FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: SHA 7216 A

Product name(s): CIAZ

Chemical active substance(s):

Boscalid, 233 g/L
Difenoconazole, 66 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

Applicant: Sharda Cropchem España S.L.

Submission date: August 2021

MS Finalisation date: 02/2022; 12/2022

Version history

When	What
02/2022	Assessment by expert
12/2022	Updated after comments

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6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on SHA 7216 A/CIAZ *

Product name and code	SHA 7216 A/CIAZ
Formulation type	Suspension concentrate [Code: SC]
Active substance(s) (incl. content)	Boscalid, 233 g/L Difenoconazole 66 g/L
Function	Fungicide
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	No
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of SHA 7216 A/CIAZ 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 SHA 7216 A/CIAZ according to Regulation (EC) No 1272/2008

Hazard class(es), categories	Carc.2, H351
Hazard pictograms or Code(s) for hazard pictogram(s)	
Signal word	Warning
Hazard statement(s)	H351- Suspected of causing cancer
Precautionary statement(s)	P260- Do not breathe vapours/spray. P280- Wear protective gloves/protective clothing/eye protection/face protection P308+P313- IF exposed or concerned: Get medical advice/attention
Additional labelling phrases	To avoid risks to man and the environment, comply with the instructions for use. [EUH401]
	Contains 1,2-benzisothiazol-3(2H)-one (CAS No. 2634-33-5). May produce an allergic reaction. [EUH208]

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for SHA 7216 A/CIAZ

	Result	PPE / Risk mitigation measures
Operators	Acceptable	Work wear (arms, body and legs covered) M/L and A + gloves during M/L

	Result	PPE / Risk mitigation measures
Workers	Acceptable	Work wear (arms, body and legs covered)
Residents	Acceptable	None

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

No unacceptable risk for operators was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in Table 6.1-3 are applied.

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

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

1	2	3	4	5	6	7	8	9	10			
Use-No.*	**Crops and situation (e.g. growth stage of crop)**	**F, Fn, Fpn G, Gn, Gpn or I ****	**Application**		**Application rate**		**PHI (d)**	**Remarks:** **(e.g. safener/synergist (L/ha))** **critical gap for operator, worker, resident or bystander exposure based on [Exposure model]**	**Acceptability of exposure assessment**			
			Method / Kind **(incl. application technique *****	**Max. number (min. interval between applications)** **a) per use** **b) per crop/ season**	**Max. application rate kg as/ha** **a) a.s. 1** **b) a.s. 2**	**Water L/ha** **min / max**			**Operator**	**Worker**	**Residents**	**Bystander**
1	Winter wheat	F	Spraying, LCTM	a)2 (14) b)2 (14)	a)0.35 b)0.1	200-400	-	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				

* 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

6.2 Toxicological Information on Active Substance(s)

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

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

	Boscalid	**Difenoconazole**
Common Name	Boscalid	Difenoconazole
CAS-No.	188425-85-6	119446-68-3
Classification and proposed labelling		
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes (s), categories:- Code(s) for hazard pictogram(s):- Signal word:- Hazard statement(s):- Precautionary statement(s):-	Hazard classes (s), categories:- Acute Tox.4, H302 Eye Irrit.2, H319 Carc.2, H351 Code(s) for hazard pictogram(s):-  Signal word:- Warning Hazard statement(s): H302- Harmful if swallowed H319- Causes serious eye irritation H351- Suspected of causing cancer Precautionary statement(s): P260- Do not breathe vapours/spray. P280- Wear protective gloves/protective clothing/eye protection/face protection P308+P313- IF exposed or concerned: Get medical advice/attention
Additional C&L proposal	-	-
Agreed EU endpoints		
AOEL systemic	0.1 mg/kg bw/d	0.16 mg/kg bw/d
Reference	SANCO/3919/2007 – rev. 5 (21 January 2008)	EFSA Journal 2011; 9(1):1967 **ECHA Committee for Risk Assessment RAC Adopted 10 June 2021**
Conditions to take into account/critical areas of concern with regard to toxicology		
According to SANCO/3919/2007 for Boscalid and EFSA Journal 2011;9(1):1967 for Difenoconazole	None	None

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for SHA 7216 A/CIAZ 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 SHA 7216 A/CIAZ

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat (OECD 423)	= 5000 mg/kg bw	Yes	None	Samruddhi Junnarkar, 2017
LD_{50} dermal, rat (OECD 402)	> 2000 mg/kg bw	Yes	None	Samruddhi Junnarkar, 2017
LC_{50} inhalation, rat (OECD 403)	>5.433mg/L air	Yes	None	Manish R. Patel, 2017
Skin irritation, rabbits (calculation)	Non-irritant	Yes	None	calculated
Eye irritation, rabbits (calculation)	Non-irritant	Yes	None	calculated
Skin sensitisation, guinea pig (OECD 406)	Non-sensitising	Yes	None	Vinay Bhimani, 2017
Supplementary studies for combinations of plant protection products	No data – not required			

Table 6.3-2: Additional toxicological information relevant for classification/labelling of SHA 7216 A/CIAZ

	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)	Boscalid (23.3% (w/w))	None	Reg. 1272/2008	Not classified
	Difenoconazole (6.6% (w/w))	~~None~~ H302/Acute Tox.4 H319/Eye Irrit.2 H351/Carc.2	~~Reg. 1272/2008~~ ECHA Committee for Risk Assessment RAC Adopted 10 June 2021	~~Not classified~~ Carc.2/ H351
Toxicological properties	1,2-benzizotiazol-3(2H)-on (CAS nr 2634-33-5)	H317/Skin Sens.1		EUH208
Toxicological properties of non-active substance(s) (relevant for classification of product)	-	-	-	-

	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)
Further toxicological information	No data – not required			

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

6.4 Toxicological Evaluation of Groundwater Metabolites

All metabolite concentrations are predicted to stay below 0.1 µg/L – no groundwater assessment is required.

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in SHA 7216 A/CIAZ are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in SHA 7216 A/CIAZ

	Boscalid		Difenoconazole	
	Value	Reference	Value	Reference
Concentrate	10%	EFSA Journal 2017;15(6):4873	10%	EFSA Journal 2017;15(6):4873
Dilution	50%	EFSA Journal 2017;15(6):4873	50%	EFSA Journal 2017;15(6):4873

6.5.1 Justification for proposed values - Boscalid

No data on dermal absorption for Boscalid in SHA 7216 A/CIAZ 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 Boscalid

	Value	Justification for value	Acceptability of justification
Concentrate	10%	Formulation is a suspension concentrate: water-base/dispersed products.	Acceptable
Dilution	50%	Formulation is a suspension concentrate: water-base/dispersed products.	Acceptable

6.5.2 Justification for proposed values - Difenoconazole

No data on dermal absorption for Difenoconazole in SHA 7216 A/CIAZ 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 Difenoconazole

	Value	Justification for value	Acceptability of justification
Concentrate	10%	Formulation is a suspension concentrate: water-base/dispersed products.	Acceptable
Dilution	50%	Formulation is a suspension concentrate: water-base/dispersed products.	Acceptable

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	SHA 7216 A/CIAZ	
Formulation type	Suspension concentrate [Code: SC]	
Category	Fungicide	
Active substance(s) (incl. content)	**Boscalid** 233 g/L	**Difenoconazole** 66 g/L
AOEL systemic	0.1 mg/kg bw/d	0.16 mg/kg bw/d
Inhalation absorption	100%	100%
Oral absorption	100%	100%
Dermal absorption	Concentrate: 10% Dilution: 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

There is only one intended GAP.

6.6.2 Operator exposure (KCP 7.2.1)

6.6.2.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of SHA 7216 A/CIAZ according to the critical use(s) is presented in Table 6.6-2. The

outcome of the estimation is presented in Table 6.6-3 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	Winter wheat (max. 1.5 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

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

		Boscalid		**Difenoconazole**	
Model data	**Level of PPE**	**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 (winter wheat)					
Application rate		0.35 kg a.s./ha		0.1 kg a.s./ha	
Spray application (AOEM**;** 95th percentile) Body weight: 60 kg	Potential exposure	0.1537900	154	0.0567433	35
	Work wear (arms, body and legs covered) M/L and A	0.0980705	**98**	0.0351184	**22**

According to the AOEM model, calculations, it can be concluded that the risk for the operator using CIAZ is acceptable for boskalid with the use work wear (arms, body and legs covered) M/L and A, but for difenoconazole even without PPE. Generally operator should use work wear (arms, body and legs covered) M/L and A + gloves during M / L ~~and A~~
Implication for labelling: P280: Wear protective gloves, protective clothing

6.6.2.2 Measurement of operator exposure

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

6.6.3 Worker exposure (KCP 7.2.3)

6.6.3.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with SHA 7216 A/CIAZ according to the critical use(s). Out-

come of the estimation is presented in Table 6.6-5 (longer term exposure). Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	Winter wheat (max. 2 × 1.5 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

Table 6.6-5: Estimated worker exposure (longer term exposure)

		Boscalid		**Difenoconazole**	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Inspection, irrigation Outdoor Work rate: 2 hours/day, DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 14 days					
Number of applications and application rate		2 × 0.35 kg a.s./ha		2 × 0.1 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm²/person/h	0.3770451	377	0.1077272	67
	Work wear (arms, body and legs covered) TC: 1400 cm²/person/h	0.0422290	42	0.0120654	8
	Work wear (arms, body and legs covered) and gloves TC: not available	–	–	–	–

According to calculations, it can be concluded that the risk to the worker is acceptable for boscalid using work clothing (with arms, body and legs folded), but for difenoconazole even without appropriate work clothing. However, in this case the worker should use work clothing (covered arms, body and legs) when checking the performed procedure.
~~**Implication for labelling: P280: Wear protective gloves, protective clothing**~~

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

If no DFR data for the specific compound are available, a conservative default value for the DFR may be taken as 3 µg/cm² (30 mg a.s./m²).

6.6.3.3 Measurement of worker exposure

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

6.6.4 Resident and bystander exposure (KCP 7.2.2)

6.6.4.1 Estimation of resident and bystander exposure

The acute exposure assessment for bystanders covers the exposure that a resident could reasonably be expected to incur in a single day. Therefore, there is no need for a separate acute risk assessment for residents.

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.

Table 6.6-6 shows the exposure model(s) used for estimation of resident and bystander exposure to Boscalid and Difenoconazole. The outcome of the estimation is presented in **Błąd! Nie można odnaleźć źródła odwołania.**7 (longer term resident exposure) and Table 6.6-8 (acute bystander exposure). Detailed calculations are in Appendix 3.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	Winter wheat (max. 2 × 1.5 L product/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

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

		Boscalid		**Difenoconazole**	
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 (winter wheat) 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: 14 days					
Number of applications and application rate		2 × 0.35 kg a.s./ha		2 × 0.1 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0235008	23.50	0.0067145	4.20
	Vapour (75th perc.)	0.0010700	1.07	0.0010700	0.67
	Deposits (75th perc.)	0.0048817	4.88	0.0013948	0.87

	Re-entry (75th perc.)	0.0509011	50.90	0.0145432	9.09
	Sum (mean)	0.0581740	58.17	0.0173854	10.87
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0056233	5.62	0.0016067	1.00
	Vapour (75th perc.)	0.0002300	0.23	0.0002300	0.14
	Deposits (75th perc.)	0.0020551	2.06	0.0005872	0.37
	Re-entry (75th perc.)	0.0282784	28.28	0.0080795	5.05
	Sum (mean)	0.0269534	26.95	0.0078653	4.92

The hazard ratio is < 1 for the worker and residents.
Therefore, combined exposure to all active substances in CIAZ is not expected to pose a risk to workers and residents. However, the hazard ratio is > 1 for resident and bystanders, therefore a further assessment was carried out
The result of the assessment indicates that with long term exposure on boscalid operator should use work wear (arms, body and legs covered) M / L and A+ gloves during M / L
Risk assessment from combined exposure – after refinement of estimated bystander exposure: indicates that Hazard Index is < 1 for worker and residents

6.6.4.2 Measurement of resident and/or bystander exposure

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

6.6.5 Combined exposure

The product is a mixture of two active substances.

6.6.5.1 Exposure assessment of Boscalid and Difenoconazole in CIAZ/SHA 7216 A

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

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

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

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
Operators – Work wear (arms, body and legs covered) M/L and A	Boscalid	0.98
	Difenoconazole	0.22
	Cumulative risk operators (HI)	**1.2**

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
Workers – Work wear (arms, body and legs covered)	Boscalid	0.42
	Difenoconazole	0.08
	Cumulative risk workers (HI)	**0.5**
Resident - child	Boscalid	
	Drift	0.24
	Vapour	0.01
	Deposits	0.05
	Re-entry	0.51
	Sum of all pathways	0.58
	Difenoconazole	
	Drift	**0.04**
	Vapour	**0.007**
	Deposits	**0.009**
	Re-entry	**0.09**
	Sum of all pathways	**0.11**
	Cumulative risk resident – child (HI)	
	Drift	**0.28**
	Vapour	**0.017**
	Deposits	**0.059**
	Re-entry	**0.6**
	Sum of all pathways	**0.69**
Resident - adult	Boscalid	
	Drift	0.06
	Vapour	0.002
	Deposits	0.02
	Re-entry	0.28
	Sum of all pathways	0.27
	Difenoconazole	
	Drift	**0.01**
	Vapour	**0.001**
	Deposits	**0.004**
	Re-entry	**0.05**
	Sum of all pathways	**0.05**
	Cumulative risk resident – adult (HI)	
	Drift	**0.07**
	Vapour	**0.003**
	Deposits	**0.024**

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
	Re-entry	**0.33**
	Sum of all pathways	**0.32**

The Hazard Index is <1 for worker and residents. Therefore combined exposure to ll active substances in SHA 7216 A/CIAZ is not expected to present a risk for workers and residents.
Howerver, Hazard Index is >1 for operators ~~and bystander~~ therefore, further refinement of the assessment is needed and presented below:

Operator:

Table 6.6-10: Exposure models for intended uses

Critical use(s)	Winter wheat (max. 1.5 L product/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

Table 6.6-11: Estimated operator exposure (long term exposure) refinement:

		Boscalid	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops (winter wheat)			
Application rate		0.35 kg a.s./ha	
Spray application (AOEM**;** 75th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) M/L and A	0.1537900	154
	Work wear (arms, body and legs covered) M/L and A + gloves during M/L	0.0251346	**25**

Table 6.6-12: Risk assessment from combined exposure – after refinement of estimated operator exposure:

Application scenario	Active ingredient	Estimated exposure / AOEL (HQ)
Operators – Work wear (arms, body and legs covered) M/L and A + gloves during M/L	Boscalid	0.25
	Difenoconazole	0.22
	Cumulative risk operators (HI)	**0.47**

Cumulative risk operators (HQ)– after refinement of estimated operator exposure is acceptable

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	Vertebrate study Y/N	Owner
KCP 7.1.1	xxxxxxxxxx	2017	Acute oral toxicity study of Boscalid 23.3% + Difenoconazole 6.6% SC in rats xxxxxxxx No. 401-1-01-16906 GLP, Unpublished	Y	SHARDA Cropchem Limited
KCP 7.1.2	xxxxxxxxxx	2017	Acute dermal toxicity study of Boscalid 23.3% + Difenoconazole 6.6% SC in rats xxxxxxxx No. 403-1-01-16907 GLP, Unpublished	Y	SHARDA Cropchem Limited
KCP 7.1.3	xxxxxxxxxx	2017	Acute inhalation toxicity study of Boscalid 23.3% + Difenoconazole 6.6% SC in rats xxxxxxxx No. 405-1-01-16908 GLP, Unpublished	Y	SHARDA Cropchem Limited
KCP 7.1.6	xxxxxxxxxx	2017	Skin sensitisation study of Boscalid 23.3% + Difenoconazole 6.6% SC in Guinea pigs [Guinea pig maximization test] xxxxxxxx report No. 408-1-01-16911 GLP, Unpublished	Y	SHARDA Cropchem Limited

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

No additional study submitted.

The following tables are to be completed by MS

List of data submitted by the applicant and not relied on

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

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

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

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

Comments of zRMS:	N/A

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	**Under the experimental conditions, the oral LD_{50} of Boscalid 23.3% + Difenoconazole 6.6% SC is 5000 mg/kg bw in rats.** **No classification is required according to Regulation (EC) No. 1272/2008.**

Reference	KCP 7.1.1
Report	Acute oral toxicity study of Boscalid 23.3% + Difenoconazole 6.6% SC in rats, xxxxxxxxxxxxxxxx, 2017, report No. 401-1-01-16906
Guideline(s)	Yes, OECD guidelines No. 423
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	Boscalid 23.3% + Difenoconazole 6.6% SC (Batch No. SCL-20245)
Species	Rat, Wistar
No. of animals (group size)	6 females
Dose(s)	2000 mg/kg bw
Exposure	Once by gavage
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table A 1: Results of acute oral toxicity study in rats of SHA 7216 A/CIAZ

Dose (mg/kg bw)	Toxicological results *	Duration of signs	Time of death	LD_{50} (mg/kg bw) (14 days)
Female rats				
2000	0/0/3	-	-	5000 cut-off
Female rats				
2000	0/0/3	-	-	5000 cut-off

* Number of animals which died/number of animals with clinical signs/number of animals used

Table A 2: Summary of findings of acute oral toxicity study in rats of SHA 7216 A/CIAZ

Mortality	No mortality occurred.
Clinical signs	No clinical signs of toxicity were observed.
Body weight	Body weight gain was considered to be normal.
Macroscopic examination	The necropsies performed at the end of the study revealed no apparent findings.

Conclusion

Under the experimental conditions, the oral LD_{50} of SHA 7216 A/CIAZ is 5000 mg/kg bw in rats. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

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

Comments of zRMS:	**Under the experimental conditions, the dermal LD_{50} of Boscalid 23.3% + Difenoconazole 6.6% SC is higher than 2000 mg/kg bw in rats.** **No classification is required according to Regulation (EC) No. 1272/2008.**

A 2.3.1 Study 1

Reference	KCP 7.1.2
Report	Acute dermal toxicity study of Boscalid 23.3% + Difenoconazole 6.6% SC in rats, xxxxxxxxxxx, 2017, report No. 403-1-01-16907
Guideline(s)	Yes, OECD guidelines No. 402
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	Boscalid 23.3% + Difenoconazole 6.6% SC (Batch No. SCL-20245)
Species	Rat, Wistar
No. of animals (group size)	5 males, 5 females
Dose(s)	2000 mg/kg bw
Exposure	24 hours (dermal, semi-occlusive)
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table A 3: Results of acute dermal toxicity study in rats of SHA 7216 A/CIAZ

Dose (mg/kg bw)	Toxicological results *	Duration of signs	Time of death	LD_{50} (mg/kg bw) (14 days)
Male rats				
2000	0/0/5	-	-	> 2000
Female rats				
2000	0/0/5	-	-	> 2000

* Number of animals which died/number of animals with clinical signs/number of animals used

Table A 4: Summary of findings of acute dermal toxicity study in rats of SHA 7216 A/CIAZ

Mortality	No mortality occurred.
Clinical signs	No clinical signs of toxicity were observed.
Body weight	Body weight gain was considered to be normal.
Macroscopic examination	The necropsies performed at the end of the study revealed no apparent findings.

Conclusion

Under the experimental conditions, the dermal LD_{50} of SHA 7216 A/CIAZ is higher than 2000 mg/kg bw in rats. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	**Under the experimental conditions, the inhalation LC_{50} of Boscalid 23.3% + Difenoconazole 6.6% SC is higher than 5.433 mg/L air in rats.** **No classification is required according to Regulation (EC) No. 1272/2008.**

A 2.4.1 Study 1

Reference	KCP 7.1.3
Report	Acute inhalation toxicity study of Boscalid 23.3% + Difenoconazole 6.6% SC in rats, xxxxxxxxxxxx, 2017, report No. 405-1-01-16908
Guideline(s)	Yes, OECD guidelines No. 403
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	Boscalid 23.3% + Difenoconazole 6.6% SC (Batch No. SCL-20245)
Species	Rat, Wistar
No. of animals (group size)	3 males, 3 females
Concentration(s)	5.433 mg/L air
Exposure	4 hours (nose only)
Vehicle/Dilution	None
Post exposure observation period	14 days
Remarks	None

Results and discussions

Table A 5: Concentration(s) and exposure conditions

Nominal conc. (mg/L air)	Actual conc. (mg/L air)	MMAD * (µm)	GSD ** (µm)
16.667	5.433	3.09	1.64

* MMAD = Mass Median Aerodynamic Diameter
** GSD = Geometric Standard Deviation

Table A 6: Results of acute inhalation toxicity study in rats of SHA 7216 A/CIAZ

Concentration (mg/L air)	Toxicological results *	Duration of signs	Time of death	LC_{50} (mg/L air) (14 days)
Male rats				
5.433	0/0/3	-	-	> 5.433
Female rats				
5.433	0/0/3	-	-	> 5.433

* Number of animals which died/number of animals with clinical signs/number of animals used

Table A 7: Summary of findings of acute inhalation toxicity study in rats of SHA 7216 A/CIAZ

Mortality	No mortality occurred.
Clinical signs	No clinical signs of toxicity were observed.

Body weight	Decrease in mean body weight was observed on day 1 which increased on days 3, 7 and 14 in male rats while decrease in mean body weight was observed on days 1 and 3 which increased on days 7 and 14 in female rats when compared to day 0 mean body weight.
Macroscopic examination	The necropsies performed at the end of the study revealed no apparent findings.

Conclusion

Under the experimental conditions, the inhalation LC_{50} of SHA 7216 A/CIAZ is higher than 5.433 mg/L air in rats. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	**Calculation is acceptable** **According to the Regulation EC No. 1272/2008, Boscalid 23.3% + Difenoconazole 6.6% SC is not classified**

Acute toxicity studies for Boscalid 23.3% + Difenoconazole 6.6% SC were **not** evaluated as part of the EU review of tefluthrin. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the calculation methodology that was used to assess the acute toxicity of Boscalid 23.3% + Difenoconazole 6.6% SC be found in an appendix to the confidential dossier of this submission (Registration Report, Part C).
The product does not contain any of co-formulants considered as skin irritant (classified as: Skin Irrit. 2; H315). Under the GHS classification system this product is not classified according to Regulation (EC) no. 1272/2008.

Conclusion
According to the Regulation EC No. 1272/2008, CIAZ is **not classified**. No signal word or hazard statement is required for this hazard.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	**Calculation is acceptable** **According to the Regulation EC No. 1272/2008, Boscalid 23.3% + Difenoconazole 6.6% SC is not classified**

Acute toxicity studies for Boscalid 23.3% + Difenoconazole 6.6% SC were **not** evaluated as part of the EU review of tefluthrin. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the calculation methodology that was used to assess the acute toxicity of Boscalid 23.3% + Difenoconazole 6.6% SC be found in an appendix to the confidential dossier of this submission (Registration Report, Part C).
The product contains < 1% of co-formulants considered as eye damage (classified as: Eye Dam. 1; H318). Under the GHS classification system this component is below the additive trigger value of the classification according to Regulation (EC) no. 1272/2008.

Conclusion
According to the Regulation EC No. 1272/2008, CIAZ is **not classified**. No signal word or hazard statement is required for this hazard.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	**Under the experimental conditions, Boscalid 23.3% + Difenoconazole 6.6% SC is not a skin sensitiser.** **No classification is required according to Regulation (EC) No. 1272/2008.**

A 2.7.1 Study 1

Reference	KCP 7.1.6
Report	Skin sensitisation study of Boscalid 23.3% + Difenoconazole 6.6% SC in Guinea pigs [Guinea pig maximization test], xxxxxxxxxxx, 2017, report No. 408-1-01-16911
Guideline(s)	Yes, OECD guidelines No. 406
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	Boscalid 23.3% + Difenoconazole 6.6% SC (Batch No. SCL-20245)
Species	Guinea pig, Hartley
No. of animals (group size)	Test substance group: 20 guinea pigs (10 males + 10 females) Vehicle control goup: 10 guinea pigs (5 males + 5 females)
Range finding	Yes
Exposure (concentration(s), no. of applications)	Intradermal injection: Injection 1: a 1:1 mixture (v/v) o Freund's Complete Adjuvant (FCA) with distilled water Injection 2: 5.0% (v/v) Boscalid 23.3% + Difenoconaole 6.6% SC in distilled water Injection 3: 5.0% (v/v) Boscalid 23.3% + Difenoconaole 6.6% SC in distilld water formulated in a 1:1 mixture (v/v) of FCA in distilled water Topical application: A patch loaded with 0.2 mL Boscalid 23.3% + Difenoconaole 6.6% SC Challenge Test: A patch loaded with 0.2 mL Boscalid 23.3% + Difenoconaole 6.6% SC
Vehicle	Distilled water
Pretreatment prior to topical application	Yes (sodium lauryl sulfate)
Reliability check	Positive control agent (α-Hexylcinnamaldehyde)
Remarks	None

Results and discussions

Table A 8: Results of skin sensitisation study of SHA 7216 A/CIAZ

	24 hours	48 hours	Total number of animals affected
	After challenge		
SHA 7216 A/CIAZ	0/20	0/20	0
Test vehicle control group	0/10	0/10	0
Positive control	Visual observation of skin post challenge exposure revealed a positive skin response of 45% at 24 and 48 h post patch removal in guinea pigs of the treatment group.		

* Number of animals with positive dermal response (scores of 1-3) /number of animals in dose group

Clinical signs:	No clinical signs of toxicity were observed.

Conclusion

Under the experimental conditions, SHA 7216 A/CIAZ is not a skin sensitiser. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

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

No data available.

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)

According to the new EFSA guidance on dermal absorption (EFSA Journal 2017;15(6):4873 adopted: 24 May 2017) a default dermal absorption value 10% (concentrate) and 50% (diluted) of may be applied for products that are water-based/dispersed [(c)] or solid-formulated[(d)]

[(c)]: Formulation types: soluble concentrate (SL), suspension concentrate (SC), flowable concentrate for seed treatment (FS), flowable (FL) (SC).

[(d)]: Formulation types: wettable powder (WP), water-dispersible granules (WG/WDG), water-soluble granules

(SG), water-soluble powder (SP), powder for dry seed treatment (DS).

A 2.11 Other/Special Studies

No data submitted.

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for Boscalid

Table A 9: Input parameters considered for the estimation of operator exposure

Formulation type	SC		Crop type	Cereals (winter wheat)
Application rate (AR)	0.35	kg a.s./ha	Application method	Downward spraying
Area treated per day (A)	50	ha	Application equipment	Vehicle-mounted
Dermal absorption (DA)	10	% (concentr.)	Indoor/outdoor	Outdoor
	50	% (dilution)	Closed cabin	No
Inhalation absorption (IA)	100	%	Drift reduction	No
Body weight (BW)	60	kg/person	Cultivation	Normal
AOEL	0.1	mg/kg bw/d	Water soluble bag	No

Table A 10: Estimation of longer term operator exposure towards Boscalid according to EFSA guidance

	Potential		**With work wear + PPE/RPE**	
Mixing and loading				
Hands			None	
Specific exposure value	4398.3317249	µg/person	4398.3317249	µg/person
Systemic exposure	**73.3055287**	**mg/kg bw/d**	**73.3055287**	**mg/kg bw/d**
Body			Work wear	
Specific exposure value	2667.4650359	µg/person	30.0456522	µg/person
Systemic exposure	**44.4577506**	**mg/kg bw/d**	**0.5007609**	**mg/kg bw/d**
Head			None	
Specific exposure value	90.7962786	µg/person	90.7962786	µg/person
Systemic exposure	**1.5132713**	**mg/kg bw/d**	**1.5132713**	**mg/kg bw/d**
Inhalation			None	
Specific exposure value	8.6761714	µg/person	8.6761714	µg/person
Systemic exposure	**0.1446029**	**mg/kg bw/d**	**0.1446029**	**mg/kg bw/d**
Application				
Hands			None	
Specific exposure value	1297.8295741	µg/person	1297.8295741	µg/person
Systemic exposure	**21.6304929**	**mg/kg bw/d**	**21.6304929**	**mg/kg bw/d**
Body			Work wear	
Specific exposure value	725.6608746	µg/person	19.9061023	µg/person
Systemic exposure	**12.0943479**	**mg/kg bw/d**	**0.3317684**	**mg/kg bw/d**
Head			None	
Specific exposure value	34.2972190	µg/person	34.2972190	µg/person
Systemic exposure	**0.5716203**	**mg/kg bw/d**	**0.5716203**	**mg/kg bw/d**

Inhalation			None	
Specific exposure value	4.3446365	µg/person	4.3446365	µg/person
Systemic exposure	**0.0724106**	**mg/kg bw/d**	**0.0724106**	**mg/kg bw/d**
Total				
Total systemic exposure	**0.1537900**	**mg/kg bw/d**	**0.0980705**	**mg/kg bw/d**
% of AOEL	**153.79**	**%**	**98.07**	**%**

Table A 11: Estimation of longer term operator exposure towards Boscalid according to EFSA guidance - refinement

	Potential		**With work wear + PPE/RPE**	
Mixing and loading				
Hands			Protective gloves	
Specific exposure value	4398.3317249	µg/person	22.1824037	µg/person
Systemic exposure	**73.3055287**	**mg/kg bw/d**	**0.3697067**	**mg/kg bw/d**
Body			Work wear	
Specific exposure value	2667.4650359	µg/person	30.0456522	µg/person
Systemic exposure	**44.4577506**	**mg/kg bw/d**	**0.5007609**	**mg/kg bw/d**
Head			None	
Specific exposure value	90.7962786	µg/person	90.7962786	µg/person
Systemic exposure	**1.5132713**	**mg/kg bw/d**	**1.5132713**	**mg/kg bw/d**
Inhalation			None	
Specific exposure value	8.6761714	µg/person	8.6761714	µg/person
Systemic exposure	**0.1446029**	**mg/kg bw/d**	**0.1446029**	**mg/kg bw/d**
Application				
Hands			None	
Specific exposure value	1297.8295741	µg/person	1297.8295741	µg/person
Systemic exposure	**21.6304929**	**mg/kg bw/d**	**21.6304929**	**mg/kg bw/d**
Body			Work wear	
Specific exposure value	725.6608746	µg/person	19.9061023	µg/person
Systemic exposure	**12.0943479**	**mg/kg bw/d**	**0.3317684**	**mg/kg bw/d**
Head			None	
Specific exposure value	34.2972190	µg/person	34.2972190	µg/person
Systemic exposure	**0.5716203**	**mg/kg bw/d**	**0.5716203**	**mg/kg bw/d**
Inhalation			None	
Specific exposure value	4.3446365	µg/person	4.3446365	µg/person
Systemic exposure	**0.0724106**	**mg/kg bw/d**	**0.0724106**	**mg/kg bw/d**
Total				
Total systemic exposure	**0.1537900**	**mg/kg bw/d**	**0.0251346**	**mg/kg bw/d**
% of AOEL	**153.79**	**%**	**25.13**	**%**

A 3.1.2 Calculations for Difenoconazole

Table A 12: Input parameters considered for the estimation of operator exposure

Formulation type	SC		Crop type	Cereals (winter wheat)
Application rate (AR)	0.1	kg a.s./ha	Application method	Downward spraying
Area treated per day (A)	50	ha	Application equipment	Vehicle-mounted
Dermal absorption (DA)	10	% (concentr.)	Indoor/outdoor	Outdoor
	50	% (dilution)	Closed cabin	No
Inhalation absorption (IA)	100	%	Drift reduction	No
Body weight (BW)	60	kg/person	Cultivation	Normal
AOEL	0.16	mg/kg bw/d	Water soluble bag	No

Table A 13: Estimation of longer term operator exposure towards Difenoconazole according to EFSA guidance

	Potential		**With work wear + PPE/RPE**	
Mixing and loading				
Hands			None	
Specific exposure value	1676.6718712	µg/person	1676.6718712	µg/person
Systemic exposure	**27.9445312**	**mg/kg bw/d**	**27.9445312**	**mg/kg bw/d**
Body			Work wear	
Specific exposure value	1105.7500945	µg/person	9.8977400	µg/person
Systemic exposure	**18.4291682**	**mg/kg bw/d**	**0.1649623**	**mg/kg bw/d**
Head			None	
Specific exposure value	25.9417939	µg/person	25.9417939	µg/person
Systemic exposure	**0.4323632**	**mg/kg bw/d**	**0.4323632**	**mg/kg bw/d**
Inhalation			None	
Specific exposure value	5.9760397	µg/person	5.9760397	µg/person
Systemic exposure	**0.0996007**	**mg/kg bw/d**	**0.0996007**	**mg/kg bw/d**
Application				
Hands			None	
Specific exposure value	370.8084497	µg/person	370.8084497	µg/person
Systemic exposure	**6.1801408**	**mg/kg bw/d**	**6.1801408**	**mg/kg bw/d**
Body			Work wear	
Specific exposure value	207.3316784	µg/person	5.6874578	µg/person
Systemic exposure	**3.4555280**	**mg/kg bw/d**	**0.0947910**	**mg/kg bw/d**
Head			None	
Specific exposure value	9.7992054	µg/person	9.7992054	µg/person
Systemic exposure	**0.1633201**	**mg/kg bw/d**	**0.1633201**	**mg/kg bw/d**
Inhalation			None	
Specific exposure value	2.3193984	µg/person	2.3193984	µg/person
Systemic exposure	**0.0386566**	**mg/kg bw/d**	**0.0386566**	**mg/kg bw/d**
Total				
Total systemic exposure	**0.0567433**	**mg/kg bw/d**	**0.0351184**	**mg/kg bw/d**
% of AOEL	**35.46**	**%**	**21.95**	**%**

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for Boscalid

Table A 14: Input parameters considered for the estimation of worker exposure

Intended use(s)	Cereals (winter wheat) , outdoor		Dislodgeable foliar residue (DFR)	3	µg/cm²/kg a.s./ha
Application rate (AR)	0.35	kg a.s./ha	Dermal absorption (DA)	50	% (worst case)
Number of applications (NA)	2		Inhalation absorption (IA)	100	%
Interval between applications	14	days	Work rate per day (WR)	2	h/d
Half-life of active substance	30	days	TC dermal (potential)	12500	cm²/h
Multiple application factor (MAF)	1.7		TC dermal (work wear)	1400	cm²/h
Body weight (BW)	60	kg/person	TC dermal (work wear, gloves)	-	cm²/h
AOEL	0.1	mg/kg bw/d	Task specific factor inhalation	-	ha/h x 10^{-3}

Table A 15: Estimation of longer term worker exposure towards Boscalid according to EFSA guidance

	Potential		**With work wear**		**With work wear and gloves**	
Worker (re-entry): Dermal exposure after application						
(DFR x TC x WR x AR x MAF x DA) / BW						
Systemic exposure	0.3770451	**mg/kg bw/d**	**0.0422290**	**mg/kg bw/d**	-	**mg/kg bw/d**
% of AOEL	**377.05**	**%**	**42.23**	**%**	-	**%**

A 3.2.2 Calculations for Difenoconazole

Table A 16: Input parameters considered for the estimation of worker exposure

Intended use(s)	Cereals (winter wheat) , outdoor		Dislodgeable foliar residue (DFR)	3	µg/cm²/kg a.s./ha
Application rate (AR)	0.1	kg a.s./ha	Dermal absorption (DA)	50	% (worst case)
Number of applications (NA)	2		Inhalation absorption (IA)	100	%
Interval between applications	14	days	Work rate per day (WR)	2	h/d
Half-life of active substance	30	days	TC dermal (potential)	12500	cm²/h
Multiple application factor (MAF)	1.7		TC dermal (work wear)	1400	cm²/h
Body weight (BW)	60	kg/person	TC dermal (work wear, gloves)	-	cm²/h
AOEL	0.16	mg/kg bw/d	Task specific factor inhalation	-	ha/h x 10^{-3}

Table A 17: Estimation of longer term worker exposure towards Difenoconazole according to EFSA guidance

	Potential	**With work wear**	**With work wear and gloves**
Worker (re-entry): Dermal exposure after application			
(DFR x TC x WR x AR x MAF x DA) / BW			

	Potential		With work wear		With work wear and gloves	
Systemic exposure	0.1077272	**mg/kg bw/d**	**0.0120654**	**mg/kg bw/d**	-	**mg/kg bw/d**
% of AOEL	**67.33**	**%**	**7.54**	**%**	-	**%**

A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for Boscalid

Table A 18: Input parameters considered for the estimation of longer term resident exposure

Intended use(s)	Cereals (winter wheat) , spraying		Drift reduction (DR)		%
Application rate (AR)	0.35	kg a.s./ha	Transfer coefficient surface deposits (TC)	7300	cm^2/h (adult)
				2600	cm^2/h (child)
Minimum water volume (V)	200	L/ha	Drift on surface (D) - 75th perc.	5.60	%
Buffer strip	2-3	m	Drift on surface (D) - mean	4.10	%
Number of applications (NA)	2		Turf Transferable Residues (TTR)	5	%
Interval between applications	14	days	Exposure duration dermal (H_D)	2	h
Half-life of active substance	30	days	Exposure duration inhal. (H_I)	24	h
Multiple application factor (MAF)	1.7		Exposure duration entry into treated crops (H_E)	0.25	h
Body weight (BW)	60	kg/person (adults)	Airborne Concentration of Vapour (VC)	0.001	mg/m^3
	10	kg/person (children)			
Dermal absorption (DA)		% ('worst case')	Dislodgeable foliar residue (DFR)	3	$\mu g/cm^2$/kg a.s.
Inhalation absorption (IA)	100	%	Light clothing adjustment factor (CF)	18	%
Oral absorption (OA)	100	%	Saliva Extraction Factor (SE)	50	%
AOEL	0.1	mg/kg bw/d	Surface Area of Hands (SA)	20	cm^2
Spray drift dermal (SD) - 75th perc.	0.47	mL spray dilution (adult)	Frequency of Hand to Mouth (Freq)	20	events/h
	0.327	mL spray dilution (child)			
Spray drift inhal. (SI) - 75th perc.	0.00010	mL spray dilution (adult)	Dislodgeable residues object to mouth (DR_{OM})	20	%
	0.00022	mL spray dilution (child)			
Spray drift dermal (SD) - mean	0.22318	mL spray dilution (adult)	Ingestion Rate for Mouthing of Grass (IgR)	25	cm^2/d
	0.18	mL spray dilution (child)			
Spray drift inhal. (SD) - mean	0.00009	mL spray dilution (adult)	TC entry into treated crops - 75th perc.	7500	cm^2/h (adult)
	0.00017	mL spray dilution (child)		2250	cm^2/h (child)
Inhalation rate (IR)	16.57	m^3/d (adult)	TC entry into treated crops -	5980	cm^2/h (adult)

	8.31	m^3/d (child)	mean:	1794	cm^2/h (child)

Table A 18: Estimation of longer term resident exposure towards Boscalid according to EFSA guidance

Adult			**Child**		
Spray drift (75th perc.)					
(SD x DA x (1- CF) + SI) x AR x MAF x V x DR/ BW					
Systemic exposure	**0.0056233**	**mg/kg bw/d**	**Systemic exposure**	**0.0235008**	**mg/kg bw/d**
% of AOEL:	**5.62**	**%**	**% of AOEL:**	**23.50**	**%**
Vapour (75th perc.)					
(VC x IR x IA) / BW					
Systemic exposure	**0.0002300**	**mg/kg bw/d**	**Systemic exposure**	**0.0010700**	**mg/kg bw/d**
% of AOEL:	**0.23**	**%**	**% of AOEL:**	**1.07**	**%**
Surface deposits (75th perc.)					
Dermal					
AR x MAF x D x TTR x TC x H_D x DA / BW					
Systemic exposure	**0.0020551**	**mg/kg bw/d**	**Systemic exposure**	**0.0043918**	**mg/kg bw/d**
Hand to mouth					
AR x MAF x D x TTR x SE x SA x Freq x H_D x OA / BW					
			Systemic exposure	**0.0003209**	**mg/kg bw/d**
Object to mouth					
AR x MAF x D x DR_{OM} x IgR x OA / BW					
			Systemic exposure	**0.0001689**	**mg/kg bw/d**
Total					
Systemic exposure	**0.0020551**	**mg/kg bw/d**	**Systemic exposure**	**0.0048817**	**mg/kg bw/d**
% of AOEL:	**2.06**	**%**	**% of AOEL:**	**4.88**	**%**
Entry into treated crops (75th perc.)					
Dermal					
AR x MAF x TC x H_D x DFR x DA / BW					
Systemic exposure	**0.0282784**	**mg/kg bw/d**	**Systemic exposure**	**0.0509011**	**mg/kg bw/d**
Hand to mouth					
AR x MAF x 100% x TTR x x SE x SA x Freq x H_D x OA / BW					
			Systemic exposure		**mg/kg bw/d**
Object to mouth					
AR x MAF x 100% x DR_{OM} x IgR x OA / BW					
			Systemic exposure		**mg/kg bw/d**
Total					
Systemic exposure	**0.0282784**	**mg/kg bw/d**	**Systemic exposure**	**0.0509011**	**mg/kg bw/d**
% of AOEL:	**28.28**	**%**	**% of AOEL:**	**50.90**	**%**
All pathways (mean)					
Systemic exposure			**0.0269534** **mg/kg bw/d**	**Systemic exposure**	**0.0581740** **mg/kg bw/d**
% of AOEL:	**26.95**	**%**	**% of AOEL:**	**58.17**	**%**

A 3.3.2 Calculations for Difenoconazole

Table A 19: Input parameters considered for the estimation of longer term resident exposure

Intended use(s)	Cereals (winter wheat), spraying		Drift reduction (DR)		%
Application rate (AR)	0.1	kg a.s./ha	Transfer coefficient surface deposits (TC)	7300	cm^2/h (adult)
				2600	cm^2/h (child)
Minimum water volume (V)	200	L/ha	Drift on surface (D) - 75th perc.	5.60	%
Buffer strip	2-3	m	Drift on surface (D) - mean	4.10	%
Number of applications (NA)	2		Turf Transferable Residues (TTR)	5	%
Interval between applications	14	days	Exposure duration dermal (H_D)	2	h
Half-life of active substance	30	days	Exposure duration inhal. (H_I)	24	h
Multiple application factor (MAF)	1.7		Exposure duration entry into treated crops (H_E)	0.25	h
Body weight (BW)	60	kg/person (adults)	Airborne Concentration of Vapour (VC)	0.001	mg/m^3
	10	kg/person (children)			
Dermal absorption (DA)	50	% ('worst case')	Dislodgeable foliar residue (DFR)	3	$\mu g/cm^2$/kg a.s.
Inhalation absorption (IA)	100	%	Light clothing adjustment factor (CF)	18	%
Oral absorption (OA)	100	%	Saliva Extraction Factor (SE)	50	%
AOEL	0.16	mg/kg bw/d	Surface Area of Hands (SA)	20	cm^2
Spray drift dermal (SD) - 75th perc.	0.47	mL spray dilution (adult)	Frequency of Hand to Mouth (Freq)	20	events/h
	0.327	mL spray dilution (child)			
Spray drift inhal. (SI) - 75th perc.	0.00010	mL spray dilution (adult)	Dislodgeable residues object to mouth (DR_{OM})	20	%
	0.00022	mL spray dilution (child)			
Spray drift dermal (SD) - mean	0.22318	mL spray dilution (adult)	Ingestion Rate for Mouthing of Grass (IgR)	25	cm^2/d
	0.18	mL spray dilution (child)			
Spray drift inhal. (SD) - mean	0.00009	mL spray dilution (adult)	TC entry into treated crops - 75th perc.	7500	cm^2/h (adult)
	0.00017	mL spray dilution (child)		2250	cm^2/h (child)
Inhalation rate (IR)	16.57	m^3/d (adult)	TC entry into treated crops - mean:	5980	cm^2/h (adult)
	8.31	m^3/d (child)		1794	cm^2/h (child)

Table A 20: Estimation of longer term resident exposure towards Difenoconazole according to EFSA guidance

Adult			Child		
Spray drift (75th perc.)					
(SD x DA x (1- CF) + SI) x AR x MAF x V x DR/ BW					
Systemic exposure	**0.0016067**	**mg/kg bw/d**	**Systemic exposure**	**0.0067145**	**mg/kg bw/d**
% of AOEL:	**1.00**	**%**	**% of AOEL:**	**4.20**	**%**
Vapour (75th perc.)					
(VC x IR x IA) / BW					
Systemic exposure	**0.0002300**	**mg/kg bw/d**	**Systemic exposure**	**0.0010700**	**mg/kg bw/d**
% of AOEL:	**0.14**	**%**	**% of AOEL:**	**0.67**	**%**
Surface deposits (75th perc.)					
Dermal					
AR x MAF x D x TTR x TC x H_D x DA / BW					
Systemic exposure	**0.0005872**	**mg/kg bw/d**	**Systemic exposure**	**0.0012548**	**mg/kg bw/d**
Hand to mouth					
AR x MAF x D x TTR x SE x SA x Freq x H_D x OA / BW					
			Systemic exposure	**0.0000917**	**mg/kg bw/d**
Object to mouth					
AR x MAF x D x DR_{OM} x IgR x OA / BW					
			Systemic exposure	**0.0000483**	**mg/kg bw/d**
Total					
Systemic exposure	**0.0005872**	**mg/kg bw/d**	**Systemic exposure**	**0.0013948**	**mg/kg bw/d**
% of AOEL:	**0.37**	**%**	**% of AOEL:**	**0.87**	**%**
Entry into treated crops (75th perc.)					
Dermal					
AR x MAF x TC x H_D x DFR x DA / BW					
Systemic exposure	**0.0080795**	**mg/kg bw/d**	**Systemic exposure**	**0.0145432**	**mg/kg bw/d**
Hand to mouth					
AR x MAF x 100% x TTR x x SE x SA x Freq x H_D x OA / BW					
			Systemic exposure		**mg/kg bw/d**
Object to mouth					
AR x MAF x 100% x DR_{OM} x IgR x OA / BW					
			Systemic exposure		**mg/kg bw/d**
Total					
Systemic exposure	**0.0080795**	**mg/kg bw/d**	**Systemic exposure**	**0.0145432**	**mg/kg bw/d**
% of AOEL:	**5.05**	**%**	**% of AOEL:**	**9.09**	**%**
All pathways (mean)					
Systemic exposure			**0.0078653** **mg/kg bw/d**	**Systemic exposure**	**0.0173854** **mg/kg bw/d**
% of AOEL:	**4.92**	**%**	**% of AOEL:**	**10.87**	**%**

A 3.4 Combined exposure calculations for Boscalid and Difenoconazole

In tables below are presented calculations for combined exposure for Boscalid and Difenoconazole.

Operator exposure:

		Boscalid (AOEL = 0.1 mg/kg bw/d)		**Difenoconazole (AOEL = 0.16 mg/kg bw/d)**		**Cumulative risk Operators (HI)[1]**
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**Estimated exposure / AOEL (HQ)**	**Total absorbed dose (mg/kg/day)**	**Estimated exposure / AOEL (HQ)**	
Tractor mounted boom spray application outdoors to low crops						
Application rate		0.35 kg a.s./ha		0.1 kg a.s./ha		
Spray application (AOEM**;** 95th percentile) Body weight: 60 kg	Potential exposure	0.1538	**1.54**	0.0567	**0.35**	**1.89**
	Work wear (arms, body and legs covered) M/L and A	0.0981	**0.98**	0.0351	**0.22**	**1.2**

Operator exposure refinement:

		Boscalid (AOEL = 0.1 mg/kg bw/d)		**Difenoconazole (AOEL = 0.16 mg/kg bw/d)**		**Cumulative risk Operators (HI)[2]**
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**Estimated exposure / AOEL (HQ)**	**Total absorbed dose (mg/kg/day)**	**Estimated exposure / AOEL (HQ)**	
Tractor mounted boom spray application outdoors to low crops						
Application rate		0.35 kg a.s./ha		0.1 kg a.s./ha		
Spray application (AOEM**;** 95th percentile) Body weight: 60 kg	Potential exposure	0.1538	**1.54**	0.0567	**0.35**	**1.89**
	Work wear (arms, body and legs covered) M/L and	0.0981	**0.25**	0.0351	**0.22**	**0.47**

[1] The Hazard Index (HI) is the sum of the individual HQs for Boscalid and Difenoconazole

	A + gloves during M/L					

The Hazard Index is < 1 for the estimation using gloves during mix/loading.

Worker exposure:

		Boscalid (AOEL = 0.1 mg/kg bw/d)		**Difenoconazole (AOEL = 0.16 mg/kg bw/d)**		**Cumula-tive risk Operators (HI)***
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**Estimated exposure / AOEL (HQ)**	**Total absorbed dose (mg/kg/day)**	**Estimated exposure / AOEL (HQ)**	
Number of applications and application rate		2 × 0.35 kg a.s./ha		2 × 0.1 kg a.s./ha		
Body weight: 60 kg	Potential TC: 12500 cm^2/person/h	0.3770	**3.77**	0.1077	**0.67**	**4.44**
	Work wear (arms, body and legs covered) TC: 1400 cm^2/person/h	0.0422	**0.42**	0.0121	**0.08**	**0.5**
	Work wear (arms, body and legs covered) and gloves TC: not available	–	–	–	–	–

The estimated exposure for workers present that the Hazard Index is < 1 for the estimation without the use of personal protective equipment.

Bystander and resident exposure:

		Boscalid (AOEL = 0.1 mg/kg bw/d)		**Difenoconazole (AOEL = 0.16 mg/kg bw/d)**		**Cumulative risk Operators (HI)***
Model data		**Total ab-sorbed dose (mg/kg/day)**	**Estimated exposure / AOEL (HQ)**	**Total ab-sorbed dose (mg/kg/day)**	**Estimated exposure / AOEL (HQ)**	
Number of applications and application rate		2 × 0.35 kg a.s./ha		2 × 0.1 kg a.s./ha		
Resident child Body weight: 10	Drift (75th perc.)	0.0234	**0.24**	0.0067	**0.04**	**0.28**
	Vapour (75th perc.)	0.0011	**0.01**	0.0011	**0.007**	**0.017**

kg	Deposits (75th perc.)	0.0049	**0.05**	0.0014	**0.009**	**0.059**
	Re-entry (75th perc.)	0.0509	**0.51**	0.0145	**0.09**	**0.6**
	Sum (mean)	0.0582	**0.58**	0.0174	**0.11**	**0.69**
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0056	**0.06**	0.0016	**0.01**	**0.07**
	Vapour (75th perc.)	0.0002	**0.002**	0.0002	**0.001**	**0.003**
	Deposits (75th perc.)	0.0021	**0.02**	0.0006	**0.004**	**0.024**
	Re-entry (75th perc.)	0.0283	**0.28**	0.0081	**0.05**	**0.33**
	Sum (mean)	0.027	**0.27**	0.0079	**0.05**	**0.32**
						2.0763

The Hazard Index is < 1. Thus combined exposure to all active substances in product CIAZ is not expected to present a risk for bystanders and residents.

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)

None.