour pressure	< 3.5 x 10^{-6} Pa at 25°C		< 8 x 10^{-10} Pa at 25°C		1.67 x 10^{-3} Pa at 25°C	
Bystanders (adult) Drift rate: 0.29% (10 m) Body weight: 60 kg	0.0000484	0.08	~~9.69 x 10^{-5}~~ 0.0001211	~~0.01~~ 0.02	0.0004843	0.16
Bystanders (children) Drift rate: 0.29% (10 m) Body weight: 16.15 kg	0.0000379	0.06	~~7.59 x 10^{-5}~~ 0.0000948	~~0.01~~ 0.01	0.0003791	0.13
Residents (adult) Drift rate: 0.29% (10 m) Body weight: 60 kg	0.0000035	0.01	~~7.10 x 10^{-6}~~ 0.0000088	~~0.001~~ 0.001	0.0000353	0.01
Residents (children) Drift rate: 0.29% (10 m) Body weight: 16.15 kg	0.0000056	0.01	~~1.02 x 10^{-5}~~ 0.0000126	~~0.001~~ 0.002	0.0000557	0.02

Results

According to the EFSA Guidance, the total estimated systemic resident exposure of children and adults to prosulfuron, nicosulfuron and dicamba, after application on the intended crops, is lower than 100 % of the AOEL.

The same is predicted with Martin *et al.*, the total estimated systemic resident and bystander exposure of children and adults to prosulfuron, nicosulfuron and dicamba, after application on the intended crops, is lower than 100 % of the AOEL.

Therefore, according to both models, it is concluded that there is no undue risk to any bystander and resident after exposure to A18385B. This has no labelling implications.

6.6.5.2 Measurement of bystander and/or resident exposure

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

6.6.6 Combined exposure

The product is a mixture of three active substances.
From a scientific point of view it is regarded necessary to take into account potential combination effects. However, the evaluation of cumulative or synergistic effects as requested by Art. 4 (3b) of Regulation (EC) No. 1107/2009 should only be performed when harmonised “scientific methods accepted by the Authority to assess such effects are available.”

6.6.6.1 Exposure assessment of prosulfuron, nicosulfuron and dicamba in A18385B

Comments of zRMS:	The combined exposure calculations for operator, workers and residents conducted by the Applicant and presented in Table 6.6-9 are accepted. The Hazard Index is < 1, therefore combined exposure to all active substances in Spandis54 WG is not expected to present a risk for operators and workers and residents. The exposure assessment for residents also covers bystander exposure, therefore combined exposure is also not expected for bystanders.

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 converted to decimal. The Hazard Index (HI) is the sum of the individual HQs.

Table 6.6-9: Risk assessment from combined exposure (longer term exposure)

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
Operators – vehicle-mounted application	Prosulfuron	0.218
	Nicosulfuron	~~0.001~~ 0.001
	Dicamba	0.091
	Cumulative risk operators (HI)	**0.319**
Workers – inspection/irrigtion cereals	Prosulfuron	0.023
	Nicosulfuron	~~0.0004~~ 0.00
	Dicamba	0.047
	Cumulative risk workers (HI)	**0.074**
Resident – child (EFSA model)	Prosulfuron	
	Drift	0.022
	Vapour	0.018
	Deposits	0.00~~03~~
	Re-entry	0.028
	Sum of all pathways	0.055
	Nicosulfuron	
	Drift	~~0.0003~~ 0.00
	Vapour	~~0.0001~~ 0.00
	Deposits	~~0.000~~ 0.00
	Re-entry	~~0.0007~~

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
		0.01
	Sum of all pathways	~~0.007~~ 0.01
	Dicamba	
	Drift	0.045
	Vapour	0.00~~0~~4
	Deposits	0.00~~1~~5
	Re-entry	0.05~~6~~3
	Sum of all pathways	0.077
	Cumulative risk resident – child (HI)	
	Drift	0.0~~6~~70
	Vapour	0.0~~18~~23
	Deposits	0.00~~1~~8
	Re-entry	0.08~~4~~8
	Sum of all pathways	**~~0.139~~ 0.142**
Resident – adult (EFSA model)	Prosulfuron	
	Drift	0.00~~1~~5
	Vapour	0.00~~0~~3
	Deposits	0.00~~0~~2
	Re-entry	0.0~~20~~15
	Sum of all pathways	0.020
	Nicosulfuron	
	Drift	~~0.0001~~ 0.00
	Vapour	~~0.000~~ 0.00
	Deposits	~~0.000~~ 0.00
	Re-entry	~~0.0002~~ 0.00
	Sum of all pathways	~~0.0003~~ 0.00
	Dicamba	
	Drift	0.0~~0~~11
	Vapour	0.000
	Deposits	0.00~~0~~2
	Re-entry	0.031
	Sum of all pathways	0.032
	Cumulative risk resident – adult (HI)	

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
	Drift	0.0~~02~~17
	Vapour	0.00~~03~~
	Deposits	0.00~~04~~
	Re-entry	0.05~~1~~48
	Sum of all pathways	**0.05~~2~~5**

The Hazard Index is < 1. Thus, combined exposure to all active substances in A18385B 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 / 01	xxxxxxx	2013a	Prosulfuron/dicamba/nicosulfuron WG (A18385B) - Acute Oral Toxicity Study in the Rat (Up and Down Procedure) Syngenta xxxxxxxxxxxxx not published Syngenta File No A18385B_10008; VV-405072	Y	SYN
KCP 7.1.2 / 01	xxxxxxxxxxxxx	2013ab	Prosulfuron/dicamba/nicosulfuron WG (A18385B) - Acute Dermal Toxicity Study in Rats Syngenta xxxxxxxxxxxxxxxxxxx not published Syngenta File No A18385B_10007; VV-405071	Y	SYN
KCP 7.1.4 / 01	xxxxxxxxxxxxxx.	2013bc	Prosulfuron/dicamba/nicosulfuron WG (A18385B) - Primary Skin Irritation Study in Rabbits Syngenta xxxxxxxxxxxxxxxxxxx not published Syngenta File No A18385B_10009; VV-405073	Y	SYN
KCP 7.1.5 / 01	xxxxxxxxxxxxxxx	2013cd	Prosulfuron/dicamba/nicosulfuron WG (A18385B) - Acute Eye Irritation Study in Rabbits Syngenta xxxxxxxxxxxxxxxxxxxxx xxxxxxxxx not published Syngenta File No A18385B_10022; VV-405644	Y	SYN
KCP 7.1.6 / 01	xxxxxxxxx	2013	Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) - Local Lymph Node Assay in the Mouse Syngenta xxxxxxxxxxxxxxxxxx not published Syngenta File No A18385B_10018; VV-405478	Y	SYN

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	Verte-brate study Y/N	Owner
KCP 7.1.1 / 02	xxxxxxxxxxxxxx	1994	CGA 152005 WG 75, (A-8714 C) - Acute oral toxicity in the rat Novartis Crop Protection AG, Basel, Switzerland xxxxxxxxxx GLP not published Syngenta File No CGA152005/0420	Y	Syngenta
KCP 7.1.1 / 03	xxxxxxxxxxxxxxxxxx	1996	Acute oral toxicity in the rat Novartis Crop Protection AG, Basel, Switzerland xxxxxxxxxxxxxxxxxxxxx GLP not published Syngenta File No CGA152005/0606	Y	Syngenta
KCP 7.1.1 / 04	xxxxxxxxxxxxx	1996a	Acute oral toxicity in the mouse Novartis Crop Protection AG, Basel, Switzerland xxxxxxxxxxxxxxxxxx GLP not published Syngenta File No CGA152005/0605	Y	Syngenta
KCP 7.1.2 / 02	xxxxxxxxxx	1994	CGA 152005 WG 75, (A-8714 C) - Acute dermal toxicity in the rat Novartis Crop Protection AG, Basel, Switzerland xxxxxxxxxxxxxxxx GLP not published Syngenta File No CGA152005/0403	Y	Syngenta
KCP 7.1.4 / 02	xxxxxxxxxxx	1994	CGA 152005 WG 75, (A-8714 C) - Acute dermal irritation/corrosion study in the rabbit Novartis Crop Protection AG, Basel, Switzerland xxxxxxxxxxxxxxxx GLP not published	Y	Syngenta

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
			Syngenta File No CGA152005/0404		
KCP 7.1.5 / 02	Marty J.H.	1994a	CGA 152005 WG 75, (A-8714 C) - Acute eye irritation/corrosion study in the rabbit Novartis Crop Protection AG, Basel, Switzerland xxxxxxxxxxxxxxxx GLP not published Syngenta File No CGA152005/0406	Y	Syngenta
KCP 7.1.6 / 02	xxxxxxxxxxx	1994b	CGA 152005 WG 75, (A-8714 C) - Skin sensitization test in the Guinea Pig - Buehler Test Novartis Crop Protection AG, Basel, Switzerland xxxxxxxxxxx GLP not published Syngenta File No CGA152005/0405	Y	Syngenta
KCP 7.3 / 01	Johnson I.	2012	Prosulfuron (A8714C) - In Vitro Absorption through Human Epidermis using [14C]-Prosulfuron Syngenta Dermal Technology Laboratory Ltd., Staffordshire, UK, JV2170-REG GLP not published Syngenta File No A8714C_11430	N	Syngenta
KCA3 5.8 / 01	Callander R.	2005	CA349707: Bacterial Mutation Assay In S. Typhimurium And E,Coli Syngenta Crop Protection AG, Basel, Switzerland Central Toxicology Laboratory (CTL), Cheshire, United Kingdom, YV6941 GLP not published Syngenta File No CGA349707/0011	N	Syngenta
KCA3 5.8 / 02	xxxxxxxxxxxxxxxxxx	2005a	CGA 349707: L5178Y TK+/- Mouse Lymphoma Mutation Assay Syngenta Crop Protection AG, Basel, Switzerland xxxxxxx GLP not published	Y	Syngenta

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
			Syngenta File No CGA349707/0012		
KCA3 5.8 / 03	Fox V.	2005a	CGA 349707: In Vitro Cytogenetic Assay In Human Lymphocytes Syngenta Crop Protection AG, Basel, Switzerland Central Toxicology Laboratory (CTL), Cheshire, United Kingdom, SV1296 GLP not published Syngenta File No CGA349707/0013	N	Syngenta
KCA3 5.8 / 04	Hertner Th.	1993	CA 1118 A - Salmonella and escherichia/liver-microsome test Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, 931097 GLP not published Syngenta File No CGA159902/0009	N	Syngenta
KCA3 5.8 / 05	Clay P.	2005ab	CGA 159902: L5178Y + / - Mouse Lymphoma Mutation Assay Syngenta Crop Protection AG, Basel, Switzerland Syngenta Limited, Cheshire, United Kingdom, VV0322 GLP not published Syngenta File No CGA159902/0014	N	Syngenta
KCA3 5.8 / 06	Fox V.	2005ab	CGA 159902: In Vitro Cytogenetic Assay In Human Lymphocytes Syngenta Crop Protection AG, Basel, Switzerland Central Toxicology Laboratory (CTL), Cheshire, United Kingdom, SV1295 GLP not published Syngenta File No CGA159902/0015	N	Syngenta
KCA3 5.8 / 07	xxxxxxxxxxxxxxxxx	2005bc	CGA 159902: In Vivo Rat Liver Unscheduled DNA Synthesis Assay Syngenta Crop Protection AG, Basel, Switzerland xxxxxxxxxxxx GLP not published	Y	Syngenta

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
			Syngenta File No CGA159902/0016		
KCA3 5.8 / 08	xxxxxxxxxxxxx	2005~~ed~~	CGA 159902: Mouse bone marrow micronucleus test Syngenta Crop Protection AG, Basel, Switzerland xxxxxxxxxxxxxx GLP not published Syngenta File No CGA159902/0017	Y	Syngenta
KCA3 5.8 / 09	Wagner Valentine, VanDyke Melissa	2009	IN-A4098: Bacterial Reverse Mutation Assay DuPont Crop Protection, Newark, USA, Syngenta BioReliance, 9630 Medical Center Drive, Rockville, Maryland 20850, USA , DuPont-28277, BioRel: AC26XC.503.BTL, WRN: 18355, SCN: 500 GLP not published Syngenta File No CGA150829_10016	N	Syngenta
KCA3 5.8 / 10	Stammberger I., Braun K.	1998	AE F059411: Bacterial Reverse Mutation Test Syngenta , 98.0717, C000993, M-181601-01-1 GLP not published Syngenta File No CGA150829_10024	N	Syngenta
KCA3 5.8 / 11	Geleick D.	1991	CGA 150`829 tech. - Salmonella and escherichia/liver-microsome test. Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Basel, Genetische Toxikologie, Basel, Switzerland, 901510 GLP not published Syngenta File No CGA150829/0002	N	Syngenta
KCA3 5.8 / 12	~~Roy S., Rao M.~~ Gudi R.	~~2016~~ 2009	IN-A4098: In Vitro Mammalian Chromosome Aberration Test E.I. Dupont Nemours & Co., Inc., Wilmington, USA BioReliance, 9630 Medical Center Drive, Rockville, Maryland 20850, USA , DuPont-28082 GLP	N	Syngenta

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
			not published Syngenta File No CGA150829_10014		
KCA3 5.8 / 13	Lloyd M.	2016~~5~~	IN-A4098: In Vitro L5178Y Gene Mutation Assay at the tk locus E.I. Dupont Nemours & Co., Inc., Wilmington, USA, Cheminova A/S, Harboore, Denmark, Rotam Agrochem International Co. Ltd., Chai Wan, Hong Kong Covance Laboratories Limited, Harrogate, UK, DuPont-42500 GLP not published Syngenta File No CGA150829_10077	N	Syngenta
KCA3 5.8 / 14	Meyer A.	1991	CGA 150`829 tech. - Cytogenetic test on Chinese hamster cells in vitro (EC-Conform). Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Basel, Genetische Toxikologie, Basel, Switzerland, 901511 GLP not published Syngenta File No CGA150829/0009	N	Syngenta
KCA3 5.8 / 15	Dollenmeier P.	1987	CGA 150`829 tech. - Chromosome studies on human lymphocytes in vitro. Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Ltd., Basel, Switzerland, 860159 GLP not published Syngenta File No CGA150829/0012	N	Syngenta
KCA3 5.8 / 16	Clarke Jane	2009	IN-A4098: In Vitro Mammalian Cell Gene Mutation Test (CHO/HGPRT Assay) DuPont Crop Protection, Newark, USA, Syngenta BioReliance, 9630 Medical Center Drive, Rockville, Maryland 20850, USA , DuPont-28083, BioRel: AC26XC.782.BTL, WRN: 18355, SCN: 515 GLP not published Syngenta File No CGA150829_10015	N	Syngenta
KCA3 5.8 / 17	xxxxxxxxxxxxxxxxxxx	1988	CGA 150`829 tech. - Autoradiographic DNA repair test on rat hepatocytes. xxxxxx	Y	Syngenta

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
			xxxxxxxxxxxxxxxxx GLP not published Syngenta File No CGA150829/0011		
KCA3 5.8 / 18	Meyer A.	1988	CGA 150`829 tech. - Autoradiographic DNA repair test on human fibroblasts. Novartis Crop Protection AG, Basel, Switzerland Ciba-Geigy Basel, Genetische Toxikologie, Basel, Switzerland, 871188 GLP not published Syngenta File No CGA150829/0010	N	Syngenta
KCA3 5.8 / 19	xxxxxxxxxxxxxxx	1988	CGA 150`829 tech. - Chromosome studies on somatic cells of Chinese hamster. Novartis Crop Protection AG, Basel, Switzerland xxxxxxxxxxxxxxxxxx GLP not published Syngenta File No CGA150829/0013	Y	Syngenta
KCA3 5.8 / 20	Sokolowski A	2010	SYN542604 - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay Syngenta - Jealott's Hill, Bracknell, United Kingdom Harlan, Cytotest Cell Research GmbH (Harlan CCR), 64380 Rossdorf, Germany, 1276501 GLP not published Syngenta File No SYN542604_10001	N	Syngenta
KCA3 5.8 / 21	Bohnenberger S	2010	SYN542604 - Chromosome Aberration Test in Human Lymphocytes In Vitro Syngenta - Jealott's Hill, Bracknell, United Kingdom Harlan, Cytotest Cell Research GmbH (Harlan CCR), 64380 Rossdorf, Germany, 1276503 GLP not published Syngenta File No SYN542604_10000	N	Syngenta
KCA3 5.8 / 22	Wollny H	2010	SYN542604 - Cell Mutation Assay at the Thymidine Kinase Locus (TK +/-) in Mouse Lymphoma L5178Y Cells	N	Syngenta

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
			Syngenta - Jealott's Hill, Bracknell, United Kingdom Harlan, Cytotest Cell Research GmbH (Harlan CCR), 64380 Rossdorf, Germany, 1276502 GLP not published Syngenta File No SYN542604_10002		
KCA3 5.8 / 23	Sokolowski A.	2013	CGA325025 - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1527201 GLP not published Syngenta File No CGA325025_10007	N	Syngenta
KCA3 5.8 / 24	Wollny H.	2013	CGA325025 - Cell Mutation Assay at the Thymidine Kinase Locus (TK+/-) in Mouse Lymphoma L5178Y Cells Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1527203 GLP not published Syngenta File No CGA325025_10008	N	Syngenta
KCA3 5.8 / 25	Bohnenberger S.	2013	CGA325025 - Chromosome Aberration Test in Human Lymphocytes In Vitro Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1527202 GLP not published Syngenta File No CGA325025_10009	N	Syngenta
KCA3 5.8 / 26	Sokolowski A.	2014	SYN547308 - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1577801 GLP not published Syngenta File No SYN547308_10002	N	Syngenta

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
KCA3 5.8 / 27	Wollny H.	2014	SYN547308 - Cell Mutation Assay at the Thymidine Kinase Locus (TK+/-) in Mouse Lymphoma L5178Y Cells Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1577803 GLP not published Syngenta File No SYN547308_10000	N	Syngenta
KCA3 5.8 / 28	Bohnenberger S.	2014	SYN547308 - In Vitro Chromosome Aberration Test in Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1577802 GLP not published Syngenta File No SYN547308_10004	N	Syngenta
KCA3 5.8 / 29	xxxxxxxxxxxxxxxx	2014	SYN547308 - Oral (Gavage) Mouse Micronucleus Test Final Report Syngenta xxxxxxxxxxxxxxxxxx GLP not published Syngenta File No SYN547308_10006	Y	Syngenta
KCA3 5.8 / 30	Sokolowski A.	2015a	CGA300406 - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1660401 GLP not published Syngenta File No CGA300406_10009	N	Syngenta
KCA3 5.8 / 31	Wollny H.	2015	CGA300406 - Cell Mutation Assay at the Thymidine Kinase Locus (TKP+/-) in Mouse Lymphoma L5178Y Cells Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1660403 GLP	N	Syngenta

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
			not published Syngenta File No CGA300406_10011		
KCA3 5.8 / 32	Sokolowski A.	2015ab	CGA300406 - Chromosome Aberration Test in Human Lymphocytes In Vitro Syngenta Harlan Cytotest Cell Research GmbH (Harlan CCR), Germany, 1660402 GLP not published Syngenta File No CGA300406_10013	N	Syngenta
KCA3 5.8 / 33	xxxxxxxxxxxxx	2015	CGA300406 - Oral (Gavage) Mouse Micronucleus Test Syngenta xxxxxxxxxxxxxx GLP not published Syngenta File No CGA300406_10015	Y	Syngenta

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

Comments of zRMS:	In the dRR Part A the Applicant provided a justification and reasons for submission of tests and studies: *This is new plant protection product, which is intended to be authorized in Member State for the first time. There is no repetition of studies involving vertebrates. Animal studies were only performed where there were no data available to address an endpoint, no extrapolation to existing data possible or the available data were not done according to modern guidelines. The testing strategy takes into account methods compliant with the 3R concept for refinement, reduction and replacement of animal testing where applicable and acceptable.* *This is new plant protection product, and there is no EU derogation allowing for these data points to be addressed by extrapolating from existing data; and there have been changes to active substance endpoints and test, study and assessment guidelines; therefore where necessary in order to obtain approval new tests and study reports are provided.*

Acute toxicity studies for A18385B have not been evaluated as part of the EU review of the nicosulfuron, dicamba or prosulfuron. Therefore, all relevant data are provided and are considered adequate.

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	The study is considered to be acceptable and used in evaluation. Acute oral toxicity was examined according to the guideline OECD Test Guideline 425 (2008); EPA OPPTS 870.1100 (2002) on rats in compliance with Principles of Good Laboratory Practice (GLP). There was no deviation during the study. Rats were treated with a single oral (gavage) dose of Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) at the limit dose of 2000 mg/kg body weight. Intermittent clonic convulsions (5/5 rats) and vocalization (3/5 rats) only occurred when the animals were handled, taken out of the cage for observation. All animals were symptom free from 48 hours after the treatment. No mortality was observed and there were no effects on body weight or body weight gain. Also there were no macroscopic observations at necropsy. The study results indicate that the acute oral median lethal dose (LD50) of the Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) was greater than 2000 mg/kg bw, therefore no classification is required for acute oral toxicity of A18385B according to Regulation (EC) 1272/2008.

A 2.2.1 Study 1

The following acute oral toxicity study, performed on A18385B, has not previously been reviewed and is provided in support of this assessment.

Reference:	7.1.1/01
Report	Title: Prosulfuron/dicamba/nicosulfuron WG (A18385B) – Acute Oral Toxicity Study in the Rat (Up and Down Procedure) Author(s): xxxxxxxxxxxxxxxxxxx Year: 2013a Report No: 13/084-001P Syngenta File No. A18385B_10008; VV-405072
Guideline(s):	Yes

	OECD 425 (2008): EPA OPPTS 870.1100 (2002)
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Executive summary

Fasted female CRL:(WI) rats, 9-11 weeks old and weighing 197-225 g. Animals were treated with a single oral (gavage) dose of Prosulfuron/dicamba/nicosulfuron WG (A18385B) at the limit dose of 2000 mg/kg body weight. Single animals were dosed sequentially at no less than approximately 48 hour intervals. Animals were observed individually for up to 14 days thereafter and necropsies were performed on all animals at the end of the study.

Treatment with Prosulfuron/dicamba/nicosulfuron WG (A18385B) at the dose level of 2000 mg/kg bw caused intermittent clonic convulsions (5/5 rats) and vocalization (3/5 rats). These signs only occurred when the animals were handled, taken out of the cage for observation. No abnormal behaviour or was seen before and after handling when left undisturbed, for animals in the first six hours. Additionally, decreased activity was observed in all animals in the first 24 hours. All animals were symptom free from 48 hours after the treatment.

There were no treatment related changes in the body weights. The body weights of the animals were within the range commonly recorded for this strain and age. There was no evidence of the observations at a dose level of 2000 mg/kg bw at necropsy.

Under the conditions of this study, the acute oral median lethal dose (LD_{50}) of the test item, Prosulfuron/dicamba/nicosulfuron WG (A18385B), was greater than 2000 mg/kg bw (limit dose) in female CRL:(WI) rats.

The acute oral toxicity was greater than 2000 mg/kg therefore no classification is required for acute oral toxicity of A18385B according to Regulation (EC) No 1272/2008 as amended.

Materials and methods

Materials:

Test Material:	Prosulfuron/dicamba/nicosulfuron WG (A18385B)
Description:	Brown Granules
Lot/Batch number:	SMU2BP004
Purity:	Content of prosulfuron – 4.32 % w/w Content of dicamba – 41.0 % w/w Content of nicosulfuron – 10.5 % w/w
Product Code:	A18385B
Stability of test compound:	Recertification date – End of September 2014

Vehicle and/or positive control: Distilled water

Test Animals:	
Species	Rat
Strain	CRL:(WI)
Age/weight at dosing	Young adult rats, 9-11 weeks old / 197-225 g
Source	Charles River Laboratories, Research Models and Services, Germany GmbH, Sandhofer Weg 7, D-97633 Sulzfeld
Housing	Individual caging
Acclimatisation period	At least 5 days
Diet	Animals received ssniff® SM R/M "Autoclavable complete diet for rats and rats – breeding and maintenance" produced by ssniff Spezialdiäten GmbH, D-59494 Soest Germany, *ad libitum*
Water	Tap water from municipal supply, provided in 500 mL bottles, *ad libitum*
Environmental conditions	Temperature: 20.1 – 24.1 °C Humidity: 34 – 70 % Air changes: 15-20 air exchanges/hour Photoperiod: 12 hours daily, from 6.00 a.m. to 6.00 p.m.

Study Design and Methods:

In-life dates: Experimental Starting Date: 18 April 2013

Experimental Completion Date: 07 May 2013

Animal assignment and treatment:

Fasted female CRL:(WI) rats, 9-11 weeks old and weighing 197-225 g. Animals were treated with a single oral (gavage) dose of Prosulfuron/dicamba/nicosulfuron WG (A18385B) at the limit dose of 2000 mg/kg body weight. Single animals were dosed sequentially at no less than approximately 48 hour intervals. Animals were observed individually for up to 14 days thereafter and necropsies were performed on all animals at the end of the study

Animals were observed individually after dosing at 30 minutes, then 1, 2, 3, 4, and 6 hours after dosing and once each day for 14 days thereafter. Individual observations were performed on the skin and fur, eyes and mucous membranes and also respiratory, circulatory, autonomic and central nervous system, somatomotor activity and behaviour pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma.

The body weights were recorded on Days -1, 0 (beginning of the experiment), 7 and 14.

All animals were euthanised at the end of the observation period by exsanguination under pentobarbital anaesthesia (Release 300 mg/mL (Pentobarbital sodium) A.U.V. inj, Lot No.: 063012, Expiry Date: January 2015, Produced by: Wirtschaftsgenossenschaft deutscher Tierarzte eG, Germany) and subjected to macroscopic examination. After an external examination,the cranial, thoracic and abdominal cavities were opened and the appearance of the tissues and organs were observed. All gross pathological changes were recorded for each animal on the post mortem record sheets.

Statistics: The LD_{50} was calculated using the AOT425StatPgm program. This program was prepared for the US Environmental Protection Agency by Westat, May 2001 and updated by the US EPA June 2003. This programme was constructed using the most appropriate method to of estimate the LD_{50}.

Results and discussions

Mortality: No mortality was observed in any animals receiving a single dose of Prosulfuron/dicamba/nicosulfuron WG (A18385B) at 2000 mg/kg bw.

Table A 1: Acute oral toxicity of Prosulfuron/dicamba/nicosulfuron WG (A18385B) formulation in the rat, application scheme and mortality data

Animal Number	Dosage [mg/kg body weight]	Dose volume [mL/animals]	Viability/Mortality
477	2000	2.0	Survived
478	2000	2.0	Survived
479	2000	2.2	Survived
480	2000	2.2	Survived
481	2000	2.3	Survived

Clinical observations: Treatment with Prosulfuron/dicamba/nicosulfuron WG (A18385B) at the dose level of 2000 mg/kg bw caused intermittent clonic convulsions (5/5 rats) and vocalization (3/5 rats). These signs only occurred when the animals were handled, taken out of the cage for observation. No abnormal behaviour was seen before and after handling when left undisturbed, for animals in the first six hours. Additionally, decreased activity was observed in all animals in the first 24 hours. All animals were symptom free from 48 hours after the treatment.

Bodyweight: There were no treatment related effects on body weight or body weight gain.

Necropsy: There was no evidence of the observations at a dose level of 2000 mg/kg bw at necropsy.

Conclusion

Under the conditions of this study, the acute oral median lethal dose (LD_{50}) of the test item, Prosulfuron/dicamba/nicosulfuron WG (A18385B), was greater than 2000 mg/kg bw (limit dose) in female CRL:(WI) rats.

The acute oral toxicity was greater than 2000 mg/kg therefore no classification is required for acute oral toxicity of A18385B according to Regulation (EC) No 1272/2008 as amended.

(xxxxxxxxxxx, 2013a)

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

Comments of zRMS:	The study is considered to be acceptable and used in evaluation. Acute dermal toxicity was examined according to the guideline OECD 402 (1987); OPPTS 870.1200 (1998); EC 440/2008 (2008) on rats in compliance with Principles of Good Laboratory Practice (GLP). There was no deviation during the study. Five male and five female CRL:(WI) Wistar rats were treated with a single semi occlusive dermal application of Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) at the limit dose of 2000 mg/kg bw. The application period was 24 hours, followed by a 14-day observation period. No mortality occurred during the study and neither adverse clinical signs nor effects on body weight and body weight gain were observed during the observation period. Also there were no macroscopic observations at necropsy. The study results indicate that the median lethal dose (LD50) of Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) after a single dermal administration was greater than 2000 mg/kg bw, therefore no classification is required for acute dermal toxicity of A18385B according to Regulation (EC) 1272/2008.

A 2.3.1 Study 1

The following acute dermal toxicity study, performed on A18385B, has not previously been reviewed and is provided in support of this assessment.

Reference: 7.1.2/01

Report	Title: Prosulfuron/dicamba/nicosulfuron WG (A18385B) – Acute Dermal Toxicity Study in Rats Author(s): xxxxxxxxxxxxxxxxxxxxx Year: 2013b Report No: 13/084-002P Syngenta File No. A18385B_10007; VV-405071
Guideline(s):	Yes OECD 402 (1987): OPPTS 870.1200 (1998); EC 440/2008 (2008)
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Executive summary

A single administration of Prosulfuron/dicamba/nicosulfuron WG (A18385B) at a dose of 2000 mg/kg body weight was applied dermally to 5 male and 5 female CRL:(WI) rats, followed by a 14-day observation period. The test item was applied as supplied. The application period was 24 hours. Clinical observations were assessed in all animals at 1 and 5 hours after dosing and daily for 14 days thereafter. Body weight was measured prior to dosing on Day 0 and on Days 7 and 14. All animals were euthanized and subjected to a gross macroscopic examination at the end of the 14-day observation period (Day 14).

On test day 0, the test item was applied at a single dose of 2000 mg/kg body weight applied uniformly over the skin and remained on the skin throughout a 24- hour exposure period.

No mortality occurred during the study.

No adverse clinical signs were observed after treatment with the test item or during the 14 day observation period and no effects were observed at the site of application.

There were no treatment related effects on body weight or body weight gain during the observation period.

There was no evidence of the any observations at a dose level of 2000 mg/kg bw at necropsy.

Under the conditions of this study, the median lethal dose of Prosulfuron/dicamba/nicosulfuron WG (A18385B) after a single dermal administration was found to be greater than 2000 mg/kg bw in male and female CRL:(WI) rats.

The acute dermal toxicity was greater than 2000 mg/kg therefore no classification is required for acute dermal toxicity of A18385B according to Regulation (EC) No 1272/2008 as amended.

Materials and methods

Materials:

Test Material:	Prosulfuron/dicamba/nicosulfuron WG (A18385B)
Description:	Brown Granules
Lot/Batch number:	SMU2BP004
Purity:	Content of prosulfuron – 4.32 % w/w Content of dicamba – 41.0 % w/w Content of nicosulfuron – 10.5 % w/w
Product Code:	A18385B
Stability of test compound:	Recertification date – End of September 2014

Vehicle and/or positive control: None

Test Animals:

Species	Rat
Strain	CRL:(WI)
Age/weight at dosing	Young adult rats, between 207 g and 278 g
Source	Charles River Laboratories, Research Models and Services, Germany GmbH, Sandhofer Weg 7, D-97633 Sulzfeld.
Housing	Individual caging Type II. polypropylene/polycarbonate.Laboratory bedding (Lignocel Hygienic Animal Bedding produced by J. Rettenmaier & Söhne GmbH+Co.KG (Holzmühle 1, 73494 Rosenberger, Germany Bedding was available to animals during the study))
Acclimatisation period	at least 5 days
Diet	ssniff® SM R/M-Z+H "Autoclavable complete feed for rats and mice – breeding and maintenance" produced by ssniff Spezialdiäten GmbH, D-59494, Soest, Germany, *ad libitum* (Lot number: 523 7816)
Water	Tap water from municipal supply, *ad libitum*
Environmental conditions	Temperature: 19.3 – 24.5 °C Humidity: 32- 69 % Air changes: 15-20 air exchanges/hour Photoperiod: 12 hours daily, from 6.00 a.m. to 6.00 p.m.

Study Design and Methods:

In-life dates: Start: 24 April 2013 End: 10 May 2013

Animal assignment and treatment: A single administration of Prosulfuron/dicamba/nicosulfuron WG (A18385B) at a dose of 2000 mg/kg body weight was applied dermally to 5 male and 5 female CRL:(WI) rats, followed by a 14-day observation period. The test item was applied as supplied. The application period was 24 hours. A limit test was carried out at 2000 mg/kg body weight (bw) in both sexes (5 rats/sex).

The backs of the animals were shaven (approximately 10% area of the total body surface) approximately 24 hours prior to treatment. Only those animals without injury or irritation on the skin were used in the test. On test day 0, the test item was applied as a single dose of 2000 mg/kg body weight, moistened with water to form a wetted paste, and distributed as uniformly as possible over the skin and remained on the skin throughout a 24- hour exposure period. Sterile gauze pads were placed on the skin of rats at the site of application. These gauze pads were kept in contact with the skin by a patch with adhesive hypoallergenic plaster. The entire trunk of the animal was then wrapped with semi occlusive plastic wrap for 24 hours. At the end of the exposure period, residual test item was removed, using body temperature water.

A clinical examination was performed on the day of treatment, at 1 and 5 hours after the application of the test item, and once each day for 14 days thereafter.

Observations included the skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous system, and somatomotor activity and behaviour pattern. Particular attention was directed to the observation of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma.

The body weights were recorded on Day 0 (beginning of the experiment) and on Days 7 and 14.

Statistics: There was no mortality in the study therefore statistical analysis was not required.

Results and discussions

Mortality: No mortality occurred after the 24-hour dermal exposure to Prosulfuron/dicamba/nicosulfuron WG (A18385B).

Table A 2: Acute dermal toxicity of Prosulfuron/dicamba/nicosulfuron WG (A18385B) in the rat, application scheme and mortality data

Dose Level (mg/kg)	Day Number	Number of Deaths	
		Male	Female
2000	1	0	0
	Total at day 14	0/5	0/5

Clinical observations: No adverse clinical signs were observed after treatment with the test item or during the 14 day observation period.

Bodyweight: There were no effects on bodyweight and body weight gain during the observation period.

Necropsy: There were no macroscopic abnormalities in any animals at a dose level of 2000 mg/kg bw at necropsy.

Conclusion

Under the conditions of this study, the median lethal dose of Prosulfuron/dicamba/nicosulfuron WG (A18385B) after a single dermal administration was found to be greater than 2000 mg/kg bw in male and female CRL:(WI) rats.

The acute dermal toxicity was greater than 2000 mg/kg therefore no classification is required for acute dermal toxicity of A18385B according to Regulation (EC) No 1272/2008 as amended.

(xxxxxxxxxxxxxxxx, 2013b)

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	Justification provided by Applicant is acceptable. Acute inhalation toxicity was determined using calculation method taking into consideration valid data available on each of the components in the mixture. The ATEmix for inhalation toxicity was calculated as 8.1 mg/L, therefore no classification is required for acute inhalation toxicity of A18385B according to Regulation (EC) No. 1272/2008.

The new data requirements for plant protection products set in the Commission Regulation (EU) n° 284/2013 specify that an acute inhalation study shall be carried out also where the plant protection product is to be applied by spraying. Spraying is the method by which A18385B is applied on crops.
Therefore, a study or a justification to not perform it under Regulation (EC) n° 1272/2008 is deemed necessary.

The acute inhalation toxicity of the product was determined on the basis of the composition and the classification declared in the confidential document (Part C). The classification of each component was determined both from the MSDS and the Annex VI of the CLP Regulation (EC) 1272/2008. The classification is based on the ingredients and using the additivity formula in Annex I, 3.1.3.6.2.3, of the CLP Regulation (EC) 1272/2008, as information is not available for all components and the total concentration of the relevant ingredients with unknown toxicity is > 10%.
Therefore, the formula adjusted for the percentage of the unknown ingredients is as follows:

$$\frac{100 - (\sum C \text{ unknown if} > 10\ \%)}{ATE_{mix}} = \sum_{n} \frac{C_i}{ATE_i}$$

The detailed calculation can be found in the confidential dossier of this submission (Registration Report - Part C).

Conclusion
According to the additivity formula in Annex I, 3.1.3.6.2.3, of the CLP Regulation (EC) 1272/2008, the formulation A18385B has an ATE_{mix} of 8.1 mg/L/4h. Therefore, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	The study is considered to be acceptable and used in evaluation. Skin irritation was examined according to the guideline OECD Test Guideline 404 (2002); EPA OPPTS 870.2500 (1998); EC No 440/2008, B.4 (2008) on rabbits in compliance with Principles of Good Laboratory Practice (GLP). The deviation in humidity during the study is considered to have no impact on the outcome of the study and interpretation of the results. Young adult New Zealand white rabbits (3 males) were exposed to 0.5g Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) for 4 hours. Skin reactions were scored at 1, 4, 24, 48 and 72 hours after removal of the dressings. No clinical signs of systemic toxicity were observed in the animals during the study and no mortality occurred. Also the body weights of all rabbits were considered to be within the normal range of variability. The study results indicate that the application of Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) did not result in any signs of skin irritation, therefore no classification is required for skin irritating properties of A18385B according to Regulation (EC) 1272/2008.

A 2.5.1 Study 1

The following acute skin irritation study, performed on A18385B, has not previously been reviewed and is provided in support of this assessment.

Reference:	7.1.4/01
Report	Title: Prosulfuron/dicamba/nicosulfuron WG (A18385B) – Primary Skin Irritation Study in Rabbits Author(s): xxxxxxxxxxxxxxxxx Year: 2013c Report No: 13/084-006N Syngenta File No. A18385B_10009; VV-405073
Guideline(s):	Yes OECD 404 (2002): OPPTS 870.2500 (1998); EC No 440/2008, B.4 (2008)
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Executive summary

Young adult New Zealand white rabbits (3 males) were exposed to 0.5 g Prosulfuron/dicamba/nicosulfuron WG (A18385B), applied to the intact shaved flank under a semi-occlusive dressing, for 4 hours. Skin reactions were scored at 1, 4, 24, 48 and 72 hours after removal of the dressings.

No clinical signs of systemic toxicity were observed in the animals during the study and no mortality occurred. As no clinical signs were observed at 72 hours after patch removal, the study was terminated after

the 72 hours observation. The body weights of all rabbits were considered to be within the normal range of variability.

The application of Prosulfuron/dicamba/nicosulfuron WG (A18385B) did not result in any signs of skin irritation. According to the Draize classification criteria Prosulfuron/dicamba/nicosulfuron WG (A18385B) is considered to be "Not Irritant" to rabbit skin.

The mean irritation scores 24 to 72 hours after application were less than the thresholds defined in Regulation (EC) No 1272/2008 as amended. Therefore, no classification is required for skin irritating properties of A18385B.

Materials and methods

Materials:

Test Material:	Prosulfuron/dicamba/nicosulfuron WG (A18385B)
Description:	Brown Granules
Lot/Batch number:	SMU2BP004
Purity:	Content of prosulfuron – 4.32 % w/w Content of dicamba – 41.0 % w/w Content of nicosulfuron – 10.5 % w/w
Product Code:	A18385B
Stability of test compound:	Recertification date – End of September 2014

Vehicle and/or positive control: None

Test Animals:	
Species	Rabbit
Strain	Young Adult New Zealand White Rabbit
Source	S&K-Lap Kft.2173 Kartal, Császár út 135, Hungary
Housing	Individual caging
Acclimatisation period	28 and 30 days
Diet	UNI diet for rabbits (AgribrandsEurope Hungary PLC, H-5300 Karcag, Madarasi út, Hungary), *ad libitum*
Water	Tap water, from an automatic system, *ad libitum*
Environmental conditions	Temperature: 17.9 – 21.8 °C Humidity: 24 – 57 % Air changes: 8-12 air exchanges/hour Photoperiod: 12 hours daily, from 6.00 a.m. to 6.00 p.m.

Study Design and Methods:

In-life dates: Start: 24 April 2013 End: 29 April

Animal assignment and treatment: The test item was ground to a powder, moistened with water to ensure good skin contact and administered at 0.5 g/animal, the dose specified in the test guidelines for a solid test item

According to EC 2004/73, B.4. and OECD Guidelines 404, a test item does not need to be tested if the pH-value is less than 2 or greater than 11.5, owing to its predictable corrosive properties. The pH of the test item was measured before the study initiation date and was found to be 5.~~0~~5.

Approximately 24 hours prior to the test the hair was clipped from the back and flanks of the animals with an electric clipper, exposing an area of approximately 100 cm^2 (10 cm x 10 cm). Animals with overt signs of skin injury or marked irritation, which may have interfered with the interpretation of the results, were not used in the test.

On the day of treatment, 0.5 g of powdered Prosulfuron/dicamba/nicosulfuron WG (A18385B) was placed on a surgical gauze pad (ca. 2.5 cm x 2.5 cm) and sufficient water was added to dampen the material to

ensure good contact with the skin. This gauze pad was applied to the intact skin of the clipped area and was kept in contact with the skin by a patch with a surrounding adhesive hypoallergenic plaster. The entire trunk of the animals was then wrapped with plastic wrap held in place with an elastic stocking. The duration of treatment was 4 hours. The dressing was then removed and the skin was flushed with lukewarm tap water to clean the application site.

Initially, a single animal was treated. As neither a corrosive effect nor a severe irritant effect were observed after the 1-hour exposure, the test was completed using the 2 remaining animals with an exposure period of 4 hours.

The viability/mortality was recorded daily from the day of application of the animals to the termination of test. Clinical signs were recorded daily and body weights were recorded on the day of application and at termination of observation.

The primary irritation index was calculated by totalling the mean cumulative scores at 24, 48 and 72 hours for all animals and then dividing by the number of data points.

Results and discussions

The mean irritation scores for erythema and oedema were 0.0.

No local dermal signs were observed in the treated animals throughout the study.

No clinical signs of systemic toxicity were observed in the animals during the study and no mortality occurred. As no clinical signs were observed at 72 hours after patch removal, the study was terminated after the 72 hours observation.

The body weights of all rabbits were considered to be within the normal range of variability.

Table A 3: Individual and mean skin irritation scores of Prosulfuron/dicamba/nicosulfuron WG (A18385B) according to the Draize scheme

Time	Erythema			Oedema		
Animal number	00213	00227	00233	00213	00227	00233
after 1 hour	0	0	0	0	0	0
after 24 hours	0	0	0	0	0	0
after 48 hours	0	0	0	0	0	0
after 72 hours	0	0	0	0	0	0
mean score 24-72 h	0	0	0	0	0	0

Conclusion

The application of Prosulfuron/dicamba/nicosulfuron WG (A18385B) did not result in any signs of skin irritation. According to the Draize classification criteria Prosulfuron/dicamba/ nicosulfuron WG (A18385B) is considered to be “Not Irritant” to rabbit skin.

The mean irritation scores 24 to 72 hours after application were less than the thresholds defined in Regulation (EC) No 1272/2008 as amended. Therefore, no classification is required for skin irritating properties of A18385B.

(xxxxxxxxxxxxxxxxx 2013c)

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	The study is considered to be acceptable and used in evaluation. Acute eye irritation was examined according to the guideline OECD 405 (2012); EPA OPPTS 870.2400 (1998); EC No 440/2008, B.5 (2008); Directive 2004/73/EC B.5 (L 152 2004) on rabbits in compliance with Principles of Good Laboratory Practice (GLP). The deviation in humidity during the study is not considered to have adversely affected the study.

	Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) was graded in the study as a moderate irritant (Class 5 on a 1 to 8 scale) to the rabbit eye according to the modified Kay and Calandra classification system. The mean irritation scores 24 to 72 hours after application were greater than the thresholds defined in Regulation (EC) No 1272/2008, therefore A18385B was concluded to have the potential to induce reversible eye irritation. Considering above, Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) should be classified for reversible eye effects, Category 2 (H319) in accordance with Regulation EC (No) 1272/2008.

A 2.6.1 Study 1

The following acute eye irritation study, performed on A18385B, has not previously been reviewed and is provided in support of this assessment.

Reference:	7.1.5/01
Report	Title: Prosulfuron/dicamba/nicosulfuron WG (A18385B) Acute Eye Irritation Study in Rabbits Author(s): xxxxxxxxxxxxxx Year: 2013d Report No: 13/084-005N Syngenta File No. A18385B_10022; VV-405644
Guideline(s):	Yes OECD 405 (2012): EPA OPPTS 870.2400 (1998): EC No 440/2008, B.5 (2008): Directive 2004/73/EC B.5 (L 152 2004 29th April)
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Executive summary

In primary eye irritation study, 0.1 g Prosulfuron/dicamba/nicosulfuron WG (A18385B) was instilled into the conjunctival sac of the left eye of 3 adult male New Zealand White rabbits. The untreated right eyes served as the control. Scoring of irritation effects was performed approximately 1, 24, 48, 72 hours and 1 week in all animals after test material instillation and 2 weeks in one animal after test material instillation. Observations with fluorescein staining were made approximately 24 hours before treatment and then 24, 48, 72 hours and 1 week after treatment in all animals and 2 weeks after the treatment in one animal.

No mortality occurred during the study.

Initial Pain Reaction/Pain reaction (IPR/PR) was not observed. Conjunctival redness (score 2), chemosis (score 2 or 3) and discharge (score 3) were seen in all rabbits at 1 hour after treatment. Conjunctival redness (score 2), chemosis (score 2) and discharge (score 3) were seen in all rabbits at 24 hours after treatment.

Conjunctival redness (score 2), chemosis (score 2) and discharge (score 2 or 3) were seen in all rabbits at 48 hours after treatment. Conjunctival redness (score 2), chemosis (score 1) and discharge (score 1 or 2) were seen in all rabbits at 72 hours after treatment. Conjunctival redness (score 1) and discharge (score 1) was seen in one rabbit at 1 week after treatment. Corneal opacity (score 1, area 3, 4 respectively) was seen in two rabbits at 1, 24, 48 and 72 hours after treatment. All symptoms had fully reversed in two animals at the 1 week observations and in one animal at two weeks observations.

Fluorescein staining was positive in the first animal at 24, 48 and 72 hours after instillation during the study. Fluorescein staining was positive in the second animal at 24, 48 and 72 hours after instillation during the

study. Fluorescein staining was positive in the third animal at 24, 48 and 72 hours after instillation during the study. Fluorescein staining was negative in all animals at 1 week after instillation and one animal 2 weeks after instillation during the study. The control eyes were symptom-free during the study. No mortality occurred during the study. The bodyweights of all rabbits were considered to be within the normal range of variability.

Prosulfuron/dicamba/nicosulfuron WG (A18385B) was graded as a moderate irritant (Class 5 on a 1 to 8 scale) to the rabbit eye according to the modified Kay and Calandra classification system.

The mean irritation scores 24 to 72 hours after application were greater than the thresholds defined in Regulation (EC) No 1272/2008 as amended. Therefore, H319 classification is required for eye irritating properties of A18385B.

Materials and methods

Materials:

Test Material:	Prosulfuron/dicamba/nicosulfuron WG (A18385B)
Description:	Brown Granules
Lot/Batch number:	SMU2BP004
Purity:	Content of prosulfuron – 4.32 % w/w Content of dicamba – 41.0 % w/w Content of nicosulfuron – 10.5 % w/w
Product Code:	A18385B
Stability of test compound:	Recertification date – End of September 2014

For the purpose of the study, the test material was used as supplied.

Test Animals:	
Species	Rabbit
Strain	Young Adult New Zealand White Rabbit
Source	S&K-Lap Kft.2173 Kartal, Császár út 135, Hungary
Housing	Individual caging
Acclimatisation period	at least 5 days
Diet	UNI diet for rabbits (AgribrandsEurope Hungary PLC, H-5300 Karcag, Madarasi út, Hungary), *ad libitum* (The batch numbers of the lots used in the study were: 0251 04 13 (expiry date of the diet: 08 July 2013)
Water	Tap water, from an automatic system, *ad libitum*
Environmental conditions	Temperature: 17.1 – 21.9°C Humidity: 37 – 83 % Air changes: 15-20 air exchanges/hour Photoperiod: 12 hours daily, from 6.00 a.m. to 6.00 p.m.

Study Design and Methods:

In-life dates: Experimental Starting Date: 10 June 2013

Experimental Completion Date: 04 July 2013

Animal assignment and treatment: Approximately 24 hours before the start of the test, both eyes of the provisionally selected test rabbits were examined for evidence of ocular irritation or defect using a hand-held slit-lamp. Only animals free of ocular damage were used.

Initially, a single rabbit was treated. A single amount of 0.1 g of the test material was placed into the conjunctival sac of the left eye, formed by gently pulling the lower lid away from the eyeball. The upper and lower eyelids were held together for several seconds immediately after treatment, to prevent loss of the test material, and then released. The right eye remained untreated and was used for control purposes. Immediately after administration of the test material, an assessment of the initial pain reaction was made. As there

was no effect observed at the 48h-observation, two further rabbits were treated. The third rabbit was treated after the 24 hour-observation of the second animal.

An assessment of eye irritation was made according to a 6 point scale at approximately 1, 24, 48 and 72 hours after instillation. The ocular reaction (i.e. corneal opacity, iridic effects, conjunctivae and chemosis) was assessed according to the Draize numerical evaluation (Draize J H 1977). The eyes were further examined using 2% fluorescein solution at least 24 hours before treatment and then 24, 48 and 72 hours after treatment.

Results and discussions

Mortality: No mortality occurred during the study.

Clinical observations: Conjunctival redness (score 2), chemosis (score 2 or 3) and discharge (score 3) were seen in all rabbits at 1 hour after treatment. Conjunctival redness (score 2), chemosis (score 2) and discharge (score 3) were seen in all rabbits at 24 hours after treatment.

Conjunctival redness (score 2), chemosis (score 2) and discharge (score 2 or 3) were seen in all rabbits at 48 hours after treatment. Conjunctival redness (score 2), chemosis (score 1) and discharge (score 1 or 2) were seen in all rabbits at 72 hours after treatment. Conjunctival redness (score 1) and discharge (score 1) was seen in one rabbit (animal no.: 01280) at 1 week after treatment. Corneal opacity (score 1, area 3, 4 respectively) was seen in two rabbits (animal no.: 01280, 01278) at 1, 24, 48 and 72 hours after treatment. All symptoms had fully reversed in two animals (animal no.: 01278, 01298) at the 1 week observations and in one animal (animal no.: 01280) at two weeks observations.

Fluorescein staining was positive in the first animal (animal no.: 01280) at 24, 48 and 72 hours after instillation during the study. Fluorescein staining was positive in the second animal (animal no.: 01278) at 24, 48 and 72 hours after instillation during the study. Fluorescein staining was positive in the third animal (animal no.: 01298) at 24, 48 and 72 hours after instillation during the study. Fluorescein staining was negative in all animals at 1 week after instillation and one animal (animal no.: 01280) 2 weeks after instillation during the study.

During the study, the control eye of all animals was symptom-free.

Table A 4: Eye irritation scores of Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) according to the Draize scheme

Time	Cornea			Iris			Conjunctiva					
							Redness			Chemosis		
Animal number	01280	01278	01298	01280	01278	01298	01280	01278	01298	01280	01278	01298
after 1 hour	1	1	0	0	0	0	2	2	2	2	3	2
after 24 hours	1	1	0	0	0	0	2	2	2	2	2	2
after 48 hours	1	1	0	0	0	0	2	2	2	2	2	2
after 72 hours	1	1	0	0	0	0	2	2	2	1	1	1
mean scores 24-72h	1.00	1.00	0.00	0.00	0.00	0.00	2.00	2.00	2.00	1.67	1.67	1.67
after 1 week	0	0	0	0	0	0	1	0	0	0	0	0
after 2 weeks	0	0	0	0	0	0	0	0	0	0	0	0

All symptoms had fully reversed in two animals (animal no.: 01278, 01298) at the 1 week observations and in one animal (animal no.: 01280) at two weeks observations.

Bodyweight: The bodyweights of all rabbits were considered to be within the normal range of variability.

Necropsy: No necropsy was performed in the study.

Conclusion

Prosulfuron/dicamba/nicosulfuron WG (A18385B) was graded as a moderate irritant (Class 5 on a 1 to 8 scale) to the rabbit eye according to the modified Kay and Calandra classification system.

The mean irritation scores 24 to 72 hours after application were greater than the thresholds defined in Regulation (EC) No 1272/2008 as amended. Therefore, H319 classification is required for eye irritating properties of A18385B.

(xxxxxxxxxxxxxxxxx 2013d)

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	The study is considered to be acceptable and used in evaluation. Skin sensitization was examined according to the guideline OECD 429 (2010); EC No 440/2008, B.42 (2008) on mouse in compliance with Principles of Good Laboratory Practice (GLP). There was no deviation during the study. The test item solutions were applied on the dorsal surface of ears of experimental animals (25 µL/ear) for 3 consecutive days. No mortality or signs of systemic toxicity was observed during the study. There were no indications of any irritancy at the site of application. Also no treatment related effects were observed on body weight. The appearance of the lymph nodes was normal. Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) was shown to have no sensitisation potential (not a skin sensitizer) in the Local Lymph Node Assay - the sensitisation rate of SI 1.6 is less than the threshold of significance (SI ≥ 3) set in Regulation (EC) No 1272/2008. Therefore no classification is required for skin sensitization properties of A18385B according to Regulation (EC) 1272/2008.

A 2.7.1 Study 1

The following skin sensitisation study, performed on A18385B, has not previously been reviewed and is provided in support of this assessment.

Reference:	7.1.6/01
Report	Title: Prosulfuron/Dicamba/Nicosulfuron WG (A18385B) Local Lymph Node Assay in the Mouse Author(s): xxxxxxxxxxxxxxxxx Year: 2013 Report No: 13/084-037E Syngenta File No. A18385B_10018; VV-405478
Guideline(s):	Yes OECD 429 (2010): EC No 440/2008 of 30 May 2008, B.42
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Executive summary

The aim of this study was to determine the skin sensitisation potential of Prosulfuron/dicamba/ nicosulfuron WG (A18385B) following dermal exposure to CBA/J Rj mice. For this purpose, the Local Lymph Node Assay method was used. The test item solutions were applied on the dorsal surface of ears of experimental animals (25 µL/ear) for 3 consecutive days (Days 1, 2 and 3). There was no treatment on Days

4, 5 and 6. On Day 6, 5 hours prior to termination, animals were intravenously injected *via* the tail vein with tritiated methyl thymidine (^{3}HTdR). Cell proliferation in the local lymph nodes was measured by incorporation of ^{3}HTdR and the values obtained were used to calculate stimulation indices (SI).

No mortality or signs of systemic toxicity was observed for the test item treated animals during the study. Alopecia was observed for all animals in the 50% (w/v) group on Days 3-6, slightly rigid ears were observed in the same group on Day 3. There were no indications of any irritancy at the site of application. No treatment related effects were observed on body weight in the test item treated groups.

The appearance of the lymph nodes was normal in all test item treated groups. The observed stimulation index values were 1.6, 0.8, and 0.6 at concentrations of 50, 25, and 10 % (w/v), respectively.

The sensitivity and reliability of the experimental technique employed was assessed by CiToxLAB Hungary Ltd. with 25% (w/v) α-Hexylcinnamaldehyde (abbreviation: HCA) at an interval no greater than 6 months using the same vehicle (Study code: 13/063-037E). The observed stimulation index value was 17.1.

The sensitisation rate of SI 1.6 is less than the threshold of significance (SI ≥ 3) set in Regulation (EC) No 1272/2008 as amended. Therefore, no classification is required for skin sensitisation properties of A18385B.

Materials and methods

Materials:

Test Material:	Prosulfuron/dicamba/nicosulfuron WG (A18385B)
Description:	Brown granules
Lot/Batch number:	SMU2BP004
Purity:	Content of prosulfuron 4.32% w/w
Product Code:	Content of dicamba 41.0% w/w Content of nicosulfuron 10.5% w/w A18385B
Recertification date:	End of September 2014
Storage conditions	Room temperature (< 30°C)

Vehicle and/or positive control: The vehicle for the test substance was 1% aqueous Pluronic PE9200 (abbreviated as 1% Pluronic).

Test Animals:	
Species	Mouse
Strain	CBA/J Rj
Age/weight at dosing	8 weeks old
Source	Elevage Janvier
Housing	Individual caging / mice were provided with glass tunnel-tubes
Acclimatisation period	5 days
Diet	ssniff SM R/M-Z+H "Autoclavable complete diet for rats and mice, *ad libitum*
Water	tap water from the municipal supply, *ad libitum*
Environmental conditions	Temperature: 19.5 – 24.9 °C Humidity: 30 - 70% Air changes: 15-20 air exchange/hour Photoperiod: 12 hours daily

Study Design and Methods:

In-life dates: Start: 29 May 2013 End: 04 June 2013

Preliminary irritation/toxicity test: A Preliminary Irritation/Toxicity Test was performed on CBA/J Rj mice using two doses (2 animals/dose), at test item concentrations of 50 and 25 % (w/v) in 1% Pluronic.

The preliminary experiment was conducted in a similar experimental manner to the main study, but it was terminated on Day 6 with a body weight measurement and the radioactive proliferation assay was not performed.

Animal assignment and treatment: Groups of four female CBA/J Rj mice were treated with 50, 25 and 10 % (w/v) Prosulfuron/dicamba/nicosulfuron WG (A18385B). The negative control group received 1% Pluronic.

The test item solutions were applied on the dorsal surface of the ears (25 µL/ear) for 3 consecutive days (Days 1, 2 and 3). There was no treatment on Days 4, 5 and 6. On Day 6, animals were killed and cell proliferation in the local lymph nodes was measured by incorporation of tritiated methyl thymidine (^{3}HTdR). The values obtained were used to calculate stimulation indices (SI).

Terminal procedures: On Day 6, animals were intravenously injected with 250 µL of sterile PBS (phosphate buffered saline) containing approximately 20 µCi of ^{3}HTdR. Five hours after intravenous injection, the mice were humanely killed and the draining auricular lymph nodes were excised, and placed in separate Petri dishes containing PBS to keep the nodes wet before processing. The nodes of each animal were processed individually.

Preparation of Lymph Node Cells: A single cell suspension (SCS) of lymph node cells (LNCs) was prepared and collected in disposable tubes by gentle mechanical disaggregating of the lymph nodes through a cell strainer. LNCs for each mouse were pelleted by centrifugation after which supernatants were discarded. Pellets were gently resuspended and 10 mL of PBS was added to the tubes. The washing step was repeated twice. This procedure was repeated for the lymph nodes of each individual animal.

After the final washing step, supernatants were removed. Pellets were gently agitated resuspended and 3 mL of 5 % (w/v) TCA solution was added to the tubes for precipitation of macromolecules.

After incubation with 5% TCA at 2-8 °C for approximately 42 hours), precipitate was recovered by centrifugation at 190 x g for 10 minutes at 4 °C, and supernatants were removed. Pellets were resuspended in 1 mL of 5% (w/v) TCA solution and dispersed using an ultrasonic water bath. Each precipitate was transferred to a suitable sized scintillation vial with 10 mL of scintillation liquid and thoroughly mixed. The vials were loaded into a β-scintillation counter and ^{3}HTdR incorporation was measured (10-minute measurement per sample).

The β-counter expresses the ^{3}HTdR incorporation as the number of radioactive disintegrations per minute (DPM). Background level was also measured in duplicates by adding 1 mL of 5 % (w/v) TCA solution into a scintillation vial filled with 10 mL of scintillation liquid.

Statistics / Data Evaluation: Disintegrations per minute (DPM) were measured for each animal of nodes (correcting for background radioactivity). The results were expressed as disintegrations per node (DPN) by dividing the DPM by the number of lymph nodes.

Stimulation index (SI =mean DPN of treated group divided by mean DPN of the appropriate control group) for each treatment group was calculated. A stimulation index of 3 or greater is the criteria for defining a positive result.

A stimulation index of 3 or greater is the criteria for defining a positive result.

Results and discussions

No mortality or signs of systemic toxicity was observed during the study. Alopecia was observed for all animals in the 50% (w/v) group on Days 3-6, slightly rigid ears were observed in the same group on Day 3. There were no indications of any irritancy at the site of application. No treatment related effects were observed on body weight.

The stimulation index values were 1.6, 0.8, and 0.6 at concentrations of 50, 25, and 10 % (w/v), respectively. The lack of any positive result under these exaggerated test conditions is considered to be evidence that Prosulfuron/dicamba/nicosulfuron WG (A18385B) is not a skin sensitizer.

Table A 5: Skin sensitisation potential of Prosulfuron/dicamba/nicosulfuron WG (A18385B)

Concentration of test substance (%w/v)	Number of lynph nodes assayed	Disintegrations per minute (dpm)	dpm per lymph node	Test : control ratio (SI)
0 (1% Pluronic)	2	123.5	61.8	N/A
	2	295.5	147.8	
	2	75.5	37.8	
	2	173.5	86.8	
	2	458.5	229.3	
50% (w/v)	2	182.5	91.3	1.6
in 1% Pluronic	2	256.5	128.3	
	2	176.5	88.3	
	2	211.5	105.8	
	2	65.5	32.8	
25% (w/v)	2	97.5	48.8	0.8
in 1% Pluronic	2	136.5	68.3	
	2	52.5	26.3	
	2	78.5	39.3	
	2	120.5	60.3	
10% (w/v)	2	117.5	58.8	0.6
in 1% Pluronic	2	123.5	61.8	
	2	295.5	147.8	
	2	75.5	37.8	
	2	173.5	86.8	

N/A = not applicable

The sensitivity and reliability of the experimental technique employed was assessed by CiToxLAB Hungary Ltd. with 25% (w/v) α-Hexylcinnamaldehyde (abbreviation: HCA) at an interval no greater than 6 months using the same vehicle (Study code: 13/063-037E). The observed stimulation index value was 17.1.

Conclusion

The sensitisation rate of SI 1.6 is less than the threshold of significance (SI ≥ 3) set in Regulation (EC) No 1272/2008 as amended. Therefore, no classification is required for skin sensitisation properties of A18385B.

(Hargitai J, 2013)

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

This product does not contain recommendations for combinations of plant protection products therefore supplementary studies are 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)

Comments of zRMS:	The explanation is accepted. The dermal absorption values for prosulfuron, nicosulfuron and dicamba in Spandis 54 WG are in accordance with Guidance on Dermal Absorption (EFSA Journal 2017;15(6): 4873).

Dermal absorption studies for A18385B have not been performed. Therefore, all relevant data are provided and are considered adequate.

Prosulfuron

Based on the Review Report for prosulfuron (SANCO/3055/99-Final; 2 July, 2002), the dermal absorption study was not conducted. Therefore, according to EFSA Guidance on Dermal Absorption the default values of dermal absorption are considered applicable for the risk assessment of A18385B.

According to the guidance, default dermal absorption value of 50% is applied for the concentrate, containing prosulfuron <5% (40 g/kg of prosulfuron in A18385B); default dermal absorption value of 50% is also applied for in-use spray dilution.

The percentage absorptions used in the operator exposure assessment are presented in table below.

Table A 6: Dermal absorption end-points for the risk assessment of prosulfuron

Endpoint	Prosulfuron
Dermal penetration	Concentrate: 50%
	Spray dilutions: 50%

Nicosulfuron

Based on the EFSA's Scientific Report (2007) 120, 1-91, the dermal absorption study was not conducted. Therefore, according to EFSA's Guidance on Dermal Absorption the default values of dermal absorption are considered applicable for the risk assessment of A18385B.

According to the guidance, default dermal absorption value of 10% is applied for the concentrate, containing nicosulfuron >5% (100 g/kg of nicosulfuron in A18385B).

Regarding the dermal absorption value for in-use dilution; the oral absorption value for nicosulfuron is established as ~40% (EFSA Scientific Report (2007) 120, 1-91), which is <75%, therefore, according to the guidance oral absorption value can be applied for diluted product.

The percentage absorptions used in the operator exposure assessment are presented in table below.

Table A 7: Dermal absorption end-points for the risk assessment of nicosulfuron

Endpoint	Nicosulfuron
Dermal penetration	Concentrate: 10%
	Spray dilutions: 40%

Dicamba

Based on the EFSA's conclusions for dicamba (EFSA Journal 2011;9(1):1965), the dermal absorption study was conducted with SL formulation. Therefore, according to EFSA Guidance on Dermal Absorption the default values of dermal absorption are considered applicable for the risk assessment of A18385B.

According to the guidance, default dermal absorption value of 10% is applied for the concentrate, containing dicamba >5% (400 g/kg of dicamba in A18385B); default dermal absorption value of 50% is applied for in-use spray dilution.

The percentage absorptions used in the operator exposure assessment are presented in table below.

Table A 8: Dermal absorption end-points for the risk assessment of dicamba

Endpoint	Dicamba
Dermal penetration	Concentrate: 10%
	Spray dilutions: 50%

A 2.11 Other/Special Studies

The following genotoxicity studies, performed on identified groundwater metabolites CGA349707, CGA159902, CGA150829, SYN542604, CGA325025, SYN547308, and CGA300406, were assessed in the EU review of prosulfuron. The reports are not enclosed with this submission as the studies were deemed to be acceptable during the EU review. However, a short conclusion of the study is provided for completeness.

A 2.11.1 CGA349707

Reference:	KCA 5.8/01
Report	Title: CGA349707: Bacterial mutation assay in *S. typhimurium* and *E. coli* Author(s): Callander, R. Year: 2005 Report No: YV6941/REG/REPT Syngenta File No. CGA349707_0011
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1997): OPPTS 870.5100 (1998): 2000/32/EEC B.13/B.14 (2000).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

Under the conditions of this assay, CGA349707 gave a negative, i.e. non-mutagenic, response in *S. typhimurium* strains TA 1535, TA 1537, TA 98 and TA 100 and in *E. coli* strains WP2 (pKM101) and WP2 *uvr*A (pKM101) in both the presence and absence of S9-mix.

Reference:	KCA 5.8/02
Report	Title: CGA349707: L5178Y TK$^{+/-}$ mouse lymphoma mutation assay. Author(s): Clay, P. Year: 2005a Report No: VV0323/REG/REPT Syngenta File No. CGA349707_0012
Guideline(s):	Yes *In Vitro* Mammalian Cell Gene Mutation Test OECD 476 (1997): OPPTS 870.5300 (1998): 2000/32/EEC B.17 (2000).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication	Not applicable

(if vertebrate study)

Conclusion

Under the conditions of this assay, CGA349707 is not mutagenic in L5178Y TK+/- cells treated *in vitro* in the presence of S9-mix.

Reference:	KCA 5.8/03
Report	Title: CGA349707: *In vitro* cytogenetic assay in human lymphocytes. Author(s): Fox, V. Year: 2005a Report No: SV1296-REG Syngenta File No. CGA349707_0013
Guideline(s):	Yes *In Vitro* Mammalian Chromosome Aberration Test. OECD 473 (1997); OPPTS 870.5375 (1998); 2000/32/EC B10 (2000); ICH S2A and S2B Genotoxicity (1997).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

Under the conditions of this assay, CGA349707 is not clastogenic to cultured human lymphocytes treated *in vitro* in either the presence or absence of S9-mix.

A 2.11.2 CGA159902

Reference:	KCA 5.8/04
Report	Title: CA1118A: Salmonella and Escherichia / liver microsome test Author(s): Hertner, T. Year: 1993 Report No: 931097 Syngenta File No. CGA159902_0009
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1983): OPPTS 798.5265 (1987): 92/69/EEC B.13/B.14 (1992): Ministry of Health & Welfare, Japan (1984).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

Based on the results of these experiments and on standard evaluation criteria, it is concluded that CA1118A and its metabolites did not induce gene mutations in the strains of *S. typhimurium* and *E. coli* used.

Reference:	KCA 5.8/05
Report	Title: CGA159902 - L5178Y TK+/- mouse lymphoma mutation assay Author(s): Clay, P. Year: 2005~~a~~b Report No: VV0322-REG Syngenta File No. CGA159902_0014
Guideline(s):	Yes *In Vitro* Mammalian Cell Gene Mutation Test OECD 476 (1997): OPPTS 870.5300 (1998): 2000/32/EEC B.17 (2000).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

Under the conditions of this assay, CGA159902 is mutagenic in L5178Y TK+/- cells treated *in vitro* in the presence of S9-mix.

Reference:	KCA 5.8/06
Report	Title: CGA159902 - *In vitro* cytogenetic assay in human lymphocytes Author(s): Fox, V. Year: 2005~~a~~b Report No: SV1295-REG Syngenta File No. CGA159902_0015
Guideline(s):	Yes *In Vitro* Mammalian Chromosome Aberration Test. OECD 473 (1997): OPPTS 870.5375 (1998): 2000/32/EC B10 (2000): ICH S2A and S2B Genotoxicity (1997).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

Under the conditions of this assay, CGA159902 is clastogenic to cultured human lymphocytes treated *in vitro* in the absence of S9-mix.

Reference:	KCA 5.8/07
Report	Title: CGA159902 - *In vivo* rat liver unscheduled DNA synthesis assay Author(s): xxxxxxxxxxxx Year: 2005~~b~~c Report No: SR1326-REG Syngenta File No. CGA159902_0016
Guideline(s):	Yes

	OECD 486 (1997): 2000/32/EEC B.39 (2000): ICH S2A and S2B (1997)
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Conclusion

Under the conditions of test, CGA159902 did not induce DNA repair, as measured by unscheduled DNA synthesis, in the rat liver *in vivo*.

Reference:	KCA 5.8/08
Report	Title: CGA159902 - Mouse bone marrow micronucleus test Author(s): xxxxxxxxxxxxxxx Year: 2005ed Report No: SM1319-REG Syngenta File No. CGA159902_0017
Guideline(s):	Yes Mouse bone marrow micronucleus test OECD 474 (1997): 2000/32/EEC B.12 (2000): US EPA OPPTS 870.5395 (1998): ICH S2A and S2B (1997)
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Conclusion

Under the conditions of test, CGA159902 is not clastogenic in the mouse bone marrow micronucleus test.

A 2.11.3 CGA150829

Reference:	KCA 5.8/09
Report	Title: IN-A4098: Bacterial reverse mutation assay Author(s): Wagner, V., VanDyke M. Year: 2009 Report No: DuPont-28277 Syngenta File No. CGA150829_10016
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1997), OPPTS 870.5100 (1998), 2000/32/EEC, B13/14 (2000), JMAFF Notification No. 12-Nousan-8147 Guideline No. 2-1-19-1 (2000 and later revisions).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication	Not applicable

(if vertebrate study)

Conclusion

Under the conditions of this study, the test substance IN-A4098 did not exhibit any mutagenic responses in either the presence or absence of Aroclor-induced rat liver S9. Therefore, the test substance was concluded to be negative in this assay.

Reference:	KCA 5.8/10
Report	Title: AE F059411; Substance, Technical, Code: AE F059411 00 1C99 0001: Bacterial reverse mutation test Author(s): Stammberger, I., Braun K. Year: 1998 Report No: 98.0717 Syngenta File No. CGA150829_10024
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1997), OPPTS 870.5100 (1998), 2000/32/EEC, B13/14 (2000), JMAFF Notification No. 12-Nousan-8147 Guideline No. 2-1-19-1 (2000 and later revisions).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

AE F059411; substance, technical was not mutagenic in this bacterial mutation test either in the absence or in the presence of exogenous metabolic activation.

Reference:	KCA 5.8/11
Report	Title: CGA150829 tech.: Salmonella and Escherichia / liver microsome test Author(s): Geleick, D. Year: 1991 Report No: 901510 Syngenta File No. CGA150829_0002
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1983): OPPTS 798.5265 (1987): 92/69/EEC B.13/B.14 (1984): Ministry of Health & Welfare, Japan (1984): Ministry of Labour Japan (1979).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

Based on the results of these experiments and on standard evaluation criteria, it is concluded that CGA150829 tech. and its metabolites did not induce gene mutations in the strains of *S. typhimurium* and

E. coli used.

Reference:	KCA 5.8/12
Report	Title: IN-A4098: *In Vitro* Mammalian Chromosome Aberration Test Author(s): Gudi, R. Year: 2009 Report No: DuPont-28082 Syngenta File No. CGA150829_10014
Guideline(s):	Yes *In Vitro* Mammalian Chromosome Aberration Test. OECD 473 (1997), OPPTS 870.5375 (1998): 2000/32/EC B10 (2000), Japanese Ministry of Agriculture, Forestry and Fisheries (JMAFF) (November 24, 2000 and later revisions).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

Based on the findings of this study, IN-A4098 was concluded to be negative for the induction of structural and numerical chromosome aberrations in both non-activated and S9-activated test systems in the *in vitro* mammalian chromosome aberration test using human peripheral blood lymphocytes.

Reference:	KCA 5.8/13
Report	Title: IN-A4098: *In Vitro* L5178Y Gene Mutation Assay at the *tk* locus Author(s): Lloyd, M. Year: 2015 Report No: 8323754 Syngenta File No. CGA150829_10077
Guideline(s):	Yes *In Vitro* Mammalian Cell Gene Mutation Test OECD 476 (1997): OPPTS 870.5300 (1998): 440/EEC B.17 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

IN-A4098 was negative in the non-activated and S9-activated test systems in the *in vitro* L5178Y gene mutation assay at the *tk* locus.

Reference:	KCA 5.8/14
Report	Title: CGA150829 technical: Cytogenetic test on Chinese hamster cells *in vitro* (EC-conform). Author(s): Meyer, A.

	Year: 1991 Report No: 901511 Syngenta File No. CGA150829_0009
Guideline(s):	Yes *In Vitro* Mammalian Chromosome Aberration Test. OECD 473 (1983): EPA 798.5375 (1987): 79/831/EEC B10 (1984).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

It is concluded that under the given experimental conditions no evidence of clastogenic effects was obtained in Chinese hamster ovary cells *in vitro* treated with CGA150829 technical.

Reference:	KCA 5.8/15
Report	Title: CGA150829 tech.: Chromosome studies on human lymphocytes *in vitro* Author(s): Dollenmeier, P. Year: 1987 Report No: 860159 Syngenta File No. CGA150829_0012
Guideline(s):	No regulatory guidelines were specified but the study method was based on Evans HJ and O'Riordan ML, 1975; Basler A, Baumann M and Röhrborn G, 1982, Ames BN, McCann J and Yamasaki E, 1975 and Obe G, Beek B and Vaidya V, 1975.
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

It is concluded that under the given experimental conditions, in the experiment with microsomal activation, CGA150829 technical exerted mutagenic effects in human lymphocytes *in vitro*.

Reference:	KCA 5.8/16
Report	Title: IN-A4098: *In Vitro* mammalian cell gene mutation test (CHO/HGPRT assay). Author(s): Clarke, J. Year: 2009 Report No: DuPont-28083 Syngenta File No. CGA150829_10015
Guideline(s):	Yes *In Vitro* Mammalian Cell Gene Mutation Test OECD 476 (1997): OPPTS 870.5300 (1998): 2000/32/EEC B.17 (2000), JMAFF 59-Nousan-4200

	(1985)
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

Under the conditions of this study, IN-A4098 did not cause a positive response in the non-activated or S9-activated systems in the CHO/HGPRT Mutation Assay. The assay was negative.

Reference:	KCA 5.8/17
Report	Title: CGA150829 tech.: Autoradiographic DNA-repair test on rat hepatocytes Author(s): Hertner, T. Year: 1988a Report No: 871186 Syngenta File No. CGA150829_0011
Guideline(s):	Yes OECD 482 (1987).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

It is concluded that, under the given experimental conditions, no evidence of induction of DNA damage by CGA150829 technical or by its metabolites was obtained that could be interpreted as suggestive of genotoxic properties of the substance.

Reference:	KCA 5.8/18
Report	Title: CGA150829 tech.: Autoradiographic DNA repair test on human fibroblasts. Author(s): Meyer, A. Year: 1988 Report No: 871188 Syngenta File No. CGA150829_0010
Guideline(s):	Yes OECD 482 (1987).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

It is concluded that, under the given experimental conditions, no evidence of induction of DNA damage by CGA150829 technical or by its metabolites was obtained that could be interpreted as suggestive of genotoxic properties of the substance.

Reference:	KCA 5.8/19
Report	Title: CGA150829 tech.: Chromosome studies on somatic cells of Chinese Hamster Author(sxxxxxxxxxxxxxxx. Year: 1988 Report No: 871187 Syngenta File No. CGA150829_0013
Guideline(s):	Yes *In Vivo* Chromosome Study on Somatic Cells of Chinese Hamster. OECD 475 (1983).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Conclusion

It is concluded that under the conditions of the experiment, no evidence of mutagenic effects was obtained in Chinese hamsters with CGA150829 tech.

A 2.11.4 SYN542604

Reference:	KCA 5.8/20
Report	Title: SYN542604 - *Salmonella Typhimurium* and *Escherichia Coli* Reverse Mutation Assay. Author(s): Sokolowski, A. Year: 2010 Report No: 2010 Syngenta File No. SYN542604_10001
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1997); OPPTS 870.5100 (1998); 2008/440/EC B.13/B.14 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion, it can be stated that during the described mutagenicity test and under the experimental conditions reported, SYN542604 did not induce gene mutations by base pair changes or frameshifts in the genome of the strains used.

Reference:	KCA 5.8/21
Report	Title: SYN542604 - *In Vitro* Chromosome Aberration Test in Human Lymphocytes Author(s): Bohnenberger, S. Year: 2010 Report No: 2010 Syngenta File No. SYN542604_10000
Guideline(s):	Yes *In Vitro* Mammalian Chromosome Aberration Test. OECD 473 (1997); OPPTS 870.5375 (1998); EC 440/2008 B.10 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion, it can be stated that under the experimental conditions reported, the test item SYN542604 did not induce structural chromosomal aberrations in human lymphocytes *in vitro* in the absence and presence of metabolic activation, when tested up to precipitating concentrations.

Reference:	KCA 5.8/22
Report	Title: SYN542604 - Cell Mutation Assay at the Thymidine Kinase Locus (TK+/-) in Mouse Lymphoma L5178Y Cells Author(s): Wollny, H. Year: 2010 Report No: 2010 Syngenta File No. SYN542604_10002
Guideline(s):	Yes *In Vitro* Mammalian Cell Gene Mutation Test OECD 476 (1997): OPPTS 870.5300 (1998): 440/EEC B.17 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion it can be stated that during the mutagenicity test described and under the experimental conditions reported the test item SYN542604 did not induce mutations in the mouse lymphoma thymidine kinase locus assay using the cell line L5178Y in the absence and presence of metabolic activation.
Therefore, SYN542604 is considered to be non-mutagenic in this mouse lymphoma assay.

A 2.11.5 CGA325025

Reference:	KCA 5.8/23

Report	Title: CGA325025 - *Salmonella Typhimurium* and *Escherichia Coli* Reverse Mutation Assay Author(s): Sokolowski, A. Year: 2013 Report No: 2013 Syngenta File No. CGA325025_10007
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1997): OPPTS 870.5100 (1998): EC 440/2008 B.13/14 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

During the described mutagenicity tests and under the experimental conditions reported, CGA325025 did not induce gene mutations by base pair changes or frameshifts in the genome of the strains used. CGA325025 is considered to be non-mutagenic in the *Salmonella typhimurium* and *Escherichia coli* reverse mutation assay.

Reference:	KCA 5.8/24
Report	Title: CGA325025 - Cell Mutation Assay at the Thymidine Kinase Locus ($TK^{+/-}$) in Mouse Lymphoma L5178Y Cells Author(s): Wollny, H. Year: 2013 Report No: 2013 Syngenta File No. CGA325025_10008
Guideline(s):	Yes *In Vitro* Mammalian Cell Gene Mutation Test OECD 476 (1997): OPPTS 870.5300 (1998): EC 440/2008 B17 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion, it can be stated that under the experimental conditions reported the test substance CGA325025 did not induce mutations in the mouse lymphoma thymidine kinase locus assay using the cell line L5178Y in the absence and presence of metabolic activation. Therefore, CGA325025 is considered to be non-mutagenic in this mouse lymphoma assay.

Reference:	KCA 5.8/25
Report	Title: CGA325025 - *In Vitro* Chromosome Aberration Test in Human Lymphocytes Author(s): Bohnenberger, S.

	Year: 2013 Report No: 2013 Syngenta File No. CGA325025_10009
Guideline(s):	Yes *In Vitro* Mammalian Chromosome Aberration Test. OECD 473 (1997); OPPTS 870.5375 (1998); EC 440/2008 B10 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion, it can be stated that under the experimental conditions reported, the test substance did not induce structural chromosomal aberrations in human lymphocytes *in vitro*. Therefore, CGA325025 is considered to be non-clastogenic in this chromosome aberration test, when tested up to cytotoxic and/or precipitating concentrations.

A 2.11.6 SYN547308

Reference:	KCA 5.8/26
Report	Title: SYN547308 - *Salmonella Typhimurium* and *Escherichia Coli* Reverse Mutation Assay. Author(s): Sokolowski, A. Year: 2014 Report No: 2014 Syngenta File No. SYN547308_10002
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1997): OPPTS 870.5100 (1998): EC 440/2008 B.13/14 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

During the described mutagenicity tests and under the experimental conditions reported, SYN547308 did not induce gene mutations by base pair changes or frameshifts in the genome of the strains used. SYN547308 is considered to be non-mutagenic in the *Salmonella typhimurium* and *Escherichia coli* reverse mutation assay.

Reference:	KCA 5.8/27
Report	Title: SYN547308 - Cell Mutation Assay at the Thymidine Kinase Locus ($TK^{+/-}$) in Mouse Lymphoma L5178Y Cells Author(s): Wollny, H. Year: 2014 Report No: 2014

	Syngenta File No. SYN547308_10000
Guideline(s):	Yes *In Vitro* Mammalian Cell Gene Mutation Test OECD 476 (1997): OPPTS 870.5300 (1998): EC 440/2008 B17 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion, it can be stated that under the experimental conditions reported the test substance SYN547308 did not induce mutations in the mouse lymphoma thymidine kinase locus assay using the cell line L5178Y in the absence and presence of metabolic activation. Therefore, SYN547308 is considered to be non-mutagenic in this mouse lymphoma assay.

Reference:	KCA 5.8/28
Report	Title: SYN547308 - *In Vitro* Chromosome Aberration Test in Human Lymphocytes Author(s): Bohnenberger, S. Year: 2014 Report No: 2014 Syngenta File No. SYN547308_10004
Guideline(s):	Yes *In Vitro* Mammalian Chromosome Aberration Test. OECD 473 (1997); OPPTS 870.5375 (1998); EC 440/2008 B10 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion, it can be stated that under the experimental conditions reported, the test substance induced structural chromosomal aberrations in human lymphocytes *in vitro*. Therefore, SYN547308 is considered to be clastogenic in this chromosome aberration test, when tested up to cytotoxic and/or precipitating concentrations.

Reference:	KCA 5.8/29
Report	Title: SYN547308 - Oral (Gavage) Mouse Micronucleus Test Author(s): xxxxxxxxxxxxxxxx Year: 2014 Report No: BFI0214 Syngenta File No. SYN547308_10006
Guideline(s):	Yes Mouse bone marrow micronucleus test. OECD 474 (1997): OPPTS 870.5395 (1998): 2000/32/EC 440/2008 B.12 (2008).

Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Conclusion

There was no evidence of clastogenicity or aneugenicity following oral (gavage) administration of SYN547308 up to the regulatory test guideline maximum dose level of 2000 mg/kg/day in male mice. Therefore, SYN547308 is considered to be non-clastogenic or aneugenic in this bone marrow micronucleus assay.

A 2.11.7 CGA300406

Reference:	KCA 5.8/30
Report	Title: CGA300406 - *Salmonella Typhimurium* and *Escherichia Coli* Reverse Mutation Assay. Author(s): Sokolowski, A. Year: 2015a Report No: 1660401 Syngenta File No. CGA300406_10009
Guideline(s):	Yes Reverse Mutation Test Using Bacteria. OECD 471 (1997); OPPTS 870.5100 (1998); 2008/440/EC B.13/B.14 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

During the described mutagenicity tests and under the experimental conditions reported, CGA300406 did not induce gene mutations by base pair changes or frameshifts in the genome of the strains used. CGA300406 is considered to be non-mutagenic in the Salmonella typhimurium and *Escherichia coli* reverse mutation assay.

Reference:	KCA 5.8/31
Report	Title: CGA300406 - Cell Mutation Assay at the Thymidine Kinase Locus (TK+/-) in Mouse Lymphoma L5178Y Cells Author(s): Wollny, H. Year: 2015 Report No: 1660403 Syngenta File No. CGA300406_10011
Guideline(s):	Yes *In Vitro* Mammalian Cell Gene Mutation Test OECD 476 (1997): OPPTS 870.5300 (1998): EC 440/2008 B17 (2008).
Deviations:	No
GLP:	Yes

Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion, it can be stated that under the experimental conditions reported, the test substance CGA300406 did not induce mutations in the mouse lymphoma thymidine kinase locus assay using the cell line L5178Y in the absence and presence of metabolic activation. Therefore, CGA300406 is considered to be non-mutagenic in this mouse lymphoma assay.

Reference:	KCA 5.8/32
Report	Title: CGA300406 - *In Vitro* Chromosome Aberration Test in Human Lymphocytes Author(s): Sokolowski, A. Year: 2015b Report No: 2015 Syngenta File No. CGA300406_10013
Guideline(s):	Yes *In Vitro* Mammalian Chromosome Aberration Test. OECD 473 (2014); EPA OPPTS 870.5375 (1998); EC 440/2008 B.10 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	Not applicable

Conclusion

In conclusion, it can be stated that under the experimental conditions reported, the test substance induced structural chromosomal aberrations in human lymphocytes *in vitro* in the absence and presence of a metabolic activation system. Therefore, CGA300406 is considered to be clastogenic in this chromosome aberration test, when tested up to the highest required concentration.

Reference:	KCA 5.8/33
Report	Title: CGA300406 - Oral (Gavage) Mouse Micronucleus Test Author(sxxxxxxxxxxxx Year: 2015 Report No: BFI0400 Syngenta File No. CGA300406_10015
Guideline(s):	Yes Mouse bone marrow micronucleus test. OECD 474 (1997): OPPTS 870.5395 (1998): 2000/32/EC 440/2008 B.12 (2008).
Deviations:	No
GLP:	Yes
Acceptability:	Yes/No/Supplementary
Duplication (if vertebrate study)	No

Conclusion

There was no evidence of clastogenicity or aneugenicity in male mice following oral (gavage) administration of CGA300406 up to the OECD 474 limit dose of 2000 mg/kg/day. Therefore, CGA300406 is considered to be neither clastogenic nor aneugenic in the mouse bone marrow micronucleus assay.

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for prosulfuron

Table A 9: Input parameters considered for the estimation of operator exposure (EFSA Guidance) (LCTM; no PPE)

Substance	Prosulfuron	Formulation = Wettable granules, soluble granules	Application rate-0.02 kg a.s. /ha	Spray dilution = 0.1 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 50	Dermal for in use diluation = 50	Oral = 100	Inhalation = 100	
RVNAS	0.06 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 10: Estimation of operator exposure towards prosulfuron using the EFSA Guidance (LCTM; no PPE)

Operator Model		Mixing, loading and application AOEM			
Potential exposure	Longer term systemic exposure mg/kg bw/day		0.0239	% of RVNAS	39.78%
	Acute systemic exposure mg/kg bw/day		0.2139	% of RVAAS	
Mixing and Loading		Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Soluble bags = No
Application		Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Closed cabin = No
Exposure (including PPE options above)	Longer term systemic exposure mg/kg bw/day		0.0131	% of RVNAS	21.77%
	Acute systemic exposure mg/kg bw/day		0.0770	% of RVAAS	

A 3.1.2 Calculations for nicosulfuron

Table A 11: Input parameters considered for the estimation of operator exposure (EFSA Guidance) (LCTM; no PPE)

Substance	Nicosulfuron	Formulation = Wettable granules, soluble granules	Application rate-0.05 kg a.s. /ha	Spray dilution = 0.25 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 10	Dermal for in use diluation = 50	Oral = 40	Inhalation = 100	
RVNAS	0.8 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 12: Estimation of operator exposure towards nicosulfuron using the EFSA Guidance (LCTM; no PPE)

Operator Model	Mixing, loading and application AOEM			
Potential exposure	Longer term systemic exposure mg/kg bw/day	0.0141	% of RVNAS	1.76%
	Acute systemic exposure mg/kg bw/day	0.1076	% of RVAAS	
Mixing and Loading	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Soluble bags = No
Application	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Closed cabin = No
Exposure (including PPE options above)	Longer term systemic exposure mg/kg bw/day	0.0086	% of RVNAS	1.07%
	Acute systemic exposure mg/kg bw/day	0.0641	% of RVAAS	

A 3.1.3 Calculations for dicamba

Table A 13: Input parameters considered for the estimation of operator exposure (EFSA Guidance) (LCTM; no PPE)

Substance	Dicamba	Formulation = Wettable granules, soluble granules	Application rate-0.2 kg a.s. /ha	Spray dilution = 1 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 10	Dermal for in use diluation = 50	Oral = 100	Inhalation = 100	
RVNAS	0.3 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 14: Estimation of operator exposure towards dicamba using the EFSA Guidance (LCTM; no PPE)

Operator Model	Mixing, loading and application AOEM			
Potential exposure	Longer term systemic exposure mg/kg bw/day	0.0442	% of RVNAS	14.75%
	Acute systemic exposure mg/kg bw/day	0.2609	% of RVAAS	
Mixing and Loading	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Soluble bags = No
Application	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Closed cabin = No
Exposure (including PPE options above)	Longer term systemic exposure mg/kg bw/day	0.0274	% of RVNAS	9.12%
	Acute systemic exposure mg/kg bw/day	0.1745	% of RVAAS	

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for prosulfuron

Table A 15: Input parameters considered for the estimation of worker exposure (EFSA Guidance) (Crop inspection)

Substance	Prosulfuron	Formulation = Wettable granules, soluble granules	Application rate-0.02 kg a.s. /ha	Spray dilution = 0.1 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 50	Dermal for in use diluation = 50	Oral = 100	Inhalation = 100	
RVNAS	0.06 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 16: Estimation of worker exposure towards prosulfuron using the EFSA re-entry model (Crop inspection)

Worker - Inspection, irrigation	Potential exposure mg/kg bw/day	0.0125	% of RVNAS	20.83%
	Working clothing mg/kg bw/day	0.0014	% of RVNAS	2.33%
	Working clothing and gloves mg/kg bw/day		% of RVNAS	

A 3.2.2 Calculations for nicosulfuron

Table A 17: Input parameters considered for the estimation of worker exposure (EFSA Guidance) (Crop inspection)

Substance	Nicosulfuron	Formulation = Wettable granules, soluble granules	Application rate-0.05 kg a.s. /ha	Spray dilution = 0.25 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 10	Dermal for in use diluation = 50	Oral = 40	Inhalation = 100	
RVNAS	0.8 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 18: Estimation of worker exposure towards nicosulfuron using the EFSA re-entry model (Crop inspection)

Worker - Inspection, irrigation	Potential exposure mg/kg bw/day	0.0313	% of RVNAS	3.91%
	Working clothing mg/kg bw/day	0.0035	% of RVNAS	0.44%
	Working clothing and gloves mg/kg bw/day		% of RVNAS	

A 3.2.3 Calculations for dicamba

Table A 19: Input parameters considered for the estimation of worker exposure (EFSA Guidance) (Crop inspection)

Substance	Dicamba	Formulation = Wettable granules, soluble granules	Application rate-0.2 kg a.s. /ha	Spray dilution = 1 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 10	Dermal for in use diluation = 50	Oral = 100	Inhalation = 100	
RVNAS	0.3 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 20: Estimation of worker exposure towards dicamba using the EFSA re-entry model (Crop inspection)

Worker - Inspection, irrigation	Potential exposure mg/kg bw/day	0.1250	% of RVNAS	41.67%
	Working clothing mg/kg bw/day	0.0140	% of RVNAS	4.67%
	Working clothing and gloves mg/kg bw/day		% of RVNAS	

A 3.3 Bystander and resident exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for prosulfuron

Table A 21: Input parameters considered for the estimation of resident exposure (EFSA model; LCTM)

Substance	Prosulfuron	Formulation = Wettable granules, soluble granules	Application rate-0.02 kg a.s. /ha	Spray dilution = 0.1 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 50	Dermal for in use diluation = 50	Oral = 100	Inhalation = 100	
RVNAS	0.06 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 22: Estimation of resident exposure towards prosulfuron using the EFSA model (LCTM)

Resident - child	Spray drift (75th percentile) mg/kg bw/day	0.0013	% of RVNAS	2.24%
	Vapour (75th percentile) mg/kg bw/day	0.0011	% of RVNAS	1.78%
	Surface deposits (75th percentile) mg/kg bw/day	0.0002	% of RVNAS	0.27%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0017	% of RVNAS	2.81%
	All pathways (mean) mg/kg bw/day	0.0033	% of RVNAS	5.46%
Resident - adult	Spray drift (75th percentile) mg/kg bw/day	0.0003	% of RVNAS	0.54%
	Vapour (75th percentile) mg/kg bw/day	0.0002	% of RVNAS	0.38%
	Surface deposits (75th percentile) mg/kg bw/day	0.0001	% of RVNAS	0.11%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0009	% of RVNAS	1.56%
	All pathways (mean) mg/kg bw/day	0.0012	% of RVNAS	1.97%

Table A 23: Input parameters considered for the estimation of bystander exposure (Martin *et al.*; LCTM)

Input parameters considered for the estimation of bystander exposure:

Intended use(s):			**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	0.02	kg a.s./ha	**Exposed Body Surface Area (BSA):**	1	m² (adults)
				0.21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.001	mg/kg a.s. (6 hours, adults)
	16.15	kg/person (children)		0.00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	50.00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Field Crops,
Inhalation absorption (IA):	100	%	**Exposure duration (T):**	5	min
AOEL:	0.06	mg/kg bw/d			

Table A 24: Estimation of bystander exposure towards prosulfuron (Martin *et al.*; LCTM)

Bystander exposure towards Prosulfuron					
Adults			**Children**		
Bystander: Dermal exposure after application in (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(2 x 0.29% x 1 x 50%) / 60			(2 x 0.29% x 0.21 x 50%) / 16.15		
External exposure	0.0058	mg/person	External exposure	0.001218	mg/person
External exposure	9.6667E-05	mg/kg bw/d	External exposure	7.5418E-05	mg/kg bw/d
Absorbed dose:	**0.0000483**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000377**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,000 / 360 x 0.02 x 20 x 5 x 100%) / 60			(0,000 / 360 x 0.02 x 20 x 5 x 100%) / 16.15		
External exposure	5.5556E-06	mg/person	External exposure	3.1928E-06	mg/person
External exposure	9.2593E-08	mg/kg bw/d	External exposure	1.977E-07	mg/kg bw/d
Absorbed dose:	**0.0000001**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000002**	**mg/kg bw/d**
Total systemic exposure: SE_B = SDE_B + SIE_B			Total systemic exposure: SE_B = SDE_B + SIE_B		
Total systemic exposure (absorbed dose)	0.00290556	mg/person	Total systemic exposure (absorbed dose)	0.00061219	mg/person
Total systemic exposure (absorbed dose)	**0.0000484**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0000379**	**mg/kg bw/d**
% of AOEL:	**0.08**	**%**	**% of AOEL:**	**0.06**	**%**

Table A 25: Input parameters considered for the estimation of resident exposure (Martin *et al.*)

Input parameters considered for the estimation of resident exposure:

Intended use(s):			**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	0.02	kg a.s./ha	**Transfer coefficient (TC):**	7300	cm^2/h (adults)
				2600	cm^2/h (children)
Number of applications (NA):	1		**Turf Transferable Residues (TTR):**	5	%
Body weight (BW):	60	kg/person (adults)	**Exposure Duration (H):**	2	h
	16.15	kg/person (children)	**Airborne Concentration of Vapour (ACV):**	none	
Dermal absorption (DA):	50.00	% ('worst case')	**Inhalation Rate (IR):**	16.57	m^3/d (adults),
Inhalation absorption (IA):	100	%		8.31	m^3/d (children)
Oral absorption (OA)	100	%	**Saliva Extraction Factor (SE):**	50	%
AOEL	0.06	mg/kg bw/d	**Surface Area of Hands (SA):**	20	cm^2
			Frequency of Hand to Mouth (Freq):	20	events/h
			Dislodgeable foliar residues (DFR):	20	%
			Ingestion Rate for Mouthing of Grass/Day (IgR):	25	cm^2/d

Table A 26: Estimation of resident exposure towards prosulfuron (Martin *et al.*)

Resident exposure towards Prosulfuron					
Adults			**Children**		
Residents: Dermal exposure after application in (via deposits caused by spray drift)					
SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW			SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW		
(0.0002 x 1 x 0.29% x 5% x 7300 x 2 x 50%) / 60			(0.0002 x 1 x 0.29% x 5% x 2600 x 2 x 50%) / 16.15		
External exposure	0.0004234	mg/person	External exposure	0.0001508	mg/person
External exposure	7.0567E-06	mg/kg bw/d	External exposure	9.3375E-06	mg/kg bw/d
Absorbed dose:	**0.0000035**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000047**	**mg/kg bw/d**
Residents: Inhalation exposure to vapour					
SIE_R = (AC_V x IR x IA) / BW			SIE_R = (AC_V x IR x IA) / BW		
(0 x 16.57 x 100%) / 60			(0 x 8.31 x 100%) / 16.15		
External exposure		mg/person	External exposure		mg/person
External exposure		mg/kg bw/d	External exposure		mg/kg bw/d
Absorbed dose:		**none**	**Absorbed dose:**		**none**
			Residents: Oral exposure (hand-to-mouth transfer)		
			SOE_H = (AR x NA x D x TTR x SE x SA x Freq x H x OA) /		
			(0.0002 x 1 x 0.29% x 5% x 50% x 20 x 20 x 2 x 100%) / 16.15		
			External exposure	0.0000116	mg/person
			External exposure	7.1827E-07	mg/kg bw/d
			Absorbed dose	**0.0000007**	**mg/kg bw/d**
			Residents: Oral exposure (object-to-mouth transfer)		
			SOE_O = (AR x NA x D x DFR x IgR x OA) / BW		
			(0.0002 x 1 x 0.29% x 20% x 25 x 100%) / 16.15		
			External exposure	0.0000029	mg/person
			External exposure	1.7957E-07	mg/kg bw/d
			Absorbed dose	**0.0000002**	**mg/kg bw/d**
Total systemic exposure: SE_R = SDE_R + SIE_R			Total systemic exposure: SE_R = SDE_R + SIE_R + SOE_H + SOE_O		
Total systemic exposure (absorbed dose)	0.0002117	mg/person	Total systemic exposure (absorbed dose)	0.0000899	mg/person
Total systemic exposure (absorbed dose)	**0.0000035**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0000056**	**mg/kg bw/d**
% of AOEL:	**0.01**	**%**	**% of AOEL:**	**0.01**	**%**

A 3.3.2 Calculations for nicosulfuron

Table A 27: Input parameters considered for the estimation of resident exposure (EFSA model; LCTM)

Substance	Nicosulfuron	Formulation = Wettable granules, soluble granules	Application rate-0.05 kg a.s. /ha	Spray dilution = 0.25 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 10	Dermal for in use diluation = 50	Oral = 40	Inhalation = 100	
RVNAS	0.8 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 28: Estimation of resident exposure towards nicosulfuron using the EFSA model (LCTM)

Resident - child	Spray drift (75th percentile) mg/kg bw/day	0.0034	% of RVNAS	0.42%
	Vapour (75th percentile) mg/kg bw/day	0.0011	% of RVNAS	0.13%
	Surface deposits (75th percentile) mg/kg bw/day	0.0004	% of RVNAS	0.05%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0042	% of RVNAS	0.53%
	All pathways (mean) mg/kg bw/day	0.0066	% of RVNAS	0.82%
Resident - adult	Spray drift (75th percentile) mg/kg bw/day	0.0008	% of RVNAS	0.10%
	Vapour (75th percentile) mg/kg bw/day	0.0002	% of RVNAS	0.03%
	Surface deposits (75th percentile) mg/kg bw/day	0.0002	% of RVNAS	0.02%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0023	% of RVNAS	0.29%
	All pathways (mean) mg/kg bw/day	0.0026	% of RVNAS	0.33%

Table A 29: Input parameters considered for the estimation of bystander exposure (Martin *et al.*; LCTM)

Intended use(s):			**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	0.05	kg a.s./ha	**Exposed Body Surface Area (BSA):**	1	m^2 (adults)
				0.21	m^2 (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.001	mg/kg a.s. (6 hours, adults)
	16.15	kg/person (children)		0.00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	50.00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Field Crops, Tractor Mounted (FCTM))
Inhalation absorption (IA):	100	%	**Exposure duration (T):**	5	min
AOEL:	0.8	mg/kg bw/d			

Table A 30: Estimation of bystander exposure towards nicosulfuron (Martin *et al.*; LCTM)

Bystander exposure towards Nicosulfuron					
Adults			**Children**		
Bystander: Dermal exposure after application in (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(5 x 0.29% x 1 x 50%) / 60			(5 x 0.29% x 0.21 x 50%) / 16.15		
External exposure	0.0145	mg/person	External exposure	0.003045	mg/person
External exposure	0.00024167	mg/kg bw/d	External exposure	0.00018854	mg/kg bw/d
Absorbed dose:	**0.0001208**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000943**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,000 / 360 x 0.05 x 20 x 5 x 100%) / 60			(0,000 / 360 x 0.05 x 20 x 5 x 100%) / 16.15		
External exposure	1.3889E-05	mg/person	External exposure	7.9821E-06	mg/person
External exposure	2.3148E-07	mg/kg bw/d	External exposure	4.9425E-07	mg/kg bw/d
Absorbed dose:	**0.0000002**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000005**	**mg/kg bw/d**
Total systemic exposure: SE_B = SDE_B + SIE_B			Total systemic exposure: SE_B = SDE_B + SIE_B		
Total systemic exposure (absorbed dose)	0.00726389	mg/person	Total systemic exposure (absorbed dose)	0.00153048	mg/person
Total systemic exposure (absorbed dose)	**0.0001211**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0000948**	**mg/kg bw/d**
% of AOEL:	**0.02**	**%**	**% of AOEL:**	**0.01**	**%**

Table A 31: Input parameters considered for the estimation of resident exposure (Martin *et al.*)

Intended use(s):			**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	0.05	kg a.s./ha	**Transfer coefficient (TC):**	7300	cm^2/h (adults)
				2600	cm^2/h (children)
Number of applications (NA):	1		**Turf Transferable Residues (TTR):**	5	%
Body weight (BW):	60	kg/person (adults)	**Exposure Duration (H):**	2	h
	16.15	kg/person (children)	**Airborne Concentration of Vapour (ACV):**	none	
Dermal absorption (DA):	50.00	% ('worst case')	**Inhalation Rate (IR):**	16.57	m^3/d (adults),
Inhalation absorption (IA):	100	%		8.31	m^3/d (children)
Oral absorption (OA)	40	%	**Saliva Extraction Factor (SE):**	50	%
AOEL	0.8	mg/kg bw/d	**Surface Area of Hands (SA):**	20	cm^2
			Frequency of Hand to Mouth (Freq):	20	events/h
			Dislodgeable foliar residues (DFR):	20	%
			Ingestion Rate for Mouthing of Grass/Day (IgR):	25	cm^2/d

Table A 32: Estimation of resident exposure towards nicosulfuron (Martin *et al.*)

Resident exposure towards Nicosulfuron					
Adults			**Children**		
Residents: Dermal exposure after application in (via deposits caused by spray drift)					
SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW			SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW		
(0.0005 x 1 x 0.29% x 5% x 7300 x 2 x 50%) / 60			(0.0005 x 1 x 0.29% x 5% x 2600 x 2 x 50%) / 16.15		
External exposure	0.0010585	mg/person	External exposure	0.000377	mg/person
External exposure	1.7642E-05	mg/kg bw/d	External exposure	2.3344E-05	mg/kg bw/d
Absorbed dose:	**0.0000088**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000117**	**mg/kg bw/d**
Residents: Inhalation exposure to vapour					
SIE_R = (AC_V x IR x IA) / BW			SIE_R = (AC_V x IR x IA) / BW		
(0 x 16.57 x 100%) / 60			(0 x 8.31 x 100%) / 16.15		
External exposure		mg/person	External exposure		mg/person
External exposure		mg/kg bw/d	External exposure		mg/kg bw/d
Absorbed dose:		**none**	**Absorbed dose:**		**none**
			Residents: Oral exposure (hand-to-mouth transfer)		
			SOE_H = (AR x NA x D x TTR x SE x SA x Freq x H x OA) /		
			(0.0005 x 1 x 0.29% x 5% x 50% x 20 x 20 x 2 x 40%) / 16.15		
			External exposure	0.000029	mg/person
			External exposure	1.7957E-06	mg/kg bw/d
			Absorbed dose	**0.0000007**	**mg/kg bw/d**
			Residents: Oral exposure (object-to-mouth transfer)		
			SOE_O = (AR x NA x D x DFR x IgR x OA) / BW		
			(0.0005 x 1 x 0.29% x 20% x 25 x 40%) / 16.15		
			External exposure	0.00000725	mg/person
			External exposure	4.4892E-07	mg/kg bw/d
			Absorbed dose	**0.0000002**	**mg/kg bw/d**
Total systemic exposure: $SE_R = SDE_R + SIE_R$			Total systemic exposure: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$		
Total systemic exposure (absorbed dose)	0.00052925	mg/person	Total systemic exposure (absorbed dose)	0.000203	mg/person
Total systemic exposure (absorbed dose)	**0.0000088**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0000126**	**mg/kg bw/d**
% of AOEL:	**0.001**	**%**	**% of AOEL:**	**0.002**	**%**

A 3.3.3 Calculations for dicamba

Table A 33: Input parameters considered for the estimation of resident exposure (EFSA model; LCTM)

Substance	Dicamba	Formulation = Wettable granules, soluble granules	Application rate-0.2 kg a.s. /ha	Spray dilution = 1 g a.s./l	Vapour pressure = low volatile substances having a vapour pressure of
Scenario	Cereals / Outdoor / Downward spraying / Vehicle-mounted			Buffer = 2-3	Number applications = 1, Application interval = 365 days
Percentage Absoprtion	Dermal for product = 10	Dermal for in use diluation = 50	Oral = 100	Inhalation = 100	
RVNAS	0.3 mg/kg bw/day		RVAAS	mg/kg bw/day	
DFR	3 µg a.s./cm2 per kg a.s./ha		DT50	30 days	

Table A 34: Estimation of resident exposure towards dicamba using the EFSA model (LCTM)

Resident - child	Spray drift (75th percentile) mg/kg bw/day	0.0134	% of RVNAS	4.48%
	Vapour (75th percentile) mg/kg bw/day	0.0011	% of RVNAS	0.36%
	Surface deposits (75th percentile) mg/kg bw/day	0.0016	% of RVNAS	0.54%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0169	% of RVNAS	5.63%
	All pathways (mean) mg/kg bw/day	0.0231	% of RVNAS	7.70%
Resident - adult	Spray drift (75th percentile) mg/kg bw/day	0.0032	% of RVNAS	1.07%
	Vapour (75th percentile) mg/kg bw/day	0.0002	% of RVNAS	0.08%
	Surface deposits (75th percentile) mg/kg bw/day	0.0007	% of RVNAS	0.23%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0094	% of RVNAS	3.13%
	All pathways (mean) mg/kg bw/day	0.0097	% of RVNAS	3.24%

Table A 35: Input parameters considered for the estimation of bystander exposure (Martin *et al.*; LCTM)

Input parameters considered for the estimation of bystander exposure:

Intended use(s):			**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	0.2	kg a.s./ha	**Exposed Body Surface Area (BSA):**	1	m² (adults)
				0.21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.001	mg/kg a.s. (6 hours, adults)
	16.15	kg/person (children)		0.00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	50.00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Field Crops, Tractor Mounted (FCTM))
Inhalation absorption (IA):	100	%	**Exposure duration (T):**	5	min
AOEL:	0.3	mg/kg bw/d			

Table A 36: Estimation of bystander exposure towards dicamba (Martin *et al.*; LCTM)

Bystander exposure towards Dicamba					
Adults			**Children**		
Bystander: Dermal exposure after application in (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(20 x 0.29% x 1 x 50%) / 60			(20 x 0.29% x 0.21 x 50%) / 16.15		
External exposure	0.058	mg/person	External exposure	0.01218	mg/person
External exposure	0.00096667	mg/kg bw/d	External exposure	0.00075418	mg/kg bw/d
Absorbed dose:	**0.0004833**	**mg/kg bw/d**	**Absorbed dose:**	**0.0003771**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,000 / 360 x 0.2 x 20 x 5 x 100%) / 60			(0,000 / 360 x 0.2 x 20 x 5 x 100%) / 16.15		
External exposure	5.5556E-05	mg/person	External exposure	3.1928E-05	mg/person
External exposure	9.2593E-07	mg/kg bw/d	External exposure	1.977E-06	mg/kg bw/d
Absorbed dose:	**0.0000009**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000020**	**mg/kg bw/d**
Total systemic exposure: SE_B = SDE_B + SIE_B			Total systemic exposure: SE_B = SDE_B + SIE_B		
Total systemic exposure (absorbed dose)	0.02905556	mg/person	Total systemic exposure (absorbed dose)	0.00612193	mg/person
Total systemic exposure (absorbed dose)	**0.0004843**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0003791**	**mg/kg bw/d**
% of AOEL:	**0.16**	**%**	**% of AOEL:**	**0.13**	**%**

Table A 37: Input parameters considered for the estimation of resident exposure (Martin *et al.*)

Input parameters considered for the estimation of resident exposure:

Intended use(s):			**Drift (D):**	0.29	% (FCTM, 10 m)
Application rate (AR):	0.2	kg a.s./ha	**Transfer coefficient (TC):**	7300	cm^2/h (adults)
				2600	cm^2/h (children)
Number of applications (NA):	1		**Turf Transferable Residues (TTR):**	5	%
Body weight (BW):	60	kg/person (adults)	**Exposure Duration (H):**	2	h
	16.15	kg/person (children)	**Airborne Concentration of Vapour (ACV):**	none	
Dermal absorption (DA):	50.00	% ('worst case')	**Inhalation Rate (IR):**	16.57	m^3/d (adults),
Inhalation absorption (IA):	100	%		8.31	m^3/d (children)
Oral absorption (OA)	100	%	**Saliva Extraction Factor (SE):**	50	%
AOEL	0.3	mg/kg bw/d	**Surface Area of Hands (SA):**	20	cm^2
			Frequency of Hand to Mouth (Freq):	20	events/h
			Dislodgeable foliar residues (DFR):	20	%
			Ingestion Rate for Mouthing of Grass/Day (IgR):	25	cm^2/d

Table A 38: Estimation of resident exposure towards dicamba (Martin *et al.*)

Resident exposure towards Dicamba					
Adults			**Children**		
Residents: Dermal exposure after application in (via deposits caused by spray drift)					
SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW			SDE_R = (AR x NA x D x TTR x TC x H x DA) / BW		
(0.002 x 1 x 0.29% x 5% x 7300 x 2 x 50%) / 60			(0.002 x 1 x 0.29% x 5% x 2600 x 2 x 50%) / 16.15		
External exposure	0.004234	mg/person	External exposure	0.001508	mg/person
External exposure	7.0567E-05	mg/kg bw/d	External exposure	9.3375E-05	mg/kg bw/d
Absorbed dose:	**0.0000353**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000467**	**mg/kg bw/d**
Residents: Inhalation exposure to vapour					
SIE_R = (AC_V x IR x IA) / BW			SIE_R = (AC_V x IR x IA) / BW		
(0 x 16.57 x 100%) / 60			(0 x 8.31 x 100%) / 16.15		
External exposure		mg/person	External exposure		mg/person
External exposure		mg/kg bw/d	External exposure		mg/kg bw/d
Absorbed dose:		**none**	**Absorbed dose:**		**none**
			Residents: Oral exposure (hand-to-mouth transfer)		
			SOE_H = (AR x NA x D x TTR x SE x SA x Freq x H x OA) /		
			(0.002 x 1 x 0.29% x 5% x 50% x 20 x 20 x 2 x 100%) / 16.15		
			External exposure	0.000116	mg/person
			External exposure	7.1827E-06	mg/kg bw/d
			Absorbed dose	**0.0000072**	**mg/kg bw/d**
			Residents: Oral exposure (object-to-mouth transfer)		
			SOE_O = (AR x NA x D x DFR x IgR x OA) / BW		
			(0.002 x 1 x 0.29% x 20% x 25 x 100%) / 16.15		
			External exposure	0.000029	mg/person
			External exposure	1.7957E-06	mg/kg bw/d
			Absorbed dose	**0.0000018**	**mg/kg bw/d**
Total systemic exposure: $SE_R = SDE_R + SIE_R$			Total systemic exposure: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$		
Total systemic exposure (absorbed dose)	0.002117	mg/person	Total systemic exposure (absorbed dose)	0.000899	mg/person
Total systemic exposure (absorbed dose)	**0.0000353**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0000557**	**mg/kg bw/d**
% of AOEL:	**0.01**	**%**	**% of AOEL:**	**0.02**	**%**

A 3.4 Combined exposure calculations for prosulfuron, nicosulfuron and dicamba

Not required.

Appendix 4 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)

Not required.