

FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: IN005B1570

Product name: ~~INDOFIL~~ Difenoconazole 250 G/L EC greener

Chemical active substance:

Difenoconazole, 250 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(Article 33: Application for authorisation)

Applicant: Indofil Industries (Netherlands) B.V.

Submission date: January 2022

MS Finalisation date: 10.2022, 05.2024, 08.2024

Version history

When	What
January 2022	V0 – Original version from applicant Indofil Industries (Netherlands) B.V. for submission to z-RMS, Poland, in the frame of the PPP Authorization according to Article 33 of Regulation (EC) No. 1107/2009
October 2022	zRMS first evaluation
May 2024	Applicant dRR update based on cMS comments
August 2024	zRMS update (third round of commenting)

Table of Contents

6	Mammalian Toxicology (KCP 7).....	5
6.1	Summary	6
6.2	Toxicological Information on Active Substance	10
6.3	Toxicological Evaluation of Plant Protection Product.....	10
6.4	Toxicological Evaluation of Groundwater Metabolites.....	12
6.5	Dermal Absorption (KCP 7.3)	12
6.5.1	Justification for proposed values - Difenoconazole.....	13
6.6	2020Exposure Assessment of Plant Protection Product (KCP 7.2).....	13
6.6.1	Selection of critical use(s) and justification	13
6.6.2	Operator exposure (KCP 7.2.1)	14
6.6.2.1	Estimation of operator exposure	14
6.6.2.2	Measurement of operator exposure.....	17
6.6.3	Worker exposure (KCP 7.2.3)	18
6.6.3.1	Estimation of worker exposure	18
6.6.3.2	Refinement of generic DFR value (KCP 7.2).....	22
6.6.3.3	Measurement of worker exposure.....	22
6.6.4	Resident and bystander exposure (KCP 7.2.2)	22
6.6.4.1	Estimation of resident and bystander exposure	22
6.6.4.2	Measurement of resident and/or bystander exposure.....	24
6.6.5	Combined exposure	24
Appendix 1	Lists of data considered in support of the evaluation	25
Appendix 2	Detailed evaluation of the studies relied upon.....	27
A 2.1	Statement on bridging possibilities.....	27
A 2.2	Acute oral toxicity (KCP 7.1.1)	27
A 2.3	Acute percutaneous (dermal) toxicity (KCP 7.1.2)	27
A 2.4	Acute inhalation toxicity (KCP 7.1.3)	28
A 2.5	Skin irritation (KCP 7.1.4).....	28
A 2.6	Eye irritation (KCP 7.1.5)	28
A 2.7	Skin sensitisation (KCP 7.1.6).....	29
A 2.8	Supplementary studies for combinations of plant protection products (KCP 7.1.7)	29
A 2.9	Data on co-formulants (KCP 7.4)	29
A 2.9.1	Material safety data sheet for each co-formulant.....	29
A 2.9.2	Available toxicological data for each co-formulant.....	29
A 2.10	Studies on dermal absorption (KCP 7.3)	29
A 2.10.1	Difenoconazole in difenoconazole 250 g/l EC greener – in005b1570	29
A 2.11	Other/Special Studies	33
Appendix 3	Exposure calculations	34
A 3.1	Operator exposure calculations (KCP 7.2.1.1)	34
A 3.1.1	Calculations for Difenoconazole.....	34
A 3.1.2	Low vegetables: Outdoor, normal, downward spraying, vehicle-mounted .	34
A 3.1.3	Low vegetables: Outdoor, normal, downward spraying, manual-hand	34

A 3.1.4	Low vegetables: Outdoor, normal, downward spraying, manual-knapsack	35
A 3.1.5	Orchard: Outdoor, normal, upward spraying, vehicle-mounted	35
A 3.1.6	Orchard: Outdoor, normal, upward spraying, manual-hand held	36
A 3.1.7	Orchard: Outdoor, normal, upward spraying, manual-knapsack	36
A 3.1.8	Orchard: Outdoor, dense, upward spraying, manual-hand held	36
A 3.1.9	Orchard: Outdoor, dense, upward spraying, manual-knapsack	37
A 3.1.10	Field crops: Outdoor, normal, downward spraying, vehicle-mounted	37
A 3.2	Worker exposure calculations (KCP 7.2.3.1)	42
A 3.2.1	Calculations for Difenoconazole.....	42
A 3.3	Resident and bystander exposure calculations (KCP 7.2.2.1)	48
A 3.3.1	Calculations for Difenoconazole.....	48
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)	51

6 Mammalian Toxicology (KCP 7)

This document reviews the mammalian toxicology for the product IN005B1570, an emulsifiable concentrate formulation containing 250 g/L difenoconazole for use on oilseed rape, pome fruits, carrot, tomato, eggplant, pepper, potato, cucumber, cauliflower, broccoli and cabbage. Difenconazole was first included in Annex I to Directive 91/414/EEC by Commission Directive 2008/69/EC of 1 July 2008.

A full risk assessment according to Uniform Principles is provided which demonstrates that the product is safe for the environment. Where appropriate this document refers to the conclusion of the EU review for difenoconazole. This will be where:

- The active substance data are relied upon in the risk assessment of the formulation; or when
- the EU review concluded that the additional data/information should be considered at national re-registration.

Note: this Part B document only reviews data (Annex II or Annex III) and additional information that has not previously been considered within the EU review process, as part of the Annex I inclusion decision. New annex II data must only be included if they are considered essential for the evaluation and in this case a full study summary must be provided. In the case where the formulation has been previously evaluated, at European level, detailed summaries have not been provided.

This product was not the representative formulation and has not been previously evaluated according to the Uniform Principles.

The EFSA Scientific report for Difenconazole (EFSA Scientific Report, 2011; 9(1):1967) is considered to provide the relevant review information or a reference to where such information can be found.

The Commission Implementation Regulation for Difenconazole (540/2011) provides specific provisions under part B which need to be considered by the applicant in the preparation of their submission and by the MS prior to granting an authorisation.

For the implementation of the uniform principles as referred to in Article 29(6) of Regulation (EC) No. 1107/2009, the conclusion of the review report for Difenconazole, and in particular Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health shall be taken into account.

In this overall assessment Member States must pay particular attention to:

- The protection of aquatic organisms.

Conditions of use shall include adequate risk mitigation measures, where appropriate.

The Commission Implementation Regulation (1100/2011) amending Implementing Regulation (EU) No 540/2011 as regards the conditions of approval of Difenconazole provides specific provisions under part B which need to be considered by the applicant in the preparation of their submission and by the MS prior to granting an authorisation.

For the implementation of the uniform principles, as referred to in Article 29(6) of Regulation (EC) No 1107/2009, the conclusions of the review report on difenoconazole, and in particular Appendices I and II thereof, as finalised in the Standing Committee on the Food Chain and Animal Health on 27 September 2011 shall be taken into account.

In this overall assessment Member States shall pay particular attention to the protection of aquatic organisms.

Conditions of use shall include adequate risk mitigation measures, where appropriate.

The notifier shall submit confirmatory information as regards:

- (a) further data on the specification of the technical material;
- (b) residues of triazole derivative metabolites (TDMs) in primary crops, rotational crops, processed commodities and products of animal origin;
- (c) the potential for endocrine disrupting effects on fish (fish full life cycle study) and the chronic risk to earthworms from the active substance and the metabolite CGA 205375 (1);
- (d) the possible impact of the variable isomer-ratio in the technical material and of the preferential degradation and/or conversion of the mixture of isomers on the worker risk assessment, the consumer risk assessment and on the environment.

The notifier shall submit to the Member States, the Commission and the Authority the information set out in point (a) by 31 May 2012, the information set out in points (b) and (c) by 30 November 2013 and the information set out in point (d) within 2 years from the adoption of specific guidance.'

Information on the detailed composition of IN005B1570 can be found in the confidential dossier of this submission (Registration Report – Part C).

6.1 Summary

Table 6.1-1: Information on IN005B1570 / Indofil Difenconazole 250 EC*

Product name and code	Indofil Difenconazole 250 EC (IN005B1570)
Formulation type	Emulsifiable concentrate [Code: EC]
Active substance(s) (incl. content)	Difenconazole; 250 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 the formulation 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 Indofil Difenconazole 250 EC (IN005B1570) according to Regulation (EC) No 1272/2008

Hazard classes, categories	Eye irritation (Category 2) Carcinogenicity (Category 2, Aquatic Acute Category 1 Aquatic Chronic Category 1
Hazard pictograms or Code(s) for hazard pictogram(s)	GHS07 GHS08 GHS09
Signal word	Warning
Hazard statement(s)	H319: Causes serious eye irritation. H351: Suspected of causing cancer. H400 : Very toxic to aquatic life H410: Very toxic to aquatic life with long lasting effects
Precautionary statement(s)	<u>WARNING SECTION OF THE LABEL (first page):</u> P201: Obtain special instructions before use. P280: Wear protective gloves, 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. P308+PP313: IF exposed or concerned: Get medical advice/attention. <u>Other section of the label:</u> P270 – Do not eat, drink or smoke when using this product. P391: Collect spillage; P273: Avoid release to the environment. P405: Store locked up. P501: Dispose of contents/container in accordance with national regulation. And P280 as follows: <u>Operator:</u> „Stosować rękawice ochronne, ochronę oczu lub twarzy oraz odzież roboczą (kombinezon) w trakcie przygotowywania cieczy roboczej oraz rękawice ochronne i odzież roboczą w trakcie wykonywania zabiegu” “Wear protective gloves, eye/face shield and work wear (coverall) during mixing/loading and protective gloves and work wear during application”. <u>Worker:</u> „Stosować odzież roboczą (długie spodnie, koszula z długim rękawem) oraz rękawice ochronne podczas prac wykonywanych na terenie poddanym zabiegowi.” “Wear workwear (long trousers, long-sleeve shirt) and protective gloves during field work carried out in the treated area.” <u>Section “First aid”:</u> P101: If medical advice is needed, have product container or label at hand. P308+PP313: IF exposed or concerned: Get medical advice/attention. 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	To avoid risks to man and the environment, comply with the instructions for use. To avoid risks to human health and the environment, comply with the instructions for use. [EUH401] 15 % of the mixture consists of ingredient(s) of unknown acute inhalation toxicity.

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for IN005B1570

	Result	PPE / Risk mitigation measures
--	--------	--------------------------------

	Result	PPE / Risk mitigation measures
Operators	Acceptable	Exposure assessment: None Classification: eye/face protection, protective gloves, work wear
Workers	Acceptable	None, work wear (orchards). Recommendation: protective gloves
Residents	Acceptable	None
Bystanders	Acceptable	None

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

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) Per application b) Per crop/season	Water L/ha min / max			Operator	Worker	Residents	Bystander
1	BRSNW (OSR) BBCH 14-18 and BBCH 60-69	F	Spraying, LCTM	2;21	a) 0.125 b) 0.250	200-300	21					
2	MABSD, PYUCO (Apples, Pears) (BBCH 57-84)	F	Spraying, HCTM	3;7	a) 0.05625 b) 0.16875	400— 1500 300-1000	21	Critical gap for operator and resident or by- stander exposure based on [EFSA Journal 2014;12(10):3874]				
3	DAUCS (Garden carrot) (from BBCH 39-40)	F	Spraying, LCTM	3;14	a) 0.125 b) 0.375	200-1000 600	14	Critical gap for resident or by- stander exposure based on [EFSA Journal 2014;12(10):3874]				
5	BRSOK (broccoli) (from BBCH 19-21)	F	Spraying, LCTM	3;7	a) 0.125 b) 0.375	200-1000	14	Critical gap for operator, worker exposure based on [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

Data gaps

Noticed data gaps are:

- None

6.2 Toxicological Information on Active Substance

Information regarding classification of the active substance 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

	Difenoconazole
Common Name	Difenoconazole
CAS-No.	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: Acute Oral Toxicity (Category 4) Eye irritation (Category 2) Carcinogenicity (Category 2) Aquatic Acute Category 1 Aquatic Chronic Category 1 Code(s) for hazard pictogram(s): GHS07 GHS08 GHS09 Signal word: Warning Hazard statement(s): H302 H319 H351 H400 H410 Precautionary statement(s): P270, P273, P280, P301+P312, P305+P351+P338, P337+P313, P391, P501
Additional C&L proposal	Not applicable
Agreed EU endpoints	
AOEL systemic	0.16 mg/kg bw/day mg/kg bw/d
Reference	EFSA Conclusion (EFSA Journal 2011;9(1):1967)
Conditions to take into account/critical areas of concern with regard to toxicology	
According to EFSA Conclusion for active substance	None

6.3 Toxicological Evaluation of Plant Protection Product

The toxicological evaluation for INDOFIL Difenoconazole 250 EC (IN005B1570) is derived from the classification of the active substance Difenoconazole and co-formulants.

IN005B1570 is not predicted to be toxic via the oral, dermal or inhalation routes. IN005B1570 is classified for eye irritation. Summaries of the evaluation are presented in Appendix 2 and details of the co-formulants and their classification and the calculation methodology are presented in the confidential dos-

sier of this submission (Registration Report - Part C).

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for IN005B1570

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD ₅₀ oral	Not submitted, not necessary. ATE _{mix} = 6612 g/kg bw	yes	none	Estimation based on the composition of the product (additivity formula) Justification presented in Appendix 2
LD ₅₀ dermal	Not submitted, not necessary. ATE _{mix} > 2000 mg/kg	yes	none	Estimation based on the composition of the product (additivity formula) Justification presented in Appendix 2
LC ₅₀ inhalation	Not submitted, not necessary. ATE _{mix} > 5.0 mg/L	yes	none	Estimation based on the composition of the product (additivity formula) Justification presented in Appendix 2
Skin irritation	Not submitted, not necessary. Not-irritating to the skin	yes	none	Estimation based on the composition of the product (additivity formula) Justification presented in Appendix 2
Eye irritation	Not submitted, not necessary. Irritating to the eye	yes	Eye Irrit.2, H319	Estimation based on the composition of the product (additivity formula) Justification presented in Appendix 2
Skin sensitisation	Not submitted, not necessary.	yes	none	Estimation based on the composition of the product (additivity formula) Justification presented in Appendix 2
Supplementary studies for combinations of plant protection products	No data – not required		none	

Table 6.3-2: Additional toxicological information relevant for classification/labelling of IN005B1570

	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	Difenoconazole (22% (w/w))	Carc. 2 Acute Tox. 4 Eye Irrit. 2	Reg. 1272/2008 / MSDS** / EFSA conclusion	Hazard statement(s): H302 H319 H351

	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)
product)		Hazard statement(s) H302 H319 (criteria $\geq 10\%$)	(EFSA Journal 2011;9(1):1967) CLH Report, 2020 RAC Opinion 2021	
Toxicological properties of non-active substance(s) (relevant for classification of product)	Please refer to the confidential dossier of this submission (Registration Report - Part C)			
Further toxicological information	No data – not required			

* Please use concentration range or concentration limit (e.g. 1-10% or > 1%) as provided in MSDS.

** Material safety data sheet by the applicant

6.4 Toxicological Evaluation of Groundwater Metabolites

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

6.5 Dermal Absorption (KCP 7.3)

Comments of ZRMs:	Dermal absorption study (Desai, K.R. 2022) is accepted without reservation. The absorption values of difenoconazole contained in the formulation IN005B1570 are acceptable and amount to 3.3 and 20 % for the concentrate and dilution, respectively.
-------------------	---

A summary of the dermal absorption rates for the active substances in IN005B1570 are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in IN005B1570

	Difenoconazole	
	Value	Reference
Concentrate	3.3%	New study (Desai, K.R. 2022) reported in Appendix 2
Dilution (dilution factor 1:2400)	19%	New study (Desai, K.R. 2022) reported in Appendix 2
Dilution (dilution factor 1:6667)	20%	New study (Desai, K.R. 2022) reported in Appendix 2

6.5.1 Justification for proposed values - Difenoconazole

Proposed dermal absorption rates for Difenoconazole are based on a dermal absorption study on the formulation INDOFIL Difenoconazole 250 EC (IN005B1570). The study results are summarised in the following table. A full summary of study on the dermal absorption of INDOFIL Difenoconazole 250 EC (IN005B1570) that has not previously been evaluated within an EU peer review process is described in detail in Appendix 2.

Table 6.5-2: Summary of the results of submitted dermal absorption studies for Difenoconazole

Test	Concentrate	Spray dilution (1:2400)	Spray dilution (1:6667)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference*
In vitro (human)	3.3%	19%	20%	INDOFIL Difenoconazole 250 EC (IN005B1570)	Yes	Not required	Justification accepted. Endpoint can be used for current product	Desai, K.R. 2022

* indicates that a study was reviewed at EU level

6.6 2020Exposure 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	INDOFIL Difenoconazole 250 EC (IN005B1570)
Formulation type	EC
Category	Fungicide
Active substance(incl. content)	Difenoconazole 250 g/L
AOEL systemic	0.16 mg/kg bw/d
Inhalation absorption	100%
Oral absorption	100%
Dermal absorption	Concentrate: 3.3% Dilution: 20% (0.0375 g/L) (Based on product (INDOFIL Difenoconazole 250 EC (IN005B1570)))

6.6.1 Selection of critical use(s) and justification

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

Justification

The application uses selected offer the worst-case scenarios for exposure to operator, worker, resident and bystander. The values used were considered to be the worst-case of each scenario.

6.6.2 Operator exposure (KCP 7.2.1)

<p>Comments of zRMS:</p>	<p>The estimations of operator exposure to difenoconazole contained in IN005B1570 (based on AOEM) performed by the Applicant are correct.</p> <p><u>Conclusions:</u></p> <p>According to the estimation based on AOEM, the use of IN005B1570 containing difenoconazole (250 g/kg) causes acceptable health risk for unprotected operator (arms, body and legs covered).</p> <p>However, taking into account the classification of the product (Eye Irrit. 2, H319), eye/face shield are mandatory during handling the undiluted product.</p> <p>Consequently, the following sentence regarding the use of PPE is recommended by the evaluator to be placed in the label:</p> <p>„Stosować rękawice ochronne, ochronę oczu lub twarzy oraz odzież roboczą (kombinezon) w trakcie przygotowywania cieczy roboczej oraz rękawice ochronne i odzież roboczą w trakcie wykonywania zabiegu.”</p> <p>“Wear protective gloves, eye/face shield and work wear (coverall) during mixing/loading and protective gloves and work wear during application”.</p> <p>04/2024</p> <p>The estimations of operator exposure to difenoconazole contained in IN005B1570 were updated by the Applicant acc. to Calcualtor OPEX version v.1.0.1. Additionally, the calculations for scenario with Manual-Hand held and Manual-Knapsack held application in pome fruit orchards, broccoli, garden carrots are provided.</p> <p><u>Conclusions for Manual held sprayer:</u></p> <p>According to the estimation based on Calcualtor OPEX version v.1.0.1, the use of IN005B1570 causes acceptable health risk for operator equipped with:</p> <ul style="list-style-type: none"> - Work wear (arms, body and legs covered) during M/L and A: broccoli, carrot; - Work wear (arms, body and legs covered) during M/L and A: pple, pear (normal crop density); - Work wear (arms, body and legs covered) and protective gloves during M/L and A: apple, pear (high crop density). <p>Taking into account the classification of the product (Eye Irrit. 2, H319, Carc. 2, H351 and the results of estimations, the following sentence regarding the use of PPE is recommended by the evaluator to be placed in the label:</p> <p>„Stosować rękawice ochronne, ochronę oczu lub twarzy oraz odzież roboczą (kombinezon) w trakcie przygotowywania cieczy roboczej oraz rękawice ochronne i odzież roboczą w trakcie wykonywania zabiegu.”</p> <p>“Wear protective gloves, eye/face shield and work wear (coverall) during mixing/loading and protective gloves and work wear during application”.</p>
--------------------------	---

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 IN005B1570 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)	Outdoor low vegetables crops : Broccoli (3 x 0.5 L product/ha) and carrot 3 x 0.5 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 EFSA (European Food Safety Authority), Buist H, Craig P, Dewhurst I, Hougaard Bennekou S, Kneuer C, Machera K, Pieper C, Court Marques D, Guillot G, Ruffo F and Chiusolo A, 2017. Guidance on dermal absorption. EFSA Journal 2017;15(6):4873, 60 pp. https://doi.org/10.2903/j.efsa.2017.4873 EFSA (European Food Safety Authority), Charistou A, Coja T, Craig P, Hamey P, Martin S, Sanvido O, Chiusolo A, Colas M and Istace F, 2022. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. https://doi.org/10.2903/j.efsa.2022.7032 Calcualtor OPEX version v.1.0.1 (01/07/2023)
Critical use(s)	Outdoor orchards high-crops Apple, Pear (3 x 0.225 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 EFSA (European Food Safety Authority), Buist H, Craig P, Dewhurst I, Hougaard Bennekou S, Kneuer C, Machera K, Pieper C, Court Marques D, Guillot G, Ruffo F and Chiusolo A, 2017. Guidance on dermal absorption. EFSA Journal 2017;15(6):4873, 60 pp. https://doi.org/10.2903/j.efsa.2017.4873 EFSA (European Food Safety Authority), Charistou A, Coja T, Craig P, Hamey P, Martin S, Sanvido O, Chiusolo A, Colas M and Istace F, 2022. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. https://doi.org/10.2903/j.efsa.2022.7032 Calcualtor OPEX version v.1.0.1 (01/07/2023)
Critical use(s)	Outdoor field use: Oilseed rape (2 x 0.5 L product/ha)
Model(s)	EFSA (European Food Safety Authority), Buist H, Craig P, Dewhurst I, Hougaard Bennekou S, Kneuer C, Machera K, Pieper C, Court Marques D, Guillot G, Ruffo F and Chiusolo A, 2017. Guidance on dermal absorption. EFSA Journal 2017;15(6):4873, 60 pp. https://doi.org/10.2903/j.efsa.2017.4873 EFSA (European Food Safety Authority), Charistou A, Coja T, Craig P, Hamey P, Martin S, Sanvido O, Chiusolo A, Colas M and Istace F, 2022. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. https://doi.org/10.2903/j.efsa.2022.7032 Calcualtor OPEX version v.1.0.1 (01/07/2023)

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

		Difenconazole	
Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Tractor mounted boom spray application outdoors to low vegetables crops Broccoli, carrot			
Application rate		3 x 0.125 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	0.03	17.2

	Work wear (arms, body and legs covered) M/L and A	0.0146 0.02	9.10% 11.3
Manual-Hand held application outdoors to low vegetables: Broccoli, carrot			
Application rate		3 x 0.125 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	0.3	191
	Work wear (arms, body and legs covered) M/L and A	0.04	23.9
Manual-Knapsack held application outdoors to low vegetables: Broccoli, carrot			
Application rate		3 x 0.125 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	0.3	193
	Work wear (arms, body and legs covered) M/L and A	0.04	25.7
Tractor mounted broadcast spray application outdoors to Orchards Normal high crops Apple, Pear			
Application rate		3 x 0.05625 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	0.03	18.2
	Work wear (arms, body and legs covered) M/L and A	0.0100	6.25% 7.1
Manual-Hand held application outdoors to Orchards Normal: Apple, pear			
Application rate		3 x 0.05625 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	0.2	105
	Work wear (arms, body and legs covered) M/L and A	0.008	5.3
Manual-Knapsack held application outdoors to Orchards Normal: Apple, pear			
Application rate		3 x 0.05625 kg a.s./ha	

Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	0.1	85.7
	Work wear (arms, body and legs covered) M/L and A	0.01	6.5
Manual-Hand held application outdoors to Orchards Dense: Apple, pear			
Application rate		3 x 0.05625 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	2.5	1586
	Work wear (arms, body and legs covered) M/L and A	0.2	98.6
Manual-Knapsack held application outdoors to Orchards Dense: Apple, pear			
Application rate		3 x 0.05625 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	2.5	1589
	Work wear + Protected hands (hands, arms, body and legs covered) M/L and A	0.2	98.5
Vehicle-mounted application outdoors to field crops: OSR			
Application rate		2 x 0.125 kg a.s./ha	
Spray application (AOEM; 75 th percentile) Body weight: 60 kg	Potential exposure	0.03	17.2
	Work wear (arms, body and legs covered) M/L and A	0.02	11.3

6.6.2.2 Measurement of operator exposure

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

6.6.3 Worker exposure (KCP 7.2.3)

Comments of zRMS:	<p>The estimations of worker exposure to the active substance contained in IN005B1570 (based on AOEM) performed by the Applicant are accepted.</p> <p><u>Conclusions:</u></p> <p>According to the estimation results, the use of IN005B1570 containing difenoconazole (250 g/kg) does not cause unacceptable health risk for a worker wearing work wear (arms, body and legs covered).</p> <p>Nevertheless, it is forbidden to re-enter area treated with IN005B1570 until spray deposit on plant surfaces has dried. Taking into account the hygienic rules during handling of the PPPs, the protective gloves are strongly recommended.</p> <p>Following sentence regarding the use of PPE is recommended by the evaluator to be placed in the section of precautions for the workers:</p> <p><i>„Stosować odzież roboczą (długie spodnie, koszula z długim rękawem) oraz rękawice ochronne podczas prac wykonywanych na terenie poddanym zabiegowi.”</i></p> <p>“Wear workwear (long trousers, long-sleeve shirt) and protective gloves during field work carried out in the treated area.”</p> <p>04/2024</p> <p>The estimations of worker exposure to difenoconazole contained in IN005B1570 were updated by the Applicant acc. to Calcualtor OPEX version v.1.0.1.</p> <p><u>Conclusions:</u></p> <p>According to the estimation results, the use of IN005B1570 containing difenoconazole (250 g/kg) does not cause unacceptable health risk for: unprotected worker (field crops: inspection; low vegetables: all field activities; orchards: inspection, harvest), worker wearing work wear (orchards: maintenance/ thinning).</p> <p>However, taking into account the hygienic rules during handling of the PPPs, the protective gloves are strongly recommended.</p> <p>Following sentence regarding the use of PPE is recommended by the evaluator to be placed in the section of precautions for the workers:</p> <p><i>„Stosować odzież roboczą (długie spodnie, koszula z długim rękawem) oraz rękawice ochronne podczas prac wykonywanych na terenie poddanym zabiegowi.”</i></p> <p>“Wear workwear (long trousers, long-sleeve shirt) and protective gloves during field work carried out in the treated area.”</p>
-------------------	--

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 INDOFIL Difenoconazole 250 EC (IN005B1570) according to the critical use(s). Outcome 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)	Outdoor low vegetables crops : Broccoli (3 x 0.5 L product/ha) and carrot 3 x 0.5 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 EFSA (European Food Safety Authority), Buist H, Craig P, Dewhurst I, Hougaard Bennekou S, Kneuer C, Machera K, Pieper C, Court Marques D, Guillot G, Ruffo F and Chiusolo A, 2017. Guidance on dermal absorption. EFSA Journal 2017;15(6):4873, 60 pp. https://doi.org/10.2903/j.efsa.2017.4873 EFSA (European Food Safety Authority), Charistou A, Coja T, Craig P, Hamey P, Martin S, Sanvido O, Chiusolo A, Colas M and Istace F, 2022. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. https://doi.org/10.2903/j.efsa.2022.7032 Calcualtor OPEX version v.1.0.1 (01/07/2023)
Critical use(s)	Outdoor orchards high-crops Apple, Pear (3 x 0.225 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 EFSA (European Food Safety Authority), Buist H, Craig P, Dewhurst I, Hougaard Bennekou S, Kneuer C, Machera K, Pieper C, Court Marques D, Guillot G, Ruffo F and Chiusolo A, 2017. Guidance on dermal absorption. EFSA Journal 2017;15(6):4873, 60 pp. https://doi.org/10.2903/j.efsa.2017.4873 EFSA (European Food Safety Authority), Charistou A, Coja T, Craig P, Hamey P, Martin S, Sanvido O, Chiusolo A, Colas M and Istace F, 2022. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. https://doi.org/10.2903/j.efsa.2022.7032 Calcualtor OPEX version v.1.0.1 (01/07/2023)
Critical use(s)	Outdoor field use: Oilseed rape (2 x 0.5 L product/ha)
Model(s)	EFSA (European Food Safety Authority), Buist H, Craig P, Dewhurst I, Hougaard Bennekou S, Kneuer C, Machera K, Pieper C, Court Marques D, Guillot G, Ruffo F and Chiusolo A, 2017. Guidance on dermal absorption. EFSA Journal 2017;15(6):4873, 60 pp. https://doi.org/10.2903/j.efsa.2017.4873 EFSA (European Food Safety Authority), Charistou A, Coja T, Craig P, Hamey P, Martin S, Sanvido O, Chiusolo A, Colas M and Istace F, 2022. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment of plant protection products. EFSA Journal 2022;20(1):7032, 134 pp. https://doi.org/10.2903/j.efsa.2022.7032 Calcualtor OPEX version v.1.0.1 (01/07/2023)

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

		Difenoconazole	
Model data	Level of PPE	Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Low vegetables (all) Inspection, irrigation Outdoor Work rate: 2 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 7 days			
Number of applications and application rate		3 x 0.125 kg a.s./ha	

Body weight: 60 kg	Potential TC: 12500 cm ² /person/h	0.08	50.2
	Work wear (arms, body and legs covered) TC: 1400 cm ² /person/h	0.009	5.6
	Work wear (arms, body and legs covered) and gloves TC: 1250 cm ² /person/h	0.008	5
Low vegetables (Brassica only) Harvest and maintenance Outdoor Work rate: 8 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 7 days			
Number of applications and application rate		3 x 0.125 kg a.s./ha	
Body weight: 60 kg	Work wear (arms, body and legs covered) TC: 5000 cm ² /person/h	0.1	80.3
Broccoli (low vegetable crop) Low vegetables (all except Brassicas -carrot-) Reaching, picking Outdoor Work rate: 8 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 7 14 days			
Number of applications and application rate		3 x 0.125 kg a.s./ha	
Body weight: 60 kg	Potential TC: 5800 cm ² /person/h	0.1493 0.1	93.32% 81.6
	Work wear (arms, body and legs covered) TC: 2500 cm ² /person/h	0.0644 0.06	40.22% 35.2
	Work wear (arms, body and legs covered) and gloves TC: 580 cm ² /person/h	0.0149 0.01	9.33% 8.2
Orchard (Apple and Pear) Maintenance/ thinning Outdoor Work rate: 8 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 7 days			
Number of applications and application rate		3 x 0.05625 kg a.s./ha	
Body weight: 60 kg	Potential TC: 22500 cm ² /person/h	0.3	163
	Work wear (arms, body and legs covered) TC: 4500 cm ² /person/h	0.05	32.5
	Work wear (arms, body and legs covered) and gloves TC: 2250 cm ² /person/h	0.03	16.3

Orchard (Apple and Pear) Inspection, irrigation Outdoor Work rate: 2 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 7 days			
Number of applications and application rate		3 x 0.05625 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm ² /person/h	0.04	22.6
	Work wear (arms, body and legs covered) TC: 1400 cm ² /person/h	0.004	2.5
	Work wear (arms, body and legs covered) and gloves TC: 1250 cm ² /person/h	0.004	2.3
Orchard (Apple and Pear) (high crop) Searchnig, reaching, picking Outdoor Work rate: 8 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 7 days			
Number of applications and application rate		3 x 0.05625 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 22500 cm ² /person/h	0.2606 0.1	162.91% 90.4
	Work wear (arms, body and legs covered) TC: 3500 4500 cm ² /person/h	0.0521 0.04	32.58% 25.3
	Work wear (arms, body and legs covered) and gloves TC: 1250 cm ² /person/h	0.01	9
Field crops (OSR) Inspection, irrigation Outdoor Work rate: 2 hours/day, DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 21 days			
Number of applications and application rate		2 x 0.125 kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm ² /person/h	0.05	31.6
	Work wear (arms, body and legs covered) TC: 1400 cm ² /person/h	0.006	3.5
	Work wear (arms, body and legs covered) and gloves TC: 1250 cm ² /person/h	0.005	3.2

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

Not required.

6.6.3.3 Measurement of worker exposure

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

6.6.4 Resident and bystander exposure (KCP 7.2.2)

Comments of zRMS:

The reference value acutely toxic active substance (RVAAS) for difenoconazole is not allocated. Consequently, it is assumed that the estimation of bystander exposure is covered by the calculation of resident exposure towards the active substance.

The estimations of resident exposure to difenoconazole presented by the Applicant are not accepted. In the worst-case scenario for low crops, the interval between multiple applications should amount to 7 days instead of 14 days. The new results of exposure of bystander/resident are presented below:

Resident - child	Spray drift (75th percentile) mg/kg bw/day	0,0034	% of RVNAS	2,10%
	Vapour (75th percentile) mg/kg bw/day	0,0011	% of RVNAS	0,67%
	Surface deposits (75th percentile) mg/kg bw/day	0,0012	% of RVNAS	0,75%
	Entry into treated crops (75th percentile) mg/kg bw/day	0,0109	% of RVNAS	6,79%
	All pathways (mean) mg/kg bw/day	0,0125	% of RVNAS	7,79%
Resident - adult	Spray drift (75th percentile) mg/kg bw/day	0,0008	% of RVNAS	0,50%
	Vapour (75th percentile) mg/kg bw/day	0,0002	% of RVNAS	0,14%
	Surface deposits (75th percentile) mg/kg bw/day	0,0004	% of RVNAS	0,27%
	Entry into treated crops (75th percentile) mg/kg bw/day	0,0060	% of RVNAS	3,77%
	All pathways (mean) mg/kg bw/day	0,0057	% of RVNAS	3,59%

The estimations of resident exposure to difenoconazole after PPP use in high crops presented by the Applicant are accepted.

Conclusions:

The results of the exposure estimations suggest that the use of IN005B1570 according to the list of intended uses presented in GAP Table cause acceptable health risk for bystander and resident (adult and child) according AOEM.

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 Difenoconazole. The outcome of the estimation is presented in Table 6.6-7 (longer term resident exposure). Detailed calculations are in Appendix 3.

Table 6.6-6: Exposure models for intended uses

Critical use(s)	Outdoor low crops: Carrot (max. 0.5 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
Critical use(s)	Outdoor high crops Apple and Pear (max. 0.255 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 6.6-7: Estimated resident exposure (longer term exposure)

		Difenoconazole	
Model data		Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Tractor mounted boom spray application outdoors to low crops Carrot 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		3 x 0.125 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75 th perc.)	0.0034	2.10%
	Vapour (75 th perc.)	0.0011	0.67%
	Deposits (75 th perc.)	0.0010	0.65%
	Re-entry (75 th perc.)	0.0095	5.93%
	Sum (mean)	0.0113	7.03%
Resident adult Body weight: 60 kg	Drift (75 th perc.)	0.0008	0.50%
	Vapour (75 th perc.)	0.0002	0.14%
	Deposits (75 th perc.)	0.0004	0.24%
	Re-entry (75 th perc.)	0.0053	3.29%
	Sum (mean)	0.0051	3.18%
Tractor mounted broadcast spray application outdoors to high crops Apple and Pear Buffer zone: 5(m) Drift reduction technology: no DT ₅₀ : 30 days DFR: 3 µg/cm ² /kg a.s./ha Interval between treatments: 7 days			
Number of applications and application rate		3 x 0.05625 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75 th perc.)	0.0157	9.80%
	Vapour (75 th perc.)	0.0011	0.67%
	Deposits (75 th perc.)	0.0015	0.95%
	Re-entry (75 th perc.)	0.0049	3.05%

	Sum (mean)	0.0164	10.25%
Resident adult Body weight: 60 kg	Drift (75 th perc.)	0.0087	5.42%
	Vapour (75 th perc.)	0.0002	0.14%
	Deposits (75 th perc.)	0.0006	0.35%
	Re-entry (75 th perc.)	0.0027	1.70%
	Sum (mean)	0.0085	5.30%

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 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

Not relevant. The product contains only one active substance.

Appendix 1 Lists of data considered in support of the evaluation

The following lists should include all product data considered in support of the evaluation, independently if they may have been evaluated previously, e.g. in the EU peer review of the active substance(s), and thus, are not summarised in this document in detail. New data evaluated for the active substance(s) should be included as well.

Please sort by data points and within one data point by name of authors

Tables considered not relevant can be deleted as appropriate.

MS to blacken authors of vertebrate studies in the version made available to third parties/public.

List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 7.3	Desai K.R.	2022	In vitro dermal absorption of difenoconazole from difenoconazole 250 g/L EC greener - IN005B1570 using human split-thickness skin in a flow through diffusion system. (2022) Report N. 617-1-06-29170 JRF GLP Unpublished	N	Indofil Industries (Netherlands) B.V.

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

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
Reference	Sweden	2006	Draft Assessment Report (DAR) on the active substance difenoconazole prepared by the rapporteur Member State Sweden in the framework of Directive 91/414/EEC, December 2006.	N	n/a
Reference	Sweden	210	. Final Addendum to Draft Assessment Report on difenoconazole, compiled by EFSA, November 2010.	N	n/a
Reference	EFSA	2011	European Food Safety Authority; Conclusion on the peer review of the pesticide risk assessment of the active substance difenoconazole. EFSA Journal 2011;9(1):1967. [71 pp.]. doi:10.2903/j.efsa.2011.1967. Available online: www.efsa.europa.eu/efsajournal.htm	N	n/a

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

The toxicological evaluation for IN005B1570 is derived from the classification of the active substance Difenconazole and co-formulants.

IN005B1570 has a predicted low oral toxicity and is predicted as not toxic via the oral, dermal or inhalation routes. IN005B1570 is classified for eye irritation. Details of the co-formulants and their classification and the calculation methodology are presented in the confidential dossier of this submission (Registration Report - Part C).

Comments of zRMS:	The classification of the formulation IN005B1570 is based on toxicological data of individual ingredients of the mixture (additivity formula). Bridging principles for the classification of mixture did not apply.
-------------------	---

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	<p>Two ingredients are taken into account for the purpose of product classification: Difenconazole: 21.93% (Acute Tox. 4, H302; LD₅₀ = 14503 mg /kg bw) Methanol: 0.19% (Acute Tox. 3, H3012; LD50: 143-187 mg/kg bw (human)).</p> <p>The ATE_{mix} of the product amounts to 6134-3214 g/kg bw.</p> <p><u>Conclusion:</u> Taking into account the composition of the product, the formulation IN005B1570 does not require classification in regards to oral acute toxicity.</p>
-------------------	---

Acute toxicity studies for IN005B1570 were not evaluated as part of the EU review of Difenconazole. 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 oral toxicity of IN005B1570 can be found in an appendix to the can be found in the confidential dossier of this submission (Registration Report - Part C). The acute oral toxicity of IN005B1570 was estimated to be ATE_{mix} > 2000 mg/kgIN005B1570 therefore does not require classification for this health hazard.

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

Comments of zRMS:	<p>The formulation IN005B1570 does not contain ingredients classified in regards to acute dermal toxicity.</p> <p><u>Conclusion:</u> Taking into account the composition of the product, the formulation IN005B1570 does not require classification in regards to acute dermal toxicity.</p>
-------------------	--

Acute toxicity studies for IN005B1570 were not evaluated as part of the EU review of Difenconazole. Therefore, all relevant data are provided here and are considered adequate. Details of the co-formulants and their classification and the methodology that was used to assess the acute dermal toxicity of IN005B1570 can be found in an appendix to the can be found in the confidential dossier of this submission (Registration Report - Part C). The acute dermal toxicity of IN005B1570 was estimated to be ATE_{mix} > 2000 mg/kgIN005B1570 therefore does not require classification for this health hazard.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	The formulation IN005B1570 does not contain ingredients classified on regards to acute inhalation toxicity.
	<u>Conclusion:</u> Taking into account the composition of the product, the formulation IN005B1570 does not require classification in regards to acute inhalation toxicity.

Acute toxicity studies for IN005B1570 were not evaluated as part of the EU review of Difenconazole. 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 inhalation toxicity of IN005B1570 can be found in the confidential dossier of this submission (Registration Report - Part C). The acute inhalation toxicity of IN005B1570 was estimated to be ATE_{mix} 5.0 mg/L, IN005B1570 therefore does not require classification for this health hazard.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	The formulation IN005B1570 does not contain ingredients classified in regards to skin irritation.
	<u>Conclusion:</u> Taking into account the composition of the product, the formulation IN005B1570 does not require classification in regards to skin irritation.

Acute toxicity studies for IN005B1570 were not evaluated as part of the EU review of Difenconazole. 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 dermal irritation of IN005B1570 can be found in an appendix to the can be found in the confidential dossier of this submission (Registration Report - Part C). IN005B1570 is not considered a potential dermal irritant and does not require classification for this endpoint according to Regulation (EC) No 1272/2008. No signal word or hazard statement is required.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	Only one ingredient is taken into account for the purpose of product classification: Difenconazole: 21.93% (Eye Irrit. 2, H319)
	<u>Conclusion:</u> Taking into account the composition of the product, the amount of the active ingredient in the product triggers classification of the formulation regarding reversible effect to the eye ($\geq 10\%$). Thus, the formulation IN005B1570 requires classification in regards to irritant effect to the eye (Eye Irrit.2, H319).

Acute toxicity studies for IN005B1570 were not evaluated as part of the EU review of Difenconazole. 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 eye irritation of IN005B1570 can be found in an appendix to the can be found in the confidential dossier of this submission (Registration Report - Part C). According to Regulation (EC) no. 1272/2008 IN005B1570 is classified as an eye irritant and Signal word "Warning" with the hazard statement "H319: Causes serious eye irritation" and the pictogram GHS07 is required.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	<p>The formulation IN005B1570 does not contain ingredients classified in regards to skin sensitization.</p> <p><u>Conclusion:</u> Taking into account the composition of the product IN005B1570, the formulation IN005B1570 does not require classification in regards to skin sensitization.</p>
-------------------	--

Acute toxicity studies for IN005B1570 were not evaluated as part of the EU review of Difenconazole. 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 skin sensitisation potential of IN005B1570 can be found in an appendix to the can be found in the confidential dossier of this submission (Registration Report - Part C). IN005B1570 is not considered a potential skin sensitizer and does not require classification for this endpoint according to Regulation (EC) No 1272/2008. No signal word or hazard statement is required..

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

No supplementary studies are 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)

A 2.10.1 Difenconazole in difenconazole 250 g/l EC greener – in005b1570

Comparative dermal absorption, in vitro using human skin

Comments of zRMS:	<p>The study of dermal absorption (Desai, K.R. 2022) is accepted without reservation. The absorption values of difenconazole contained in the formulation IN005B1570 are acceptable and amount to 3.3 and 20 % for the concentrate and dilution, respectively. These value are used for the exposure estimations.</p>
-------------------	---

Reference KCA 7.3

Report *In vitro* dermal absorption of difenconazole from difenconazole 250 g/L EC

	greener using human split-thickness skin in a flow through diffusion system. (2022) Karishma R. Desai. Report N. 617-1-06-29170
Guideline(s)	OECD GD 428 EFSA, 2017: “Guidance on Dermal Absorption”. EFSA Journal 15(6):4873
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Executive summary

This study was designed for the evaluation of the dermal absorption of Difenconazole from Difenconazole 250 g/L EC Greener – IN005B1570 through human split-thickness skin in an *in vitro* study.

Test preparations containing (^{14}C - Difenconazole) were tested at three target concentrations of Difenconazole: 250 g/L, 0.1 g/L and 0.0375 g /L. Mass balance analysis was conducted by measuring the radioactivity (Liquid Scintillation Counting - LSC) in the receptor fluid, donor and receptor chamber washes, the residues remaining in/on the skin and in the *stratum corneum*.

The corrected dermal absorption value based on EFSA, 2017 was 3.3% for the formulation concentrate, 19% for the spray dilution 1 (0.1g/L) and 20% for spray dilution 2 (0.0375 g/L).

Materials and methods

Test material	Name (Lot/Batch No.)	Difenconazole, [4-chlorophenyl ring- ^{14}C (U)]-
	Test preparation	spiking
	Specific activity	56.6 mCi/mmol
	Radiochemical purity	100%
Product	Name (Lot/Batch No.)	Difenconazole 250 g/L EC Greener (IND_F021_0321_1)
	Company code	IN005B1570
	Concentration a.s.	250 g/L
	Formulation type	EC
Blank product	Name (Lot/Batch No.)	Placebo Difenconazole 250 g/L EC Greener (IND_F021_0321_1)
	Concentration a.s.	0 g/L

Test system		
Diffusion cell	Cell type	dynamic
	(if dynamic) Flow rate	1.6 ml/h
	Exposed skin area	0.64 cm ²
	Cover	occlusive
Membrane	Skin type	Dermatomed
	Skin thickness range	300-400 µm
	Skin donors age	Not stated
	Skin donors sex	m+f
	Location	abdomen and breast
	Source	Surgical waste
	Integrity test	Yes
Receptor	Receptor medium	Dulbecco's phosphate buffered saline (DPBS) with pH 7.4, supplemented with 6% PEG, 0.01%

		sodium azide and antibiotics, i.e. penicillin (50 IU/mL) and streptomycin (50 µg/mL)
	Solubility in receptor medium	>100 µg/mL
Sample Time	Exposure time	6h
	Observation time	24h
Sampling	Sample intervals	0 h (before exposure), 0-1 h, 1-2 h, 2-4 h, 4-6 h, 6-8 h, 8-10 h, 10-12 h, 12-16 h, 16-20 h, and 20-24 h
Washing		post exposure
Final Procedure	Tape stripping	yes
	TS1-2 analysed separately	yes

Tested doses	Concentrate	Spray dilution 1	Spray dilution 2
Target concentration [mg/ml]	250	0.1	0.0375
Area dose [µg/cm²]	2500	1	0.375
Total dose [µg/cell]	1600	0.64	0.24
Specific activity [MBq/ml]	≈ 5.8	≈ 0.5	≈ 0.2
No. of replicates/donors	8 from 4 donors	8 from 4 donors	8 from 4 donors
No of cells used/valid cells	8/8	8/8	8/8

This study was designed for the evaluation of the dermal absorption of Difenconazole from Difenconazole 250 g/L EC Greener – IN005B1570 through human split-thickness skin in an *in vitro* study.

DPBS supplemented with 6% PEG, 0.01% sodium azide and antibiotics (i.e., penicillin (50 IU/mL) and streptomycin (50 µg/mL), was selected as the receptor fluid in this study. For this study, flow-through diffusion cells were used, with the volume being replenished continuously with a flow rate of 1.6 mL/h.

Human split-thickness skin membranes (thickness between 300 and 400 µm) were placed in the flow-through diffusion cells with 0.64 cm² exposure area and exposed at 32 ± 1°C and ambient humidity. Eight cells using material across 4 human donors were used per test item dose level. Before an integrity check, the skin membranes were hydrated for approx. 12 h to close small holes such as open hair channels. The integrity of the skin membranes was determined by measuring the permeability coefficient (Kp) for the tritiated water (≈ 0.1 µCi/skin membrane). Skin membranes having a Kp ≤ 4.5 x 10⁻³ cm/h were considered acceptable and used in the study.

Difenconazole 250 g/L EC Greener – IN005B1570 was tested at three target concentrations of Difenconazole: 250 g/L (Concentrate), 0.1 g/L (Spray dilution 1) and 0.0375 g/L (Spray dilution 2). For the preparation of field spray dilution, distilled water was used as a vehicle in this study. The test preparations were formulated by an addition of 313 µCi of ¹⁴C- Difenconazole to the Concentrate, 70 µCi to Spray dilution 1 and 28 µCi of ¹⁴C- Difenconazole to Spray dilution 2.

The contact time was 6h ± 10 minutes, and the post-exposure time was 18 h ± 10 minutes. Skin membranes were washed at 6 h ± 10 minutes and 24 h ± 10 minutes after applying the test preparation to remove any excess test preparation from the skin surface. Receptor fluid samples were collected for analysis at 0 h (before exposure), 0-1 h, 1-2 h, 2-4 h, 4-6 h, 6-8 h, 8-10 h, 10-12 h, 12-16 h, 16-20 h, and 20-24 h after application of the test preparations. Following the 24 h sampling and skin washing, the diffusion cells were dismantled, and the skin membranes were retained for tape stripping and analysis for radioactivity. The *stratum corneum* was collected by tape stripping the skin membranes up to 15-times. All tape strips were individually extracted and analysed for radioactivity. The epidermis (after tape stripping) and dermis were also separated using forceps and analysed separately. Mass balance analysis was conducted by measuring the radioactivity (Liquid Scintillation Counting - LSC) in the receptor fluid, donor and receptor chamber washes, the residues remaining in/on the skin and in the *stratum corneum*.

Results and discussions

The mean cumulative absorption of Difenconazole from Difenconazole 250 g/L EC Greener – IN005B1570 (Concentrate) into the receptor fluid after 24 h was 0.29% of the applied dose. The respective mean maximal flux was 1.063 µg/cm²/h and the mean lag time was -0.93 h. The mean total recovery

of Difenconazole was 99.32% from Test Preparation I (Concentrate). The mean of total unabsorbed doses recovered from skin washings, donor compartment, and first two tape strips was 96.85% from Test Preparation I (Concentrate). The mean of the absorbed dose of Difenconazole from Difenconazole 250 g/L EC Greener – IN005B1570 was 2.47%. Absorption was considered incomplete as the amount permeated into the receptor fluid at 12 h (0.24%) was <75 % of the amount permeated at 24 h (0.29%). Therefore, the corrected dermal absorption value based on EFSA, 2017 was 3.3%.

The mean cumulative absorption of Difenconazole from Spray dilution 1 into the receptor fluid after 24 h was 6.45% of the applied dose. The respective mean maximal flux was 0.002 µg/cm²/h and the mean lag time was 0.96 h. The mean total recovery of Difenconazole was 101.16% for Spray dilution 1. The mean total unabsorbed dose (recovered from skin washings, donor compartment, and the first two tape strips) was 85.81%. The mean of the absorbed dose through human split-thickness skin was 15.35%. Absorption was considered incomplete as the amount permeated into the receptor fluid at 12 h (3.59%) was <75 % of the amount permeated at 24 h. Therefore, the corrected dermal absorption value for Spray dilution 1 based on EFSA, 2017 was 19%.

The mean cumulative absorption of Difenconazole from Spray dilution 2 into the receptor fluid after 24 h was 8.52% of the applied dose. The respective mean maximal flux was 0.0013 µg/cm²/h and the mean lag time was 0.42 h. The mean total recovery for spray dilution 2 was 99.42%. The mean total unabsorbed dose was 83.97%. The absorbed dose of Difenconazole from Spray dilution 2 was 15.45%. Absorption was considered incomplete as the amount permeated into the receptor fluid at 12 h (4.90%) was <75 % of the amount permeated at 24 h. Therefore, the corrected dermal absorption value for Spray dilution 2 based on EFSA, 2017 was 20%.

Tape stripping of the skin membranes (15 per skin membrane) treated with the formulation concentrate, Spray dilution 1 and Spray dilution 2 showed a gradual decrease in Difenconazole recovery with an increase in the number of tape strips. The mean recovery from the tape strips was around 2.64% 5.52%, and 4.03% from the skin membranes exposed to the formulation concentrate, Spray dilution 1 and Spray dilution 2, respectively.

A summary of an estimate of the percentage of the dose absorbed in different compartments after exposure of human skin to Difenconazole from Difenconazole 250 g/L EC Greener – IN005B1570 is provided in the table below:

Table A 1: In-vitro dermal penetration of Difenconazole formulated as Difenconazole 250 g/L EC Greener – IN005B1570 through human skin - Recovery data

Dose group	High dose (Formulation concentrate)		Mid dose (Spray dilution 1:2400)		Low dose (Spray dilution 1:6667)	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Target concentration [mg/mL]	250		0.1		0.0375	
Target dose [µg/cm ²]	2500		1		0.375	
Mean actual applied dose [µg/cm ²]	2511.3		0.99		0.380	
	Recovery [%]		Recovery [%]		Recovery [%]	
	Mean	S.D.	Mean	S.D.	Mean	S.D.
Dislodgeable dose	95.64	8.58	83.6	6.83	82.4	8.55
e.g. Skin washing after 6 h	88.47	4.04	79.11	5.80	77.82	6.72
e.g. Skin washing after 24 h	4.92	2.39	4.39	0.95	4.50	1.78
Donor chamber wash	2.25	2.15	0.10	0.08	0.08	0.05
Dose associated to skin	3.39	1.89	11.03	7.29	8.25	6
Tape strips: 1 st sample, strips 1 + 2	1.21	0.85	2.22	1.53	1.57	1.69
Tape strips: 2 nd sample; strips 3 - n	1.43	0.64	3.30	1.90	2.46	0.94
Dermis	0.18	0.13	2.65	1.54	1.84	0.93
Epidermis (without <i>stratum corneum</i>)	0.57	0.27	2.86	2.32	2.38	2.44

Absorbed dose						
Receptor fluid	0.29	0.45	6.45	2.15	8.52	2.47
Receptor chamber wash	0.01	0.00	0.09	0.05	0.26	0.16
Total recovery¹	99.32	1.50	101.16	1.32	99.42	1.90
Absorption essentially complete at end of study (>75% absorption within half the study duration) [% Absorption at t _{0.5}]	No [49.40% ±12.63]		No [45.39% ±9.10]		Yes No [52.83% ±4.91]	
If no: Absorption estimates = absorbed dose + skin preparation + tape strips sample 2) ²	2.47	0.98	15.35	4.58	15.45	5.42
If yes: Absorption estimates = absorbed dose + skin preparation	N/A	N/A	N/A	N/A	N/A	N/A
Absorption estimate normalised ³	N/A		N/A		N/A	
Relevant absorption estimate ⁴	3.289		19.204		20.001	
Absorption estimates used for risk assessment⁵	3.3		19		20	

¹ Values may not calculate exactly due to rounding of figures

² In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873 EFSA Journal 2012;10(4):2665) the radioactivity in the second tape-strip pool (3rd to nth tape strip) is considered potentially absorbable if less than 75% of the absorption occurred in the first half of the study (see Table 7.6.2-1) Finally, the skin preparation is also considered potentially absorbable.

³ According to the EFSA Guidance on Dermal Absorption, cells with insufficient recovery (< 95%) can be corrected by normalisation of absorption estimate to 100% recovery; explanation should be included.

⁴ In accordance with the EFSA Guidance on Dermal Absorption, one standard deviation was added to the mean% dermal penetration in cases where the standard deviation was ≥ 25% of the mean value.

⁵ Relevant absorption estimate was rounded to the required number of significant figures.

N/A: not applicable

Conclusion/endpoint:

The dermal penetration of difenoconazole when formulated in the product Difenoconazole 250 g/L EC Greener - IN005B1570 through human dermatomed skin was determined *in vitro*. The amount of applied dose penetrating within 24 hours was determined to be 2.47% ± 0.98, 15.35% ± 4.58 and 15.45 ± 5.42 for the formulation concentrate, the 1:2400 spray dilution, and the 1: 6667 spray dilution respectively. The corrected dermal absorption value based on EFSA, 2017 was 3.3% for the formulation concentrate, 19% for the 1:2400 spray dilution 1 and 20% for the 1: 6667 spray dilution 2.

A 2.11 Other/Special Studies

No other/special studies are required.

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for Difenoconazole

Product name	Neodif (IN005B1570)
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.
Product category	Other
Name of active substance	Difenoconazole
Concentration of active substance [g a.s./l or kg]	250
AOEL [mg/kg bw/day]	0.16
AAOEL [mg/kg bw]	
Inhalation absorption [%]	100
Oral absorption [%]	100
Dermal absorption [%] (concentrate)	3.3

A 3.1.2 Low vegetables: Outdoor, normal, downward spraying, vehicle-mounted

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% system error AC
Low vegetables/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percent Crop density: Norrr			
Difenoconazole	Number of applications and application rate: 3 x 0.125 kg a.s./l		
	Dermal absorption (concentrate): 3.3		
	Dermal absorption (in-use dilution): 20		
	M/L: Workwear	0.02	11
	App: Workwear		

A 3.1.3 Low vegetables: Outdoor, normal, downward spraying, manual-hand

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% system error AC
Low vegetables/Outdoor/Downward spraying/Manual-hand held/Drift reduction: 0 %/75th percent Crop density: Normal			
Difenoconazole	Number of applications and application rate: 3 x 0.125 kg a.s./ha		
	Dermal absorption (concentrate): 3.3 %		
	Dermal absorption (in-use dilution): 20 %		
	M/L: Workwear App: Workwear	0.04	25

A 3.1.4 Low vegetables: Outdoor, normal, downward spraying, manual-knapsack

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% system error AC
Low vegetables/Outdoor/Downward spraying/Manual-knapsack/Drift reduction: 0 %/75th percent Crop density: Normal			
Difenoconazole	Number of applications and application rate: 3 x 0.125 kg a.s./ha		
	Dermal absorption (concentrate): 3.3 %		
	Dermal absorption (in-use dilution): 20 %		
	M/L: Workwear App: Workwear	0.04	25

A 3.1.5 Orchard: Outdoor, normal, upward spraying, vehicle-mounted

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOE L
Orchards/Outdoor/Upward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile Crop density: Normal			
Difenoconazole	Number of applications and application rate: 3 x 0.05625 kg a.s./ha		
	Dermal absorption (concentrate): 3.3 %		
	Dermal absorption (in-use dilution): 20 %		
	M/L: Workwear App: Workwear	0.01	7.1

A 3.1.6 Orchard: Outdoor, normal, upward spraying, manual-hand held

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of sys-temic AOEL
Orchards/Outdoor/Upward spraying/Manual-hand held/Drift reduction: 0 %/75th percentile Crop density: Normal			
Number of applications and application rate: 3 x 0.05625 kg a.s./ha			
Difenconazole	Dermal absorption (concentrate): 3.3 %		
	Dermal absorption (in-use dilution): 20 %		
	M/L: Workwear		
	App: Workwear	0.008	5.3

A 3.1.7 Orchard: Outdoor, normal, upward spraying, manual-knapsack

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of sys-temic AOEL
Orchards/Outdoor/Upward spraying/Manual-knapsack/Drift reduction: 0 %/75th percentile Crop density: Normal			
Number of applications and application rate: 3 x 0.05625 kg a.s./ha			
Difenconazole	Dermal absorption (concentrate): 3.3 %		
	Dermal absorption (in-use dilution): 20 %		
	M/L: Workwear		
	App: Workwear	0.01	6.5

A 3.1.8 Orchard: Outdoor, dense, upward spraying, manual-hand held

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of sys-temic AOEL
Orchards/Outdoor/Upward spraying/Manual-hand held/Drift reduction: 0 %/75th percentile Crop density: Dense			

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of sys-temic AOEL
Number of applications and application rate: 3 x 0.05625 kg a.s./ha			
Difenconazole	Dermal absorption (concentrate): 3.3 %		
	Dermal absorption (in-use dilution): 20 %		
	M/L: Workwear	0.2	98.6
	App: Workwear		

A 3.1.9 Orchard: Outdoor, dense, upward spraying, manual-knapsack

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of sys-temic AOEL
Orchards/Outdoor/Upward spraying/Manual-knapsack/Drift reduction: 0 %/75th percentile Crop density: Dense			
Number of applications and application rate: 3 x 0.05625 kg a.s./ha			
Difenconazole	Dermal absorption (concentrate): 3.3 %		
	Dermal absorption (in-use dilution): 20 %		
	M/L: Workwear + Protected hands	0.2	98.5
	App: Workwear		

A 3.1.10 Field crops: Outdoor, normal, downward spraying, vehicle-mounted

Model data	Level of PPE	Total absorbed dose [mg/kg bw per day]	% of sys-temic AOEL
Field crops/Outdoor/Downward spraying/Vehicle-mounted/Drift reduction: 0 %/75th percentile Crop density: Normal			
Number of applications and application rate: 2 x 0.125 kg a.s./ha			
Difenconazole	Dermal absorption (concentrate): 3.3 %		
	Dermal absorption (in-use dilution): 20 %		
	M/L: Workwear	0.02	11.3
	App: Workwear		

Table A 2: Input parameters considered for the estimation of operator exposure (Broccoli)

Operator exposure for Difeno Greener outdoor spray applications				
Application rate of active substance	0.125	kg a.s./ha	<i>L_AppRate</i>	
Assumed area treated	50	ha/day	<i>d_AreaTreated</i>	
Amount of active substance applied	6.25	kg a.s./day	<i>L_AmountAS</i>	
Dermal absorption of the product	3.30%		<i>L_AbsorpProduct</i>	
Dermal absorption of in-use dilution	20.00%		<i>L_AbsorpInuse</i>	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.			
Indoor or Outdoor application	Outdoor			
Application method	Downward spraying			
Application equipment	Vehicle-mounted			
Season	not relevant			
Mixing and loading	Exposure values	µg exposure/day mixed and loaded		Reference
		75 th centile	95 th centile	Comment
	Hands	19909	74139	AOEM
	Body	12935	122660	AOEM
	Head	324	1778	AOEM
	Protected hands (gloves)	113	1238	AOEM
	Protected body (workwear or protective garment and sturdy footwear)	121	914	AOEM
	Protected head (hood and face shield)	5	101	AOEM
	Inhalation	6	30	AOEM
Application	Protective Equipment	Select for inclusion		Penetration factor
	Gloves	No		Inhalation Protection factor
	Clothing	work wear - arms, body and legs covered		ncl. in AOEM model
	Head and respiratory PPE	None		1
	Water soluble bag	No		1
	Exposure values	µg exposure/day applied		Reference
		75 th centile	95 th centile	Comment
	Hands	927	8771	AOEM
	Body	518	2672	AOEM
	Head	24	74	AOEM
	Protected hands (gloves)	115	4127	AOEM
	Protected body (workwear or protective garment and sturdy footwear)	14	35	AOEM
	Inhalation	3	8	AOEM
	Protective Equipment	Select for inclusion		Penetration factor
	Gloves	No		Inhalation Protection factor
	Clothing	work wear - arms, body and legs covered		ncl. in AOEM model
	Head and respiratory PPE	None		1
	Closed cab	No		vehicle mounted upward spraying

Table A 3: Estimation of longer term operator exposure towards Difenconazole according to EFSA guidance (Broccoli)

1. Total			
	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	1.3975184	0.8738106	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0232920	0.0145635	
% of RVNAS	14.56%	9.10%	
Acute			
Total systemic exposure from mixing, loading and application (mg a.s./day)	8.8948182	4.3497983	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.1482470	0.0724966	
% of RVAAS	#DIV/0!	#DIV/0!	

Table A 4: Input parameters considered for the estimation of operator exposure (Apple and Pear)

Operator exposure for Difeno Greener outdoor spray applications

Application rate of active substance	0.05625 kg a.s./ha	<i>L AppRate</i>
Assumed area treated	10 ha/day	<i>L AreaTreated</i>
Amount of active substance applied	0.5625 kg a.s./day	<i>L AmountAS</i>
Dermal absorption of the product	3.30%	<i>L AbsorpProduct</i>
Dermal absorption of in-use dilution	20.00%	<i>L AbsorpInuse</i>
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Indoor or Outdoor application	Outdoor	
Application method	Upward spraying	
Application equipment	Vehicle-mounted	
Season	not relevant	

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75 th centile	95 th centile		
Mixing and loading	Hands	3119	11370	AOEM	
	Body	2381	60937	AOEM	
	Head	29	160	AOEM	
	Protected hands (gloves)	24	111	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	14	82	AOEM	
	Protected head (hood and face shield)	0	9	AOEM	
	Inhalation	3	28	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	
Application	Exposure values	µg exposure/day applied		Reference	Comment
		75 th centile	95 th centile		
	Hands	1515	3508	AOEM	No data available for a drift reduction scenario
	Body	4957	28922	AOEM	
	Head	651	3998	AOEM	
	Protected hands (gloves)	20	517	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	65	126	AOEM	
	Inhalation	46	47	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		Incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying only	

Table A 5: Estimation of longer term operator exposure towards Difenconazole according to EFSA guidance (Apple and Pear)

1. Total			
	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	1.6562387	0.5997672	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0276040	0.0099961	
% of RVNAS	17.25%	6.25%	
Acute			
Total systemic exposure from mixing, loading and application (mg a.s./day)	9.7517727	1.9845085	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.1625295	0.0330751	
% of RVAAS	#DIV/0!	#DIV/0!	

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for Difenoconazole

A 3.2.1.1 Low vegetables

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Inspection, irrigation (All) / Outdoor Work rate: 2 hours/day Interval: 7 days Body weight: 60 kg TC (potential): 12500 cm ² /h TC (workwear (arms, body and legs covered)): 1400 cm ² /h TC (workwear (arms, body and legs covered) and gloves): 1250 cm ² /h TC (gloves): NA cm ² /h			
Number of applications & application rate: 3 x 0.125 kg a.s./ha Dermal absorption: 20 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Potential	0.08	50.2	0
Workwear	0.009	5.6	0
Workwear and gloves	0.008	5	0
Hands covered, no workwear			
Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Harvest (Brassica only) / Outdoor Work rate: 8 hours/day Interval: 7 days Body weight: 60 kg TC (potential): NA cm ² /h TC (workwear (arms, body and legs covered)): 5000 cm ² /h TC (workwear (arms, body and legs covered) and gloves): NA cm ² /h TC (gloves): NA cm ² /h			
Number of applications & application rate: 3 x 0.125 kg a.s./ha Dermal absorption: 20 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Potential			
Workwear	0.1	80.3	0
Workwear and gloves			

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Hands covered, no workwear			
Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Maintenance (Brassica only) / Outdoor Work rate: 8 hours/day Interval: 7 days Body weight: 60 kg TC (potential): NA cm²/h TC (workwear (arms, body and legs covered)): 5000 cm²/h TC (workwear (arms, body and legs covered) and gloves): NA cm²/h TC (gloves): NA cm²/h			
Number of applications & application rate: 3 x 0.125 kg a.s./ha Dermal absorption: 20 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days			
Potential			
Workwear	0.1	80.3	0
Workwear and gloves			
Hands covered, no workwear			
Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Reaching, picking (all except Brassica) / Outdoor Work rate: 8 hours/day Interval: 14 days Body weight: 60 kg TC (potential): 5800 cm²/h TC (workwear (arms, body and legs covered)): 2500 cm²/h TC (workwear (arms, body and legs covered) and gloves): 580 cm²/h TC (gloves): NA cm²/h			
Number of applications & application rate: 3 x 0.125 kg a.s./ha Dermal absorption: 20 % DFR: 3 µg/cm² foliage per kg a.s./ha DT50: 30 days			
Potential	0.1	81.6	0
Workwear	0.06	35.2	0
Workwear and gloves	0.01	8.2	0
Hands covered, no workwear			

A 3.2.1.2 Orchard

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Maintenance/thinning / Outdoor Work rate: 8 hours/day Interval: 7 days Body weight: 60 kg TC (potential): 22500 cm ² /h TC (workwear (arms, body and legs covered)): 4500 cm ² /h TC (workwear (arms, body and legs covered) and gloves): 2250 cm ² /h TC (gloves): NA cm ² /h			
Number of applications & application rate: 3 x 0.05625 kg a.s./ha Dermal absorption: 20 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Potential	0.3	163	22
Workwear	0.05	32.5	0
Workwear and gloves	0.03	16.3	0
Hands covered, no workwear			
Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Inspection, irrigation / Outdoor Work rate: 2 hours/day Interval: 7 days Body weight: 60 kg TC (potential): 12500 cm ² /h TC (workwear (arms, body and legs covered)): 1400 cm ² /h TC (workwear (arms, body and legs covered) and gloves): 1250 cm ² /h TC (gloves): NA cm ² /h			
Number of applications & application rate: 3 x 0.05625 kg a.s./ha Dermal absorption: 20 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Potential	0.04	22.6	0
Workwear	0.004	2.5	0
Workwear and gloves	0.004	2.3	0
Hands covered, no workwear			
Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Searching, reaching, picking / Outdoor Work rate: 8 hours/day Interval: 7 days Body weight: 60 kg TC (potential): 12500 cm ² /h TC (workwear (arms, body and legs covered)): 3500 cm ² /h TC (workwear (arms, body and legs covered) and gloves): 1250 cm ² /h TC (gloves): NA cm ² /h			
Number of applications & application rate: 3 x 0.05625 kg a.s./ha Dermal absorption: 20 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Potential	0.1	90.4	0
Workwear	0.04	25.3	0
Workwear and gloves	0.01	9	0
Hands covered, no workwear			

A 3.2.1.3 Field crops

Level of PPE	Total absorbed dose [mg/kg bw per day]	% of systemic AOEL	Re-entry restriction [days]
Inspection, irrigation / Outdoor Work rate: 2 hours/day Interval: 21 days Body weight: 60 kg TC (potential): 12500 cm ² /h TC (workwear (arms, body and legs covered)): 1400 cm ² /h TC (workwear (arms, body and legs covered) and gloves): 1250 cm ² /h TC (gloves): NA cm ² /h			
Number of applications & application rate: 2 x 0.125 kg a.s./ha Dermal absorption: 20 % DFR: 3 µg/cm ² foliage per kg a.s./ha DT50: 30 days			
Potential	0.05	31.6	0
Workwear	0.006	3.5	0
Workwear and gloves	0.005	3.2	0
Hands covered, no workwear			

Table A 6: Input parameters considered for the estimation of worker exposure (Broccoli)

Worker exposure from residues on foliage for Difeno Greener		
Crop type	Brassica vegetables	
Indoor or outdoor	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Worker's task	Reaching, picking	
Main body parts in contact with foliage	Hand and body	
Application rate of active substance	0.125 kg a.s./ha	i_AppRate
Number of applications	3	i_AppNo
Interval between multiple applications	7 days	i_AppInt
Half-life of active substance	30 days	d_HalfLifeAS
Multiple application factor	2.6	d_MAF
Dermal absorption of the product	3.30%	i_AbsorpProduct
Dermal absorption of the in-use dilution	20.00%	i_Absorplnuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.375 µg a.s./cm ²	d_DFR
Working hours	8 hr	d_WorkHr
Dermal transfer coefficient - Total potential exposure	5800 cm ² /hr	d_DermTcUCV
Dermal transfer coefficient - arms, body and legs covered	2500 cm ² /hr	d_DermTcCV1
Dermal transfer coefficient - hands, arms, body and legs covered	580 cm ² /hr	d_DermTcCV2
Inhalation transfer coefficient for automated applications	NA ha/hr*10 ⁻³	d_InhalTcAut
Inhalation transfer coefficient for cutting ornamentals	NA ha/hr*10 ⁻³	d_InhalTcCut
Inhalation transfer coefficient for sorting / bundling ornamentals	NA ha/hr*10 ⁻³	d_InhalTcSort

Table A 7: Estimation of longer term worker exposure towards Difenconazole according to EFSA guidance (Broccoli)

1. Total	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	8.9585702	3.8614527	0.8958570	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.1493095	0.0643575	0.0149310	
% of RVNAS	93.32%	40.22%	9.33%	

Table A 8: Input parameters considered for the estimation of worker exposure (Apple and Pear)

Worker exposure from residues on foliage for Difeno Greener		
Crop type	Pome fruit	
Indoor or outdoor	Outdoor	
Application method	Upward spraying	
Application equipment	Vehicle-mounted	
Worker's task	Searching, reaching, picking	
Main body parts in contact with foliage	Hand and body	
Application rate of active substance	0.05625 kg a.s./ha	i_AppRate
Number of applications	3	i_AppNo
Interval between multiple applications	7 days	i_AppInt
Half-life of active substance	30 days	d_HalfLifeAS
Multiple application factor	2.6	d_MAF
Dermal absorption of the product	3.30%	i_AbsorpProduct
Dermal absorption of the in-use dilution	20.00%	i_Absorpnuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.16875 µg a.s./cm ²	d_DFR
Working hours	8 hr	d_WorkHr
Dermal transfer coefficient - Total potential exposure	22500 cm ² /hr	d_DermTcUCV
Dermal transfer coefficient - arms, body and legs covered	4500 cm ² /hr	d_DermTcCV1
Dermal transfer coefficient - hands, arms, body and legs covered	2250 cm ² /hr	d_DermTcCV2
Inhalation transfer coefficient for automated applications	NA ha/hr*10 ⁻³	d_InhalTcAut
Inhalation transfer coefficient for cutting ornamentals	NA ha/hr*10 ⁻³	d_InhalTcCut
Inhalation transfer coefficient for sorting / bundling ornamentals	NA ha/hr*10 ⁻³	d_InhalTcSort

Table A 9: Estimation of longer term worker exposure towards Difenconazole according to EFSA guidance (Grape)

1. Total	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	15.6388833	3.1277767	1.5638883	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.2606481	0.0521296	0.0260648	
% of RVNAS	162.91%	32.58%	16.29%	

A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for Difenoconazole

Table A 10: Input parameters considered for the estimation of longer term resident exposure (Carrot)

Resident exposure for Difeno Greener		
Croptype	Root and tuber vegetables	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	i_FormVal
Buffer strip	2-3 m	i_Buffer
Application rate of the product	0.125 kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	0.625 g a.s./l	d_ConcAS
Dermal absorption of product	3.30%	i_AbsorpProduct
Dermal absorption of in-use dilution	20.00%	i_AbsorpInuse
Oral absorption	100.00%	i_AbsorpOrallnuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.375 µg a.s./cm ²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa	i_Volat
Concentration in air	0.001 mg/m ³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	0.47 ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327 ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010 ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022 ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318 ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18 ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009 ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017 ml spray dilution/person	
Exposure duration dermal	2 hours	d_ReExpDur
Exposure duration inhalation	24 hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25 hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%	d_ClothAF
Breathing rate adult	0.23 m ³ /day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07 m ³ /day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	5.60%	
Drift percentage on surface (mean)	4.10%	
Turf transferable residues percentage	5.00%	d_Turf
Transfer coeff. of surface deposits-adult	7300 cm ² /hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600 cm ² /hour	d_ReTCCh
Saliva extraction percentage	50.00%	d_SalExt
Surface area of hands mouthed	20 cm ²	d_AreaHM
Frequency of hand to mouth activity	9.5 events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25 cm ²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%	d_DRP
Transfer coefficient for entry into treated crops (75th percentile)	7500 cm ² /h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile)	2250 cm ² /h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980 cm ² /h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794 cm ² /h	d_TcEntryCh

Table A 11: Estimation of longer term resident exposure towards Difenoconazole according to EFSA guidance (Carrot)

1. Total					
1.1 1-3 year old child					
	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0336550	0.0107000	0.0104611	0.0948072	0.1125082
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0033655	0.0010700	0.0010461	0.0094807	0.0112508
% of RVNAS	2.10%	0.67%	0.65%	5.93%	7.03%
1.2 Adult					
	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0482375	0.0138000	0.0229672	0.3160240	0.3055239
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0008040	0.0002300	0.0003828	0.0052671	0.0050921
% of RVNAS	0.50%	0.14%	0.24%	3.29%	3.18%

Table A 12: Input parameters considered for the estimation of longer term resident exposure (Apple and Pear)

Resident exposure for Difeno Greener		
Croptype	Pome fruit	
Application method	Upward spraying	
Application equipment	Vehicle-mounted	i_AppEquip
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	i_FormVal
Buffer strip	5 m	i_Buffer
Application rate of the product	0.05625 kg a.s./ha	i_AppRate
Concentration of active substance (in-use dilution for liquid applications)	0.5625 g a.s./l	d_ConcAS
Dermal absorption of product	3.30%	i_AbsorpProduct
Dermal absorption of in-use dilution	20.00%	i_Absorplnuse
Oral absorption	100.00%	i_AbsorpOrallnuse
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.16875 µg a.s./cm ²	d_DFR
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10 ⁻³ Pa	i_Volat
Concentration in air	0.001 mg/m ³	d_AirCon
Resident dermal spray drift exposure 75th percentile - adult	5.63 ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	1.689 ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00210 ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00164 ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	3.68 ml spray dilution/person	
Resident dermal spray drift exposure mean - child	1.11 ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00170 ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00133 ml spray dilution/person	
Exposure duration dermal	2 hours	d_ReExpDur
Exposure duration inhalation	24 hours	d_ReExpDurInhal
Exposure duration entry into treated crops	0.25 hours	d_ExpDurTreatCrop
Light clothing adjustment factor	18.0%	d_ClothAF
Breathing rate adult	0.23 m ³ /day/kg	d_BreathRAd
Breathing rate child (1-3 year old)	1.07 m ³ /day/kg	d_BreathRCh
Drift percentage on surface (75th percentile)	15.79%	
Drift percentage on surface (mean)	11.69%	
Turf transferable residues percentage	5.00%	d_Turf
Transfer coeff. of surface deposits-adult	7300 cm ² /hour	d_ReTCAd
Transfer coeff. of surface deposits-child (1-3 year old)	2600 cm ² /hour	d_ReTCCh
Saliva extraction percentage	50.00%	d_SalExt
Surface area of hands mouthed	20 cm ²	d_AreaHM
Frequency of hand to mouth activity	9.5 events/hour	d_ReFreqHM
Ingestion rate for mouthing of grass per day	25 cm ²	d_MouthGrass
Dislodgeable residues percentage transferability for object to mouth	20.00%	d_DRP
Transfer coefficient for entry into treated crops (75th percentile)	7500 cm ² /h	d_TcEntryAd
Transfer coefficient for entry into treated crops (75th percentile)	2250 cm ² /h	d_TcEntryCh
Transfer coefficient for entry into treated crops (mean) - adult	5980 cm ² /h	d_TcEntryAd
Transfer coefficient for entry into treated crops (mean) - child	1794 cm ² /h	d_TcEntryCh

Table A 13: Estimation of longer term resident exposure towards Difenoconazole according to EFSA guidance (Apple and Pear)

1. Total					
1.1 1-3 year old child					
	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.1567347	0.0107000	0.0152050	0.0488715	0.1640696
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0156735	0.0010700	0.0015205	0.0048872	0.0164070
% of RVNAS	9.80%	0.67%	0.95%	3.05%	10.25%
1.2 Adult					
	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.5205488	0.0138000	0.0333824	0.1629050	0.5088402
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0086758	0.0002300	0.0005564	0.0027151	0.0084807
% of RVNAS	5.42%	0.14%	0.35%	1.70%	5.30%

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 relevant.