European Commission

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ISOFLUCYPRAM

Volume 3 – B.6 (PPP) – Isoflucypram EC 50

Rapporteur Member State : United Kingdom
Co-Rapporteur Member State : France

Version History

When	What
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B.6. TOXICOLOGY AND METABOLISM DATA AND ASSESSMENT OF RISKS FOR HUMANS

The representative product, ISY EC 50 (also referred to as Isoflucyram EC 50) is an emulsifiable concentrate (EC) containing 5% isoflucypram. It is used as a professional fungicide on cereal crops.

B.6.1. ACUTE TOXICITY OF PLANT PROTECTION PRODUCT

There are no studies addressing the acute toxicity, skin and eye irriation or skin sensitization potentential of the respresenative product ISY EC 50 (Isoflucypram EC 50). The toxicological data requirements for the representative product have been addressed by applying the calculation method of Regulation (EC) No 1272/2008 to its components. Information on the acute toxicity and other hazard properties of all components has been obtained from the SDS (Safety Data Sheets) provided by the applicant. The outcome of the calculation is summarized below. For further details please see volume 4, section C.1.3.

For each co-formulant described in Vol 4, section C.1.3, the Applicant has also provided alternative components. These are considered toxicologically equivalent.

B.6.1.1. Oral

The representative formulation ISY EC 50 contains no ingredients relevant for calculation of an oral ATEmix. Therefore, ISY EC 50 should not be classified for oral toxicity according to Regulation (EC) 1272/2008.

B.6.1.2. Dermal

The representative formulation ISY EC 50 contains no ingredients relevant for calculation of an oral ATEmix. Therefore, ISY EC 50 should not be classified for dermal toxicity according to Regulation (EC) 1272/2008.

B.6.1.3. Inhalation

The representative formulation ISY EC 50 contains two ingredients (the active substance and one co-formulants) relevant to the calculation of an inhalation ATEmix. The calculation method shows that the presence of these two ingredients does not require that ISY EC 50 to be classified for inhalation toxicity.

B.6.1.4. Skin irritation

The representative formulation ISY EC 50 contains no ingredients classified for skin corrosive Category 1. However, it contains a component classified for skin irritation in category 2 at 37.75%. This level is above the generic concentration limit of ≥ 10% for classification of the mixture. Therefore, ISY EC 50 should be classified with Skin Irrit Category 2; H315 (Causes skin irritation).

B.6.1.5. Eye irritation

The representative formulation ISY EC 50 contains no ingredients classified for eye damage effects Category 1. However, it contains a component classified for eye irritation in category 2 at 37.75%. This level is above the generic concentration limit of ≥ 10% for classification of the mixture. Therefore, ISY EC 50 should be classified with Eye Irrit Category 2; H319 (Causes serious eye irritation).

B.6.1.6. Skin sensitization

The representative formulation ISY EC 50 contains the active substance isoflucypram which is proposed to be classified as category 1B for skin sensitization. The concentration of isoflucypram in the mixture at 5.15% is greater than the trigger value of ≥ 1% for classification for skin sensitization Category 1. Therefore, ISY EC 50 should be classified with Skin Sens 1; H317 (May cause an allergic skin reaction).

B.6.1.7. Supplementary studies on the plant protection product

Not required.

B.6.1.8. Supplementary studies for combinations of plant protection products

Not required.

B.6.2. DERMAL ABSORPTION

An *in vitro* dermal absorption study in human skin with ISY EC 50 was submitted with the original dossier. In September 2018, a triple-pack (including an *in vivo* dermal absorption study in the rat) was submitted by the Applicant. These additional studies were generated by the Applicant for the planned registration of the substance in North America. The UK RMS has evaluated only the *in vitro* dermal absorption study in human skin and disregarded the triple-pack approach as this involves vertebrate testing. Consideration of the triple-pack approach would be in breach of Art 62 of Regulation 1107/2009.

In vitro human dermal absorption study with ISY EC 50

Study	BCS-CN88460 EC 50 [14C]-BCS-CN88460 - In vitro dermal absorption study using human skin
Reference	Blanck, 2017
Test facility	Bayer S.A.S. Crop Science Division, Sophia Antipolis Cedex, France
Report reference	SA 16319
Guideline(s)	OECD No.: 428 (2004)
Deviations from the guideline	None
GLP	Yes. Signed QA and GLP certificates provided
Test material	14C-labelled isoflucypram; Batch: KML 10306, Purity >99% w/w ; specific activity : 4.22 MBq/mg
Study acceptable	Yes

The *in vitro* dermal penetration of isoflucypram formulated as ISY EC 50 through human skin has been investigated. The available study was conducted in accordance with OECD test guideline 428, with GLP certification and has been evaluated in accordance with the EFSA guidance on dermal absorption (2012).

Method, guideline, GLP status, reference	**Species**	**Test substance, dose levels, duration of exposure**	**Dermal absorption results**
In vitro dermal penetration OECD 428 GLP compliant	Human abdominal skin, dermatomed (split thickness), thickness of 350-450 µm 6 donors per concentration Receptor fluid: Eagle's medium supplemented with 5% bovine serum albumin and gentamycin	Isoflucypram concentrate 50 mg/ml Spray dilution 0.1875 mg/ml (g/L) 8-hour exposure 24-hour sampling	High-dose concentrate = 2% Low-dose spray dilution =5%

In an *in vitro* experiment, the dermal penetration through human dermatomed skin of isoflucypram was investigated at two concentrations corresponding to the neat product (50 g /L =5%) and one representative spray dilution (0.1875 g/L = 0.01875%). The formulation used in this experiment was the emulsifiable concentrate ISY EC 50 (containing 50 g/L isoflucypram).

Both the emulsifiable concentrate and the representative spray dilution were applied to human (abdomen) dermatomed skin from 6 female donors each, at the rate of 10 µl/cm² exposed skin. The skin was mounted into modified Franz-type flow-through diffusion cells. The exposure of the skin to the test material lasted 8 hours; thereafter, the skin was thoroughly washed with freshly prepared 1% v/v Tween 80 in PBS. Samples of the receptor fluid were taken at hourly intervals for the duration of the study (24 hours) after the start of the exposure in order to determine kinetic parameters (lag phase, absorption rate and permeability constant). Prior to the experiment, the skin-sample integrity was determined by measurement of the trans-epidermal electrical resistance, the trans-epidermal water loss and visual inspection. At the end of the experiment, cells were assessed to be valid if total recoveries fulfilled guideline requirements (a total recovery per membrane of 100 ± 10%) and if clearly aberrant, penetration kinetics and aberrant skin wash after the 8-hour exposure period were not observed. Good recovery was obtained for the neat formulation and the spray dilution, with mean total recoveries of radioactivity in the range of 96% to 102% of the applied dose.

At the end of the study (24 hour after application), each skin preparation was tape-stripped to remove the *stratum corneum*. This involved the application of Monaderm adhesive tape (Monaderm, Monaco) for 5 seconds before the tape was carefully removed against the direction of hair growth. This procedure was continued until a 'shiny' appearance of the epidermis was evident, which indicated that the stratum corneum had been removed. The tape-strips (from a minimum of 6 to a maximum of 10 tape strips) were collected into scintillation vials for analysis. The skin surrounding the application site (surrounding skin) was separated from the treated skin. Both surrounding skin and tape-stripped treated skin were retained for analysis.

The mean recoveries of the different compartments are presented in the table below. For the formulation concentrate, 4 cells were used to determine the dermal penetration value, and for the spray dilution 6. For the concentrate, 2 skin preparations (H03 and H04) were excluded from the calculation of the dermal absorption value as they were clear outliers and failed the acceptance criteria. Total recovery in these two cells was low (87 - 88% compared to a mean for the reaming 4 cells of 101.6%) with skin wash at 8 hour also being unusually low (36 – 75% compared to a mean for the remaining 4 cells of 98%). Four cells is the minimum for an acceptable study.

No information on lag times was available. The achieved concentrations were at least 10 times lower than the determined solubility concentration. Therefore, solubility of the test material in the receptor fluid was not a rate-limiting step. Measurements of the homogeneity of the two concentrations of formulation applied indicated that it was acceptable.

The full recoveries and overall dermal penetration rates are shown in the table below. In both groups, absorption was incomplete; at 12 hours, the total penetrated radioactivity recovered in the receptor medium for the concentrate and spray dilution was 24% and 62%, respectively. Isoflucypram was demonstrated to be soluble in the receptor fluid at a concentration of 0.6 mg/ml. The maximal concentration per hour of [14C] isoflucypram in the receptor fluid was 39 ng/ml.

Summary table of recoveries and overall dermal penetration

Dose Group	**High Dose (concentrate)**	**Low Dose (dilution) 0.1875 g/l**
Target Concentration (mg/ml)	50	0.1875
Target Dose (µg/cm²])	500	1.1875
Valid Cells	4	6
	Amount recovered as % of dose (mean+/-SD)	**Amount recovered as % of dose (mean+/-SD)**
Unabsorbed Dose		
Skin washing – 8 h	98.1 ± 5.61	85.3 ± 1.16
Skin washing - 24h	0.91 ± 0.996	2.89 ± 0.795
Donor Chamber wash	0.27 ± 0.297	0.45 ± 0.37
Dose associated with skin		
Tape strips (1 and 2)	0.98 ± 0.943	2.53 ± 0.306
Remainig 15 tape strips (excluding 1 and 2)	*0.51 ± 0.327*	*2.78 ± 0.613*
Skin preparation	*0.70 ± 0.491*	*0.86 ± 0.445*
Total absorobed from skin compartment	***1.21 ± 0.795***	***3.63 ± 0.663***

Absorbed dose		
Sum of receptor samples 0-24h	*0.11 ± 0.074*	*1.48 ± 0.831*
Residual Receptor fluid*	*0.02 ± 0.016*	*0.07 ± 0.040*
Receptor chamber wash	*0.04 ± 0.088*	*ND*
Total absorbed from the receptor compartment	***0.17 ± 0.142***	***1.55 ± 0.867***
Total Recovery	**101.6 ± 5.00**	**96.3 ± 1.01**
Absorption essentially complete at the end of the study (>75% absorption within half of the study duration)	**No -** % of dose in the receptor fluid up to 12 hours was 24%	**No** - % of dose in the receptor fluid up to 12 hours was 62%
SD greater than 25% of mean	Yes	No
Recovery < 95%	No	No
STUDY: **Total % Potentially Absorbable**[b]	**Give the Mean +/- SD** **1.39 ± 0.907** (65% of mean)	**Give the Mean +/- SD** **5.19 ± 1.09** (21% of mean)
Absorption estimate for risk assessment	**2.3 % (rounded off to 2%)**	**5.19% (rounded off to 5%)**

[a] In accordance with the EFSA Guidance on Dermal Absorption (2012) one standard deviation was added to the mean % dermal penetration in cases where the standard deviation was ≥ 25 % of the mean value. This value was then rounded to the required number of significant figures.

[b]: total % absorbed from receptor compartment + total % absorbed from the skin compartment. The presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the excel software

*Residual receptor fluid = the receptor fluid remaining in the cell and outlet tubing at the end of the experiment

In line with the EFSA Guidance on Dermal Absorption (EFSA Journal 2012;10(4):2665), the radioactivity from the following samples was regarded to have been absorbed. If the sample period is 24 hours and over 75 % of the total absorption (receptor fluid) occurred within half the duration of the sampling period (12h), then absorption = receptor fluid + receptor chamber washes + skin samples (excluding all tape strips). If the percentage of radioactivity found in the receptor fluid during the first 12 hours is below 75% of the total directly absorbed fraction, the radioactivity found in the *stratum corneum* (except tape strips 1 and 2) has to be included in the potentially absorbable fraction.

The following dermal absortion values can be calculated:

Concentrate (5% isoflucypram)
Total in the receptor compartment (0.17%) + Skin + tape strips excluding strips 1 and 2 (0.7+0.51) = 1.39% (SD = 0.907). The SD represents 65% of the mean. By adding the SD, a value of 2.3% is calculated. This can be rounded off to **2%.**

Tested Dilution (0.01875% isoflucypram)
Total in the receptor compartment (1.55%) + Skin + tape strips excluding strips 1 and 2 (0.86+2.78) = 5.19 (SD = 1.09). The SD represents 21% of the mean and therefore it does not need to be added. Overall, a dermal absorption of 5.19% can be calculated. This can be rounded off to **5%**.

Overall, dermal absorption values of **2%** and **5%** for isoflucypram in the **concentrate** (5% = 50 g/L) and **tested dilution** (0.01875% = 0.1875 g/L) of ISY EC 50, respectively can be determined.

Extrapolation to in-use dilution of ISY EC 50
It should be noted that the highest in-use dilution of ISY EC 50 from the GAP Table (0.1875 g/L) corresponds to the tested dilution. Therefore, a dermal absorption of 5% is appropriate for the highest in-use dilution and conservative for the lowest in-use dilution.

B.6.3. AVAILABLE TOXICOLOGICAL DATA RELATING TO CO-FORMULANTS

SDS have been submitted for all of the co-formulants listed in Vol 4, section C.1.3. Co-formulants classified for acute toxicity, skin and eye irritation and skin sensitisation have been considered above. In addition to these, ISY EC 50 contains one co-formulant (at 37.5%) in excess of the concentration limit (20%) triggering classification for STOT-SE category 3 (respiratory irriation) (H335). It also contains one co-formulant (at 20%) in excess of the concentration limit (10%) triggering classification for aspiration hazard, Category 1 (H304). Furthermre, as the kinematic viscosity is below 20.5 mm2/s, ISY EC 50 requires classification with H304 (May be fatal if swallowed and enters the airways).

For further details please see volume 4, section C.1.3.

Overall toxicological classification of ISY EC 50

Skin Irrit 2; H315 (Causes skin irritation)
Eye Irrit 2; H319 (Causes serious eye irritation)
Skin Sens 1; H317 (May cause an allergic skin reaction)
STOT SE 3; H335(May cause respiratory irritation)
Asp Tox 1; H304 (May be fatal if swallowed and enters the airways)

Overall toxicological classification of the in use dilution of ISY EC 50

ISY EC 50 concentrate is diluted 67 times (1.5 L of product with 100 L of water). In the in-use dilution, the concentrations of those ingredients which trigger the classification of the concentrated product are all below the relevant concentration limits. Therefore, the in-use dilution does not require classification for any toxicological hazard.

B.6.4. EXPOSURE DATA

'ISY EC 50' is an emulsifiable concentrate (EC) containing 50 g isoflucypram /L. It is used as a professional fungicide on cereal crops. A summary of the application parameters pertinent to operator, worker, resident and bystander exposure assessment for the 'ISY EC 50' are presented in Table B 6.4-1. Table B 6.4-2 presents the toxicological endpoints used to estimate systemic exposure to isoflucypram and the classification of 'ISY EC 50' for human health effects.

Estimates of operator, worker, bystander and resident exposure were conducted in line with the EFSA guidance (EFSA Journal 2014;12(10):3874, 55 pp.,) and the respective calculator (Version: 30 March 2016). It is noted that the product 'ISY EC 50' contains isoflucypram that has no significant acute toxicity and/or the potential to exert effects after a single dose and hence in this instance an acute exposure risk assessment is not required. 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.

Table B.6.4-1: Summary of 'ISY EC 50' application parameters pertinent to the operator, bystander, resident and worker exposure assessment

'ISY EC 50'	
Formulation type	EC containing 50 g/L isoflucypram
Use	Fungicide on cereal crops
Application method	Field crop boom sprayer
Max individual dose	1.5 L product/ha (0.075 kg a.s/ha)
Max total dose	1.5 L product/ha (0.075 kg a.s/ha)
Application volume	100 – 400 L/ha
Spray concentration	0.1875 g/L - 0.75 g/L
Number of applications	1
Timing of application	BBCH 30 - BBCH 69
Vapour pressure	$< 5 \times 10^{-5}$ Pa at 25 °C

Table B.6.4-2: Summary of 'ISY EC 50' toxicological endpoints and classification for human health effects

'ISY EC 50'	
Systemic AOEL	0.04 mg/kg bw/day
Dermal absorption	2 % concentrate (50 g/L) 5 % spray dilution (0.1875 g/L)
Product classification	Skin Irrit 2; H315 (Causes skin irritation) Eye Irrit 2; H319 (Causes serious eye irritation) Skin Sens 1; H317 (May cause an allergic skin reaction) STOT SE 3; H335(May cause respiratory irritation) Asp Tox 1; H304 (May be fatal if swallowed and enters the airways)
Spray classification	Unclassified for human health effects

B.6.4.1. Operator exposure

Exposure was calculated for application with a vehicle mounted boom sprayer with standard nozzles, and with standard work clothing. The dermal absorption value of 5% corresponding to the highest spray dilution of 0.1875 g a.s./L was applied to calculate exposure during application and this estimate is considered to cover also exposure for higher spray concentrations. A summary of the estimated long term exposure is provided in the Table B.6.4.1-1 with outputs from the EFSA calculator provided in Appendix A, estimate 1.

Table B.6.4.1- 1 EFSA calculator estimates of long-term exposure to isoflucypram for operators applying 'ISY EC 50' through field crop boom sprayers

Model data	**Isoflucypram**	
	Total absorbed dose (mg/kg bw/day)	**% of systemic AOEL**
Scenario: Cereals / Outdoor / Downward spraying / Vehicle-mounted Formulation type: Emulsifiable Concentrate Work rate: 50 ha Season: Not relevant		
Application rate	0.075 kg a.s/ha	
Level of PPE	Work wear (arms, body and legs covered) M/L and A	
Spray application outdoor (AOEM**;** 75th percentile) Body weight: 60 kg	0.0052	12.94%
M/L = mixing and loading A = application		

The estimated long-term operator exposure to isoflucypram is calculated to be within acceptable limits and equal to 13% of the AOEL for an operator that applies the product 'ISY EC 50' without using PPE.

Local effects risk assessment
The product 'ISY EC 50', is classified for human health effects as eye irritant Cat 2, skin irritant Cat 2 and skin sensitizer Cat 1, hence the following PPE is required: suitable protective clothing (coveralls), suitable protective gloves and face protection (face shield) when handling the concentrate.

B.6.4.2. Bystander and resident exposure

The product 'ISY EC 50' contains the active substances isoflucypram that does not have significant acute toxicity or the potential to exert toxic effects after a single exposure, therefore no bystander risk assessment is required and

the exposure risk assessment for residents also covers bystander exposure. It is noted that the spray dilution is not classified for human health effects, thus no local effect risk assessment is required for bystanders and residents. Systemic exposure was calculated for application with a vehicle mounted boom sprayer with standard nozzles and for 2-3m buffer zones. Following the conservative approach resident exposure was calculated for the scenario of 100 L/ha spray dilution and using the 5% dermal absorption value. A summary of the estimated resident exposure and comparison with the AOEL is provided in the Table B.6.4.2- 1 with outputs from the EFSA calculator provided in Appendix A, estimate 2.

Table B.6.4.2- 1 EFSA calculator estimate of resident exposure to isoflucypram for the proposed use of 'ISY EC 50' through a field crop boom sprayer

		Isoflucypram	
Model data	**Exposure**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Scenario: Cereals / Outdoor / Downward spraying / Vehicle-mounted Formulation type: Emulsifiable Concentrate Buffer zone: 2-3 m Drift reduction technology: not applicable DT_{50}: 30 days (default) Initial DFR: 3 µg/cm^2/kg a.s./ha (default) Season: not applicable			
Number of applications and application rate:		1 x 0.075 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0010	2.56%
	Vapour (75th perc.)	0.0011	2.68%
	Deposits (75th perc.)	0.0001	0.29%
	Re-entry (75th perc.)	0.0006	1.58%
	Sum (mean)	0.0022	5.56%
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0002	0.61%
	Vapour (75th perc.)	0.0002	0.58%
	Deposits (75th perc.)	0.0000	0.06%
	Re-entry (75th perc.)	0.0004	0.88%
	Sum (mean)	0.0006	1.61%

An acceptable resident (and bystander) exposure to isoflucypram is predicted for an unprotected child and adult for individual pathways and the mean of all pathways for which exposure is 5.6% (child) and 1.6% (adult) of the AOEL respectively.

B.6.4.3. Worker exposure

A first-tier exposure assessment for workers undertaking crop inspection/irrigation activities in a cereal crop was undertaken using the EFSA calculator. A summary of the estimated long-term exposure and comparison with the AOEL is provided in the Table B.6.4.3-1 with outputs from the EFSA calculator provided in Appendix A, estimate 3.

Table B.6.4.3.1-1: EFSA calculator estimate of worker exposure to isoflucypram for the proposed use of 'ISY EC 50' through a field crop boom sprayer

Model data	**Level of PPE**	**Isoflucypram**	
		Total absorbed dose (mg/kg bw/day)	**% of systemic AOEL**
Outdoor cereals Inspection / irrigation Work rate: 2 hours/day, DT50: 30 days (default) Initial DFR: 3 µg/cm^2/kg a.s./ha (default)			
Number of applications and application rate:		1 x 0.075 kg a.s/ha	
Body weight: 60 kg	Work wear (arms, body and legs covered) TC: 1400 cm^2/person/h	0.0005	1.31%

The resultant worker exposure was equal to 1.3% of the AOEL for isoflucypram, for a worker performing crop inspection/ irrigation activities without the use of PPE. As worker re-entry activities will take place outdoors, it is assumed that workers will be wearing normal work wear (arms, body and legs covered).

B.6.5. EXPOSURE AND RISK ASSESSMENT

The non-dietary human exposure risk assessment is presented above for isoflucypram based on the representative product 'ISY EC 50' which is used as a fungicide in cereals and contains 50 g a.s./ L. Exposure was estimated using the EFSA guidance (EFSA Journal 2014;12(10):3874, 55 pp.,) and the respective calculator. For operators, workers, bystanders and resident the exposure risk assessment was conducted using the default values in accordance with the EFSA guidance, the highest spray concentration and the highest dermal absorption value established based on the dermal absorption studies. It was assumed that the product is applied using standard spray nozzles. The product 'ISY EC 50' contains the active substances isoflucypram that does not have significant acute toxicity or the potential to exert toxic effects after a single exposure, therefore no acute risk assessment is required. 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. Thus, long-term exposure assessment also covers acute exposure assessment.

The operator exposure assessment undertaken indicates that the proposed uses of 'ISY EC 50' through field crop boom sprayers will result in acceptable systemic operator exposure, equal to 13% of the AOEL for isoflucypram, for an operator that applies the product 'ISY EC 50' wearing normal workwear (arms, legs and body covered) and no PPE. It is noted that due to the classification of the representative product 'ISO EC 50' for human health effects, the following PPE is required for operators: suitable protective clothing (coveralls), suitable protective gloves and face protection (face shield) when handling the concentrate. The resident (and bystander) exposure assessment undertaken indicates that the proposed uses of 'ISY EC 50' through field crop boom sprayers will result in acceptable risk to an unprotected child and adult. The resident exposure (see Table B.6.4.2- 2) was acceptable for individual pathways and the mean of all pathways for which exposure is 5.6% (child) and 1.6% (adult) of the AOEL for isoflucypram respectively. The worker exposure assessment undertaken indicates that the proposed uses of 'ISY EC 50' through field crop boom sprayers will result in acceptable risk for workers performing crop inspection/ irrigation activities without the use of PPE. The worker exposure (see Table B.6.4.3.1-1) is predicted to be 1.3% of the AOEL for isoflucypram for a worker wearing normal workwear (arms, legs and body covered).

In conclusion, the operator, bystander, resident and worker risk assessment presented above demonstrates an acceptable risk to isoflucypram under conditions of intended uses of the representative product 'ISY EC 50', thus a safe use can be concluded and a further risk assessment is not required.

B.6.6. REFERENCES 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	Data protection claimed Y/N	Justification if data protection is claimed	Owner	Previous evaluation
KCP 7.3 / 01	Blanck, M.	2017	BCS-CN88460 EC 50 [14C]-BCS-CN88460 - In vitro dermal absorption study using human skin Bayer S.A.S., Crop Science Division, Sophia Antipolis, France Bayer Report No.: SA 16319 Date: 2017-04-28 GLP/GEP: Yes, unpublished	N	Y	New data for a new active substance	Bayer	No

B.6.7. APPENDIX A: EXPOSURE CALCULATIONS

Estimate 1: Operator Exposure – Standard Nozzles, workwear

Operator exposure for ISY EC 50 outdoor spray applications

Application rate of active substance	0.075	kg a.s./ha	*i_AppRate*
Assumed area treated	50	ha/day	*d_AreaTreated*
Amount of active substance applied	3.75	kg a.s./day	*i_AmoutAS*
Dermal absorption of the product	2.00%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	5.00%		*i_AbsorInuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

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

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	13436	49808	AOEM	
	Body	9033	105742	AOEM	
	Head	195	1067	AOEM	
	Protected hands (gloves)	81	743	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	77	548	AOEM	
	Protected head (hood and face shield)	3	60	AOEM	
	Inhalation	5	30	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	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	556	6034	AOEM	
	Body	311	1603	AOEM	
	Head	15	44	AOEM	
	Protected hands (gloves)	87	3888	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	9	21	AOEM	
	Inhalation	2	6	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	

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.5048591	0.3106090
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0084143	0.0051768
% of RVNAS	21.04%	12.94%

Estimate 2: Resident Exposure – Standard Nozzles, 2-3 m buffer zone

Resident exposure for ISY EC 50				
Croptype	Cereals			
Application method	Downward spraying			
Application equipment	Vehicle-mounted			*i_AppEquip*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.			*i_FormVal*
Buffer strip	2-3	m		*i_Buffer*
Application rate of the product	0.075	kg a.s./ha		*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	0.75	g a.s./l		*d_ConcAS*
Dermal absorption of product	2.00%			*i_AbsorpProduct*
Dermal absorption of in-use dilution	5.00%			*i_AbsorpInuse*
Oral absorption	100.00%			*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.225	µg a.s./cm^2		*d_DFR*
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa		*i_Volat*
Concentration in air	0.001	mg/m^3		*d_AirCon*
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person		
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person		
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person		
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person		
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person		
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person		
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person		
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person		
Exposure duration dermal	2	hours		*d_ReExpDur*
Exposure duration inhalation	24	hours		*d_ReExpDurInhal*
Exposure duration entry into treated crops	0.25	hours		*d_ExpDurTreatCrop*
Light clothing adjustment factor	18.0%			*d_ClothAF*
Breathing rate adult	0.23	m^3/day/kg		*d_BreathRAd*
Breathing rate child (1-3 year old)	1.07	m^3/day/kg		*d_BreathRCh*
Drift percentage on surface (75th percentile)	5.60%			
Drift percentage on surface (mean)	4.10%			
Turf transferable residues percentage	5.00%			*d_Turf*
Transfer coeff. of surface deposits-adult	7300	cm^2/hour		*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour		*d_ReTCCh*
Saliva extraction percentage	50.00%			*d_SalExt*
Surface area of hands mouthed	20	cm^2		*d_AreaHM*
Frequency of hand to mouth activity	9.5	events/hour		*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2		*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20.00%			*d_DRP*
Transfer coefficient for entry into treated crops (75th percentile) - adı	7500	cm^2/h		*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile) - chi	2250	cm^2/h		*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h		*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h		*d_TcEntryCh*

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0102203	0.0107000	0.0011550	0.0063281	0.0222538
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0010220	0.0010700	0.0001155	0.0006328	0.0022254
% of RVNAS	2.56%	2.68%	0.29%	1.58%	5.56%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0145275	0.0138000	0.0015330	0.0210938	0.0386714
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0002421	0.0002300	0.0000256	0.0003516	0.0006445
% of RVNAS	0.61%	0.58%	0.06%	0.88%	1.61%

Estimate 3: Worker exposure

Worker exposure from residues on foliage for ISY EC 50			
Crop type	Cereals		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0.075	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.0		*d_MAF*
Dermal absorption of the product	2.00%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	5.00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0.225	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	0.2812500	0.0315000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0046875	0.0005250		
% of RVNAS	11.72%	1.31%		