REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: IND002B1760

Product name(s): --

Chemical active substance:

Cymoxanil, 450 g/kg

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(New authorisation)

Applicant: Indofil Industries (Netherlands) B.V.

Submission date: August 2022, updated May 2023

MS Finalisation date: May 2023 (initial Core Assessment)

September 2023, updated April 2024 (final Core Assessment)

Version history

When	What
August 2022	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
May 2023	Applicants' update according to Data Gap Clarification requests.
May 2023	Initial zRMS assessment The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are ~~struck through~~ and shaded for transparency.
September 2023	Final report (Core Assessment updated following the commenting period) Additional information/assessments included by the zRMS in the report in response to comments received from the cMS and the Applicant are highlighted in yellow. Information no longer relevant ~~is struck through~~ and shaded.
April 2024	Final report (Core Assessment updated following the commenting period) Additional information/assessments included by the zRMS in the report in response to comments received from the cMS and the Applicant are highlighted in blue. Not agreed or not relevant information are ~~struck through~~ and shaded for transparency.

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Reviewer comments:

This application has been submitted to support the authorization of the new product IN002B1760 in accordance with Article 33 of Regulation (EC) n. 1107/2009. The product is a WG formulation containing 450 g/kg cymoxanil; it was not the representative formulation of the EU review, but it is a new product not previously evaluated.
Poland is zRMS for this registration and assessed the application submitted for the first authorization of this product in Poland and in other MSs of the Central zone for field uses. This dossier is submitted in accordance with the Commission Regulation (EU) No 284/2013. In the Central zone, IN002B1760 is fungicide for the control of late blight in potato.

Cymoxanil was included into Annex I of Directive 91/414 according to Commission Directive 2008/125/EC of 19 December 2008 and approved under Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009.

In support of this application, reference is made to active substance data, please refer to the list of endpoints (EFSA Scientific Report (2008) 167, 1-116; SANCO/179/08 – 09/07/2010; original DAR and Final Addendum to the Draft Assessment Report-updated September 2008).

For the current product registration, APPL provided an assessment of the toxicological potential based on calculation method (ATEmix; for details refer Part C). zRMS PL, in accordance with the EC recommendations to avoid tests on animals, for the purposes of hazard classification use the data obtained using the calculation method and do not request for *in vivo* data.

NDE assessment for operator, workers and B&R exposure to the cymoxanil considering all critical use(s) and all tasks, identify safe use of the product IN002B1760.

The following risk mitigation measures (RMM) are required for field crops:
Operator:
Potato (max. 6 x 0.33 kg product/ha, interval 5 days)
- Tractor-mounted boom sprayer, downwards: Work-wear during mixing/loading and application,
- Manual, hand-held application (lance and knapsack): Work wear during mixing/loading and application and gloves in case of application with lance,
Workers:
Potato (max. 6 x 0.33 kg product/ha, interval 5 days)
- Work wear (arms, body and legs covered) during all worker re-entry tasks.

Note: Additional RMM resulting from hazard classification are required during handling and application of the PPP Protective clothing is always recommended; in addition protective gloves/eye protection/face protection for all tasks due to the hazardous properties of the product.

6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on IND002B1760 *

Product name and code	IND002B1760
Formulation type	formulation type [Code: WG]
Active substances (incl. content)	Cymoxanil (450 g/kg)
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 IND002B1760 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 IND002B1760 according to Regulation (EC) No 1272/2008

Hazard classes, categories	Acute oral tox cat.4 Skin Sens. 1, Repro. 2, STOT RE 2; Eye Irrit. 2
Hazard pictograms or Code(s) for hazard pictogram(s)	GHS07 GHS08
Signal word	Warning
Hazard statement(s)	H302 H317 H361fd H373 H319
Precautionary statement(s)	P201, P260, P273, P280, P308+P313, P305 + P351 + P338, P391, P501
Additional labelling phrases	~~To avoid risks to man and the environment, comply with the instructions for use.~~ [EUH401] To avoid risks to human health and the environment, comply with the instructions for use.

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for IND002B1760

	Result	PPE / Risk mitigation measures
Operators	Acceptable	Workwear is recommendend in all the tasks. Gloves in the manual application with lance. **zRMS:** Additional RMM resulting from hazard classyfication which are required during handling and aplication of the PPP: Protective clothing is always recommended; in addition protective gloves/eye protection/face protection for all tasks due to the hazardous properties of the product.
Workers	Acceptable	Potato: work wear for inspection and irrigation
Residents	Acceptable	None
Bystanders	Acceptable	None

The use of gloves and glasses are recommended for mixing and loading tasks due to the hazardous properties of the product (skin sensitizer and eye irritant).

No unacceptable risk for operators, workers, residents and bystanders was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in

Table 6.1-3 are applied.

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

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

1	2	3	4	5	6	7	8	9	10			
Use-No.*	**Crops and situation (e.g. growth stage of crop)**	**F, Fn, Fpn G, Gn, Gpn or I ******	**Application**		**Application rate**		**PHI (d)**	**Remarks:** **(e.g. safener/synergist (L/ha))** **critical gap for operator, worker, resident or bystander exposure based on [Exposure model]**	**Acceptability of exposure assessment**			
			Method / Kind **(incl. application technique *****)**	**Max. number (min. interval between applications)** **a) per use** **b) per crop/ season**	**Max. application rate kg as/ha** **a) a.s. 1**	**Water L/ha** **min / max**			**Operator**	**Worker**	**Residents**	**Bystander**
1	Potato (BBCH 12-95)	F	Sprayer LCTM	6 (5); 6 (5)	a) 0.1485	300 – ~~1000~~ 500	~~7~~ 5	EFSA Journal 2014;12(10):3874				
			Sprayer LCKH									
			Sprayer LCHH									

* 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:
No data gaps were identified.

6.2 Toxicological Information on Active Substance(s)

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

Table 6.2-1: Information on active substance

	Active substance
Common Name	Cymoxanil
CAS-No.	57966-95-7
Classification and proposed labelling	
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Acute oral tox. cat.4, Skin sens cat. 1, STOT RE 2 (blood, thymus), Repro cat. 2 GHS07 GHS08 H302, H317, H373 H361fd
Additional C&L proposal	-
Agreed EU endpoints	
AOEL systemic	0.01 mg/kg bw/d (corrected for 75% oral absorption)
Reference	EFSA Scientific Report (2008) 167, 1-116
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

A summary of the toxicological evaluation for IND002B1760 is given in the following tables. The justifications according to CLP calculation method are reported in detail in Appendix 2.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for IND002B1760

~~Type of test, species, model system (Guideline)~~ **Endpoint**	**Result**	**Acceptability**	**Classification (acc. to the criteria in Reg. 1272/2008)**	**Reference**
LD_{50} oral	> 300 mg/kg bw and < 2000 mg/kg bw	Yes	H302	Calculation method
LD_{50} dermal	> 2000 mg/kg bw	Yes	None	Calculation method
LC_{50} inhalation	> 5.0 mg/L air	Yes	None	Calculation method
Skin irritation	Non-irritant	Yes	None	Calculation method
Eye irritation	Irritant	Yes	H319	Calculation method
Skin sensitisation	Skin sensitising	Yes	H317	Calculation method
Supplementary studies for combinations of plant protection products	No data – not required	--		

According to the above toxicological conclusions the use of gloves and glasses are recommended for mixing and loading tasks due to the hazardous properties of the product.

Table 6.3-2: Additional toxicological information relevant for classification/labelling of IND002B1760

	Substance (concentration in product, % w/w)	**Classification of the substance (acc. to the criteria in Reg. 1272/2008)**	**Reference**	**Classification of product (acc. to the criteria in Reg. 1272/2008)**
Toxicological properties of active substance(s) (relevant for classification of product)	cymoxanil (45% (w/w))	Acute oral tox. cat.4 (criteria ≥ 25%) Skin sens cat.1 (criteria ≥ 1%) Repro. cat. 2 (criteria ≥ 3%) STOT RE cat. 2 (criteria ≥ 10%)	Annex VI Reg. 1272/2008	Acute oral tox cat.4; H302 Skin sens. cat.1; H317 Repro. cat. 2, H361fd STOT RE cat. 2 H373
Toxicological properties of non-active substance(s) (relevant for classification of product)	Coformulant 3 (2.9% (w/w))	Acute oral tox. cat.4 (criteria ≥ 25%) Skin irrit. cat 2 (criteria ≥ 10%) Eye Corr. cat. 1 (criteria ≥ 3%)	MSDS*	Eye Irrit. cat.2 H319
Further toxicological information	No data - not required			

* Material safety data sheet by the applicant

6.4 Toxicological Evaluation of Groundwater Metabolites

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

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in IND002B1760 are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in IND002B1760

	Cymoxanil	
	Value	**Reference**
Concentrate	0.38%	New study reported in Appendix 2
Dilution (1:4000)	28%	New study reported in Appendix 2

6.5.1 Justification for proposed values - cymoxanil

Proposed dermal absorption rates for cymoxanil are based on dermal absorption study on IND002B1760. The study results are summarised in the following table. Full summaries of study on the dermal absorption of IND002B1760 that have not previously been evaluated within an EU peer review process are described in detail in Appendix 2.

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

Test	Concentrate	Spray dilution (1:4000)	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference*
In vitro (human)	0.38%	28%	IND002B1760	Yes	Yes (see Appendix A 2.10)	Justification accepted. Endpoint can be used for current product (see Appendix A 2.10)	[redacted] 2022

* indicates that a study was reviewed at EU level

6.6 Exposure Assessment of Plant Protection Product (KCP 7.2)

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

Product name and code	IND002B1760
Formulation type	WG
Category	Fungicide
Active substance (incl. content)	**Cymoxanil** 450 g/kg
AOEL systemic	0.01 mg/kg bw/d
Inhalation absorption	100%
Oral absorption	75%
Dermal absorption	Concentrate: 0.38% Dilution: 28% (0.1125 g/L) (Based on product (formulation))

6.6.1 Selection of critical use(s) and justification

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

Justification

The applications use selected (potatoes) offers the worst-cases scenario for exposure to operator, worker, resident and bystander. The values used were considered to be the worst-case of each scenario.

For manual downward applications, the EFSA model for estimating operator exposure for hand-held application via a downward spray does not cover application rates < 1.5 kg a.s./ha and therefore it greatly overestimates the potential levels of exposure. Therefore, operator exposure has been estimated basing on upward spraying to obtain a more realistic assessment.

The assessment was performed considering default DT_{50} (30 days) and DFR (3 µg/cm^2 per kg a.s./ha) for first instance as required by the guideline. When the risk was not acceptable, some specific refinements are proposed (DT_{50}) were used.

6.6.2 Operator exposure (KCP 7.2.1)

6.6.2.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of IND002B1760 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 uses	**Potato (max. 6 x 0.33 kg product/ha, interval 5 days)**
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

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

		Cymoxanil	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to potato			
Application rate		0.1485 kg a.s./ha	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.0100	100.38
	Work wear (arms, body and legs covered) M/L and A	0.0069	69.30
Manual hand-held spray application outdoors to potato			
Application rate		0.1485 kg a.s./ha	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.2747	2747
	Work wear (arms, body and legs covered) M/L and A + gloves	0.0070	69.50
Manual knapsack spray application outdoors to potato			
Application rate		0.1485 kg a.s./ha	
Spray application (AOEM; 75th percentile) Body weight: 60 kg	Potential exposure	0.2171	2171
	Work wear (arms, body and legs covered) M/L and A	0.0091	90.78

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.

Conclusion

Potato (max. 6 x 0.33 kg product/ha, interval 5 days)

- Tractor-mounted boom sprayer, downwards
  ⇨ Work-wear during mixing/loading and application
- Manual, hand-held application (lance and knapsack)

⇨ Work wear during mixing/loading and application and gloves in case of application with lance

6.6.3 Worker exposure (KCP 7.2.3)

6.6.3.1 Estimation of worker exposure

Table 6.6-4 shows the exposure model(s) used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with IND002B1760 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)	**Potato (max. 6 x 0.33 kg product/ha, interval 5 days)**
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

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

		Cymoxanil	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Inspection and irrigation of potato Outdoor Work rate: 2 hours/day, DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: ~~7~~ 5 days			
Number of applications and application rate		6 x 0.1485kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm²/person/h	0.2382	2382
	Work wear (arms, body and legs covered) TC: 1400 cm²/person/h	0.0267	267
	Work wear (arms, body and legs covered) and gloves TC: - cm²/person/h	NA	NA
Refinement 1 - DT_{50}: 1 day **Inspection and irrigation of potato** Outdoor Work rate: 2 hours/day, DT_{50}: ~~30 days~~ 1 day DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: ~~7~~ 5 days			

Number of applications and application rate		6 x 0.1485kg a.s./ha	
Body weight: 60 kg	Potential TC: 12500 cm^2/person/h	0.0537	536.52
	Work wear (arms, body and legs covered) TC: 1400 cm^2/person/h	0.0060	60.09
	Work wear (arms, body and legs covered) and gloves TC: - cm^2/person/h	NA	NA

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

~~Not required.~~

Reviewer comment: Data summarized below has been update by the Applicant on zRMS request

The default DFR (Dislodgeable foliar residue) value was assumed to be 3 µg a.s./cm^2 /kg a.s./ha and used in the first tier. However, the risk is considered not acceptable taking into account this default. Therefore, a refinement DFR is proposed taking into account the behaviour of cymoxanil in some crops at the light of the available information.
DFR studies on tomatoes and grapes using IN002B1760 were performed by the Applicant in order to support the risk assessment for workers and residents in Southern zone. These obtained residue data together with the extrapolation from DFR studies and residue data to refine DT_{50} foliar of cymoxanil were used for a second tier of the risk assessment.

The residue data on potatoes, grapes and tomatoes were used to propose a DT_{50} foliar based on the behaviour of cymoxanil in different crops.
A short detail of DFR (Dislodgeable foliar residue) studies are reported below in order to show the kinetic behaviour and extrapolate a proper DT50 foliar on the base of the obtained data.

The proposed DT_{50} value for cymoxanil relied on the following experimental studies:

- in the residue studies (Koenings, I., 2009) conducted on grapes (low residue on day 0 in NEU trials A7115 BM1, A7115 CT1 and in SEU trials A7115 IT1, A7115 GR1)
- in the residue studies (Semrau, J. 2010) conducted on potato (no residue after the day of the application: N-EU trials F07W133R, G07W344R, S08-02370-01, PL07W020R; SEU trials: S07W130R, F07W135R, S08-02371-01, S07W131R as reported in Section B7.
- in the residue studies on tomato (Sala A., 2021) no residue found after three days after last application BF 21 03 BPL IT 01: 81047 and BF 21 03 BPL IT 02: 80031
- Two DFR studies conducted on grapes (Sala A., 2021a) and tomatoes (Sala A., 2021b)

Overall, the data contained in the study report can be used to determine the DT_{50} of residues on grape and tomato leaves. First order kinetic plot indicates that the DT_{50} of residues on grapes is about 1 day.

The two last studies on the product IN002B1760 will be analyzed deeply to support such affirmation. Please refer to dRR GH for the mentioned KCP.

- **KCP 7.2/01 (Sala A.; 2021 a) – Grapes (Trial 1 in Italy and Trial 2 in Spain)**

This study was conducted after five applications of IN002B1760 (cymoxanil 450 g/kg) to the grape. Overall, the data contained in the study report can be used to determine the DT_{50} of residues on grape

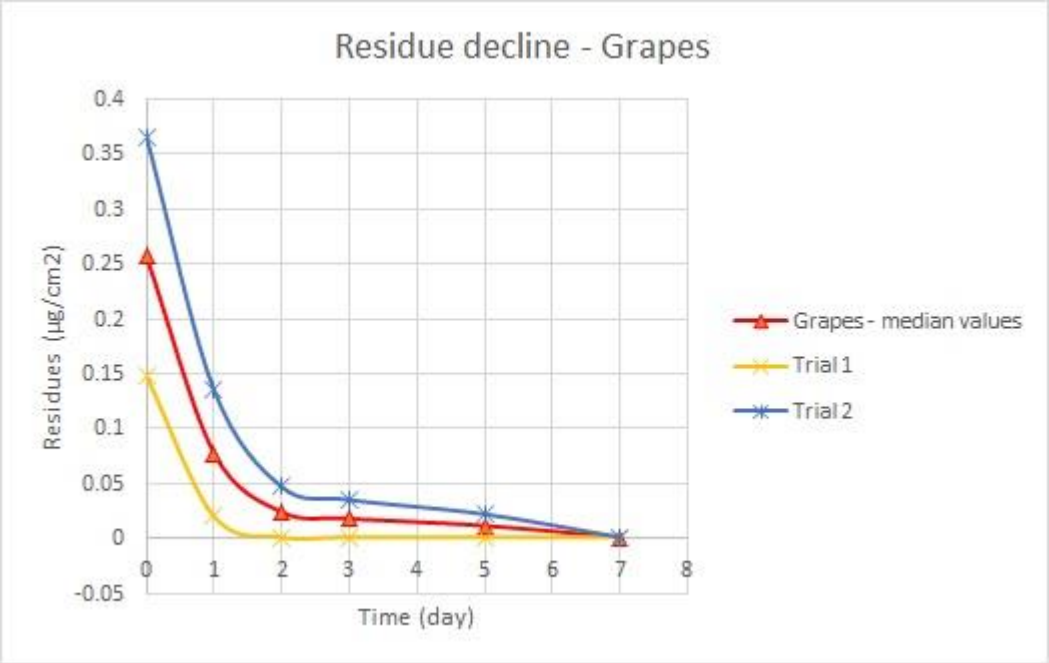
leaves. The table below summarizes the measured residues present of vine leaves and the dissipation curve.

The measured and median values for trial 1 and trial 2 are summarized in the following table.

Table a. Grapes foliar residues

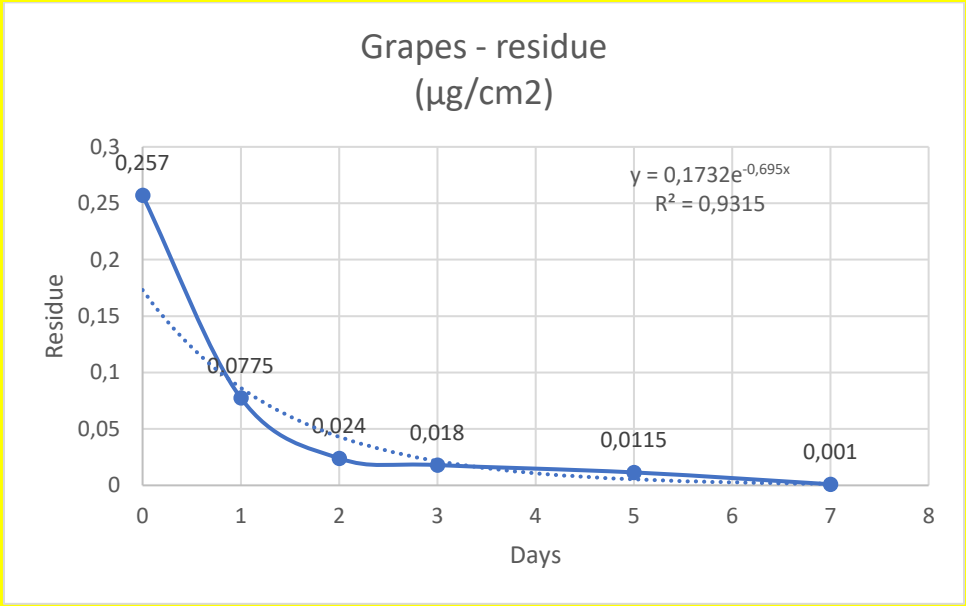
t (day)	residue Trial 1 (µg/cm²)	residue Trial 2 (µg/cm²)	residue Median value (µg/cm²)
0	0.148	0.366	0.257
1	0.02	0.135	0.0775
2	0.001	0.047	0.024
3	0.001	0.035	0.018
5	0.001	0.022	0.0115
7	0.001	0.001	0.001
10	0.001	0.001	0.001
14	0.001	0.001	0.001

Figure 1. Dissipation curve - First order kinetic of grapes in the different trials



First order kinetic plots indicate that the DT_{50} of residues on vine leaves is about 1.0 days.

Figure 2. Grape – sum of two trials results



Grapes – trial 1 - Italy

14.8 WEATHER CONDITIONS DURING APPLICATIONS

The weather conditions during application are reported in the following table:

Table 10: Wheather conditions at applications GLP-STUDY-21-45 Trial 1 – Italy

Application	Date	Plot	Air temp (°C)	Rainfall within 24 hours	Relative humidity (%)	Soil condition/ temperature (°C)	Foliage moisture	Cloud cover (%)	Wind speed range and direction (m/s)
A1	28/07/2021	T	28.9	No rain	37	Dry / 25.7	Dry	30	E→W / 0.5
A2	04/08/2021	T	27.8	No rain	41	Dry / 26.1	Dry	0	N→S / 0.7
A3	11/08/2021	T	28.5	No rain	44	Dry / 25.8	Dry	40	E→W / 1.0
A4	18/08/2021	T	27.8	No rain	32	Dry / 24.7	Dry	50	N.A. / 0
A5	25/08/2021	T	28.0	No rain	49	Dry / 25.4	Dry	20	E→W / 0.9

Grapes – trial 2 – Spain

Table 17: Weather conditions at applications

Application	Date	Plot	Air temp (°C)	Rainfall within 24 hours	Relative humidity (%)	Soil condition/ temperature (°C)	Foliage moisture	Cloud cover (%)	Wind speed range and direction (m/s)
A1	17/07/2021	T	19.7	No rain	75.9	Dry / 25.4	Dry	0	0 / N.A.[1]
A2	22/07/2021	T	24.4	No rain	37.9	Dry / 29.6	Dry	0	0 / N.A.
A3	28/07/2021	T	23.0	No rain	55.2	Dry / 27.5	Dry	0	0 / N.A.
A4	04/08/2021	T	21.4	No rain	60.3	Dry / 25.5	Dry	0	0 / N.A.
A5	11/08/2021	T	21.5	No rain	81.0	Dry / 26.7	Dry	60	0 / N.A.

[1]Not applicable

- **KCP 7.2/02 (Sala A.; 2021 b) – Tomatoes (Trial 1 in Italy and Trial 2 in Spain)**

This study was conducted after five applications of IN002B1760 (cymoxanil 450 g/kg) to the tomato. Overall, the data contained in the study report can be used to determine the DT_{50} of residues on tomato leaves. The table below summarizes the measured residues present of tomato leaves and the dissipation curve.

Table b. Tomatoes foliar residues

t (day)	residue Trial 1 (µg/cm²)	residue Trial 2 (µg/cm²)	residue Median value (µg/cm²)
0	0.179	0.107	0.143
1	0.052	0.022	0.037
2	0.008	0.006	0.007
3	0.001	0.001	0.001
5	0.001	0.001	0.001
7	0.001	0.001	0.001
10	0.001	0.001	0.001
14	0.001	0.001	0.001

First order kinetic plots indicate that the DT_{50} of residues on tomato leaves are about 1.0 days.

Figure 2. Dissipation curve - First order kinetic of tomatoes in the different trials

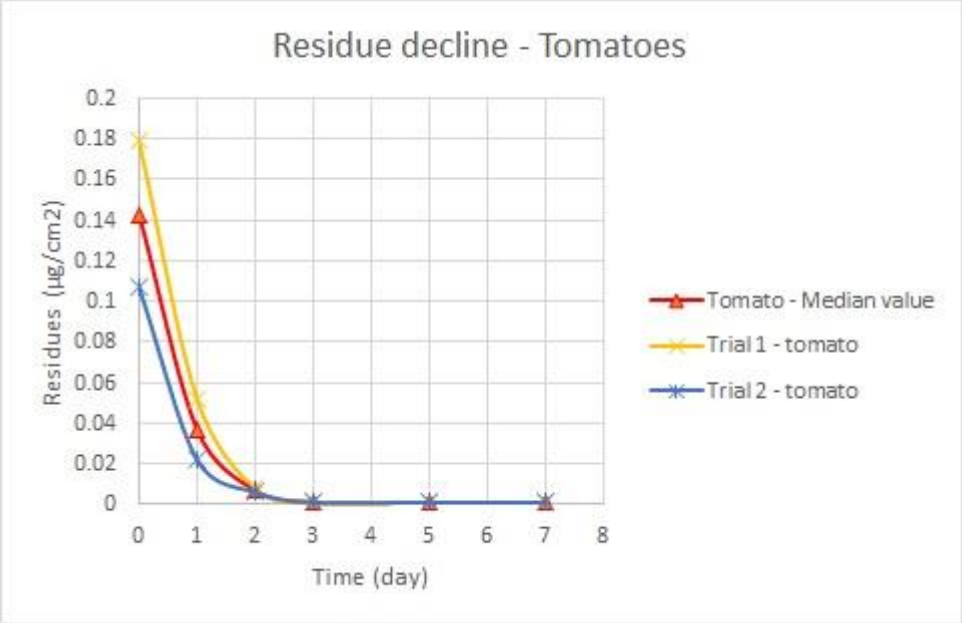
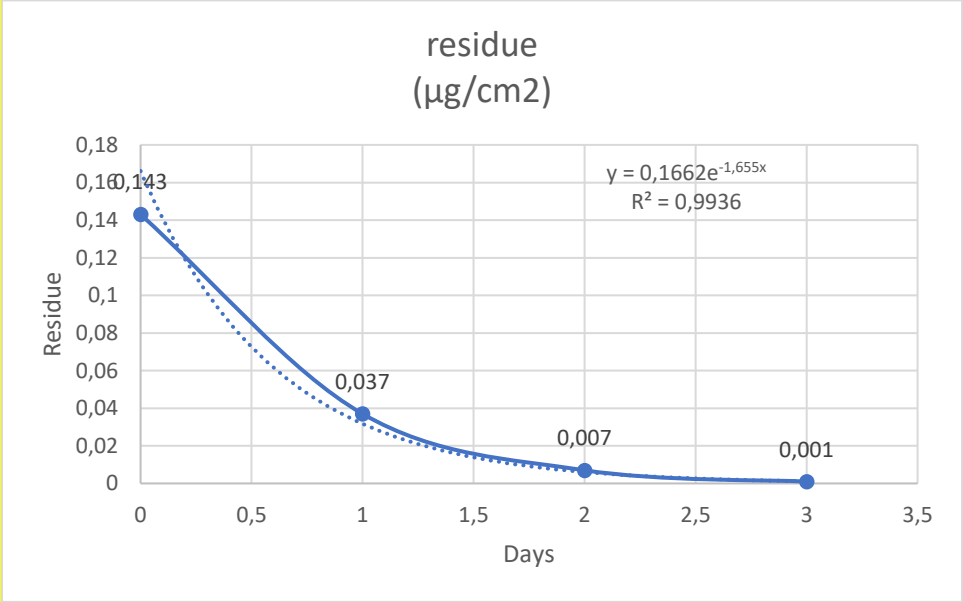


Figure 3. Tomato – sum of two trials results



Tomato – trial 1 - Italy

Table 10: Wheather conditions at applications

Application	Date	Plot	Air temp (°C)	Rainfall within 24 hours	Relative humidity (%)	Soil condition/ temperature	Foliage moisture	Cloud cover (%)	Wind speed range and direction (m/s)
A1	27/07/2021	T	28.2	No rain	32	Dry / 25.7	Dry	50	E→W / 0.7
A2	03/08/2021	T	27.4	No rain	44	Dry / 26.0	Dry	30	W→E / 1.1
A3	10/08/2021	T	28.0	No rain	80	Dry / 25.9	Dry	100	E→W / 0.4
A4	17/08/2021	T	27.0	No rain	39	Dry / 25.1	Dry	20	N.A. / 0
A5	24/08/2021	T	27.4	No rain	47	Dry / 24.9	Dry	50	W→E / 0.9

Tomato – trial 2 – Spain

15.8 WEATHER CONDITIONS DURING APPLICATIONS

The weather conditions during applications are reported in the following table:

Table 17: Wheather conditions at applications

Application	Date	Plot	Air temp (°C)	Rainfall within 24 hours	Relative humidity (%)	Soil condition/ temp. °C	Foliage moisture	Cloud cover (%)	Wind speed range and direction (m/s)
A1	02/08/2021	T	16.4	No rain	60.2	Moist / 19.4	Dry	0	0 / N.A.[1]
A2	09/08/2021	T	19.3	No rain	79.2	Moist / 20.8	Dry	100	0 / N.A.
A3	16/08/2021	T	19.6	No rain	72.0	Dry / 22.0	Dry	0	0 / N.A.
A4	23/08/2021	T	22.0	No rain	76.2	Dry / 17.8	Dry	0	0 / N.A.
A5	30/08/2021	T	18.2	No rain	68.7	Moist / 18.7	Dry	0	0 / N.A.

[1]Not applicable

Overall summaries on two DFR studies for DT_{50}

Since the dislodgeable residue results were in good accordance between the trials, the values obtained were considered together, and a median value was calculated as it was considered the more representative parameter.

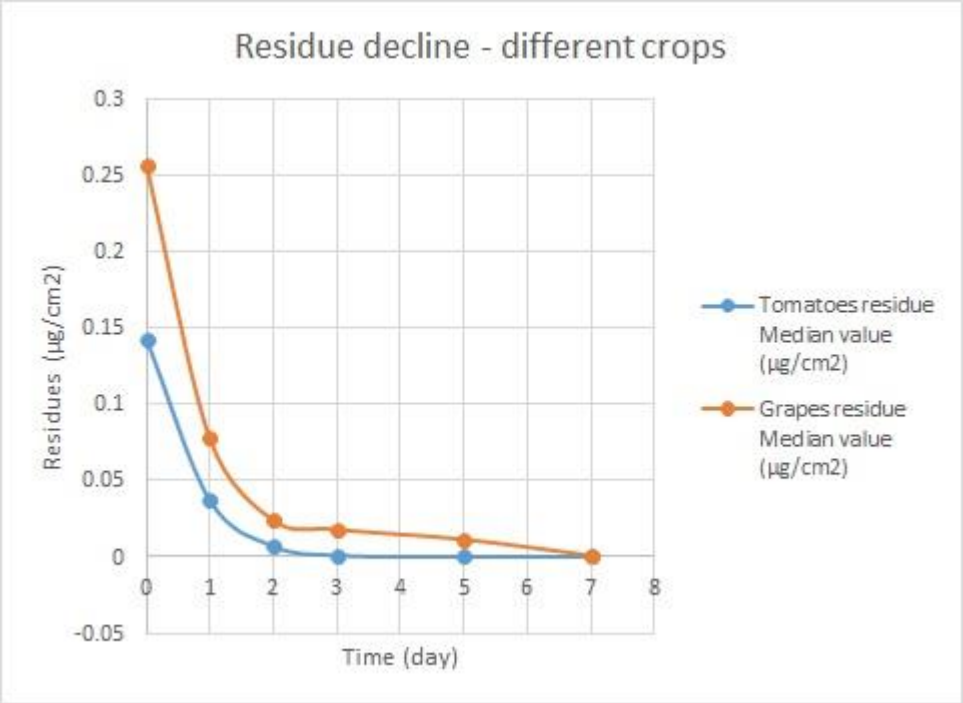
The measured and median values for trial 1 and trial 2 are summarized in the following table

Taking into account the two crops (grapes and tomatoes) in different conditions and the comparison of their residue behavior show how theirs first order kinetic is similar and they graphically allow extrapolating DT_{50} foliar value to apply in the crops.

Table c. Grapes and tomatoes median foliar residues

time	Tomatoes residue Median value (µg/cm^2)	Grapes residue Median value (µg/cm^2)
0	0.143	0.257
1	0.037	0.0775
2	0.007	0.024
3	0.001	0.018
5	0	0.0115
7	0	0.001

Figure 3.Comparison of dissipation curves - First order kinetic of grapes and tomatoes



First order kinetic plots indicate that the DT_{50} of residues on vine and tomato leaves are about 1.0 days.

Discussion

The first order kinetic plots of each trial in both crops show how is similar the behavior of cymoxanil after its application on different crops.

Moreover, the two studies are the lasts of lots residue studies on different crops for IN002B1760 and cymoxanil in general as cited above.

The same behavior was shown in all mentioned studies on different crops even if they are not directly performed in order to obtain for the determination of median dissipation foliar time.

The evidence of its dissipation after few hours is come into light graphically.

Furthermore, the cymoxanil behavior in soil could be considered as support since it is expected the same first order kinetic in that different matrix.

From residue point of view the comparability among potatoes and tomatoes is considered robust and reliable; however, it has been also considered the available data on grapes since the different data give further evidence of the wide behavior of cymoxanil.

Cymoxanil reveals the same behavior in the different matrices for different crops. It is expected and overall, it is reasonable to assume that the DT_{50} value of cymoxanil residues on the raw commodity samples would be approximately 1 day.

Overall, on the base of the above dissertation the resident exposure is refined with foliar DT_{50} of 1 day (tier 2, as cited in Table A.10).

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.

Conclusion

Based on the above calculations, the worker exposure for the intended GAP uses of IND002B1760is below the limit of 100% AOEL if the following label restrictions are taken into account:

Potato (max. 6 x 0.33 kg product/ha, interval 5 days)

- ⇨ Work wear (arms, body and legs covered) during all worker re-entry tasks

6.6.4 Resident and bystander exposure (KCP 7.2.2)

6.6.4.1 Estimation of resident and bystander exposure

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 exposure to cymoxanil. 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 uses	**Potato (max. 6 x 0.33 kg product/ha in 300 L/ha, interval 5 days)**
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

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

		Cymoxanil	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to potato in field 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: ≠ 5 days			
Number of applications and application rate		6 x 0.1485 kg a.s./ha	
Resident child	Drift (75th perc.)	0.0037	37.27

Body weight: 10 kg	Vapour (75th perc.)	0.0011	10.70
	Deposits (75th perc.)	0.0032	31.89
	Re-entry (75th perc.)	0.0322	321.56
	Sum (mean)	0.0311	310.90
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0009	8.91
	Vapour (75th perc.)	0.0002	2.30
	Deposits (75th perc.)	0.0013	12.98
	Re-entry (75th perc.)	0.0179	178.65
	Sum (mean)	0.0158	158.48
Refinement 1 - DT_{50}: 1 day; **Tractor mounted boom spray application outdoors to potato in field** Buffer zone: 2-3 m Drift reduction technology: no DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: ~~7~~ 5 days			
Number of applications and application rate		6 x 0.1485 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0037	37.27
	Vapour (75th perc.)	0.0011	10.70
	Deposits (75th perc.)	0.0007	7.18
	Re-entry (75th perc.)	0.0072	72.43
	Sum (mean)	0.0094	94.17
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0009	8.91
	Vapour (75th perc.)	0.0002	2.30
	Deposits (75th perc.)	0.0003	2.92
	Re-entry (75th perc.)	0.0040	40.24
	Sum (mean)	0.0041	40.76

6.6.4.2 Measurement of resident and/or bystander exposure

Reviewer comment:
DFR studies on tomatoes and grapes using IN002B1760 were performed by the Applicant in order to support the risk assessment for workers and residents in Southern zone. These obtained residue data together with the extrapolation from DFR studies and residue data to refine DT_{50} foliar of cymoxanil were used for a second tier of the risk assessment.
The residue data on potatoes, grapes and tomatoes were used to propose a DT_{50} foliar based on the behaviour of cymoxanil in different crops.
A short detail of DFR (Dislodgeable foliar residue) studies are reported at point 6.6.3.2 in order to show the kinetic behaviour and extrapolate a proper DT_{50} foliar on the base of the obtained data.

Since the resident and/or bystander exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for cymoxanil 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.

Conclusion
The calculations according to the EFSA model demonstrate that residents of any age are not at risk during and after application of IND002B1760 on potato in the field. The effects of cymoxanil are within the limits of 100 % AOELs for all scenarios. A bystander risk assessment is not required for PPPs that do not have significant acute toxic effects or the potential to exert toxic effects after a single exposure.

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

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	[redacted]	2022	In vitro dermal absorption of cymoxanil from Indofil cymoxanil 45 WG using human split-thickness skin in a flow through diffusion system [redacted] GLP Unpublished	N	Indofil Industries (Netherlands) BV
KCP 7.2/01	Sala A.	2021a	Determination of Dislodgeable Foliar Residues of Cymoxanil after 5 applications of IN002B1760 on grapes (Southern Europe – 2 trials, year 2021 - open field) Multisite study Company Report No. GLP-STUDY-21-45 LabAnalysis S.r.l. GLP Unpublished	N	Indofil Industries (Netherlands) BV
KCP 7.2/02	Sala A.	2021b	Determination of Dislodgeable Foliar Residues of Cymoxanil after 5 applications of IN002B1760 on tomato (Southern Europe – 2 trials, year 2021 - open field) Multisite study Company Report No. GLP-STUDY-21-46 LabAnalysis S.r.l. GLP Unpublished	N	Indofil Industries (Netherlands) BV

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

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

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
-	-	-	-	-	-

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

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

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

The classification of IND002B1760 has been determined by calculation. The assessment of all acute toxicological properties of IND002B1760 is derived from the classification of the active compound and co-formulants as shown below. For confidentiality reasons, the names and contents of each co-formulant is disclosed in Part C:

Component	% w/w	Acute oral toxicity	Acute dermal toxicity	Acute inhalation toxicity	Skin irritation	Eye irritation	Sensitizing potential
Cymoxanil	45	**300-2000 mg/kg (H302)**	> 2000 mg/kg	> 5.06 (max att. dose) mg/L	Not irritant	Not irritant*	**Skin sensitizer (H317)**
Co-formulant 1	xx	> 10700 mg/kg*	> 20000 mg/kg*	> 1.3 (max att. dose) mg/L*	Not irritant*	Eye irritant* (H319)	Not sensitizer*
Co-formulant 2	xx	> 5000 mg/kg*	> 2000 mg/kg*	> 5.0 mg/L*	Not irritant*	**Eye irritant* (H319**)	Not sensitizer*
Co-formulant 3	xx	**1800 mg/kg* (H302)**	> 2000 mg/kg*	> 5.0 mg/L*	**Irritant* (H315)**	**Corrosive* (H318)**	Not sensitizer*
Co-formulant 4	xx	> 5000 mg/kg*	> 2000 mg/kg*	> 5.0 mg/L*	Not irritant*	Not irritant*	Not sensitizer*
Co-formulant 5	xx	> 5000 mg/kg*	> 2000 mg/kg*	> 5.0 mg/L*	**Skin Irritant* (H315)**	**Eye irritant* (H319)**	Not sensitizer*
Co-formulant 6	xx	> 2000 mg/kg*	> 2000 mg/kg*	> 5.07 mg/L*	Not irritant*	Not irritant*	Not sensitizer*

* Data gathered from each co-formulant MSDS.

Comments of zRMS:	Not applicable.

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	Hazard assessment and proposed classification of the product is based on content ingredients of the mixture (Additivity formula) (for details see Part C). Calculation accepted.

The acute oral toxicity classification for IND002B1760 is calculated as follows:

$$\frac{100}{ATE_{mix}} = \sum_{r} \frac{C_i}{ATE_i}$$

Or

$$\frac{100}{ATE_{mix}} = \sum_{r} \frac{C_i}{ATE_i}$$

$$\boldsymbol{ATE_{mix} = \frac{100}{\sum_r \frac{C_i}{ATE_i}}}$$

where:
Ci = concentration of ingredient i (% w/w or % v/v)

i = the individual ingredient from 1 to n
n = the number of ingredients
ATEi = Acute Toxicity Estimate of ingredient i.

No acute oral toxicity study has been performed with IND002B1760; since acute oral toxicity was calculated according to Annex I criteria of Regulation (EU) No 1272/2008.
Cymoxanil is classified in category 4.

According to Table 3.1.2 (Conversion from experimentally obtained acute toxicity range values (or acute toxicity hazard categories) to acute toxicity point estimates for use in the formulas for the classification of mixtures) reported below, the value of ~~500~~ **360 mg/kg*** should be used in the calculation.

Exposure routes	Classification Category or experimentally obtained acute toxicity range estimate	Converted acute toxicity point estimate (see Note 1)
Oral (mg/kg bw/d)	0< Category 1 ≤ 5 5 < Category 2 ≤ 50 50 < Category 3 ≤ 300 300 < Category 4 ≤ 2000	0,5 5 100 500

*Note: RAC opinion on the active substance cymoxanil (CLH-O-0000007044-81-01/F, 09/2021) propose an ATE value of 360 mg/kg bw.

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

$$ATE_{mix} = \frac{500}{active\ substance} + \frac{1800}{co-formulant\ 3}$$

ATE mix = 632 mg/kg bw/day

According to the calculation method of CLP the ATEmix is in the range 300-2000 mg/kg bw/day.

The oral LD_{50} of IND002B1760 is in the range 300-2000 mg/kg bw/day according to CLP calculation method. Thus, IND002B1760 should be classified as Acute oral tox., cat.4 (H302) according to Regulation (EC) No. 1272/2008.

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

Comments of zRMS:	Hazard assessment and proposed classification of the product is based on content ingredients of the mixture (Additivity formula) (for details see Part C). Calculation accepted.

The acute dermal toxicity classification for IND002B1760 is calculated as follows:

$$\frac{100}{ATE_{mix}} = \sum_{r} \frac{C_i}{ATE_i}$$

$$\boldsymbol{ATE_{mix} = \frac{100}{\sum_r \frac{C_i}{ATE_i}}}$$

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

No acute dermal toxicity study has been performed with the formulation IND002B1760; since acute dermal toxicity has been calculated according to Annex I criteria of Regulation (EU) No 1272/2008.

No component is classified as harmful or toxic.

According to annex I of CL Regulation calculation method the dermal LD_{50} of IND002B1760 is higher than 2000 mg/kg bw. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	Hazard assessment and proposed classification of the product is based on content ingredients of the mixture (Additivity formula) (for details see Part C). Calculation accepted.

The acute inhalation toxicity classification for IND002B1760 is calculated as follows:

$$\frac{100}{ATE_{mix}} = \sum_{r} \frac{C_i}{ATE_i}$$

$$\boldsymbol{ATE_{mix} = \frac{100}{\sum_r \frac{C_i}{ATE_i}}}$$

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

No acute inhalation toxicity study has been performed with the formulation IND002B1760; since acute inhalation toxicity was calculated according to Annex I criteria of Regulation (EU) No 1272/2008.

No component is classified as harmful or toxic.

According to annex I of CL Regulation calculation method the inhalation LC_{50} of IND002B1760 is higher than 5.0 mg/L. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	Hazard assessment and proposed classification of the product is based on content ingredients of the mixture (for details see Part C). Calculation accepted.

No skin irritation study has been performed with the formulation IND002B1760; since skin irritation was calculated according to Annex I criteria of Regulation (EU) No 1272/2008.

Based on Table 3.2.3 of Annex I of CLP Regulation (EC) n. 1272/2008 (Generic concentration limits of ingredients classified as skin corrosion (Category 1, 1A, 1B or 1C)/skin irritation (Category 2) that trigger classification of the mixture as skin corrosion/skin irritation where the additivity approach applies) the calculation method used to determine which category IND002B1760 placed in is reported below.

n.	Sum of ingredients classified as:	Concentration triggering classification of a mixture as:	
		Skin corrosion	Skin irritation
		Category 1	Category 2
a	Skin corrosion Sub- Category 1A, 1B, 1C or Category 1	≥ 5 %	≥ 1 % but < 5 %
b	Skin irritation Category 2	-	≥ 10 %
c	10 × (Skin corrosion Sub-Category 1A, 1B, 1C or Skin corrosion Category 1 + Skin irritation Category 2	-	≥ 10 %

The product contains < 10% of co-formulants (co-formulant 3 and co-formulant 5) considered as skin irritant (classified as: Skin Irrit. 2; H315).
Under the CLP classification system these components are below the additive trigger value of the classification according to Regulation (EC) no. 1272/2008.

Conclusion
The product IND002B1760 is not considered a skin irritant according to CLP calculation method. Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	Hazard assessment and proposed classification of the product is based on content ingredients of the mixture (for details see Part C). Calculation accepted.

No eye irritation toxicity has been performed on IND002B1760 since eye irritation/corrosion was calculated according to Annex I criteria of Regulation (EU) No 1272/2008.

Based on Table 3.3.3 of Annex I of CLP Regulation (EC) n. 1272/2008 (Generic concentration limits of ingredients classified as skin corrosion (Category 1, 1A, 1B or 1C) and/or serious eye damage (Category 1) or eye irritation (Category 2) that trigger classification of the mixture as serious eye damage/eye irritation where the additivity approach applies), the calculation method used to determine which category IND002B1760 placed in is reported below.

n.	Sum of ingredients classified as:	Concentration triggering classification of a mixture as:	
		Serious eye damage	Eye irritation
		Category 1	Category 2
a	Skin corrosion Sub- Category 1A, 1B, 1C or Category 1 + Serious eye damage (Category 1)	≥ 3 %	≥ 1 % but < 3 %
b	Eye Effects Category 2	-	≥ 10 %
c	10 × (Skin corrosion Sub-Category 1A, 1B, 1C or Skin corrosion Category 1 + Serious eye damage (Category 1)) + Eye irritation (Category 2)	-	≥ 10 %

The product contains ≥ 1 % but < 3 % of co-formulants (co-formulant 3) considered as eye corrosive (classified as: ~~Eye Corr.1; H318~~ Eye Irrit. 2, H319) - case a.
Under the CLP classification system it is below the additive trigger value of the classification according to Regulation (EC) no. 1272/2008.

Conclusion

The product IND002B1760 is considered an eye corrosive according to CLP calculation method.
Therefore, the classification as ~~Eye Corr.1; H318~~ Eye Irrit. 2, H319 is required according to Regulation (EC) No. 1272/2008.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	Hazard assessment and proposed classification of the product is based on content ingredients of the mixture (for details see Part C). Calculation accepted.

No skin sensitization study has been performed with the formulation IND002B1760; since skin sensitization has been calculated according to Annex I criteria of Regulation (EU) No 1272/2008.
The cymoxanil is harmonized as skin sensitizer, cat 1. Taking into account the content of the active substance in the formulation and the cut-off criteria according to Annex I of CLP (1%), the product IND002B1760 should be classified for this hazard class.

Conclusion

IND002B1760 is a skin sensitizer; thus, the classification as Skin Sens cat.1 (H317) is required according to Regulation (EC) No. 1272/2008.

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

None.

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 Study 1 – Cymoxanil in IND002B1760

Comparative dermal absorption, in vitro using rat and human skin

Comments of zRMS:	Study is considered to be acceptable and dermal absorption for a.s. cymoxanil is covered by this study. DA values obtained from the study are reliable and can be used for risk assessment.

Reference	KCP 7.3
Report	In vitro dermal absorption of cymoxanil from Indofil cymoxanil 45 WG using human split-thickness skin in a flow through diffusion system [redacted], 2022
Guideline(s)	OECD 428
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material	Name (Lot/Batch No.)	Cymoxanil, [acetyl-2-14C] Batch No.: XXV/66/C/1 (Serial Number)
	Test preparation	radioformulation
	Specific activity	1517 MBq/mmol (41 mCi/mmol or 7.595 MBq/mg)
	Radiochemical purity	100%
Product	Name (Lot/Batch No.)	IN002B1760 (Lot. #64)
	Company code	IN002B1760
	Concentration a.s.	[450g/kg]
	Formulation type	WG
Blank product	Name (Lot/Batch No.)	Cymoxanil 45 WG (IN 002B1760) Placebo (Batch N.: IND_F040_0421_1)
	Concentration a.s.	0 g/kg

Test system		
Diffusion cell	Cell type	dynamic
	(if dynamic) Flow rate	1.6 ml/h
	Exposed skin area	0.64 cm²
	Cover	open
Membrane	Skin type	dermatomed

	Skin thickness range	200-400 µm
	Location	abdomen
	Source	ex vivo
	Integrity test	Yes
Receptor	Receptor medium	y
	Solubility in receptor medium	y
Sample Time	Exposure time	6h – 24h
	Observation time	18 hr + 10 minutes
Sampling	Sample intervals	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	y
	TS1-2 analysed separately	y
Remarks:		

Tested doses	Concentrate	Spray dilution 1
Target concentration [mg/ml]	450	0.1125
Area dose [µg/cm²]	2250	1.125
Specific activity	11.6 MBq/g	0.86 MBq/mL
No. of donors	6	6
No of cells used/valid cells*	12/12	12/12

* Justification for excluded cells, if applicable

Results and discussions

Table A 1: In-vitro dermal penetration of cymoxanil formulated as product code/name through human skin - Recovery data

	Test Preparation I (Concentrate)		**Test Preparation II** (Field spray dilution)	
Test Formulation Concentration	450 g/kg		0.1125 g/L	
Applied Dose (µg/cm²)	2250 µg/cm²		1.125 µg/cm²	
Number of replicates	12 from 6 donors		12 from 6 donors	
Cumulative Absorption into the Receptor Fluid	% of dose	µg/cm²	% of dose	µg/cm²
after 12 h	0.15	3.3433	24.18	0.2691
after 24 h	0.18	4.0848	24.97	0.2779
Mean Maximal Flux (µg/cm²/h)	0.493		0.113	
Lag Time (h)	-0.09		0.76	
	Recovery of [^{14}C]-Cymoxanil (% of dose)			
	Mean	SD	Mean	SD
Receptor Fluid (0-24h)	0.18	0.11	24.97	2.12
Receptor Compartment Wash	0.01	0.01	0.04	0.02
Dermis	0.04	0.02	0.39	0.12
Epidermis (without *stratum corneum*)	0.04	0.03	0.99	0.29
Tape Strips (1-2)	0.01	0.01	0.15	0.11
Tape Strips (3 to 15)	0.02	0.02	1.22	0.74
Stratum corneum	0.03	0.03	1.36	0.85
Skin Wash at 6h	96.78	2.34	68.92	2.25
Skin Wash at 24h	1.21	1.58	1.26	0.69
Donor Compartment Wash	0.12	0.18	0.07	0.08
Total Recovery	98.40	1.53	98.00	0.74
[1]Absorbed dose I	0.23	0.12	25.39	2.11
[2]Absorbed dose II	0.27	0.13	26.38	2.06
[3]Absorbed dose III	0.29	0.14	27.60	1.93
[4]Unabsorbed dose	98.11	1.53	70.40	1.83
Dermal Absorption Corrected Values as per EFSA 2017				

LLC of t_0.5 absorption	71.68	8.24	96.15	0.68
Absorption complete?	No		Yes	
Measured absorption, if LLC of t_0.5<=75%	0.29	0.14	N/A	N/A
Measured absorption, if LLC of t_0.5>75%	N/A	N/A	26.38	2.06
Measured absorption corrected	0.29	0.14	26.38	2.06
Relevant absorption estimate	0.381		27.699	
Final estimate (rounded)	0.38		28	

1Absorbed dose I was calculated from the amounts recovered in the receptor fluid, the receptor compartment wash, and the vascular dermis.

2Absorbed dose II was calculated from the absorbed dose I, plus the non-vascular epidermis (without stratum corneum). The absorbed dose II can be considered conservative.

3Absorbed dose III was calculated from the absorbed dose II plus the dead stratum corneum (tape strips 3 to last). The absorbed dose III can be considered highly conservative.

4Unabsorbed dose was calculated from the amounts recovered from skin washings at 6h and 24h, donor compartment wash and the first two tape strips

LLC = Lower limit of confidence; Mean T0.5 value corrected for standard deviation (lower 95% confidence value of mean)

T0.5 = Amount permeated into the receptor fluid at 12 h of amount permeated at 24 h.

Summary of Absorbed dose from Test preparation I and II:

The mean cumulative absorption of Cymoxanil from Indofil Cymoxanil 45 WG (Test Preparation I – Concentrate) into the receptor fluid after 24 h was 0.18% of the applied dose. The respective mean maximal flux was 0.493 µg/cm2/h and the mean lag time was -0.09 h. The mean total recovery of Cymoxanil was 98.40% from Test Preparation I (Concentrate). The mean of total unabsorbed doses recovered from skin washings, donor compartment, and first two tape strips was 98.11% from Test Preparation I (Concentrate). The mean of the absorbed dose I, II, and III of Cymoxanil from Indofil Cymoxanil 45 WG was 0.23%, 0.27%, and 0.29%, respectively. Absorption was considered incomplete as the amount permeated into the receptor fluid at 12 h (71.68%) was lower than 75 % of the amount permeated at 24 h. Therefore, the corrected dermal absorption value based on EFSA, 2017 was 0.38%.

The mean cumulative absorption of Cymoxanil from Indofil Cymoxanil 45 WG (Test Preparation II – Spray dilution) into the receptor fluid after 24 h was 24.97% of the applied dose. The respective mean maximal flux was 0.113 µg/cm^2/h and the mean lag time was 0.76 h. The mean total recovery of Cymoxanil was 98% from Test Preparation II (Spray dilution). The mean total unabsorbed dose (recovered from skin washings, donor compartment, and the first two tape strips) was 70.40% from Test Preparation II (Spray dilution). The mean of the absorbed doses I, II, and III of Cymoxanil from Indofil Cymoxanil 45 WG (Test Preparation II – Spray dilution) through human split-thickness skin was 25.39%, 26.38%, and 27.60%, respectively. Absorption was considered complete as the amount permeated into the receptor fluid at 12 h (96.15%) was higher than 75 % of the amount permeated at 24 h. Therefore, the corrected dermal absorption value based on EFSA, 2017 was 28%.

Conclusion/endpoint:
The dermal penetration of cymoxanil formulated as IND002B1760 through human dermatomed skin was determined in vitro. The amount of applied dose penetrating within 24 hours was determined to be:

Species	**Parameters**	**Test Preparation I (Concentrate)**	**Test Preparation II (Spray dilution)**
		Mean ± SD	**Mean ± SD**
Human Skin	Absorbed dose I (%)	0.23 ± 0.12	25.39 ± 2.11
	Absorbed dose II (%)	0.27 ± 0.13	26.38 ± 2.06
	Absorbed dose III (%)	0.29 ± 0.14	27.60 ± 1.93

Species	Parameters	Test Preparation I (Concentrate)	Test Preparation II (Spray dilution)
		Mean ± SD	**Mean ± SD**
	Dermal absorption corrected values as per EFSA 2017	0.38	28
	Maximal flux [µg/cm^2/h]	0.493 ± 0.379	0.113 ± 0.023

for the formulation concentrate and the spray dilution, respectively. The dermal penetration estimates to be used for risk assessment were set at 0.38% and 28% for the formulation concentrate and the spray dilution based on the EFSA guidance criteria.

(Desai K. R.)

A 2.11 Other/Special Studies

None.

Appendix 3 Exposure calculations

List of scenarios performed:

- Operator exposure Cymoxanil from Table A 2 to Table A 7
- Worker exposure Cymoxanil from Table A 8 to Table A 11
- Resident exposure Cymoxanil from Table A 12 to Table A 15

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for cymoxanil

Tractor mounted boom spray application outdoors to potato

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

Formulation type	WG		Crop type	Potato and fruiting vegetables
Application rate (AR)	0.1485	kg a.s./ha	Application method	Downward spraying
Area treated per day (A)	50	ha	Application equipment	Vehicle-mounted
Dermal absorption (DA)	0.38	% (concentr.)	Indoor/outdoor	Outdoor
	28	% (dilution)	Closed cabin	No
Inhalation absorption (IA)	100	%	Drift reduction	No
Body weight (BW)	60	kg/person	Cultivation	Normal
AOEL	0.01	mg/kg bw/d	Water soluble bag	No
AAOEL	NA	mg/kg bw/d		

Table A 3: Estimation of longer term operator exposure towards cymoxanil according to EFSA guidance

Operator Model	Mixing, loading and application AOEM			
Potential exposure	Longer term systemic exposure mg/kg bw/day	0.0100	% of RVNAS	100.38%
	Acute systemic exposure mg/kg bw/day	0.0708	% of RVAAS	
Mixing and Loading	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Soluble bags = No
Application	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Closed cabin = No
Exposure (including PPE options above)	Longer term systemic exposure mg/kg bw/day	0.0069	% of RVNAS	69.30%
	Acute systemic exposure mg/kg bw/day	0.0544	% of RVAAS	

Manual hand-held spray application outdoors to potato

Table A 4: Input parameters considered for the estimation of operator exposure

Formulation type	WG		Crop type	Potato and fruiting vegetables
Application rate (AR)	0.1485	kg a.s./ha	Application method	Upward spraying as per the overestimation on manual applications model, it is recommended to use upward spraying option
Area treated per day (A)	4	ha	Application equipment	~~Manual knapsack~~ Manual hand-held.
Dermal absorption (DA)	0.38	% (concentr.)	Indoor/outdoor	Outdoor
	28	% (dilution)	Closed cabin	No
Inhalation absorption (IA)	100	%	Drift reduction	No
Body weight (BW)	60	kg/person	Cultivation	Normal
AOEL	0.01	mg/kg bw/d	Water soluble bag	No
AAOEL	NA	mg/kg bw/d		

Table A 5: Estimation of longer term operator exposure towards cymoxanil according to EFSA guidance

Operator Model		Mixing, loading and application AOEM		
Potential exposure	Longer term systemic exposure mg/kg bw/day	0.2747	% of RVNAS	2746.99%
	Acute systemic exposure mg/kg bw/day	0.8685	% of RVAAS	
Mixing and Loading	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Soluble bags = No
Application	Gloves = Yes	Clothing = Work wear - arms, body and legs covered	RPE = None	Closed cabin = No
Exposure (including PPE options above)	Longer term systemic exposure mg/kg bw/day	0.0070	% of RVNAS	69.50%
	Acute systemic exposure mg/kg bw/day	0.0194	% of RVAAS	

Manual knapsack spray application outdoors to potato

Table A 6: Input parameters considered for the estimation of operator exposure

Formulation type	WG		Crop type	Potato and fruiting vegetables
Application rate (AR)	0.1485	kg a.s./ha	Application method	Upward spraying as per the overestimation on manual applications model, it is recommended to use upward spraying option
Area treated per day (A)	1	ha	Application equipment	Manual knapsack
Dermal absorption (DA)	0.38	% (concentr.)	Indoor/outdoor	Outdoor
	28	% (dilution)	Closed cabin	No
Inhalation absorption (IA)	100	%	Drift reduction	No
Body weight (BW)	60	kg/person	Cultivation	Normal
AOEL	0.01	mg/kg bw/d	Water soluble bag	No
AAOEL	NA	mg/kg bw/d		

Table A 7: Estimation of longer term operator exposure towards cymoxanil according to EFSA guidance

Operator Model	Mixing, loading and application AOEM			
Potential exposure	Longer term systemic exposure mg/kg bw/day	0.2171	% of RVNAS	2171.08%
	Acute systemic exposure mg/kg bw/day	0.8342	% of RVAAS	
Mixing and Loading	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Soluble bags = No
Application	Gloves = No	Clothing = Work wear - arms, body and legs covered	RPE = None	Closed cabin = No
Exposure (including PPE options above)	Longer term systemic exposure mg/kg bw/day	0.0091	% of RVNAS	90.78%
	Acute systemic exposure mg/kg bw/day	0.0237	% of RVAAS	

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for cymoxanil

Re-entry **inspection and irrigation** tasks for potato

Table A 8: Input parameters considered for the estimation of worker exposure

Intended use(s)	potato, inspection and irrigation, outdoor		Dislodgeable foliar residue (DFR)	3	µg/cm²/kg a.s./ha
Application rate (AR)	0.1485	kg a.s./ha	Dermal absorption (DA)	28	% (worst case)
Number of applications (NA)	6		Inhalation absorption (IA)	100	%
Interval between applications	5	days	Work rate per day (WR)	2	h/d
Half-life of active substance	30	days	TC dermal (potential)	12500	cm²/h
Multiple application factor (MAF)	3.7		TC dermal (work wear)	1400	cm²/h
Body weight (BW)	60	kg/person	TC dermal (work wear, gloves)	NA	cm²/h
AOEL	0.01	mg/kg bw/d	Task specific factor inhalation	0.001	ha/h x 10^{-3}
AAOEL	NA	mg/kg bw/d			

Table A 9: Estimation of longer term worker exposure towards cymoxanil according to EFSA guidance

Worker - Inspection, irrigation	Potential exposure mg/kg bw/day	0.2382	% of RVNAS	2381.96%
	Working clothing mg/kg bw/day	0.0267	% of RVNAS	266.78%
	Working clothing and gloves mg/kg bw/day		% of RVNAS	

Re-entry **inspection and irrigation** tasks for potato - refinement 1

Table A 10: Input parameters considered for the estimation of worker exposure

Intended use(s)	potato, inspection and irrigation, outdoor		Dislodgeable foliar residue (DFR)	3	µg/cm^2/kg a.s./ha
Application rate (AR)	0.1485	kg a.s./ha	Dermal absorption (DA)	28	% (worst case)
Number of applications (NA)	6		Inhalation absorption (IA)	100	%
Interval between applications	5	days	Work rate per day (WR)	2	h/d
Half-life of active substance	1	days	TC dermal (potential)	12500	cm^2/h
Multiple application factor (MAF)	1		TC dermal (work wear)	1400	cm^2/h
Body weight (BW)	60	kg/person	TC dermal (work wear, gloves)	NA	cm^2/h
AOEL	0.01	mg/kg bw/d	Task specific factor inhalation	0.001	ha/h x 10^{-3}
AAOEL	NA	mg/kg bw/d	Refinement	1	

Table A 11: Estimation of longer term worker exposure towards cymoxanil according to EFSA guidance

Worker - Inspection, irrigation	Potential exposure mg/kg bw/day	0.0537	% of RVNAS	536.52%
	Working clothing mg/kg bw/day	0.0060	% of RVNAS	60.09%
	Working clothing and gloves mg/kg bw/day		% of RVNAS	

A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for cymoxanil

Resident exposure to potato

Table A 12: Input parameters considered for the estimation of longer term resident exposure

Intended use(s)	Potato, spray application		Drift reduction (DR)	-	%
Application rate (AR)	0.1485	kg a.s./ha	Transfer coefficient surface deposits (TC)	7300	cm^2/h (adult)
				2600	cm^2/h (child)
Minimum water volume (V)	300	L/ha	Drift on surface (D) - 75th perc.	5.60	%
Buffer strip	2-3	m	Drift on surface (D) - mean	4.10	%
Number of applications (NA)	6		Turf Transferable Residues (TTR)	5	%
Interval between applications	5	days	Exposure duration dermal (H_D)	2	h
Half-life of active substance	30	days	Exposure duration inhal. (H_I)	24	h
Multiple application factor (MAF)	4.6		Exposure duration entry into treated crops (H_E)	0.25	h
Body weight (BW)	60	kg/person (adults)	Airborne Concentration of Vapour (VC)	0.001	mg/m^3
	10	kg/person (children)			
Dermal absorption (DA)	28	% ('worst case')	Dislodgeable foliar residue (DFR)	1	$\mu g/cm^2/kg$ a.s.
Inhalation absorption (IA)	100	%	Light clothing adjustment factor (CF)	18	%
Oral absorption (OA)	75	%	Saliva Extraction Factor (SE)	50	%
AOEL	0.01	mg/kg bw/d	Surface Area of Hands (SA)	20	cm^2
Spray drift dermal (SD) - 75th perc.	0.47	mL spray dilution (adult)	Frequency of Hand to Mouth (Freq)	20	events/h
	0.327	mL spray dilution (child)			
Spray drift inhal. (SI) - 75th perc.	0.00010	mL spray dilution (adult)	Dislodgeable residues object to mouth (DR_{OM})	20	%
	0.00022	mL spray dilution (child)			
Spray drift dermal (SD) - mean	0.22318	mL spray dilution (adult)	Ingestion Rate for Mouthing of Grass (IgR)	25	cm^2/d
	0.18	mL spray dilution (child)			
Spray drift inhal. (SD) - mean	0.00009	mL spray dilution (adult)	TC entry into treated crops - 75th perc.	7500	cm^2/h (adult)
	0.00017	mL spray dilution (child)		2250	cm^2/h (child)
Inhalation rate (IR)	16.57	m^3/d (adult)	TC entry into treated crops - mean:	5980	cm^2/h (adult)
	8.31	m^3/d (child)		1794	cm^2/h (child)

Table A 13: Estimation of longer term resident exposure towards cymoxanil according to EFSA guidance

Resident - child	Spray drift (75th percentile) mg/kg bw/day	0.0037	% of RVNAS	37.27%
	Vapour (75th percentile) mg/kg bw/day	0.0011	% of RVNAS	10.70%
	Surface deposits (75th percentile) mg/kg bw/day	0.0032	% of RVNAS	31.89%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0322	% of RVNAS	321.56%
	All pathways (mean) mg/kg bw/day	0.0311	% of RVNAS	310.90%
Resident - adult	Spray drift (75th percentile) mg/kg bw/day	0.0009	% of RVNAS	8.91%
	Vapour (75th percentile) mg/kg bw/day	0.0002	% of RVNAS	2.30%
	Surface deposits (75th percentile) mg/kg bw/day	0.0013	% of RVNAS	12.98%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0179	% of RVNAS	178.65%
	All pathways (mean) mg/kg bw/day	0.0158	% of RVNAS	158.48%

Resident exposure to potato - refinement 1 (DT_{50}: 1 day)

Table A 14: Input parameters considered for the estimation of longer term resident exposure

Intended use(s)	Potato , spray application		Drift reduction (DR)	-	%
Application rate (AR)	0.1485	kg a.s./ha	Transfer coefficient surface deposits (TC)	7300	cm^2/h (adult)
				2600	cm^2/h (child)
Minimum water volume (V)	300	L/ha	Drift on surface (D) - 75th perc.	5.60	%
Buffer strip	5 2-3m	m	Drift on surface (D) - mean	4.10	%
Number of applications (NA)	6		Turf Transferable Residues (TTR)	5	%
Interval between applications	5	days	Exposure duration dermal (H_D)	2	h
Half-life of active substance	**1**	days	Exposure duration inhal. (H_I)	24	h
Multiple application factor (MAF)	**1**		Exposure duration entry into treated crops (H_E)	0.25	h
Body weight (BW)	60	kg/person (adults)	Airborne Concentration of Vapour (VC)	0.001	mg/m^3
	10	kg/person (children)			
Dermal absorption (DA)	28	% ('worst case')	Dislodgeable foliar residue (DFR)	0.4455	$\mu g/cm^2/kg$ a.s.
Inhalation absorption (IA)	100	%	Light clothing adjustment factor (CF)	18	%
Oral absorption (OA)	75	%	Saliva Extraction Factor (SE)	50	%
AOEL	0.01	mg/kg bw/d	Surface Area of Hands (SA)	20	cm^2
Spray drift dermal (SD) - 75th perc.	0.47	mL spray dilution (adult)	Frequency of Hand to Mouth (Freq)	20	events/h
	0.327	mL spray dilution (child)			
Spray drift inhal. (SI) - 75th perc.	0.00010	mL spray dilution (adult)	Dislodgeable residues object to mouth (DR_{OM})	20	%
	0.00022	mL spray dilution (child)			
Spray drift dermal (SD) - mean	0.22318	mL spray dilution (adult)	Ingestion Rate for Mouthing of Grass (IgR)	25	cm^2/d
	0.18	mL spray dilution (child)			
Spray drift inhal. (SD) - mean	0.00009	mL spray dilution (adult)	TC entry into treated crops - 75th perc.	7500	cm^2/h (adult)
	0.00017	mL spray dilution (child)		2250	cm^2/h (child)
Inhalation rate (IR)	16.57	m^3/d (adult)	TC entry into treated crops - mean:	5980	cm^2/h (adult)
	8.31	m^3/d (child)		1794	cm^2/h (child)

Table A 15: Estimation of longer term resident exposure towards cymoxanil according to EFSA guidance

Resident - child	Spray drift (75th percentile) mg/kg bw/day	0.0037	% of RVNAS	37.27%
	Vapour (75th percentile) mg/kg bw/day	0.0011	% of RVNAS	10.70%
	Surface deposits (75th percentile) mg/kg bw/day	0.0007	% of RVNAS	7.18%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0072	% of RVNAS	72.43%
	All pathways (mean) mg/kg bw/day	0.0094	% of RVNAS	94.17%
Resident - adult	Spray drift (75th percentile) mg/kg bw/day	0.0009	% of RVNAS	8.91%
	Vapour (75th percentile) mg/kg bw/day	0.0002	% of RVNAS	2.30%
	Surface deposits (75th percentile) mg/kg bw/day	0.0003	% of RVNAS	2.92%
	Entry into treated crops (75th percentile) mg/kg bw/day	0.0040	% of RVNAS	40.24%
	All pathways (mean) mg/kg bw/day	0.0041	% of RVNAS	40.76%

Table A 16 verified resident exposure - potato

Resident exposure for			
Croptype	Root and tuber vegetables		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		*i_AppEquip*
Formulation type	Wettable granules, soluble granules		*i_FormVal*
Buffer strip	2-3	m	*i_Buffer*
Application rate of the product	0,1485	kg a.s./ha	*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	0,495	g a.s./l	*d_ConcAS*
Dermal absorption of product	0,38%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	28,00%		*i_AbsorpInuse*
Oral absorption	75,00%		*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	0,4455	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) - adult	7500	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentile) - child	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)	0,0372731	0,0107000	0,0071829	0,0724297	0,0941668
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0037273	0,0010700	0,0007183	0,0072430	0,0094167
% of RVNAS	37,27%	10,70%	7,18%	72,43%	94,17%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0,0534659	0,0138000	0,0175462	0,2414323	0,2445577
Total systemic exposure per kg body weight (mg/kg bw/day)	0,0008911	0,0002300	0,0002924	0,0040239	0,0040760
% of RVNAS	8,91%	2,30%	2,92%	40,24%	40,76%

2. Resident exposure 75th Percentile

	Systemic exposure [mg a.s. /day]	Systemic exposure [mg a.s./kg bw/day]	Formula	Comments
1-3 year old child				
Spray drift	0,0372731	0,0037273	*((C16*i_AbsorpInuse*(1-d_ClothAF))+C18)*d_ConcAS*	
Vapour	0,0107000	0,0010700	*d_AirCon*d_BreathRCh*d_BwChild*	
Surface deposits				
Dermal	0,0062493	0,0006249	*(i_AppRate/100)*C29*d_Turf*d_ReTCCh*d_ReExpDur*MAX(i_AbsorpProduct,i_AbsorpInuse)*d_MAF*IF(i_AppEquip = "Vehicle-mounted-Drift Reduction",0.5,1))*	
Hand to mouth	0,0006116	0,0000612	*(i_AppRate/100)*C29*d_Turf*d_SalExt*d_AreaHM*d_ReFreqHM*d_ReExpDur*i_AbsorpOralInuse*d_MAF*	
Object to mouth	0,0003219	0,0000322	*(i_AppRate/100)*C29*d_DRP*d_MouthGrass*i_AbsorpOralInuse*d_MAF*	
Entry into treated crops				
Dermal	0,0724297	0,0072430	*(d_TcEntryCh*0.25*d_DFR*d_MAF)/1000*MAX(i_AbsorpProduct,i_AbsorpInuse)*	
Hand to mouth			*(i_AppRate/100)*d_Turf*d_MAF*d_SalExt*d_AreaHM*d_ReFreqHM*d_ReExpDur*i_AbsorpOralInuse*	Considered only for application on grassland and lawns and for application on golf course, turf or other sports lawns.
Object to mouth			*(i_AppRate/100)*d_DRP*d_MouthGrass*i_AbsorpOralInuse*d_MAF*	Considered only for application on grassland and lawns and for application on golf course, turf or other sports lawns.
Adult				
Spray drift	0,0534659	0,0008911	*(C15*i_AbsorpInuse*(1-d_ClothAF))+C17)*d_ConcAS*	
Vapour	0,0138000	0,0002300	*d_AirCon*d_BreathRAd*d_BwAdult*	
Surface deposits (dermal)	0,0175462	0,0002924	*(i_AppRate/100)*C30*d_Turf*d_ReTCAd*d_ReExpDur*i_AbsorpInuse*	
Entry into treated crops (dermal)	0,2414323	0,0040239	*(d_TcEntryAd*0.25*d_DFR*d_MAF)/1000*MAX(i_AbsorpProduct,i_AbsorpInuse)*	

Appendix 4 Detailed evaluation of exposure and/or DFR studies relied upon (KCP 7.2, KCP 7.2.1.1, KCP 7.2.2.1, KCP 7.2.3.1)

~~Not required.~~

A 4.1.1 Study 1

Reference	KCP 7.2/01
Report	Determination of Dislodgeable Foliar Residues of Cymoxanil after 5 applications of IN002B1760 on **grapes** (Southern Europe - 2 trials, year 2021 - open field) Multisite study 2021a, Sala, A. Doc. N. GLP-STUDY-21-45
Guidelines	Iwata, Y., J.B. Knaak, R.C. Spear and R.J. Foster (1977). SANTE/2019/12752 SANTE/2020/12830 Rev.1
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Material and methods

The objective of the study was to quantify the amount of cymoxanil residue that can be dislodged from grapevine leaves following five applications of IN002B1760 (cymoxanil 450 g/kg), applied at 0.27 L product/ha, diluted with water immediately prior to application to a target spray volume of 500 L/ha.

Two dislodgeable foliar residue trials were conducted on grapevine during 2021 in Italy (GLP-STUDY-21-45 Trial 1 - Italy) and Spain (GLP-STUDY-21-45 Trial 2 – Spain).

Following each application of IN002B1760, a WG formulation containing 450 g/kg cymoxanil, leaf disc samples were taken at pre-defined sampling times pre and post application. The foliar residues were dislodged using an aqueous solution and the dislodged solution specimens were analysed for cymoxanil.

40 leaf disks (leaf disks dimensions: 2.5 cm diameter/10 cm^2 - double side area) per sample were collected using a leaf puncher (Ø 2.5 cm). Each sample was placed in a glass bottle with jar and keep in blue ice (cool condition) until dislodging procedure. Leaf disks were randomly collected from the plots, from top, bottom, exposed and covered parts of the plants.

Leaf disc specimens were collected from the untreated plot, before the first application, after the last application and 14 days after the last application. Leaf disc specimens were collected from the treated plot before and after each application, and 1, 2, 3, 5, 7, 10, 14 days after the last application.

After sampling, the leaf discs were immediately transported to the Test site where the dislodging procedure was carries out within 4 hours from sampling. The foliage was mechanically shaken for 10 minutes with two sequential 100mL washes with an aqueous solution of 0.01% Aerosol OT100 (dislodging solution).

The analytical method for the determination of Cymoxanil in Grapes leaf disks samples consisted in a dilution of the samples with a mixture water/methanol 60/40 (v/v) and a final analysis by HPLC/HRMS/MS. The analytical method for the determination of Cymoxanil (AM1-GLP-STUDY-21-

45) was validated under GLP compliance according to SANTE/2020/12830 Rev.1 guideline in this GLP study.

The limit of quantitation for cymoxanil was set at 10 µg/L / 0.005 µg/cm^2.

Procedural recoveries run concurrently with test specimen at levels of 10 µg/L and 10 mg/L gave an overall mean recovery of 103.0-104.4%.

Results

A summary of the residues found on DFR solution samples (200 mL of dislodging foliar solution: water containing 0.01% OT100) is reported in the following table, the results were calculated using the primary MS/MS transition:

Table 8: Field samples - result summary - Trial code: GLP-STUDY-21-45 Trial 1

Specimen code	Plot	Sampling	Sampling time[1]	Cymoxanil [2] DFR (µg/cm^2)	DFR (µg/cm^2) Mean value
GLP-SMPL-21-1476	C	S1	0 DBA1	**N.D.**	**N.D.**
GLP-SMPL-21-1478	T1			**N.D.**	**N.D.**
GLP-SMPL-21-1479	T2			**N.D.**	
GLP-SMPL-21-1480	T3			**N.D.**	
GLP-SMPL-21-1482	T1	S2	0 DAA1	**0.078**	**0.099**
GLP-SMPL-21-1483	T2			**0.101**	
GLP-SMPL-21-1484	T3			**0.117**	
GLP-SMPL-21-1486	T1	S3	0 DBA2	**N.D.**	**N.D.**
GLP-SMPL-21-1487	T2			**N.D.**	
GLP-SMPL-21-1488	T3			**N.D.**	
GLP-SMPL-21-1490	T1	S4	0 DAA2	**0.114**	**0.121**
GLP-SMPL-21-1491	T2			**0.105**	
GLP-SMPL-21-1492	T3			**0.144**	
GLP-SMPL-21-1494	T1	S5	0 DBA3	**<LOQ**	**<LOQ**
GLP-SMPL-21-1495	T2			**N.D.**	
GLP-SMPL-21-1496	T3			**N.D.**	
GLP-SMPL-21-1498	T1	S6	0DAA3	**0.123**	**0.132**
GLP-SMPL-21-1499	T2			**0.153**	
GLP-SMPL-21-1500	T3			**0.121**	
GLP-SMPL-21-1502	T1	S7	0DBA4	**N.D.**	**N.D.**
GLP-SMPL-21-1503	T2			**N.D.**	
GLP-SMPL-21-1504	T3			**N.D.**	
GLP-SMPL-21-1506	T1	S8	0 DAA4	**0.183**	**0.153**
GLP-SMPL-21-1507	T2			**0.133**	
GLP-SMPL-21-1508	T3			**0.142**	

GLP-SMPL-21-1510	T1	S9	0 DBA5	**N.D.**	**N.D.**
GLP-SMPL-21-1511	T2			**N.D.**	
GLP-SMPL-21-1512	T3			**N.D.**	
GLP-SMPL-21-1514	C	S10	0 DAA5	**N.D.**	**N.D.**
GLP-SMPL-21-1516	T1			**0.177**	**0.148**
GLP-SMPL-21-1517	T2			**0.196**	
GLP-SMPL-21-1518	T3			**0.072**	
GLP-SMPL-21-1520	T1	S11	1 DAA5	**0.021**	**0.020**
GLP-SMPL-21-1521	T2			**0.027**	
GLP-SMPL-21-1522	T3			**0.013**	
GLP-SMPL-21-1524	T1	S12	2 DAA5	**<LOQ**	**<LOQ**
GLP-SMPL-21-1525	T2			**<LOQ**	
GLP-SMPL-21-1526	T3			**<LOQ**	
GLP-SMPL-21-1528	T1	S13	3 DAA5	**N.D.**	**N.D.**
GLP-SMPL-21-1529	T2			**N.D.**	
GLP-SMPL-21-1530	T3			**N.D.**	
GLP-SMPL-21-1532	T1	S14	5 DAA5	**N.D.**	**N.D.**
GLP-SMPL-21-1533	T2			**N.D.**	
GLP-SMPL-21-1534	T3			**N.D.**	
GLP-SMPL-21-1536	T1	S15	7 DAA5	**N.D.**	**N.D.**
GLP-SMPL-21-1537	T2			**N.D.**	
GLP-SMPL-21-1538	T3			**N.D.**	
GLP-SMPL-21-1540	T1	S16	10 DAA5	**N.D.**	**N.D.**
GLP-SMPL-21-1541	T2			**N.D.**	
GLP-SMPL-21-1542	T3			**N.D.**	
GLP-SMPL-21-1544	C	S17	14 DAA5	**N.D.**	**N.D.**
GLP-SMPL-21-1546	T1			**N.D.**	**N.D.**
GLP-SMPL-21-1547	T2			**N.D.**	
GLP-SMPL-21-1548	T3			**N.D.**	

[1]DBA: Days before Application; DAA: Days after application
[2] Calculated considering 200 mL as overall volume of foliar dislodging solution and 400 cm^2 as overall surface of sampled leaves ($\mu g/cm^2$ = µg/L * 0.2 L / 400 cm^2)

Table 9: Field samples - result summary - Trial code: GLP-STUDY-21-45 Trial 2

Specimen code	Plot	Sampling	Sampling time[1]	Cymoxanil [2] DFR (µg/cm²)	DFR (µg/cm²) Mean value
GLP-SMPL-21-1550	C	S1	0 DBA1	N.D.	N.D.
GLP-SMPL-21-1552	T1			N.D.	N.D.
GLP-SMPL-21-1553	T2			N.D.	
GLP-SMPL-21-1554	T3			N.D.	
GLP-SMPL-21-1556	T1	S2	0 DAA1	0.428	0.444
GLP-SMPL-21-1557	T2			0.429	
GLP-SMPL-21-1558	T3			0.476	
GLP-SMPL-21-1560	T1	S3	0 DBA2	0.008	0.005
GLP-SMPL-21-1561	T2			<LOQ	
GLP-SMPL-21-1562	T3			<LOQ	
GLP-SMPL-21-1564	T1	S4	0 DAA2	0.351	0.404
GLP-SMPL-21-1565	T2			0.410	
GLP-SMPL-21-1566	T3			0.453	
GLP-SMPL-21-1568	T1	S5	0 DBA3	<LOQ	0.006
GLP-SMPL-21-1569	T2			0.006	
GLP-SMPL-21-1570	T3			0.009	
GLP-SMPL-21-1572	T1	S6	0DAA3	0.358	0.363
GLP-SMPL-21-1573	T2			0.388	
GLP-SMPL-21-1574	T3			0.343	
GLP-SMPL-21-1576	T1	S7	0DBA4	N.D.	<LOQ
GLP-SMPL-21-1577	T2			<LOQ	
GLP-SMPL-21-1578	T3			<LOQ	
GLP-SMPL-21-1580	T1	S8	0 DAA4	0.430	0.455
GLP-SMPL-21-1581	T2			0.455	
GLP-SMPL-21-1582	T3			0.480	
GLP-SMPL-21-1584	T1	S9	0 DBA5	<LOQ	<LOQ
GLP-SMPL-21-1585	T2			<LOQ	
GLP-SMPL-21-1586	T3			<LOQ	
GLP-SMPL-21-1588	C	S10	0 DAA5	N.D.	N.D.
GLP-SMPL-21-1590	T1			0.403	0.366
GLP-SMPL-21-1591	T2			0.317	
GLP-SMPL-21-1592	T3			0.377	
GLP-SMPL-21-1594	T1	S11	1 DAA5	0.126	0.135
GLP-SMPL-21-1595	T2			0.106	
GLP-SMPL-21-1596	T3			0.173	
GLP-SMPL-21-1598	T1	S12	2 DAA5	0.041	0.047

GLP-SMPL-21-1599	T2			**0.057**	
GLP-SMPL-21-1600	T3			**0.042**	
GLP-SMPL-21-1602	T1	S13	3 DAA5	**0.036**	**0.035**
GLP-SMPL-21-1603	T2			**0.040**	
GLP-SMPL-21-1604	T3			**0.029**	
GLP-SMPL-21-1606	T1	S14	5 DAA5	**0.028**	**0.022**
GLP-SMPL-21-1607	T2			**0.023**	
GLP-SMPL-21-1608	T3			**0.016**	
GLP-SMPL-21-1610	T1	S15	7 DAA5	**<LOQ**	**<LOQ**
GLP-SMPL-21-1611	T2			**0.005**	
GLP-SMPL-21-1612	T3			**<LOQ**	
GLP-SMPL-21-1614	T3	S16	10 DAA5	**0.006**	**<LOQ**
GLP-SMPL-21-1615	T1			**<LOQ**	
GLP-SMPL-21-1616	T2			**<LOQ**	
GLP-SMPL-21-1618	C	S17	14 DAA5	**N.D.**	**N.D.**
GLP-SMPL-21-1620	T1			**N.D.**	**N.D.**
GLP-SMPL-21-1621	T2			**N.D.**	
GLP-SMPL-21-1622	T3			**N.D.**	

[1]DBA: Days before Application; DAA: Days after application
[2] Calculated considering 200 mL as overall volume of foliar dislodging solution and 400 cm^2 as overall surface of sampled leaves ($\mu g/cm^2$ = µg/L * 0.2 L / 400 cm^2)

Conclusion

A median value of 0.11 $\mu g/cm^2$ (trial 1) and 0.25 $\mu g/cm^2$ (trial 2) is obtained. The highest obtained value is 0.455 $\mu g/cm^2$.

(Sala A., 2021a)

A 4.1.2 Study 2

Reference	KCP 7.2/02
Report	Determination of Dislodgeable Foliar Residues of Cymoxanil after 5 applications of IN002B1760 on **tomato** (Southern Europe - 2 trials, year 2021 - open field) Multisite study 2021b, Sala, A., Doc. N. GLP-STUDY-21-46
Guidelines	Iwata, Y., J.B. Knaak, R.C. Spear and R.J. Foster (1977). SANTE/2019/12752 SANTE/2020/12830 Rev.1
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Material and methods

The objective of the study was to quantify the amount of cymoxanil residue that can be dislodged from tomato leaves following five applications of IN002B1760. (cymoxanil 450 g/kg), applied at 0.27 L product/ha, diluted with water immediately prior to application to a target spray volume of 500-800 L/ha.

Two dislodgeable foliar residue trials were conducted on tomato during 2021 in Italy (GLP-STUDY-21-46 Trial 1 - Italy) and Spain (GLP-STUDY-21-46 Trial 2 - Spain).

Following each application of IN002B1760, a WG formulation containing 450 g/kg cymoxanil, leaf disc samples were taken at pre-defined sampling times pre and post application. The foliar residues were dislodged using an aqueous solution and the dislodged solution specimens were analysed for cymoxanil.

40 leaf disks (leaf disks dimensions: 2.5 cm diameter/10 cm^2 - double side area) per sample were collected using a leaf puncher (Ø 2.5 cm). Each sample was placed in a glass bottle with jar and keep in blue ice (cool condition) until dislodging procedure. Leaf disks were randomly collected from the plots, from top, bottom, exposed and covered parts of the plants.

Leaf disc specimens were collected from the untreated plot, before the first application, after the last application and 14 days after the last application. Leaf disc specimens were collected from the treated plot before and after each application, and 1, 2, 3, 5, 7, 10, 14 days after the last application.

After sampling, the leaf discs were immediately transported to the Test site where the dislodging procedure was carries out within 4 hours from sampling. The foliage was mechanically shaken for 10 minutes with two sequential 100mL washes with an aqueous solution of 0.01% Aerosol OT100 (dislodging solution).

The analytical method for the determination of Cymoxanil in Grapes leaf disks samples consisted in a dilution of the samples with a mixture water/methanol 60/40 (v/v) and a final analysis by HPLC/HRMS/MS. The analytical method for the determination of Cymoxanil (AM1-GLP-STUDY-21-46) was validated under GLP compliance according to SANTE/2020/12830 Rev.1 guideline in this GLP study.

The limit of quantitation for cymoxanil was set at 10 µg/L / 0.005 µg/cm^2.

Procedural recoveries run concurrently with test specimen at levels of 10 µg/L, and 10 mg/L gave an overall mean recovery of 102.1-105.9%.

Results

A summary of the residues found on DFR solution samples (200 mL of dislodging foliar solution: water containing 0.01% OT100) is reported in the following table, the results were calculated using the primary MS/MS transition:

Table 10: Field samples - result summary - Trial code: GLP-STUDY-21-46 Trial 1

Specimen code	Plot	Sampling	Sampling time[1]	Cymoxanil [2] DFR (µg/cm²)	DFR (µg/cm²) Mean value
GLP-SMPL-21-1652	C	S1	0 DBA1	N.D.	**N.D.**
GLP-SMPL-21-1654	T1			N.D.	**N.D.**
GLP-SMPL-21-1655	T2			N.D.	
GLP-SMPL-21-1656	T3			N.D.	
GLP-SMPL-21-1658	T1	S2	0 DAA1	0.196	**0.258**
GLP-SMPL-21-1659	T2			0.292	
GLP-SMPL-21-1660	T3			0.285	
GLP-SMPL-21-1662	T1	S3	0 DBA2	N.D.	**N.D.**
GLP-SMPL-21-1663	T2			N.D.	
GLP-SMPL-21-1664	T3			N.D.	
GLP-SMPL-21-1666	T1	S4	0 DAA2	0.267	**0.254**
GLP-SMPL-21-1667	T2			0.234	
GLP-SMPL-21-1668	T3			0.260	
GLP-SMPL-21-1670	T1	S5	0 DBA3	N.D.	**N.D.**
GLP-SMPL-21-1671	T2			N.D.	
GLP-SMPL-21-1672	T3			N.D.	
GLP-SMPL-21-1674	T1	S6	0DAA3	0.068	**0.120**
GLP-SMPL-21-1675	T2			0.119	
GLP-SMPL-21-1676	T3			0.172	
GLP-SMPL-21-1678	T1	S7	0DBA4	N.D.	**N.D.**
GLP-SMPL-21-1679	T2			N.D.	
GLP-SMPL-21-1680	T3			N.D.	
GLP-SMPL-21-1682	T1	S8	0 DAA4	0.175	**0.228**
GLP-SMPL-21-1683	T2			0.260	
GLP-SMPL-21-1684	T3			0.249	
GLP-SMPL-21-1686	T1	S9	0 DBA5	N.D.	**N.D.**
GLP-SMPL-21-1687	T2			N.D.	
GLP-SMPL-21-1688	T3			N.D.	
GLP-SMPL-21-1690	C	S10	0 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1692	T1			0.202	**0.179**
GLP-SMPL-21-1693	T2			0.155	
GLP-SMPL-21-1694	T3			0.179	
GLP-SMPL-21-1696	T1	S11	1 DAA5	0.045	**0.052**
GLP-SMPL-21-1697	T2			0.050	
GLP-SMPL-21-1698	T3			0.062	
GLP-SMPL-21-1700	T1	S12	2 DAA5	0.007	**0.008**

GLP-SMPL-21-1701	T2			0.008	
GLP-SMPL-21-1702	T3			0.010	
GLP-SMPL-21-1704	T1	S13	3 DAA5	<LOQ	**<LOQ**
GLP-SMPL-21-1705	T2			<LOQ	
GLP-SMPL-21-1706	T3			0.005	
GLP-SMPL-21-1708	T1	S14	5 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1709	T2			N.D.	
GLP-SMPL-21-1710	T3			N.D.	
GLP-SMPL-21-1712	T1	S15	7 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1713	T2			N.D.	
GLP-SMPL-21-1714	T3			N.D.	
GLP-SMPL-21-1716	T1	S16	10 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1717	T2			<LOQ	
GLP-SMPL-21-1718	T3			N.D.	
GLP-SMPL-21-1720	C	S17	14 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1722	T1			N.D.	**N.D.**
GLP-SMPL-21-1723	T2			N.D.	
GLP-SMPL-21-1724	T3			N.D.	

[1]DBA: Days before Application; DAA: Days after application
[2] Calculated considering 200 mL as overall volume of foliar dislodging solution and 400 cm^2 as overall surface of sampled leaves ($\mu g/cm^2$ = µg/L * 0.2 L / 400 cm^2)

Table 11: Field samples - result summary - Trial code: GLP-STUDY-21-46Trial 2

Specimen code	Plot	Sampling	Sampling time[1]	Cymoxanil [2] DFR ($\mu g/cm^2$)	DFR ($\mu g/cm^2$) Mean value
GLP-SMPL-21-1726	C	S1	0 DBA1	N.D.	**N.D.**
GLP-SMPL-21-1728	T1			N.D.	**N.D.**
GLP-SMPL-21-1729	T2			N.D.	
GLP-SMPL-21-1730	T3			N.D.	
GLP-SMPL-21-1732	T1	S2	0 DAA1	0.247	**0.272**
GLP-SMPL-21-1733	T2			0.280	
GLP-SMPL-21-1734	T3			0.289	
GLP-SMPL-21-1736	T1	S3	0 DBA2	<LOQ	**<LOQ**
GLP-SMPL-21-1737	T2			<LOQ	
GLP-SMPL-21-1738	T3			<LOQ	
GLP-SMPL-21-1740	T1	S4	0 DAA2	0.143	**0.146**
GLP-SMPL-21-1741	T2			0.167	
GLP-SMPL-21-1742	T3			0.129	
GLP-SMPL-21-1744	T1	S5	0 DBA3	N.D.	**<LOQ**

GLP-SMPL-21-1745	T2			<LOQ	
GLP-SMPL-21-1746	T3			<LOQ	
GLP-SMPL-21-1748	T1	S6	0DAA3	0.133	**0.155**
GLP-SMPL-21-1749	T2			0.159	
GLP-SMPL-21-1750	T3			0.173	
GLP-SMPL-21-1752	T1	S7	0DBA4	N.D.	**N.D.**
GLP-SMPL-21-1753	T2			N.D.	
GLP-SMPL-21-1754	T3			N.D.	
GLP-SMPL-21-1756	T1	S8	0 DAA4	0.072	**0.094**
GLP-SMPL-21-1757	T2			0.098	
GLP-SMPL-21-1758	T3			0.111	
GLP-SMPL-21-1760	T1	S9	0 DBA5	N.D.	**N.D.**
GLP-SMPL-21-1761	T2			N.D.	
GLP-SMPL-21-1762	T3			N.D.	
GLP-SMPL-21-1764	C	S10	0 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1766	T1			0.115	**0.107**
GLP-SMPL-21-1767	T2			0.099	
GLP-SMPL-21-1768	T3			0.106	
GLP-SMPL-21-1770	T1	S11	1 DAA5	0.023	**0.022**
GLP-SMPL-21-1771	T2			0.024	
GLP-SMPL-21-1772	T3			0.019	
GLP-SMPL-21-1774	T1	S12	2 DAA5	<LOQ	**0.006**
GLP-SMPL-21-1775	T2			<LOQ	
GLP-SMPL-21-1776	T3			0.008	
GLP-SMPL-21-1778	T1	S13	3 DAA5	<LOQ	**<LOQ**
GLP-SMPL-21-1779	T2			<LOQ	
GLP-SMPL-21-1780	T3			<LOQ	
GLP-SMPL-21-1782	T1	S14	5 DAA5	<LOQ	**<LOQ**
GLP-SMPL-21-1783	T2			<LOQ	
GLP-SMPL-21-1784	T3			<LOQ	
GLP-SMPL-21-1786	T1	S15	7 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1787	T2			N.D.	
GLP-SMPL-21-1788	T3			N.D.	
GLP-SMPL-21-1790	T1	S16	10 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1791	T2			N.D.	
GLP-SMPL-21-1792	T3			N.D.	
GLP-SMPL-21-1794	C	S17	14 DAA5	N.D.	**N.D.**
GLP-SMPL-21-1796	T1			N.D.	**N.D.**

GLP-SMPL-21-1797	T2			N.D.	
GLP-SMPL-21-1798	T3			N.D.	

[1]DBA: Days before Application; DAA: Days after application
[2] Calculated considering 200 mL as overall volume of foliar dislodging solution and 400 cm^2 as overall surface of sampled leaves ($\mu g/cm^2$ = µg/L * 0.2 L / 400 cm^2)

Conclusion

A median value of 0.18 $\mu g/cm^2$ (trial 1) and 0.11 $\mu g/cm^2$ (trial 2) is obtained. The highest value is 0.272 $\mu g/cm^2$.

(Sala A., 2021b)