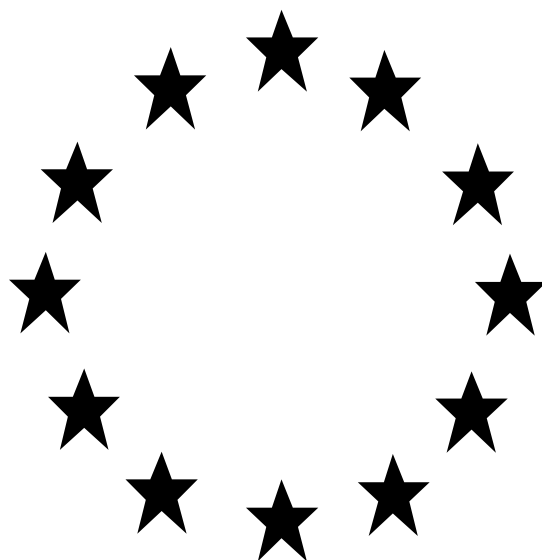




Draft Assessment Report (DAR)

- public version -

**Initial risk assessment provided by the rapporteur Member State
Austria for the existing active substance**

CYMOXANIL

**of the third stage (part B) of the review programme
referred to in Article 8(2) of Council Directive 91/414/EEC**

Volume 1

October 2007

Federal Office for Food Safety

**Spargelfeldstraße 191
1226 Vienna
Austria**

**Monograph prepared in the context of inclusion of following active substance in Annex I of
the Council Directive 91/414/EEC**

Cymoxanil



Volume 1

Report and Proposed Decision

Draft: June 2007

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Reason must not be granted on the basis of this document.

The monograph was prepared under the responsibility of:

Physical and chemical properties and methods of analysis

Klaus Hutter, Angelina Jirgal

Toxicology and metabolism

Albert Bergmann, Christian Prohaska

Residue data

Andreas Heinrich-Lenz (Coordinator)

Environmental fate and behaviour

Michael Stemmer

Ecotoxicology

Angelika Steininger, Anja Bartels

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Contents

	Page
Statement of Subject Matter and Purpose of Monograph	4
1.1 Purpose for which the monograph was prepared (Dossier Document A)	5
1.2. Summary and assessment of information relating to the collective assessment of dossiers (Dossier Document B)	5
1.3 Identity of the active substance (Annex IIA 1, Dossier Documents J, K-II and L-II)	5
1.4 Identity of the plant protection product	8
1.5 Use of the plant protection product	10
Overall Conclusions	19
2.1 General information	20
2.2 Methods of analysis	28
2.3 Impact on human and animal health	29
2.4 Residues	44
2.5 Fate and behaviour in the environment	54
2.6 Effects on non-target organisms	69
Overall Conclusions, including a listing of critical end points	77
Appendix 1	78
Appendix 2	89
Appendix 3	92
Proposed Decision with Respect to the Application for Inclusion of the Active Substance in Annex I	150
3.1 Background to the proposed decision	151
3.2 Proposed decision concerning inclusion in Annex I	153
3.3 Rational for the postponement of the decision to include the active substance in Annex I, or for the conditions and restrictions to be associated with a proposed inclusion in Annex I, as appropriate	154
Demand for Further information	155
4.1 Identity of the active substance	156
4.2 Physical and chemical properties of the active substance	156
4.3 Data on application and further information	156
4.4 Classification, packaging and labelling	156
4.5 Methods of analysis	156
4.6 Toxicology and metabolism	157
4.7 Residue data	157
4.8 Environmental fate and behaviour	157
4.9 Ecotoxicology	157

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Level 1

Cymoxanil

Statement of Subject Matter and Purpose of
Monograph

WARNING: This document forms part of an EC evaluation data package and should not be used for registration. Registration must not be granted on the basis of this document.

e-mail

Alternate Contact:

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Telephone:

[REDACTED]

Telefax:

[REDACTED]

Manufacturer of the active ingredient:

Name:

[REDACTED]

Address:

[REDACTED]
[REDACTED]

Contact Person:

[REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Telephone:

[REDACTED]

Telefax:

[REDACTED]

Location of plants:

see confidential information, Volume 4, Annex C

Applicant B:

Name:

OXON Italia SpA

Address:

Via Sempione 195
20016 Pero (MI), Italy

Contact Person:

[REDACTED]

Telephone:

[REDACTED]

Telefax:

[REDACTED]

e-mail:

[REDACTED]

Alternate Contact:

[REDACTED]
[REDACTED]
[REDACTED]

Telephone:

[REDACTED]

Telefax:

[REDACTED]

e-mail:

[REDACTED]

Manufacturer of the active ingredient:

Name: [REDACTED]
Address: [REDACTED]
[REDACTED]
Contact Person: [REDACTED]
Telephone: [REDACTED]
Telefax: [REDACTED]
e-mail: [REDACTED]

Location of plants: see confidential information, Volume 4, Annex C

1.3.2 Common name and synonyms (Annex IIA 1.3)

Cymoxanil

1.3.3 Chemical name (Annex IIA 1.4)

IUPAC: 1-(2-cyano-2-methoxyiminoacetyl)-3-ethylurea
CA: 2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide

1.3.4 Manufacturer's development code number (Annex IIA 1.5)

Applicant A (DuPont): DPX-T3217, IN-T3217, T3217

Applicant B (Oxon): No specific manufacturer's code number was defined

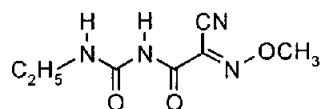
1.3.5 CAS, EEC and CIPAC numbers (Annex IIA 1.6)

CAS: 57966-95-7
EEC: 261-043-0
CIPAC: 419

1.3.6 Molecular formula, structural formula, molecular mass (Annex IIA 1.7)

Molecular formula: $C_7H_{10}N_4O_3$

Structural formula:



Molecular mass: 198.2 g/mol

1.3.7 Manufacturer or manufacturers of the active substance (Annex IIA 1.2)

Confidential Information - see Annex C

1.3.8 Method or methods of manufacture (Annex IIA 1.8)

Confidential Information - see Annex C

1.3.9 Specification of purity of the active substance (Annex IIA 1.9)

FAO Specification 419/TC (April 2005): 970 g/kg (declared minimum content of technical material).

Applicant A (DuPont): 970 g/kg (minimum purity)

Applicant B (Oxon): 970 g/kg (minimum purity)

From an analytical point of view, the technical material of both applicants is equivalent (for details see Volume 4, Annex C).

1.3.10 Identity of isomers, impurities and additives (Annex IIA 1.10)

Confidential Information - see Annex C

1.3.11 Analytical profile of batches (Annex IIA 1.11)

Confidential Information - see Annex C

1.4 Identity of the plant protection product

Applicant A (DuPont):

Name: Du Pont de Nemours (Deutschland) GmbH

Address: DuPont Strasse 1
61350 Bad Homburg, Germany

Contact Person:

Telephone:

Telefax:

e-mail

Alternate Contact:

Telephone:

Telefax:

Manufacturer of the active ingredient:

Name:

Address: [REDACTED]
[REDACTED]

Contact Person: [REDACTED]
[REDACTED]
[REDACTED]
[REDACTED]

Telephone: [REDACTED]

Telefax: [REDACTED]

Location of plants: see confidential information, Volume 4, Annex C

Applicant B:

Name: OXON Italia SpA
Address: Via Sempione 195
20016 Pero (MI), Italy

Contact Person: [REDACTED]

Telephone: [REDACTED]

Telefax: [REDACTED]

e-mail: [REDACTED]

Manufacturer:

Address: [REDACTED]
[REDACTED]
[REDACTED]

Contact Person: [REDACTED]

Telephone: [REDACTED]

Telefax: [REDACTED]

e-mail: [REDACTED]

Location of plant: see above

**1.4.1 Current, former and proposed trade names and development code numbers
(Annex IIIA 1.3)**

Applicant A (DuPont):

Trade name: Tanos®
Code number: DPX-KP481 50WG

Applicant B (Oxon):

Trade names: SIPCAM C50 (UK registered)
LIFE 50 WP (Italy proposed)

Code numbers: SIP40904 (years 1999-2000)
Cymoxanil 50 WP (years 2000-2002)

1.4.2 Manufacturer or manufacturers of the plant protection product (Annex IIIA 1.2)

Confidential Information - see Annex C

1.4.3 Type of the preparation and code (Annex IIIA 1.5)

Applicant A (DuPont): Water Dispersible Granule (WG)

Applicant B (Oxon): Wettable Powder (WP)

1.4.4 Function (Annex IIA 3.1, Annex IIIA 1.6)

Fungicide

1.4.5 Composition of the preparation (Annex IIIA 1.4)

Confidential Information - see Annex C

1.5 Use of the plant protection product

1.5.1 Field of use (Annex IIA 3.3, Annex IIIA 3.1)

Agriculture and horticulture

1.5.2 Effects on harmful organisms (Annex IIA 3.2, Annex IIIA 3.2)

Cymoxanil prevents spore germination, haustorial formation and mycelial growth of the target pathogens. Cymoxanil acts as a fungicide (contact, protective) for the control of *Phytophthora infestans* in potatoes and *Bremia lactucae* in lettuce.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

1.5.3 Summary of intended uses (Annex IIA 3.4, Annex IIIA 3.3 to 3.7, 3.9)

Crop and/or situation	Member state or Country (a)	Product Name (b)	F G or I (c)	Pests or Groups of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks (e)
					Type	Conc. of as	method kind	growth stage (d)	Number min max	Interval between application	kg as/ha min max	water l/ha min max	kg as/ha min max		
Lettuce	South	CYM 50	F	<i>Bremia lactucae</i>	WP	500 g/kg	Spray	40-49	3-4	7	0.03-0.048	500-800	0.240	10	Oxon
Potato	North	CYM 50	F	<i>Phytophthora infestans</i>	WP	500 g/kg	Spray	21-95	4	7-10	0.026-0.060-	200-450	0.120	7	Oxon
	South	CYM 50			WP	500 g/kg	Spray	21-95	5	7	0.012-0.024	500-1000	0.120	7	Oxon
	North	Tanos	F	<i>Phytophthora infestans</i>	WG	250g/kg	Spray	21-95	6-8	7-10	0.029-0.058	300-600	0.175	14	DuPont
	South														

(a) Southern Europe (South) Northern Europe (North).

(b) CYM 50 = Cymoxanil 50 %WP; Tanos = Cymoxanil/Famoxadone 250:250g/kg.

(c) Outdoor or field use (F), glasshouse application (G) or indoor application (I).

(d) Growth stage at the first application according to BBCH system for a uniform coding of phenologically similar growth stages of all mono- and dicotyledonous plant species.

(e) GAP for products supported by Oxon or DuPont.

1.5.4 Information on authorisation in EU Member States (Annex IIIA 12.1)

Applicant A (DuPont):

DuPont authorized uses on potatoes (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)	Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)
Austria Pests controlled: <i>Phytophthora, Alternaria</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: BBCH 29-79 Maximum Number Applications: 6 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Belgium Pests controlled: <i>Phytophthora infestans</i> Max. Application Rate: 0.15 kg cymoxanil/ha Growth Stage: Not specified Maximum Number Applications: 6 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Cyprus Pests controlled: <i>Phytophthora infestans Alternaria solani</i> Application Rate: 0.125 kg cymoxanil/ha Growth Stage: Not specified Maximum Number Applications: Not specified PHI: 8 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Czech Republic Pests controlled: <i>Phytophthora infestans</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: BBCH 10-92 Maximum Number Applications: 4 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Estonia Pests controlled: <i>Phytophthora infestans, alternaria solani</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: BBCH 21-35 Maximum Number Applications: 6 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Finland Pests controlled: <i>Phytophthora infestans, alternaria solani</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: Not specified Maximum Number Applications: 3 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.

DuPont authorized uses on potatoes (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)	Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)
France Pests controlled: Mildew Application Rate: 0.12kg cymoxanil/ha Growth Stage: not specified Maximum Number Applications: 4 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Germany Pests controlled: <i>Phytophthora infestans</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: BBCH 29-79 Maximum Number Applications: 8 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Greece Pests controlled: <i>Phytophthora infestans</i>, <i>Alternaria solani</i> Application Rate: 0.16 kg cymoxanil/ha Growth Stage: BBCH 14-89 Maximum Number Applications: 8 PHI: 15 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Hungary Pests controlled: <i>Alternaria</i>, <i>Phytophthora infestans</i> Application Rate: 0.16 kg cymoxanil/ha Growth Stage: Post plant, pre-emergence Maximum Number Applications: 9 PHI: 7 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Ireland Pests controlled: <i>Phytophthora infestans</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: Not specified Maximum Number Applications: 6 PHI: 14 day	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Italy Pests controlled: <i>Peronospora</i>, <i>Phytophthora infestans</i>, <i>Alternaria solani</i>, <i>Botrytis</i>, <i>A. lycopersici</i> Application Rate: 0.12 Growth Stage: Not specified Maximum Number Applications: 8 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
Latvia Pest controlled: <i>Phytophthora infestans</i>, <i>Alternaria solani</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: Not specified Maximum Number Applications: 6 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.

DuPont authorized uses on potatoes (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)	Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)
<u>Lithuania</u> Pests controlled: <i>Phytophthora, Alternaria</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: Not specified Maximum Number Applications: 6 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
<u>The Netherlands</u> Pests controlled: <i>Phytophthora infestans</i> Application Rate: 0.15 kg cymoxanil/ha Growth Stage: BBCH 10-60 Maximum Number Applications: 3 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
<u>Poland</u> Pests controlled: <i>Phytophthora infestans, Alternaria tenuis</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: BBCH 31-90 Maximum Number Applications: 3 PHI: 11 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
<u>Portugal</u> Pests controlled: <i>Phytophthora infestans</i> Application Rate: 0.12 kg cymoxanil/ha Growth Stage: n/a Maximum Number Applications: 9 PHI: 7 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
<u>Slovakia</u> Pests controlled: <i>Phytophthora infestans</i> Application Rate: 0.15 kg cymoxanil/ha Growth Stage: BBCH 10-92 Maximum Number Applications: 6 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
<u>Slovenia</u> Pests controlled: <i>Phytophthora infestans</i> Application Rate: 0.12 kg cymoxanil/ha Growth Stage: n/a Maximum Number Applications: 4 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
<u>Spain</u> Pests controlled: <i>Phytophthora infestans, Alternaria solani, Septoria, mildew</i> Application Rate: 0.12 kg cymoxanil/ha Growth Stage: n/a Maximum Number Applications: 5 PHI: 15 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.

DuPont authorized uses on potatoes (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)	Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)
Sweden Pests controlled: <i>Phytophthora</i>, <i>Alternaria</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: Not specified Maximum Number Applications: 3 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.
United Kingdom Pests controlled: <i>Phytophthora infestans</i> Application Rate: 0.175 kg cymoxanil/ha Growth Stage: Not specified Maximum Number Applications: 6 PHI: 14 days	Actual use rate is similar to registered use rate but actual number of applications is normally less than maximum number registered.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Applicant B (Oxon):

Authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)		Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season) ¹
Belgium:		
Potato	<u>mix MZ² (4.5-65 WP³)</u>: target: <i>Phytophthora infestans</i>, // rate: 90-112 g a.i./ha // timing: intervals of 7-10 days between treatments // PHI: 21 days <u>mix CTN (50-375 g/l)</u>: target: <i>Phytophthora infestans</i>, // rate: 100 g a.i./ha // timing: intervals of 7-10 days between treatments // PHI: 21 days.	
France:		
Grape	<u>mix Cu sul+MZ (3.43-18-11.5 WP)</u>: target: <i>Plasmopara viticola</i> // rate: 120g a.i./ha <u>mix MZ (6-70 WP)</u>: target: <i>Plasmopara viticola</i>, <i>Phomopsis viticola</i>, Guignardia bidwellii, <i>Pseudopeziza tracheiphila</i> // rate: 120 g a.i./ha <u>mix FOL (40-334 SC)</u>: target: <i>Plasmopara viticola</i>, <i>Phomopsis viticola</i> // rate: 120 g a.i./ha	
Potato	<u>mix MZ (6-70 WP)</u>: target: <i>Phytophthora infestans</i>, // rate: 100 g a.i./ha // n° appl.: max 6/yr. <u>mix CTN (50-375 SC)</u>: target: <i>Phytophthora infestans</i> // rate: 150 g a.i./ha // n° appl.: max 2/yr.	
Greece:		
Grape	<u>mix MZ (4-40 WP)</u> : target: <i>Plasmopara viticola</i> // rate: g 250-300 fp./hl (100-120 g a.i./ha) // timing: intervals of 7-14 days between treatments // n° appl.: max 4/yr // PHI: 28 days	
Potato	<u>mix MZ (4-40 WP)</u> : target: <i>Phytophthora infestans</i> // rate: g 250-300 fp./hl (100-120 g a.i./ha) // timing: intervals of 7-14 days between treatments // n° appl.: max 4/yr // PHI: 15 days	
Tomato	<u>mix MZ (4-40 WP)</u> : target: <i>Phytophthora infestans</i> // rate: g 250-300 fp./hl (100-120 g a.i./ha) // timing: intervals of 7-14 days between treatments // n° appl.: max 4/yr // PHI: 7-15 days	
Hungary :		
Grape	<u>mix Cu ox. (4-40 WP)</u> : target: <i>Plasmopara viticola</i> <i>Pseudopeziza tracheiphila</i> , <i>Uncinula necator</i> // rate: 120 g a.i./ha // timing: intervals of 7-10 days between treatments // n° appl.: max 4/yr // PHI: 21 days	

¹ generally cymoxanil is applied at the maximum registered rate but often with a lower number of applications than the maximum authorised number of applications

² BEN= Benalaxyl, CTN= Chlorothalonil, Cu hyd= Copper Hydroxide, Cu ox= Copper Oxychloride, Cu sul= Copper sulphate, FOL= Folpet, Fos Al= Fosetyl Aluminium, MZ= Mancozeb

³ values indicate % of ai in the formulated product, first value in bold indicate % of Cymoxanil

Authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)		Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season) ⁴
Italy:		
Artichoke	CYM alone (45 WG, 21.14 WP): target: <i>Bremia lactucae</i> // rate: 180-240 g a.i./ha // timing: intervals of 8-10 days between treatments mix Cu ox. (4-20 WP); mix Cu hyd. (2-10 WP): target: <i>Bremia lactucae</i> // rate: 120 g a.i./ha // timing: intervals of 8-10 days between treatments mix Cu ox. (2.3-20 WP): target: <i>Bremia lactucae</i> // rate: 69 g a.i./ha // timing: intervals of 8-10 days between treatments	
Courgettes	CYM alone (45 WG, 21.14 WP): target: <i>Pseudoperonospora cubensis</i> // rate: 180-240 g a.i./ha // timing: intervals of 8-10 days between treatments mix Cu ox. (4-20 WP); mix Cu hyd. (2-10 WP): target: <i>Pseudoperonospora cubensis</i> // rate: 120 g a.i./ha // timing: intervals of 8-10 days between treatments mix Cu ox. (2.3-20 WP): target: <i>Pseudoperonospora cubensis</i> // rate: 69 g a.i./ha // timing: intervals of 8-10 days between treatments	
Garlic	CYM alone (45 WG, 21.14 WP): target: <i>Peronospora schleideni</i> // rate: 180-240 g a.i./ha // timing: intervals of 8-10 days between treatments mix Cu ox. (4-20 WP); mix Cu hyd. (2-10 WP): target: <i>Peronospora schleideni</i> // rate: 120 g a.i./ha // timing: intervals of 8-10 days between treatments mix Cu ox. (2.3-20 WP): target: <i>Peronospora schleideni</i> // rate: 69 g a.i./ha // timing: intervals of 8-10 days between treatments	
Grape	CYM alone (45 WG, 21.14 WP): target: <i>Plasmopara viticola</i> // rate: 180-240 g a.i./ha // timing: intervals of 8-10 days between treatments mix Cu ox. (4-20 WP); mix Cu hyd. (2-10 WP): target: <i>Plasmopara viticola</i> // rate: 120 g a.i./ha // n° appl: 4/yr. mix Cu ox. (2.3-20 WP): target: <i>Plasmopara viticola</i> // rate: 69 g a.i./ha // n° appl: 4/yr. mix MZ (4-40 WP, 2-20 WP): target: <i>Plasmopara viticola</i> // rate: 80-120 g a.i./ha // timing: intervals of 8-10 days between treatments mix MZ (2.2-40 WP): target: <i>Plasmopara viticola</i> // rate: 44-66 g a.i./ha // timing: intervals of 8-10 days between treatments mix FOL+MZ (4-16-20 WP): target: <i>Plasmopara viticola</i> // rate: 100-120 g a.i./ha // timing: intervals of 8-10 days between treatments mix Fos Al+MZ (2.18-32.5-25 WP): target: <i>Plasmopara viticola</i> // rate: 87 g a.i./ha // timing: intervals of 4 days between treatments	

⁴ generally cymoxanil is applied at the maximum registered rate but often with a lower number of applications than the maximum authorised number of applications

Authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)		Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season) ⁵
Lettuce	<u>CYM alone (45 WG, 21.14 WP): target: <i>Bremia lactucae</i> // rate: 180-240 g a.i./ha // timing: intervals of 8-10 days between treatments</u> <u>mix Cu ox. (4-20 WP); mix Cu hyd. (2-10 WP): target: <i>Bremia lactucae</i> // rate: 120 g a.i./ha // timing: intervals of 8-10 days between treatments</u> <u>mix Cu ox. (2.3-20 WP): target: <i>Bremia lactucae</i> // rate: 69 g a.i./ha // timing: intervals of 8-10 days between treatments</u>	
Levant garlic	<u>CYM alone (45 WG, 21.14 WP): target: <i>Phytophthora porri</i> // rate: 180-240 g a.i./ha // timing: intervals of 8-10 days between treatments</u> <u>mix Cu ox. (4-20 WP); mix Cu hyd. (2-10 WP): target: <i>Phytophthora porri</i> // rate: 120 g a.i./ha // timing: intervals of 8-10 days between treatments</u> <u>mix Cu ox. (2.3-20 WP): target: <i>Phytophthora porri</i> // rate: 69 g a.i./ha // timing: intervals of 8-10 days between treatments</u>	

⁵ generally cymoxanil is applied at the maximum registered rate but often with a lower number of applications than the maximum authorised number of applications

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Level 2

Cymoxanil

Overall Conclusions

WARNING: This document forms part of an EC evaluation data package and should not be used for registration. Registration must not be granted on the basis of this document.

1. Reasoned statement of the overall conclusions drawn by the Rapporteur Member State

2.1 General information

2.1.1 Identity, including a listing of end points relating to identity

All points (Annex II and III) have been addressed and the information supplied is acceptable.

2.1.2 Physical and chemical properties, including a listing of end points relating to physical and chemical properties

Cymoxanil pure and technical active substance is a white to pale peach/pink solid. The melting point for the technical active substance is 161 °C – 162 °C. Cymoxanil is thermally stable. The relative density of Cymoxanil determined at 20 °C is ranging from 1.32 - 1.33 for the technical and pure active substance. The vapour pressure of the active substance is low, ranging from 1.50×10^{-4} Pa (20 °C) to 4.50×10^{-5} Pa (25 °C).

The Henry's law constant is calculated to be 3.3×10^{-5} Pa.m³.mol⁻¹ at pH 5 and 3.8×10^{-5} Pa.m³.mol⁻¹ at pH 7, respectively. The IR-, MS- and NMR spectra are in agreement with the chemical structure. There are no known impurities of Cymoxanil of toxicological, ecotoxicological, or environmental significance. Cymoxanil has a low solubility in water. The active substance is slightly to moderately soluble in most medium polarity organic solvents, but only slightly soluble in non-polar hydrocarbons and octanol. The partition coefficient of Cymoxanil is 3.89 at pH 5, 4.66 at pH 7 and 4.37 in an unbuffered solution. The pKa value for the pure active substance at 20° C is determined to be 9.7 ± 0.2 or 9.0, respectively. The surface tension of an aqueous solution is 68.7 mN/ at 19 ± 0.5 ° C, indicating that Cymoxanil has no surface active properties. Cymoxanil is not highly flammable, auto-flammable or explosive. Nevertheless, unambiguous determination of the oxidizing properties of Cymoxanil is required.

Applicant A (DuPont):

DPX-KP481 50WG is a solid brown water-dispersible granule with a sweet odour, containing the two active ingredients Cymoxanil and Famoxadone. DPX-KP481 50WG is not explosive nor an oxidizer. The preparation DPX-KP481 50WG is not considered flammable. The pH of an aqueous suspension of DPX-KP481 50WG is 5.8 at room temperature. The bulk density is 0.60 g/mL. The preparation was tested for dustiness and found to be nearly dust-free. From these properties no particular problems are expected, when the product is used as recommended. DPX-KP481 50WG is stable under accelerated storage conditions (14 days, 54 °C) and over a period of two years at room temperature, since no decrease of Cymoxanil concentration or significant changes of technical properties was observed during storage.

The relevant technical properties of the product (wettability, persistence of foaming, suspensibility, flowability, attrition resistance, etc.) show acceptable technical performance when using the product as recommended. DPX-KP481 50WG is chemically and physically compatible with a lot of commonly used insecticides and fungicides.

Applicant B (Oxon):

Cymoxanil 50%WP is a homogeneous powder with a clear ivory colour, having a characteristic odour. The product is not explosive and not oxidizing. It has a flash point of 178 ± 2 °C and is not highly flammable. The product is not autoflammable. The pH of an aqueous suspension of Cymoxanil 50%WP is 6.8 at room temperature. The bulk density is 0.364 g/mL. From these properties no particular problems are expected, when the product is used as recommended. Cymoxanil 50%WP is stable under accelerated storage conditions (14 days, 54° C) and over a period of two years at room temperature, since no decrease of Cymoxanil concentration or significant changes of technical properties was observed during storage. The relevant technical properties of the product (wettability, persistence of foaming and suspensibility) show acceptable technical performance. No differences in technical properties are observed when using the formulated product with and without water soluble bag. Particle size analysis shows a median diameter of 6.9 µm. Cymoxanil 50%WP is physically and chemically compatible with mancozeb and fluazinam containing products.

2.1.3 Details of uses and further information

2.1.3.1 Details of uses

Cymoxanil acts as a fungicide (contact, protective) for the control of *Phytophthora infestans* in potatoes and *Bremia lactucae* in lettuce.

2.1.3.2 Further information

Information on handling, storage, transport or fire, destruction or decontamination, and emergency measures for the active substance as manufactured and information on packaging, cleaning procedures, handling, storage, transport or fire, emergency measures, and procedures for destruction or decontamination for the suspension concentrate have been supplied and are acceptable.

2.1.4 Classification and labelling

Active Substance

On the basis of the available data the following classification and labelling is proposed according to Directive 67/548/EEC in combination with Directive 93/21/EEC:

Hazard symbols:		Black St. Andrew's Cross on orange square
		Dead fish, dead tree
Indication of danger:	Xn	Harmful
	Xi	Irritant
	N	Dangerous for the environment
Risk phrases:	R22	Harmful if swallowed

Hazard symbols:		Black St. Andrew's Cross on orange square
		Dead fish, dead tree
	R43	May cause sensitisation by skin contact
	R48/22	Harmful: danger of serious damage to health by prolonged exposure if swallowed
	R63	Possible risk of harm to the unborn child
	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases:	S2	Keep out of the reach of children
	S13	Keep away from food, drink and animal feedingstuffs
	S20/21	When using do not eat, drink or smoke
	S24	Avoid contact with skin
	S36/37	Wear suitable protective clothing and gloves
	S46	If swallowed, seek medical advice immediately and show this container or label
	S56	Dispose of this material and its container to hazardous or special waste collection point.
	S57	Use appropriate container to avoid environmental contamination.
	S60	This material and its container must be disposed of as hazardous waste.
	S61	Avoid release to the environment. Refer to special instructions/safety data sheets.

Justification for the proposal with respect to health effects:

R22 ("harmful if swallowed"): The risk phrase is proposed because the active substance showed an LD₅₀ of 960 mg/kg bw in the rat.

R43 ("may cause sensitisation by skin contact"): With respect to skin sensitisation of cymoxanil, 3 Maximisation tests have been submitted. These studies have been conducted according to OECD Guideline 406 and meet the GLP criteria; regarding the study design, the studies are comparable and differ only in the vehicle used. The results of two studies indicate no skin sensitising property of cymoxanil. However, in the third study (Allan, 1994), in all test animals dermal reactions have been observed after challenge (slight to moderate erythema and slight to well defined oedema). In contrast to the notifier's opinion, that "the weight of evidence would suggest that cymoxanil is not a skin sensitizer", a possible skin sensitizing property of cymoxanil cannot be excluded.

It should be mentioned that also in directive 2000/32/EC (26th ATP; 19 May 2000) cymoxanil has been classified and labelled with respect to its sensitizing properties.

R48/22 ("Harmful: danger of serious damage to health by prolonged exposure if swallowed"):

Based on the results of all subchronic toxicity studies, effects on testes/epididymides caused by cymoxanil technical is evident in rats and dogs as well:

- In the 28 days dietary study in rats (*Ramesh, 1999a*), animals of the two highest dose levels in rats showed changes in testes and epididymides weight, which might be linked to the reduction in body weight and body weight gain that occurred at the two higher dose groups. However, no histology has been performed in this study.
- In a 90 days dietary rat study (*Malek, 1992*), increase of testes weight of animals of the two highest dose levels had been accompanied by histological changes in testes and epididymides (spermatid degeneration, multinucleated spermatids, cell debris, hypospermia).
- Also in one out of two 90 days dog study (*Tompkins, 1993*), "small" testes, reduced epididymides weight as well as aspermatogenesis were reported at a dose level of 500 ppm. These effects could not be confirmed in the first 1 year dietary study. However, the highest dose administered (200 ppm) was much lower than the "effect dose" in the 90 days study.
- Nevertheless, in the second 1 year dog study (*Teunissen, 2003*), pathological examination exhibited finding in testes and epididymides at the high dose group (200 ppm): reduced size of testis as well as reduced size of epididymides and thickened epididymides: The histological findings comprised atrophic changes of testes and epididymides (seminiferous cell debris).
- In addition, it has to be mentioned that increased incidences of elongate spermatid degeneration and multinucleated spermatids were also observed in a chronic study on rats (see B.6.5.).

According to directive 2001/59/EC, substances have to be classified for their possible health effects by prolonged exposure, when morphological and functional changes after repeated exposure are evident (subchronic studies at and below a dose level of 50 mg/kg bw). The effects in testes mentioned have been observed in a 90 days toxicity study in rats at dose levels of 47.6 mg/kg bw (testes) as well as 102 and 224 mg/kg bw (testes and epididymides). However, findings in testes were also evident in the 90 days dog study at dose levels of 10.56 mg/kg bw and in the 1 year dog study at 5.6 mg/kg bw, too.

Although the respective findings were not seen consistently in all relevant studies, adverse effects on testes/epididymides are clearly evident in rats and dogs after subchronic administration of cymoxanil. Despite of no functional impairment of reproductive performance in multigeneration studies in rats indicative for testes effects, possible classification of cymoxanil with **Xn, R 48/22 ("Harmful: danger of serious damage to health by prolonged exposure if swallowed")** should be considered based on these morphological changes.

R63 ("Possible risk of harm to the unborn child"): With respect to teratogenicity, cymoxanil should be classified into Repro Cat 3 considering the following reasons:

Taking into account the results of all developmental studies available, there is strong evidence that cymoxanil can impair fetal development producing also malformations (demonstrated in

one out of two studies in rats and in three out of four studies in rabbits) and has to be classified into Repro Cat 3 (**Xn, R 63 “Possible risk of harm to the unborn child”**) considering the following reasons:

- In the first rat study (*Murray, 1993*) increased incidences of malformations (hemi vertebra, exencephalic head and fused ribs; findings above the range of historical control) were observed at maternal toxic dose levels.
- Also in the second rat study (*Veena, 1998*) increased incidences of variants and minor anomalies even at not maternal toxic dose levels indicate the potential of cymoxanil to disturb the development of foetuses.
- In one rabbit study (*Palmer et al., 1981*), there was a clear dose dependent increase of “vertebra and/or rib alterations”, sometimes associated with scoliosis at maternal toxicity, without statistical significance but above the historical control data.
- In a further rabbit study (*Feussner et al., 1982*) increased incidences of malformations (hydrocephaly, cleft palates) occurred at the highest dose tested. Incidences were statistically significant increased and above historical background of these findings.
- Finally the incidence of dilation of heart ventricles of a third study in rabbits (*Ponnana, 1999*) was statistically significant increased in the high dose animals and was above the historical control data.

The safety phrases **S2, S13, S20/21** and **S46** follow a general precautionary approach. The safety phrase **S24** (Avoid contact with skin) is proposed because of the skin sensitising properties; **S36/37** (Wear suitable protective clothing and gloves) has to be applied caused by R43, R48/22 and R63.

Justification for the proposal with respect to environmental effects:

N follows from R50/53

R50/53 follows from the toxicity of the active substance to algae (*Pseudokirchneriella subcapitata*: $E_{rC_{50}}$ (72 h) = 0.63 mg/L, Bell et al. (1996); *Anabaena flos-aquae*: $E_{rC_{50}}$ (72 h) = 0.254 mg/L, Hughes et al. (1996a)) and from the results of a biodegradation study where it was shown that cymoxanil is not readily biodegradable (Luit, 2001).

S56, S 57, S60 and S61 follow from the toxicity to aquatic organisms and potential long-term adverse effects to the aquatic environment.

Formulation Cymoxanil 50 % WP

On the basis of the available data the following classification and labelling is proposed according to Directive 67/548/EEC in combination with Directive 93/21/EEC:

Hazard symbols:		Black St. Andrew's Cross on orange square
		Dead fish, dead tree
Indication of danger:	Xn	Harmful
	N	Dangerous for the environment
Risk phrases:	R22	Harmful if swallowed
	R48/22	Harmful: danger of serious damage to health by prolonged exposure if swallowed
	R63	Possible risk of harm to the unborn child
	R51/53	Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases:	S2	Keep out of the reach of children
	S13	Keep away from food, drink and animal feedingstuffs
	S20/21	When using do not eat, drink or smoke
	S36/37	Wear suitable protective clothing and gloves
	S46	If swallowed, seek medical advice immediately and show this container or label
	S56	Dispose of this material and its container to hazardous or special waste collection point.
	S57	Use appropriate container to avoid environmental contamination.
	S60	This material and its container must be disposed of as hazardous waste.
	S61	Avoid release to the environment. Refer to special instructions/safety data sheets.

Justification for the proposal with respect to health effects:

R22: is proposed because the active substance showed an LD₅₀ of 1200 mg/kg bw in the rat.

Remark: R43 is not justified since a Maximizations test conducted with the preparation indicates no sensitising properties of the formulation "Cymoxanil 50 % WP".

R48/22 and **R63** are necessary because of proposed classification and labelling of the active ingredient cymoxanil (51.5 %).

The safety phrases **S2**, **S13**, **S20/21** and **S46** follows a general precautionary approach. The safety phrases **S36/37** have to be applied caused by R48/22 and R63 together with the risk assessment with respect to operator exposure. In these calculations, a safe use could only be identified if appropriate personal protective equipment is considered.

Justification for the proposal with respect to environmental effects:

N follows from R51/53

R51/53 follows from the toxicity of the formulation Cymoxanil 50 % WP to algae

(*Pseudokirchneriella subcapitata*: E_rC_{50} (72 h) = 4.72 mg/L, Bogers (1999b)

and from the results of a biodegradation study where it was shown that the active substance is not readily biodegradable (Luit, 2001).

S56, S 57, S60 and S61 follow from the toxicity to aquatic organisms and potential long-term adverse effects to the aquatic environment.

Formulation TANOS

On the basis of the available data the following classification and labelling is proposed according to Directive 67/548/EEC in combination with Directive 93/21/EEC:

Hazard symbols:		Black St. Andrew's Cross on orange square
		Dead fish, dead tree
Indication of danger:	Xn	Harmful
	N	Dangerous for the environment
Risk phrases:	R22	Harmful if swallowed
	R43	May cause sensitisation by skin contact
	R48/22	Harmful: danger of serious damage to health by prolonged exposure if swallowed
	R63	Possible risk of harm to the unborn child
	R50/53	Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Safety phrases:	S2	Keep out of the reach of children
	S13	Keep away from food, drink and animal feedingstuffs
	S20/21	When using do not eat, drink or smoke
	S24	Avoid contact with skin
	S36/37	Wear suitable protective clothing and gloves
	S46	If swallowed, seek medical advice immediately and show this container or label
	S56	Dispose of this material and its container to hazardous or special waste collection point.
	S57	Use appropriate container to avoid environmental contamination.
	S60	This material and its container must be disposed of as hazardous waste.

Hazard symbols:	 	Black St. Andrew's Cross on orange square Dead fish, dead tree
	S61	Avoid release to the environment. Refer to special instructions/safety data sheets.

Justification for the proposal with respect to health effects:

R22: is proposed because the formulation showed an LD₅₀ of 1200 mg/kg bw in the rat.

R43: With respect to possible skin sensitization properties of "TANOS", only a modified Buehler test showing the formulation to be non-sensitizing has been provided. Since the active substance is judged to be a possible skin sensitizer based on a Maximisation test, such a study would have been more appropriate to investigate the possible skin sensitization of the formulation "TANOS". In conclusion and as a precautionary principle, "TANOS" has to be classified and labelled with respect to its sensitisation by skin contact.

R48/22 and **R63** are necessary because of proposed classification and labelling of the active ingredient cymoxanil (51.5 %).

The safety phrases **S2**, **S13**, **S20/21** and **S46** follows a general precautionary approach. The safety phrase **S24** (Avoid contact with skin) is proposed because of the skin sensitising properties; **S36/37** (Wear suitable protective clothing and gloves) has to be applied caused by R43, R48/22 and R63.

According to the second active ingredient (famoxadone), no additional classification and labelling of TANOS is considered necessary.

Justification for the proposal with respect to environmental effects:

N follows from R50/53

R50/53 follows from the toxicity of the formulation Tanos to fish (*Oncorhynchus mykiss*: LC50 (96 h) = 0.0287 mg/L, Brown, (1997a)), the toxicity to aquatic invertebrates (*Daphnia magna*: EC50 (48 h) = 0.0555 mg/L, Brown (1997b)) and from the results of a biodegradation study where it was shown that the active substance cymoxanil is not readily biodegradable (Luit, 2001).

S56, **S 57**, **S60** and **S61** follow from the toxicity to aquatic organisms and potential long-term adverse effects to the aquatic environment.

WARNING: This document forms part of an application for registration of a pesticide and should not be relied upon for any purpose other than the evaluation of the application. No warranty is made by the Ministry of Agriculture, Fisheries and Forestry as to the accuracy or completeness of the information contained in this document. This document is not to be used as a basis for any legal proceedings.

2.2 Methods of analysis

2.2.1 Analytical methods for analysis of the active substance as manufactured

The submitted methods for the active substance and impurities are suitable for the determination of Cymoxanil and impurities in the technical material [RP-HPLC-UV]. All applied methods for the active substance and impurities were fully validated by both applicants. The CIPAC method 419/TC/M/3 can be used for the determination of the active substance in technical Cymoxanil.

2.2.2 Analytical methods for formulation analysis

Applicant A (DuPont):

The submitted method is suitable and sufficiently validated for the determination of the active substance in the formulation [HPLC-UV].

In addition, the CIPAC method 419/WG/M/3 is available for the determination of Cymoxanil active substance in Cymoxanil water-dispersible granules.

Applicant B (Oxon):

The submitted method is suitable and sufficiently validated for the determination of the active substance in the formulation [HPLC-UV].

The notifier stated that CIPAC method 419/WP/M/3 is considered to be applicable to a Cymoxanil 50 % WP preparation. This method has not been specifically proved for its applicability to the lead formulation.

2.2.3 Analytical methods for residue analysis

The analytical method for residues in food/feed of plant origin is successfully validated. Mean recovery rates at each fortification level are in the range of 70 to 110 % with a relative standard deviation of ≤ 20 %. The analytical calibration extend over a range appropriate to the lowest and highest nominal concentration of the analyte $\pm$ at least 20% for this analytical method. No interfering blanks (< 30 % of the LOQ) occurred. An ILV (GC-MSD) confirmed the validity of the applied method. Readily available equipment and reagents are used.

Matrix	Residue definition	LOQ	Residue limit/ Toxic concentration for non-target organisms
Food of plant origin: Potatoes Lettuce	Cymoxanil	0.05 mg/kg 0.05 mg/kg	0.05 ^{#)} mg/kg proposed MRL 0.05 mg/kg proposed MRL
Food of animal origin	Not required, no residue definition/no MRL is proposed		
Soil	Cymoxanil	0.01 mg/kg	EC ₅₀ > 1 g/kg soil dw earth worm
Drinking water	Cymoxanil	0.10 µg/L	0.10 µg/L EU drinking water limit
Surface water	Cymoxanil	0.10 µg/L	NOEC 58.1 µg/L <i>Cyprinodon variegatus</i>
Air	Cymoxanil	0.46 µg/m ³	6 µg/m ³ based on a proposed

Matrix	Residue definition	LOQ	Residue limit/ Toxic concentration for non-target organisms
			AOEL _{systemic} of 0.02 mg/kg bw/day
Body fluids	Not necessary, the active substance is not classified as toxic or very toxic		

#) Proposed setting based on LOQ study of Freshi G. (2001b) and in correspondence with residue trials

The methods for determination of residues in soil, water and air were validated sufficiently. Confirmatory analyses were performed for each matrix to demonstrate the validity of the applied methods. For body fluids and tissues no analytical method was submitted, because Cymoxanil is not classified as toxic or highly toxic.

2.3 Impact on human and animal health

2.3.1 Effects having relevance to human and animal health arising from exposure to the active substance or to impurities contained in the active substance or to their transformation products

Adsorption, distribution, metabolism, excretion

Absorption: Based on all studies submitted (single oral low and high dose; multiple dosing) the radiolabelled test substance is absorbed to a great extent in rats. The urinary excretion (including cage wash) accounted for 63.7 – 79.5 % of the administered radioactivity. Biliary excretion of cymoxanil could be observed as well and was in the range of 6.2 – 9.6 % of administered dose. The **enteral resorption** after oral administration in respective studies investigating separately excretion via bile, urine and faeces can therefore be quantified to be **in the range of 76.0 to 81.1 %** (amount of radioactivity excreted via urine including radioactivity detected in cage wash, bile, expired air and carcass). With respect to T_{max} , a rapid absorption is evident; T_{max} -values for whole blood and plasma are in the range of 0.5 – 3 hours after dosing.

Pharmacokinetic parameter: The elimination half live ($t_{1/2}$) was shown to be 11.7 – 24.1 hours after single oral dosing; a slightly increase could be observed for animals administered multiple daily doses ($t_{1/2}$ of 30.8 – 31.7 hours). Plasma/whole blood ratios decrease 8 hours after administration < 1 indicating a reincorporation of ^{14}C -residues into erythrocytes. No significant differences were found between males and females at the different dosages tested.

Distribution: Tissue/blood ratios did not indicate a selective accumulation of ^{14}C -residues in any organ/tissue investigated with the exception of kidneys and liver as the main metabolism/excretion organs showing higher residue levels when compared to the whole blood. The half lives for the elimination of radioactivity from the mentioned organs are in the range of 23.4 – 32.9 hours (kidneys) and 28.3 – 37.9 hours (liver).

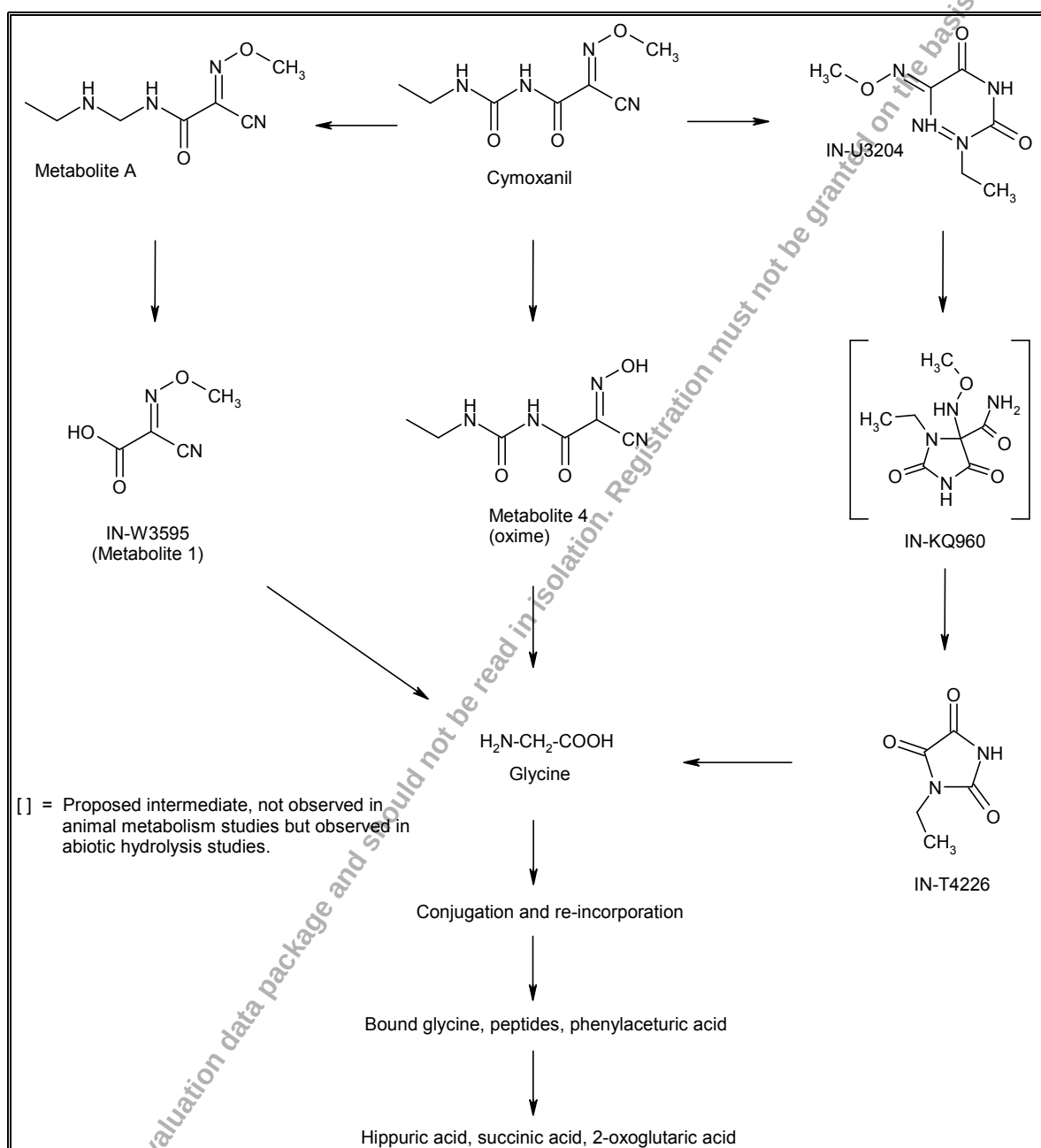
The respective tissue/plasma ratios up to 24 hours post dosing do not show any possible accumulation as well. 120 hours after administration, the ratios increase above 1 for all organs/tissues investigated. The increase of tissue/plasma ratios is conclusive, since the ^{14}C -

residues are incorporated into red blood cells. The residual radioactivity of all organs/tissues declines with time after treatment. For fat only, an increase of radioactive residues could be observed; this finding can be explained by the extensive metabolism of cymoxanil in rats indicating re-incorporation of the ^{14}C -labelled carbon atom (statistical significance was not given with respect to the increase of residues in fat). It can be concluded, that no potential of bioaccumulation can be assumed.

Excretion: After oral application of radioactive labelled cymoxanil (all dose levels tested), the major route of excretion was via urine (63.7 – 79.5 % of administered radioactivity including cage wash); feces contained 14.3 – 29.9 %. > 80 % of the applied radioactivity could be excreted within 48 hours; at the termination of the studies submitted (i.e. 48 – 168 hours after administration), 81.6 – 96.4 % of administered radioactivity was shown to be excreted via urine, feces and bile or were found in cage wash and expired air. Biliary excretion accounted for 2.0 – 9.6 %. Repeated dosing did not show any impact on the rate and extent of excretion.

Metabolism: Cymoxanil was shown to be extensively metabolised: no parent compound could be detected in any samples investigated (feces, urine, bile). The main portion of the urine radioactivity could be attributed to a polar fraction containing mainly bound glycine (conjugated with endogenous substances). One further metabolite quantified >10 % was shown to be 2-cyano-2-methoxyiminoacetic acid (IN-W3595) with levels up to 41.8 %. Degradation products like 2-cyano-N-[(ethylamino)methylene]-2-methoxyiminoacetamide, 1-ethyl 5,6-di-2,4(1H,3H) pyridinedione (IN-U3204), 1-(2-cyano-2-hydroxyiminoacetyl)-3-ethylurea (oxime) and hippuric acid were found only in trace amounts. For faeces, only about 30 – 40 % of the recovered radioactivity could be extracted; the main fraction found in extracts was again bound glycine. The radioactive residues found in bile were shown to be again mainly polar components and metabolite IN-W3595. All metabolites identified could be considered potentially intermediates leading to the formation of glycine used in physiological processes leading to conjugation and incorporation. The proposed metabolic pathway is shown in figure 2.3.1-1.

Figure B.2.3.1-1: Proposed metabolic pathway of cymoxanil in mammals



Acute toxicity

Acute toxicity tests with cymoxanil showed a moderate acute oral toxicity in rats (LD₅₀: 960 mg/kg bw). After dermal and inhalative administration, cymoxanil is of low toxicity. Cymoxanil is non-irritating to the skin and only very slightly irritant to eyes of the New Zealand White rabbit.

With respect to skin sensitisation of cymoxanil, 3 Maximisation tests have been submitted. These studies have been conducted according to OECD Guideline 406 and meet the GLP criteria; regarding the study design, the studies are comparable and differ only in the vehicle used. The results of two studies indicate no skin sensitising property of cymoxanil. However, in the third study (Allan, 1994), in all test animals dermal reactions have been observed after challenge (slight to moderate erythema and slight to well defined oedema). In contrast to the

notifier's opinion, that "the weight of evidence would suggest that cymoxanil is not a skin sensitizer", possible skin sensitizing properties of cymoxanil cannot be excluded. Based on the results of the acute toxicity studies available, cymoxanil should be classified and labelled with respect to acute oral toxicity (**Xn – harmful; R 22 – harmful if swallowed**) and skin sensitisation (**Xi – irritant; R 43 – may cause sensitisation by skin contact**).

Short term toxicity

The short term toxicity of cymoxanil has been investigated after oral application in rats (28 and 90 days of exposure), mice (28 and 90 days of exposure) and dogs (90 days and 1 year of exposure). In addition, a 28 days dermal study in rats has been conducted.

In oral rat studies, the main treatment-related findings were effects on body weight (gain) and food intake; main target organs/tissues were the liver and also kidneys. There were also some associated changes in clinical chemistry and to a minor degree in hematological parameters. In addition, histological alterations were evident in testes and epididymides (together with spermatid alterations) at higher dose levels.

In the 28 days dietary study in rats (*Ramesh, 1999a*), the NOAEL was set at 750 ppm (equivalent to 74.4 mg/kg bw) for males and 3000 ppm (equivalent to 287.8 mg/kg bw) for females, based on relative organ weight changes of liver and kidneys together with reduced body weight gain at 1500 ppm (males) and at 5000 ppm (females).

In the first 90 days dietary study in rats (*Malek, 1992*), the NOAEL can be set at 100 ppm (equivalent to 6.5 mg/kg bw) in males and 1500 ppm (equivalent to 137 mg/kg bw) in females, based on histological findings in testes at 750 ppm in males and on reduced body weight, body weight gain as well as increased food consumption, relative organ weight changes and alterations of clinical chemical parameter at 3000 ppm in females. Concerning the histological findings in testes and epididymides, incidences were statistically significant at the highest dose level tested (3000 ppm); no statistical significance has been observed for the animals of the 750 and 1500 ppm dose group with respect to this finding, but incidences at these dose groups clearly show a dose-relationship and indicate a treatment-related effect. Therefore, the 750 dose group is considered to be the LOAEL with respect to histopathological findings in testes.

In the second 90 days dietary study in rats (*Ramesh, 1999b*), treatment resulted in changes with respect to haematology and clinical chemistry even at the lowest dose (500 ppm) administered but values at this dose level were within historical background data. Based on relative organ weight changes (liver and kidneys) as well as alterations of haematological and clinical chemical parameter at ≥ 1000 ppm, the NOAEL can be set at 500 ppm (equivalent to 42.6 mg/kg bw for males and 48.1 mg/kg bw for females).

Also in mice, similar findings as a result of cymoxynil administration were observed. In a 28 days dietary study in mice (*Krishnappa, 1999a*), treatment-related effects were reduced food consumption at ≥ 1500 ppm (males) and reduced body weight plus reduced food consumption at ≥ 3000 ppm (females). The NOAEL can be set at 750 ppm (equivalent to 172.7 mg/kg bw) for males and 1500 ppm (equivalent to 329.9 mg/kg bw) for females.

In a 90 days dietary study in mice (*Krishnappa, 1999b*) the NOAEL can be set at 150 ppm (equivalent to 28.7 mg/kg bw for males and 32.9 mg/kg bw for females) based on clinical chemistry and histological changes (hepatocellular vacuolation) at 450 ppm.

In the first 90 days dietary study in dogs (*Tompkins, 1993*), clinical signs, reduced body weight gain and changes in haematology as well as in clinical chemistry parameters were observed at ≥ 200 ppm. In addition, aspermatogenesis was evident in 2/4 animals of the top dose (500 ppm). So the NOAEL was set at 100 ppm (equivalent to 3 mg/kg bw for both males and females). Also in the second 90 days (*Venugopala, 1999*) dietary study in dogs, reduced body weight gain and histological findings in the thymus (males and females) as well as organ weight changes (liver and thymus in females) were seen at ≥ 400 ppm. Therefore, the NOAEL can be set at 200 ppm (equivalent to 4.9 mg/kg bw for males and 5.2 mg/kg bw for females). Considering the dosing regime used in the first 1 year dietary study in dogs (*Tompkins, 1994*), the amount of compound administered was rather low. Possible effects on testes and epididymides, as found in a 90 days study in dogs, could not be confirmed in the 1 year dog study due to low amount administered (highest dose applied for males: 200 ppm). However, based on changes of haematology and clinical chemistry parameters in males, the NOAEL can be set at 100 ppm (equivalent to 3.0 mg/kg bw for males and 3.1 mg/kg bw for females). In females, no treatment related effects could be found even at the highest dose tested (100 ppm). In the second 1 year dietary study in dogs (*Teunissen, 2003*), again the amount of compound administered was rather low. Nevertheless, macroscopic examination exhibited a reduced size of testes in one animal of the high dose group as well as reduced size of epididymides or thickened epididymides (one animal each of the high dose group). The histological findings with respect to testes (3 animals of the highest dose group showed atrophy) and epididymides (seminiferous cell debris and atrophy of one animal of the high dose group each) were described in the study report to be within the range of background pathology in Beagle dogs of this age and strain. However, with respect to the results of one 90 days dietary study in dogs (*Tompkins, 1993*), a treatment related effect of cymoxanil to testes/epididymides cannot be excluded. Based on organ weight changes of the thymus and also on macroscopic as well as microscopic changes in testes/epididymides and eyes, the NOAEL can be set at 100 ppm (equivalent to 2.8 mg/kg bw in males and 2.9 mg/kg bw in females).

In a 28 days dermal toxicity rat study, no treatment related effects could be detected in animals of all dose groups tested. The NOAEL is higher than the highest dose administered (1000 mg/kg bw for males and females).

Genotoxicity

Cymoxanil was tested in a sufficient range of *in vitro* and *in vivo* mutagenicity assays measuring different mutagenic endpoints like gene mutation in bacterial and mammalian cells *in vitro* and chromosomal mutations and unscheduled DNA synthesis *in vitro* as well as *in vivo*.

Studies on gene mutation *in vitro* (bacterial tests, HPRT test on Chinese hamster ovaries) did not show any mutagenic potential caused by cymoxanil.

With respect to chromosomal aberrations, one of two *in vitro* studies showed positive results indicating chromosomal damage in human lymphocytes induced by the test substance. However, the results of a second study submitted on chromosomal aberrations on Chinese hamster ovary cells did not confirm the potential of cymoxanil with respect to possible genotoxicity. Furthermore, the results of 3 *in vivo* studies provided (2 micronucleous tests on mice, one *in vivo* chromosomal aberration assay in rats – bone marrow) did not show any potential of the test substance to produce chromosomal damage.

One *in vitro* UDS assay in primary rat hepatocytes indicated that under the test conditions used cymoxanil induces unscheduled DNA synthesis; again, the results of an *in vivo* study on unscheduled DNA synthesis (hepatocytes and spermatocytes) could not confirm the possible influence of cymoxanil to unscheduled DNA synthesis: the net nuclear grains observed in both hepatocytes and spermatocytes of treated animals were not statistically increased when compared to the negative (solvent) control.

Based on the results of all studies provided, the weight of evidence suggests no genotoxic potential caused by cymoxanil.

Long term toxicity/carcinogenicity:

The long term toxicity and carcinogenicity has been investigated in rats and mice (two studies each):

In the first 2-year combined chronic toxicity/carcinogenicity study in rats (Cox, 1994a), treatment related effects were increased incidences of clinical findings (increased hyperactivity and aggressiveness), reductions in body weight and weight gain and adverse macroscopic/ histopathological changes in various organs (degenerative and or inflammatory effects of the retina, nerves, lung, liver, pancreas, testes): The NOAEL was established at 100 ppm (equivalent to 4.1 mg/kg bw for males and 5.4 mg/kg bw for females). Histological findings with respect to testes (elongate spermatid degeneration, multinucleated spermatids) were found at ≥ 700 ppm supporting the conclusions drawn on the results of the studies on short term toxicity.

Based on the treatment related findings of the second chronic toxicity/carcinogenicity study on rats (Malleappa, 2003) the NOAEL for males was set at 100 ppm (equivalent to 4.7 mg/kg bw) based on reduced body weight and body weight gain as well as histological findings in different organs (rectum, lung, testes). In females, treatment related effects had been observed at 1200 ppm (changes in haematological and clinical parameter, histological findings in colon and lung); therefore the NOAEL for females can be set at 500 ppm (equivalent to 31.6 mg/kg bw).

In the first carcinogenicity study in mice (Cox, 1994b), the NOAEL was set at 30 ppm (equivalent to 4.19 mg/kg bw for males and 5.83 mg/kg bw for females) based on clinical symptoms, reduction of body weight gain, organ weight changes and histological findings in some organs (centrilobular hepatocellular hypertrophy, testicular atrophy, epididymal oligospermia and focal sperm cyst/cystic dilatation).

The results of the second carcinogenicity study on mice (Krishnaappa, 2002) indicated treatment related findings with respect to reduced food consumption, changes in the

differential leukocyte count and also macroscopic findings (haemorrhagic mesenteric lymph nodes in males) as well as histological alterations (follicular cysts in ovaries) in the highest dose group. The NOAEL can be set at 600 ppm (equivalent to 91.4 mg/kg bw for males and 91.9 mg/kg bw for females).

In all four studies, cymoxanil did not reveal any oncogenic potential up to and including the highest dose levels tested.

Reproductive toxicity:

With respect to reproductive toxicity, two multigeneration studies in rats have been submitted: Based on the results of the first two generation study (Kreckmann, 1993) the reproductive parameters investigated did not indicate a possible reproductive influence caused by cymoxanil up to 1500 ppm in the diet. For parental animals, reduced body weight of females (F_1 generation during gestation/lactation), reduced body weight gain as well as reduced food consumption of males (F_0 generation) and reduced relative testes weight (adults of the F_0 generation) were shown to be of statistical significance at the mid dose group (500 ppm) and above. Litter data: 0 – 4 day viability was statistically significantly reduced for the F_1 pups (this finding was not evident at both F_2 -generations). Concerning pup weight, statistically significant reductions were evident at 1500 ppm (all generations) and also at the mid dose level of 500 ppm for the F_{2b} -generation.

Based on these findings, the NOAEL for both parental and offspring effects is to be set at 100 ppm equivalent to 6.5 mg/kg bw/day (males) and 6.65 mg/kg bw/day (females); the reproductive NOAEL is 1500 ppm (equivalent to 97.9 mg/kg bw/day – males – and 103 mg/kg bw/day – females).

In the second two generation study (Ganiger, 2001), parental toxicity was evident by reduced body weights of the males (F_1 generation) and of females (F_0 and F_1 generation during pre-mating) as well as reduced food consumption (F_0 females during pre-mating and gestation) at the mid and high dose groups. With respect to reproductive parameters, there was a statistically significant decrease in the percentage of live pups born together with a reduced mean number of corpora lutea, mean number of implantations and an increased percentage of post-implantation loss in the high dosed F_1 generation. Concerning pup development, statistically significant decreased body weights were observed for F_1 and F_2 pups (males, females and combined sex) at the mid dose level of 450 ppm and above.

Based on findings in the second study, the NOAEL for both parental and offspring effects can be set at 150 ppm equivalent to 10.5 mg/kg bw/day (males) and 14.9 mg/kg bw/day (females); the reproductive NOAEL is 450 ppm (equivalent to 31.6 mg/kg bw/day in males and 42.8 mg/kg bw/day in females).

Developmental toxicity of cymoxanil was investigated in rats (2 studies) and rabbits (4 studies): In the first study in rats (Murray, 1993) statistically significant reductions of mean maternal body weights, reduced body weight gain and reduced food consumption indicate dose related maternal toxicity at 25 mg/kg bw and above. Concerning fetotoxicity, increased incidences of treatment related variations (partially ossified and unossified sternebra, wavy ribs and partially ossified pelvis) could be observed at maternal toxic dose levels. Concerning malformations,

incidences for hemi vertebra, exencephalic head and fused ribs were shown to be above the range of historical control at dose levels of clear maternal toxicity. Although incidences of these malformations observed were low, treatment-relation with respect to these findings cannot be excluded.

Based on all findings, the NOAEL for maternal toxicity is to be set at 10 mg/kg bw/day; the foetal NOAEL can be established at 10 mg/kg bw/day.

In the second developmental rat study (Veena, 1998), the NOAEL for maternal toxicity can be established at 60 mg/kg bw/d (highest dose level tested) based on the findings with respect to body weight, body weight gain, food consumption and reproductive parameters at the highest dose level tested (120 mg/kg bw/day). Concerning fetal findings with respect to skeletal observations, no NOAEL can be derived: incidences for minor anomalies (dumb-bell shaped thoracic vertebra 6/13) were shown to be statistically significant increased and above the historical control data even at the lowest dose tested (i.e. 30 mg/kg bw/day). These alterations are demonstrating an impact of the test material to the development of fetuses. Therefore, only a fetal LOAEL of 30 mg/kg bw/day can be established.

In the first developmental rabbit study (Cozens *et al.*, 1980), both maternal and foetal NOAEL were above the highest dose level tested, i.e. 16 mg/kg bw/day. No treatment related effects regarding maternal toxicity, litter data and foetal parameter could be observed at any dose level. However, the small number of litters available limited the validity for the assessment of developmental effects. Therefore, the study was regarded as supplementary information only. In the second developmental rabbit study (Palmer *et al.*, 1981), maternal toxicity (body weight gain and clinical observations) was evident in the mid (16 mg/kg bw/d) and high dose females (32 mg/kg bw/d). Therefore, the maternal NOAEL was set at 8 mg/kg bw/day. Concerning fetal findings, increased incidences of skeletal malformations (scoliosis and the presence of cervical ribs including "borderline cases between malformations and variants") have been observed in all dose group, but revealed no statistical significance. Even after re-evaluation and re-categorisation of these findings ("vertebra and/or rib alterations" associated with scoliosis) increased incidences (but without statistical significance) could be observed. For the high dose group, the number of fetuses with these malformations was above the historical control data submitted. Therefore the foetal NOAEL can be established at 16 mg/kg bw/day.

In the third study in rabbits (Feussner *et al.*, 1982), no maternal toxicity occurred, even at the highest dose (32 mg/kg bw/d). Concerning foetal findings, hydrocephaly was found in two fetuses of the highest dose group; the increased number of fetuses affected was without statistical significance but clearly above the range of historical control data. In addition, incidences of fetuses with cleft palates were found in the highest dose tested, the increased number of fetuses affected showed statistical significance and was above the range of historical control. These malformations occurring in the highest dose group were found in two fetuses from dams that showed anorexia. The maternal NOAEL of this study is above the highest dose level tested, i.e. 32 mg/kg bw/day. For foetal effects, the NOAEL can be established at 8 mg/kg bw/day based on increased incidences of visceral malformations at the highest dose level tested.

In the fourth developmental study in rabbits (Ponnana, 1999), maternal toxicity was evident for high dose females (reduced body weight gain and reduced food consumption). Concerning fetal findings the incidence of dilation of heart ventricles was statistically significant increased in the high dose animals and was above historical control data, too. As dilation of heart ventricles must be classified as structural change that could impair foetal survival, development or function, this alteration should be indicated as major malformation rather than an anomaly. In addition, the incidences of visceral variants (slight renal pelvis dilation) and skeletal variants (incomplete/poor ossification of fore limb) as well as skeletal anomalies (accessory floating rib no. 13) were shown to be relevant at maternal toxic dose levels, too. The NOAEL for maternal and foetal toxicity can therefore be established at 15 mg/kg bw/day.

Taking into account the results of all developmental studies available, there is strong evidence that cymoxanil can impair fetal development producing also malformations (demonstrated in one out of two studies in rats and in three out of four studies in rabbits) and has to be classified into Repro Cat 3 (**Xn, R 63 "Possible risk of harm to the unborn child"**).

Neurotoxicity:

With respect to the possible neurotoxicological potential of cymoxanil, a subchronic neurotoxicity study as well as a developmental neurotoxicity study in rats have been submitted.

Based on the results of a 90 day neurotoxicity study on rats (the study is designed as a subchronic study as well as a study on neurotoxicity) no treatment related effects with respect to neurotoxicity have been observed; the NOAEL for neurotoxic effects can be set to be higher than the highest dose administered, i.e. 3000 ppm (corresponding to 224 – 333 mg/kg bw).

In the developmental neurotoxicity study, parental female rats showed statistically significant reduced body weight gain and feed consumption at 50 mg/kg bw/day. Therefore, the maternal NOAEL was considered at the next lower dose of 5 mg/kg bw/day. With respect to litter observation/reproductive parameters, the number of pups found dead/cannibalized, the viability index, the lactation indices, the number of surviving pups and the live litter size were considered to be treatment related altered in the high dose group (100 mg/kg bw/day). In addition, body weight reduction of male and female pups together with clinical observations ("cold to touch", not nursing and nesting) were evident in this dose group as well. Therefore, the developmental NOAEL was 50 mg/kg bw/day. The observation of the pups with respect to possible developmental neurotoxic effects (neurohistological evaluation, passive avoidance testing, watermaze performance, motor activity testing, auditory startle response) showed no treatment related changes even at the highest dose tested. Based on the findings, the test substance has no developmental neurotoxic potential.

Supplementary studies:

The acute oral toxicity of metabolite IN-3204 has been investigated in male rats (two studies). Both studies provided were poorly described (a summary reporting sheet available only) and considered of limited validity. Nevertheless, the metabolite could be shown to be of low acute

oral toxicity and is not to be classified according to EC Council Directive 67/548/EEC. In addition this metabolite has been identified in rat metabolism studies (minor amount).

Concerning immunotoxic effects of cymoxanil, 2 studies have been provided.

In the *28-day study in rats*, no effects on immunotoxicity could be observed. However, general toxicity (decreased body weight gain and body weight) were evident at the two highest dose groups. Based on these alterations, the NOAEL was set at 800 ppm (equivalent to 53.9 mg/kg bw) in males and 400 ppm (equivalent to 31.3 mg/kg bw) in females. The NOAEL for immunotoxicity was established at > 1600 ppm (equivalent to 107.7 mg/kg bw in male rats and 117.4 mg/kg bw in female rats).

In *28-day study in mice*, again, no effects on immunotoxicity (thymus and spleen weight; humoral immune function) were seen. Findings of general toxicity (decreased body weight gain) were evident at the highest dose group females. Based on these findings, the NOAEL was set at 1200 ppm (equivalent to 218.4 mg/kg bw in males and 268.5 mg/kg bw in females), and the NOAEL for immunotoxicity could be established at > 1200 ppm (equivalent to 218.4 mg/kg bw) in males and >2400 ppm (equivalent to 552.4 mg/kg bw) in females, i.e. the highest dose tested.

Medical data:

Based on the documentation submitted by the notifier, no health disturbances caused by cymoxanil have been observed in personnel involved in product manufacturing and from the formulation plants. No cases of acute cymoxanil intoxication have been reported and also no specific clinical signs are expected from acute and/or accidental exposure to humans.

2.3.2 ADI

The estimation of the Acceptable Daily Intake (ADI) is based on the relevant lowest no-observed adverse effect level (NOAEL) observed in studies with respect to subchronic and chronic toxicity, neurotoxicity (if available and necessary), carcinogenicity and reproductive toxicity. Considering all results from relevant studies as summarised in table B.6.10.2-1, the **lowest NOAEL of 2.8 – 3.1 mg/kg bw/day** (100 ppm) was found in both 1-year studies in dogs (*DuPont* and *OXON*). This NOAEL is based on changes with respect to clinical chemistry as well as haematological parameters and macroscopic and histological alterations at the next higher dose level of 200 ppm. Cymoxanil is concluded to be of no mutagenic, carcinogenic and reproductive potential; with respect to teratogenicity, the substance is to be classified with Xn, R 63. However a **safety factor of 100** is considered appropriate to be applied to the NOAEL from the 1-year studies in dog mentioned resulting in an **ADI of 0.03 mg/kg bw/day** (with respect to the teratogenic effects seen at dose levels of 25 – 75 mg/kg bw/day, a margin of safety of at least 800 is evident).

Table B.2.3.1-1 Summary of toxicity studies relevant for setting the ADI/AOEL/ARfD

Study	Dose levels	NOAEL	LOAEL	Effects observed at the LOAEL
28 day study in rats (OXON)	0, 750, 1500, 3000, 5000 ppm/diet	750 ppm [♂] and 3000 ppm [♀] 74.4 [♂]/287.8 [♀] mg/kg bw/day	1500 ppm [♂] and 5000 ppm [♀] 143.5 [♂]/415.9 [♀] mg/kg bw/day	<u>Males:</u> - increased organ weight (liver, testes, kidneys) <u>Females:</u> - reduced body weight and body weight gain - increased organ weight
28 day study in mice (OXON)	0, 750, 1500, 3000, 6000 ppm/diet	750 ppm [♂] and 1500 ppm [♀] 172.7 [♂]/329.9 [♀] mg/kg bw/day	1500 ppm [♂] and 3000 ppm [♀] 303.4 [♂]/679.3 [♀] mg/kg bw/day	<u>Males:</u> - reduced feed consumption <u>Females:</u> - reduced body weight and feed consumption
90 day study in rats (DuPont)	0, 100, 750, 1500, 3000 ppm/diet	100 ppm [♂] and 750 ppm [♀] 6.54 [♂]/137 [♀] mg/kg bw/day	750 ppm [♂] and 3000 ppm [♀] 47.6 [♂]/333 [♀] mg/kg bw/day	<u>Males:</u> - histological alterations in testes <u>Females:</u> - reduced body weight and body weight gain - clinical chemistry - increased relative organ weight (liver, spleen)
90 day study in rats (OXON)	0, 500, 1000, 2000 ppm/diet	500 ppm 42.6 [♂]/48.1 [♀] mg/kg bw/day	1000 ppm 85.1 [♂]/97.8 [♀] mg/kg bw/day	<u>Males:</u> - clinical chemistry - increased organ weight (kidneys) <u>Females:</u> - haematology
90 day study in mice (OXON)	0, 150, 450, 1350 ppm/diet	150 ppm 28.7 [♂]/32.9 [♀] mg/kg bw/day	450 ppm 84.4 [♂]/97.3 [♀] mg/kg bw/day	<u>Males:</u> - clinical chemistry - histology (liver) <u>Females:</u> - clinical chemistry - histology (liver)
90 day study in dogs (DuPont)	0, 100, 200, 250/500 ppm/diet	100 ppm 3 mg/kg bw/day [♂]/[♀]	200 ppm 5.13 [♂]/5.27 [♀] mg/kg bw/day	<u>Males:</u> - clinical signs - haematology - clinical chemistry <u>Females:</u> - clinical signs - decreased body weight gain - clinical chemistry
90 day study in dogs (OXON)	0, 200, 400, 800 ppm/diet	200 ppm 4.9 [♂]/5.2 [♀] mg/kg bw/day	400 ppm 9.7 [♂]/9.9 [♀] mg/kg bw/day	<u>Males:</u> - reduced body weight - clinical chemistry - histology (thymus) <u>Females:</u> - reduced body weight gain - haematology - organ weight changes (liver, thymus) - histology (thymus)

Study	Dose levels	NOAEL	LOAEL	Effects observed at the LOAEL
1 year study in dogs (<i>DuPont</i>)	0, 50, 100, 200 ppm/diet [♂] 0, 25, 50, 100 ppm/diet [♀]	100 ppm 3.0 [♂]/3.1 [♀] mg/kg bw/day	200 ppm [♂]/> 100 ppm [♀] 5.7 [♂]/>3.1 [♀] mg/kg bw/day	<u>Males:</u> - haematology - clinical chemistry <u>Females:</u> - no substance related effects
1 year study in dogs (<i>OXON</i>)	0, 50, 100, 200 ppm/diet [♂] 0, 25, 50, 100 ppm/diet [♀]	100 ppm 2.8 [♂]/2.9 [♀] mg/kg bw/day	200 ppm [♂]/> 100 ppm [♀] 5.6 [♂]/>2.9 [♀] mg/kg bw/day	<u>Males:</u> - clinical chemistry - macroscopic examinations - histology <u>Females:</u> - no substance related effects
Combined chronic toxicity/ oncogenicity study in rats – 23 months (<i>DuPont</i>)	0, 50, 100, 700, 2000 ppm/diet	100 ppm 4.08 [♂]/5.36 [♀] mg/kg bw/day	700 ppm 30.3 [♂]/38.4 [♀] mg/kg bw/day	<u>Males:</u> - clinical observations - reduced body weight and body weight gain - clinical chemistry - histology (testes, retina) <u>Females:</u> - macroscopic findings - histology (several organs))
Combined chronic toxicity/ oncogenicity study in rats – 24 months (<i>OXON</i>)	0, 100, 500, 1200 ppm/diet	100 ppm [♂] and 500 ppm [♀] 4.7 [♂]/31.6 [♀] mg/kg bw/day	500 ppm [♂] and 1200 ppm [♀] 23.5 [♂]/67.3 [♀] mg/kg bw/day	<u>Males:</u> - reduced body weight and body weight gain - histology (several organs) <u>Females:</u> - haematology - clinical chemistry - histology (several organs)
Oncogenicity study in mice – 18 months (<i>DuPont</i>)	0, 30, 300, 1500, 3000 ppm/diet	30 ppm 4.19 [♂]/5.83 [♀] mg/kg bw/day	300 ppm 42.0 [♂]/58.1 [♀] mg/kg bw/day	<u>Males:</u> - histology (liver, testes) <u>Females:</u> - histology (liver, jejunum)
Oncogenicity study in mice – 18 months (<i>OXON</i>)	0, 60, 120, 600, 1200 ppm/diet	600 ppm 91.4 [♂]/91.9 [♀] mg/kg bw/day	1200 ppm 178.3 [♂]/179.1 [♀] mg/kg bw/day	<u>Males:</u> - haematology - macroscopic findings (lymph nodes) <u>Females:</u> - histology (stomach)
2-generation study in rats (<i>DuPont</i>)	0, 100, 500, 1500 ppm/diet	100 ppm (parental/ offspring) 6.5 [♂]/6.6 [♀] mg/kg bw/day	500 ppm (parental/ offspring) 32.1 [♂]/34.7 [♀] mg/kg bw/day	<u>Parental effects:</u> - decreased body weight and body weight gain - increased testis weight <u>reproductive effects:</u> - none <u>offspring effects:</u> - reduced 0 – 4 day viability - reduced pup weight

Study	Dose levels	NOAEL	LOAEL	Effects observed at the LOAEL
2-generation study in rats (OXON)	0, 150, 450, 1350 ppm/diet	150 ppm (parental/offspring) 10.5 [♂]/14.9 [♀] mg/kg bw/day	450 ppm (parental/offspring) 31.6 [♂]/42.8 [♀] mg/kg bw/day	<u>Parental effects:</u> - reduced body weight - reduced feed consumption <u>reproductive effects:</u> - none <u>offspring effects:</u> - reduced pup weight
Teratogenicity study in rats (DuPont)	0, 10, 25, 75, 150 mg/kg bw/day	<u>Maternal:</u> 10 mg/kg bw/day <u>Foetal:</u> 10 mg/kg bw/day	<u>Maternal:</u> 25 mg/kg bw/day <u>Foetal:</u> 25 mg/kg bw/day	<u>Maternal effects:</u> - reduced body weight gain <u>Foetal effects:</u> increased incidences of skeletal variations
Teratogenicity study in rats (OXON)	0, 30, 60, 120 mg/kg bw/day	<u>Maternal:</u> 60 mg/kg bw/day <u>Foetal:</u> not established	<u>Maternal:</u> 120 mg/kg bw/day <u>Foetal:</u> 30 mg/kg bw/day	<u>Maternal effects:</u> - reduced body weight and body weight gain - increased late resorptions and post-implantation loss <u>Foetal effects:</u> - increased incidences of skeletal variants and minor anomalies
Teratogenicity study in rabbits (DuPont)	0, 4, 8, 16 mg/kg bw/day	<u>Maternal and foetal NOAEL:</u> > 16 mg/kg bw/day	-	No effects even at the highest dose tested; study of limited validity only
Teratogenicity study in rabbits (DuPont)	0, 8, 16, 32 mg/kg bw/day	<u>Maternal:</u> 8 mg/kg bw/day <u>Foetal:</u> 16 mg/kg bw/day	<u>Maternal:</u> 16 mg/kg bw/day <u>Foetal:</u> 32 mg/kg bw/day	<u>Maternal effects:</u> - clinical observations - alterations in body weight gain <u>Foetal effects:</u> - increased incidences of skeletal malformations
Teratogenicity study in rabbits (DuPont)	0, 1, 4, 8, 32 mg/kg bw/day	<u>Maternal:</u> > 32 mg/kg bw/day <u>Foetal:</u> 8 mg/kg bw/day	- <u>Foetal:</u> 32 mg/kg bw/day	<u>Maternal effects:</u> - no adverse effects even at the highest dose tested <u>Foetal effects:</u> - increased incidences of visceral malformations
Teratogenicity study in rabbits (OXON)	0, 5, 15, 25 mg/kg bw/day	<u>Maternal and foetal NOAEL:</u> 15 mg/kg bw/day	<u>Maternal and foetal LOAEL:</u> 25 mg/kg bw/day	<u>Maternal effects:</u> - reduced body weight gain <u>Foetal effects:</u> - increased incidences on visceral and skeletal variants - increased incidences of minor skeletal anomalies - increased incidences of visceral malformation
Developmental neurotoxicity study in rats** (DuPont)	0, 5, 50, 100 mg/kg bw/day	<u>Maternal NOAEL:</u> 5 mg/kg bw/day <u>Developmental/foetal NOAEL:</u> 50 mg/kg bw/day	<u>Maternal LOAEL:</u> 50 mg/kg bw/day <u>Developmental/foetal NOAEL:</u> 100 mg/kg bw/day	<u>Maternal effects:</u> - reduced body weight gain <u>Developmental/foetal effects:</u> - effects on litter data/reproductive parameters - reduced pup body weight - clinical observations in pups

Study	Dose levels	NOAEL	LOAEL	Effects observed at the LOAEL
Immunotoxicity study in rats (28 days) (DuPont)	0, 200, 400, 800, 1600 ppm/diet	800 ppm [♂] and 400 ppm [♀] 53.9 [♂]/31.3 [♀] mg/kg bw/day	1600 ppm [♂] and 800 ppm [♀] 107.7 [♂]/59.0 [♀] mg/kg bw/day	<u>Males:</u> - reduced body weight gain <u>Females:</u> - reduced body weight and body weight gain
Immunotoxicity study in mice (28 days) (DuPont)	0, 30, 300, 600, 1200 ppm/diet [♂] 0, 30, 300, 1200 and 2400 ppm/diet [♀]	1200 ppm[♂]/[♀] 218.4 [♂]/268.5 [♀] mg/kg bw/day	>1200 ppm [♂] and 2400 ppm [♀] <218.4 [♂]/552.4 [♀] mg/kg bw/day	<u>Males:</u> no effects observed at the highest dose tested (i.e. 1200 ppm) <u>Females:</u> - reduced body weight gain

** 5 mg/kg bw/day (maternal effects) not considered relevant for setting the ARfD, because of the dosing regime (step between 5 mg/kg bw and 50 mg/kg bw) when compared to the other developmental toxicity studies in rats considering the same effects, i.e. body weight gain and feed consumption, that could be first observed at 10 mg/kg bw/day

2.3.3 ARfD (acute reference dose)

For the determination of the ARfD, results from oral studies that used acute or short term exposure are considered to be the most relevant.

Cymoxanil is of moderate toxicity in the acute oral toxicity study in rats. In the short term (90 days) studies, no acute effects have been noted. Studies on subacute toxicity (28 day studies in rats and mice) are available, but range finding studies and therefore only a limited range of parameters has been investigated.

Based on the results of all studies regarding developmental toxicity provided by both notifiers, there is clear evidence that cymoxanil has a foetotoxic/teratogenic potential. It seems therefore justified to set an Acute Reference Dose (ARfD) for cymoxanil based on these studies.

The **lowest relevant NOAEL of 8 mg/kg bw/d** was derived from a rabbit developmental toxicity study with respect to maternal toxicity. At the next higher dose level of 16 mg/kg bw/day maternal toxicity (clinical observations and alterations in body weight gain) was observed. A **safety factor of 100** is judged to be appropriate for setting the ARfD. In conclusion, the **ARfD was calculated to be 0.08 mg/kg bw/day**.

2.3.4 AOEL

According to the principles of Annex VI to Directive 91/414/EC, the proposed Acceptable Operator Exposure Level (AOEL) should be established on the basis on the highest dose at which no adverse effect is observed in relevant studies in the most sensitive species. The setting of an AOEL is usually based on mid-term studies (studies on subacute/subchronic, reproductive, developmental toxicity) since the results of these studies can be considered appropriate for the actual operator risk assessment.

The most relevant NOAEL from all appropriate studies for setting the AOEL is the NOAEL of the 90-day study (DuPont) and 1-year studies in dogs (DuPont and OXON) showing the dog to be the most sensitive species. The **lowest NOAEL of 2.8 – 3.1 mg/kg bw/day** (100 ppm)

was found in all three studies mentioned. This NOAEL is based on changes with respect to clinical signs, decreased body weight gain, clinical chemistry as well as haematological parameters and macroscopic and histological alterations at the next higher dose level of 200 ppm.

The **enteral resorption rate** after oral administration was in the range of 65.4 to 86.5 %. Therefore an additional correction factor of 0.75 should be used for establishing the AOEL. Cymoxanil has no mutagenic or carcinogenic properties. Concerning reproductive toxicity, the substance has to be classified with Xn, R 63. However, a **safety factor of 100** is considered appropriate to be applied to the NOAEL from the 90-day and 1-year studies in dog mentioned. Taking into account the limited enteral resorption, the **AOEL is established at 0.02 mg/kg bw/day**.

2.3.5 Drinking water limit

The determination of a maximum allowable concentration (MAC) value in drinking water is not necessary. According to Directive 98/83/EC a drinking water limit of 0.1 µg cymoxanil/l is established.

2.3.6 Impact on human or animal health arising from exposure to the active substance or to impurities contained in it

Dermal absorption:

For the representative formulation presented by DuPont ("**TANOS**", i.e. DPX-KP481 50 Wettable Granulate) two studies on dermal penetration have been submitted:

The undiluted concentrate as well as the aqueous dilution of "TANOS" was applied to rat skin *in vivo* for an exposure time of 6 hours. Since radioactivity was still detected in excreta even 21 days post exposure, the amount of radioactivity detected in treated skin after tape-stripping was considered as systemically available and included in the amount of totally absorbed dose. For risk assessment purposes, the absorbed dose found 18 hours post exposure was considered. Therefore, the dermal absorption rates in rats were 1.19 % for the concentrate ("mixing/loading") and 7.55 % for the aqueous 0.75 g/l-dilution ("application"). These *in vivo* dermal absorption rates have to be adjusted in the light of the relative absorption in rat and human skin *in vitro* using the correction factor of 25.2 for the concentrate and 3.5 for the spray dilution. Thus, the dermal absorption of cymoxanil in the formulation "TANOS" can be estimated to be 0.05 % for the concentrate (representing "mixing/loading") and 2.2 % for the spray dilution (representing "application").

Concerning the second formulation "**Cymoxanil 50 % WP**", no study on dermal absorption has been provided from the notifier [OXON]. Based on physical/chemical properties of cymoxanil, a dermal absorption rate of 100 % would be applicable. The results of the ADME studies provided showed an enteral absorption rate of about 75 % and was used for refinement of the dermal absorption rate. It can be assumed, that the dermal absorption will not exceed the enteral absorption. Based on these assumptions, a dermal absorption rate of 75 % (default value) for "Cymoxanil 50% WP" would be appropriate.

Exposure assessments:

For "*Cymoxanil 50 % WP*", the results of the **operator exposure** calculation according to the UK POEM model showed an exceeding of the proposed AOEL (without PPE) for both intended uses (lettuce, potatoes). Considering gloves during mixing and loading as well as application, the AOEL is still exceeded. The total estimated exposure for operator according to the BBA-model was below the proposed AOEL with specified PPE, i.e. gloves during mixing/loading and application as well as overall during application (38.37 – 76.75 % of the AOEL) for both intended uses. Based on the results of the operator exposure models used, no possible risk for the operator can be identified if appropriate PPE (gloves during mixing/loading and application and overall during application) is worn.

The results of the **bystander exposure** estimation based on the spray drift deposits reported by *Ganzelmeier et al., 1997*, showed a systemic exposure for bystanders below the AOEL (5.25 – 10.5 %). With regard to exposure assessments based on measurements (*Lloyd et al., 1983*), the total systemic burden was calculated to be 0.32 – 0.41 % of the AOEL. Based on the results of these exposure calculations, no possible risk for bystanders could be identified.

The results of the **operator exposure** calculations according to the UK POEM model with respect to the second formulation "*TANOS*" did not show an exceeding of the proposed AOEL (56.5 %) even when no PPE are worn for the intended use (potatoes). Considering gloves during mixing and loading as well as application, the total systemic exposure is further reduced to 0.002 mg/kg bw/day corresponding to 9.9 % of the AOEL).

The total estimated exposure for operators according to the BBA-model was also below the proposed AOEL without specified PPE (13.72 % of the AOEL). Considering PPE during mixing/loading (gloves) and spraying (gloves, overall), the systemic exposure was shown to be 3.04 % of the AOEL. It can be concluded, that based on the results of the operator exposure models used, no possible risk for operators can be identified even if no PPE is worn.

The results of the **bystander exposure** estimation based on the spray drift deposits reported by *Ganzelmeier et al., 1997*, show a systemic exposure for bystander far below the AOEL (0.22 %). With regard to exposure measurements reported by *Lloyd et al., 1983*, the total systemic burden was calculated to be 0.04 % of the AOEL. Based on the results of these exposure calculations, no possible risk for bystanders could be identified.

2.4 Residues

An Annex II data sharing between the notifiers DuPont and Oxon has been agreed.

Storage stability

Without significant decrease in the residue level, the storage stability of cymoxanil under frozen conditions (about -20 °C and darkness) was demonstrated at least for 30 days in homogenised lettuce and 12 months in whole lettuce plant (Oxon). On the above described

conditions, potato tuber homogenates were stable at least for 12.5 months (DuPont). A storage stability for whole potato tuber was not performed.

Plant metabolism

The metabolism of ^{14}C -cymoxanil in plants was investigated in lettuce (*Lactuca sativa*, leaf vegetable) and potato (roots and tuber vegetables). Each notifier (DuPont or Oxon) submitted one metabolism study per crop group. All four studies were performed under outdoor conditions using pots or containers. The total radioactive residue (TRR) of plant samples was determined by combustion/liquid scintillation counting (LSC). Cymoxanil and structurally relevant proposed metabolites were identified and quantified by validated chromatographic methods (in particular by HPLC).

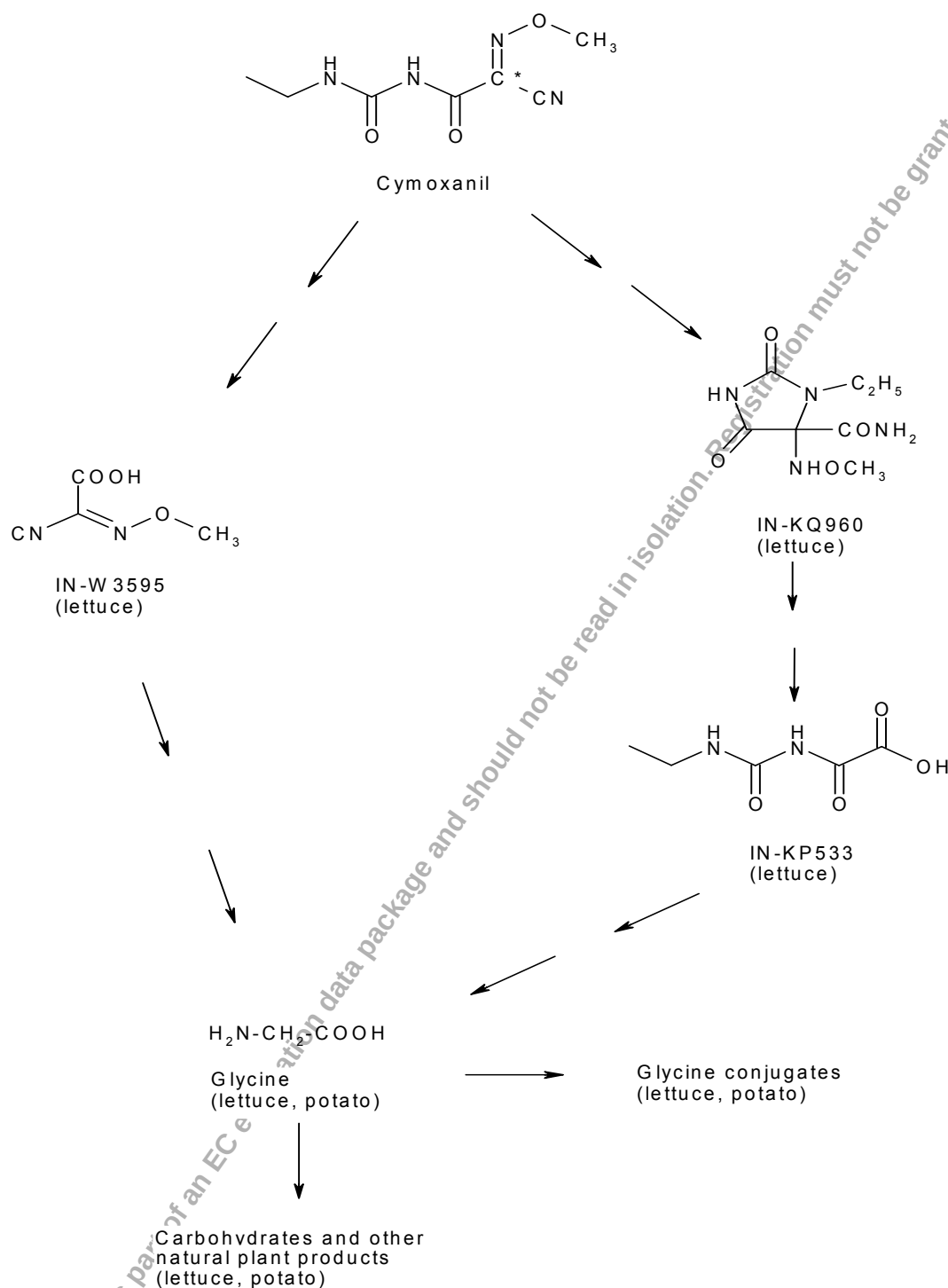
Lettuce (*Lactuca sativa*): A total amount equivalent to 0.072 (Oxon) to 3.360 (DuPont) kg labelled cymoxanil/ha was applied by spraying (BBCH about 12 to 47) 3 to 4 times on lettuce. In both studies submitted the lettuce foliage was analysed only. A small amount of parent compound was identified in both studies (DuPont: 2.1 % of TRR or 0.23 mg eq/kg in surface wash only; Oxon: 1.4 % of TRR or 0.015 mg eq/kg in organosoluble fraction of unwashed lettuce). Conjugated glycine was identified as a main metabolite in both studies, with range of approx. 13.0 % of TRR or 0.139 mg eq/kg (Oxon) to 30.6 % of TRR or 3.30 mg eq/kg (DuPont). In the study submitted by DuPont only a further main metabolite, i.e. glucose, was detected with 21.2 % of TRR or 2.28 mg eq/kg. Another main polar metabolite, i.e. IN-W3595 up to 18.1 % of TRR or 0.193 mg eq/kg, was identified in one study (Oxon) only. As minor polar metabolites IN-KQ960 (7.4 % of TRR, 0.80 mg eq/kg) and IN-KP533 (2.8 % of TRR, 0.31 mg eq/kg) were detected in the aqueous fraction of DuPont presented study only (with significant higher amount of total applied ^{14}C -cymoxanil and lower PHI than in the Oxon study). The two submitted studies provide supplementary and feasible information on the metabolism pathway of cymoxanil in lettuce foliage. An extensive metabolism of cymoxanil on/in lettuce can be considered with intermediate metabolites (like IN-W3595, IN-KQ960 or IN-KP533), glycine as main and relevant metabolite, which can be form conjugates or be incorporated in natural plant products (like carbohydrates, peptides or proteins).

Potato: The potato plants were treated (BBCH about 122, 45-50 to 95-97) 3 to 8 x times with labelled cymoxanil by spray application equivalent to 0.432 (Oxon) - 1.212 (DuPont) kg as/ha. The potato tuber only was analysed in both submitted studies. The parent compound was not detected in relevant concentrations in/on mature potato tuber regarding both studies. The main metabolite was glycine identified after acid hydrolysis of mature potato tuber homogenate in both studies. The released glycine was detected in a concentration range from 27.5 % of TRR or 0.280 mg eq/kg (Oxon) to 78.5 % of TRR or 0.54 mg eq/kg (DuPont). As minor metabolite, glucose (originating from starch) was detected at a concentration level of 8.1 % of TRR (0.06 mg eq/kg) after acid hydrolysis of mature potato tuber pellet only in the DuPont submitted study (with significant higher applied amount of total ^{14}C -cymoxanil and lower PHI). No further metabolites were identified in the study presented by Oxon. The both

studies submitted show an extensive metabolism of cymoxanil resulting in glycine (conjugated/incorporated with/in natural substances) as main detected metabolite and glucose (primarily originating from starch). Intermediate metabolites were not identified in the two presented studies on potato tubers.

Lettuce and potato: The submitted metabolism studies on lettuce heads (*Lactuca sativa*) and potato tubers indicated a rapid and extensive degradation of parent compound. Cymoxanil was metabolised (in lettuce only over intermediates like IN-W3595, IN-KQ960 or IN-KP533) to glycine, which was further conjugated or incorporated with or in natural substances (e.g. carbohydrates, peptides or proteins). The proposed metabolic pathway of cymoxanil in plant matrices (lettuce leaves and potato tubers) is summarised in figure 2.4-1.

Figure 2.4-1 Proposed metabolic pathway of cymoxanil in plant matrices (lettuce leaves and potato tubers)



* indicates radioactive label site

Cymoxanil ... 2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide, E-isomer, CAS reg. no: 57966-95-7

IN-KQ960 3-Ethyl-4-(methoxyamino)-2,5-dioxo-4-imidazolidinecarboxamide

IN-KP533 ... [[[(Ethylamino)carbonyl]amino]oxoacetic acid, CAS reg. no. 105919-00-4

IN-W3595 ... 2-cyano-2-methoxyiminoacetic acid, CAS reg. no. 78325-17-4

Livestock metabolism

Since there is evidence of a “non residue” situation of cymoxanil (< LOQ, < 0.05 mg/kg) in the plant raw agriculture commodities as shown in the supervised residue trials (lettuce and potato), rotational crop studies (lettuce, sugar beets and spring wheat) and plant metabolism studies (potato), no metabolism study in livestock is regarded necessary. Nevertheless, DuPont only submitted additionally a metabolism study on lactating goat (including an in vitro fluid bovine rumen test). The total radioactive residue (TRR) of goat samples was determined by combustion/liquid scintillation counting (LSC). Cymoxanil and structurally relevant proposed metabolites were identified and quantified by validated chromatographic methods (in particular by HPLC).

Lactating goat: After three consecutive single daily doses, equivalent to 10 mg ¹⁴C-cymoxanil per kg diet and day, a majority of the recovered administered radioactivity 23.6 % and 18.3 % of applied dose on one lactating goat was detected in excreta and urine, respectively. Goat milk contained 2.6 %, liver 3.5 % and kidney 0.1 % of administered dose. The total recovery of dosed radioactivity on the goat was low and amounted to 68.8 %. The labelled methane formed by goat rumen was not collected for analysis.

The major ¹⁴C-cymoxanil derived residue detected in goat milk was lactose, which represents 46.4 % of milk TRR (0.13 mg eq/L). Fatty acids (i.e. caproic, caprylic, capric, lauric, arachidonic, myristic, lionleic, oleic acids) accounted for 5.7 % of milk TRR (0.02 mg eq/L). About half of the radioactivity associated with the milk pellet was released (10.7 % of milk TRR, 0.03 mg eq/L) after protease digestion and acid hydrolysis, but remained unidentified.

“Formic acid” (i.e hydrolysable formyl group) was identified as the primary meatbolite in goat liver. The total “formic acid” (after acid hydrolysis of extracts or proteolytic digestion of pellet) represents 68.9 % of liver TRR (1.47 mg eq/kg). Acetic acid was released after proteolytic and acid hydrolysis at a concentration level of 14.0 % of liver TRR (0.30 mg eq/kg) from the pellet. 1.8 % of liver TRR (0.04 mg eq/kg) was identified as ¹⁴C-glycerol, whereas 1.4 % of TRR (0.03 mg eq/kg) was solvent extractable.

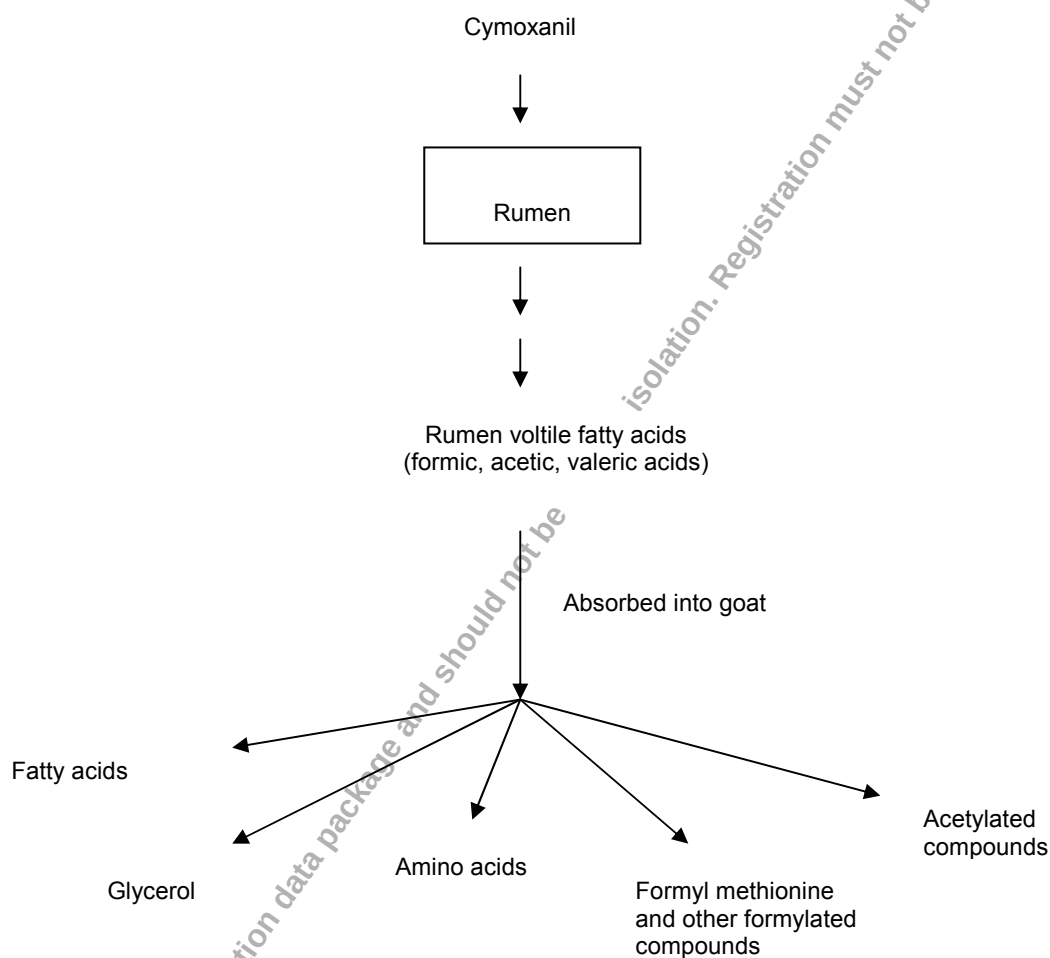
In the goat kidney a hydrolysabe formic acid group, accounted for 28.3 % of kidney TRR (0.13 mg eq/kg) was primarily identified. Radioactive glycerol and acetic acid were detected at 8.6 % and 10.9 % of kidney TRR (0.04 and 0.05 mg eq/kg), respectively.

Residues in composite goat muscle or fat fractions were low and remained unidentified. Radioactivity in goat urine was very polar and the conclusively identified metabolites after acid hydrolysis were glycine and “formic acid”. No significant characterisation of residues in feces was attempted.

Cymoxanil was metabolised by one tested lactating goat essentially to natural products including fatty acids, glycerol, glycine and other amino acids, lactose and hydrolysable formyl

and acetyl group. ^{14}C -Methan was hypothesised as a metabolite. Neither ^{14}C -cymoxanil nor structurally related metabolites were detected in any goat tissue, milk, urine (radioactivity in feces was not further determined) or from the in vitro fluid bovine rumen test. Figure 2.4-2 presents the proposed metabolic pathway of cymoxanil in lactating goat.

Figure 2.4-2 Proposed metabolic pathway of cymoxanil in lactating goat



Supervised residue field trials

According to the intended uses of DuPont/Oxon, supervised residue field trials were performed outdoor on two crop groups, i.e. leaf vegetables (lettuce, only S-EU) and root and tuber vegetables (potato, N-EU and S-EU). Regarding lettuce, respective trials were submitted by Oxon only. Concerning potato, respective trials were submitted by DuPont and Oxon.

Lettuce and potato:

A residue level of cymoxanil at or above the LOQ (< 0.05 mg/kg) in mature lettuce leaves or potato tuber matrix could not be detected in one of the 6 and 31 submitted residue trial studies on lettuce and potato, respectively. Nevertheless, cymoxanil was quantified only in the lettuce decline studies in a range from 0.48 to 4.29 mg/kg at 0 days after treatment (DAT), 0.45 to 2.72 mg/kg at 1 DAT and <0.05 to 0.95 mg/kg at 3 DAT. The field trials were performed in accordance to the intended uses by DuPont (potato: N-EU and S-EU) and Oxon (lettuce: S-EU; potato: N-EU and S-EU). The submitted residue data from the residue trials are considered as sufficient and valid to propose a "non residue" situation under the intended GAP of DuPont and Oxon, respectively. A proposal of MRLs for lettuce and potato tuber is possible.

Table B.2.4-1 Key results of crop residue trials conducted with cymoxanil (with relevance to MRL-estimation)

Crop	Application [kg as/ha]	Region *)	No. of trials	PHI [days]	Lowest residue at harvest [mg/kg] **)	Highest residue at harvest [mg/kg] **)	Remarks
lettuce	4 x 0.225-0.252	S-EU	6	0-1-3-(9)-10	<0.05	<0.05	Oxon
potato	4 x 0.118-0.128	N-EU	4	0-1-3-(6)-7	<0.05	<0.05	Oxon
potato	5 x 0.091-0.125	S-EU	15	0-1-3-7-14	<0.05	<0.05	Oxon
potato	11-12 x 0.176-0.235	N-EU	6	14	<0.05	<0.05	DuPont
potato	6-8 x 0.221-0.294	S-EU	6	14	<0.05	<0.05	DuPont

*) N-EU: Northern Region of Europe; S-EU: Southern Region of Europe

**) Residues expressed as cymoxanil

Note: LOQ for cymoxanil in lettuce or potato is 0.05 mg/kg by GC-NPD.

Rotational crops

In the study submitted by DuPont only, no accumulation of cymoxanil or related metabolites was observed in the tested rotational crops (lettuce, sugar beet and spring wheat) at 30 and 120 days rotational crop intervals (RCIs) harvested at mature. Significant amounts of TRR (the major parts were extractable) without definite decrease of radioactivity from 30 to 120 days RCI were detected in wheat grain (≤ 0.05 mg eq/kg) and wheat straw (≤ 0.14 mg eq/kg).

Livestock feeding studies

With regard to the results of metabolism studies and residue trials on potato (cymoxanil residues are < LOQ, < 0.05 mg/kg), livestock feeding studies are regarded as not necessary

for cymoxanil. Additionally, the metabolism study of lactating goat indicates an extensive metabolism and no accumulation of cymoxanil in goat organs, tissues or milk.

Processing studies

These studies (industrial processing and/or household preparation) are considered as not necessary, due to the evidence of a "non residue" situation (no residues above the LOQ, i.e. 0.05 mg/kg, are expected based on the results of residue trials on lettuce and potatoes with regard to the intended GAP by the applicants).

2.4.1 Definition of the residues relevant to MRLs

For definition of relevant residues of cymoxanil in raw agricultural commodities (RAC) the following facts were taken into account:

Studies on the uptake and metabolism of cymoxanil in lettuce (leaf vegetable) and potato (root and tuber vegetable) were evaluated. After spray application (intended growth stage for lettuce BBCH 40-49 and potato BBCH 21-95) cymoxanil was metabolised rapidly and resulted essentially to polar substances (like glycine), which were further incorporated or conjugated in or with natural products (like carbohydrates and others). Intermediates were detected in lettuce only: IN-W3595 only was found up to 18.1 % of TRR in the lettuce study submitted by Oxon. IN-KQ960 and IN-KP533 with 7.4 % of TRR and 2.8 % of TRR, respectively, were detected in lettuce samples according to the DuPont study only. Based on the results of toxicological studies provided, no toxicological relevance with respect to metabolites IN-W3595 and IN-KQ960 is evident. Metabolite IN-KP533 was found in one of two lettuce metabolism studies only at low amounts and was not tested in the rat model system. Nevertheless, cymoxanil only is proposed as residue of concern.

The supervised residue trials on lettuce and potatoes showed no cymoxanil at or above the LOQ (= 0.05 mg/kg per each crop) at commercial harvest time. Similarly, the tested rotational crops, i.e. lettuce (head), sugar beets (tops or roots) and spring wheat (forage, straw or grain) show no evidence of cymoxanil or structurally related metabolites. The trigger value of 0.1 mg residue/kg dry feed regarding intake by livestock is formally open for potato use (i.e. pig and beef cattle diet). Note, the respective trigger value is not explicit based on dry weight in for the data submitter available and in forced DG Sanco doc. 7031/VI/95, rev. 4, 22 July 1996, livestock feeding studies. Nevertheless, a lactating goat metabolism study (including an in vitro bovine rumen test) has been submitted, which showed "no residues" of cymoxanil or structurally related metabolites in the goat organs, tissues or milk. Cymoxanil was rapidly metabolised in the goat model system and the radioactivity determined in natural polar products (like fatty acids, glycerol, lactose, amino acids) or formylated or acetylated compounds.

In consideration of the above presented arguments, the proposed residue definition for plant products (essentially based on the lettuce and potato metabolism studies) for risk assessment and monitoring purpose is cymoxanil (parent compound).

A residue definition for food of animal origin (primarily based on “non residue” situation in potato tubers and on the supplementary lactating goat metabolism study) is not regarded necessary.

2.4.2 Residues relevant to consumer safety

Estimation of chronic exposure

For the estimations of cymoxanil on the chronic exposure through human diet (lettuce and potato), proposed values of ADI (acceptable daily intake) of 0.03 mg/kg bw/day and MRLs (maximum residue levels) of 0.05 mg/kg for lettuce or potato tubers each, were assumed.

Table 2.4.2-1 shows the results of chronic risk assessment on cymoxanil.

Table 2.4.2-1 Chronic consumer risk assessment on cymoxanil

Diet Model	Theoretical maximum daily intake (TMDI) [mg/person/day]	% ADI
WHO, European diet, 1994, adult: 60.0 kg	0.013465	0.7
German VELs, 2006, child: 16.15 kg	0.002140	0.4
UK (PSD), 2006, 10 consumer groups *) elderly-residential (61.6 kg bw) infant (8.7 kg bw)	0.010472 0.005046	0.5 1.9

*) lowest and highest % ADI value is shown

Estimation of acute exposure

Based on proposed values of AfRD (acute reference dose) of 0.08 mg/kg bw/day and MRLs of 0.05 mg/kg (lettuce and potato each) the estimations of cymoxanil on the acute exposure through human diet of the two crops were performed. Table 2.4.2-2 summarises the results of acute risk assessment on cymoxanil.

Table 2.4.2-2 Acute consumer risk assessment on cymoxanil

Diet Model	National estimate of short term intake (NESTI) [mg/kg bw/day]	% AfRD
German VELs, 2006, child: 16.15 kg lettuce potato	0.0008071 0.0023492	1.0 2.9
UK (PSD), 2006, 10 consumer groups *) lettuce, 4-6 year old child (20.5 kg bw) potato, infant (8.7 kg bw)	0.00089 0.00769	1.1 9.6

*) highest % AfRD values per crop commodity are shown

2.4.3 Residues relevant to worker safety

Lettuce (*lactuca sativa*)

For the application of "Cymoxanil 50 % WP" in lettuce (Oxon), the earliest re-entry into treated areas and a possible contamination of workers with the active ingredient cymoxanil could be at harvest (*Krebs et al., 2000*: Uniform Principles for Safeguarding the Health of Workers Re-Entering Crop Growing Areas after Application of Plant Protection Products). However, at this time point (PHI = 10 days), residues of cymoxanil in lettuce were below the LOQ (i.e. 0.01 mg/kg) in all residue trials submitted. No dislodgeable residues will be present on the crop and therefore no contamination would take place for workers when harvesting lettuce.

Potatoes

Concerning the use of "Cymoxanil 50 % WP" or "Tanos" in potatoes it is not necessary to enter the treated area immediately after spraying. Since potatoes are considered to be a highly mechanised crop, the possible exposure to workers cannot be anticipated. Based on these considerations, no risk for the worker can be identified.

2.4.4 Proposed EU MRLs and compliance with existing MRLs

Lettuce (*lactuca sativa*)

The results of 6 supervised residue trials (3 harvest + 3 decline curve studies, covering 2 growing years) performed in Southern Europe are regarded as relevant according to the intended uses (Oxon only). Since at harvest no residue at or above the LOQ could be detected in/on any lettuce head samples analysed, a **MRL of 0.05 mg/kg** (= LOQ) expressed as parent compound is proposed for lettuce.

Potatoes

According to the intended uses of DuPont and Oxon the results of 10 supervised residue trials (DuPont: 6 harvest studies covering 1 growing year, Oxon: 2 harvest + 2 decline curve studies covering 1 growing year) performed in Northern Europe and 21 supervised residue trials (DuPont: 6 harvest studies covering 1 growing year, Oxon: 12 harvest studies covering 2 growing years + 3 decline curve studies covering 1 growing year) performed in Southern Europe are considered as relevant. Since at harvest no residue at or above the LOQ could be detected in/on any potato tuber samples analysed, a **MRL of 0.05 mg/kg** (= LOQ) expressed as parent compound is proposed for potato tubers.

2.4.5 Proposed EU import tolerances and compliance with existing MRLs

Currently no EU-MRLs are set for cymoxanil. The notifiers (DuPont/Oxon) did not request to set import tolerances.

2.4.6 Basis for differences, if any, in conclusion reached having regard to established or proposed CAC MRLs

There are no CAC MRLs for cymoxanil currently existing.

2.5 Fate and behaviour in the environment

The Annex II dossier for cymoxanil is prepared collectively (shared) by E.I. du Pont de Nemours and Company (DuPont) and Oxon Italia S.p.A (Oxon). Therefore, available Annex II data of both companies are handled as a collective irrespective of the notifier. Annex III data were prepared and handled separately by both notifiers for the formulations TANOS 50 WG (DuPont) and CYMOXANIL 50 % WP (Oxon).

2.5.1 Definition of the residues relevant to the environment

In soil, the parent cymoxanil and the metabolites IN-U3204, IN-W3595 and IN-JX915 are considered major compounds (> 10 % of AR), the latter observed > 10 % of AR in soil photolysis study only.

In surface water and sediment, cymoxanil and the metabolites IN-U3204, IN-W3595, IN-KQ960, IN-T4226, IN-KP533, metabolite fraction M5, IN-JX915 and IN-R3273 are considered major (> 10 % of AR), the two latter observed > 10 % of AR in water photolysis studies only. Additional input into the water body via soil runoff and drainage has to be considered for all compounds mentioned with the exception of the metabolite fraction M5, which was only observed in the water/sediment system.

In groundwater cymoxanil and soil metabolites are considered non-relevant as predicted 80th percentile annual average concentrations were clearly < 0.1 µg L⁻¹ in all FOCUS scenarios. Groundwater modellings for cymoxanil and metabolites were confirmed by a representative lysimeter study conducted in Germany.

Cymoxanil has a low volatility and undergoes rapid photochemical degradation. Thus, PEC_A is expected to be minimal and long range transport is unlikely to occur.

2.5.2 Fate and behaviour in soil

Note: One of the 9 soils investigated to establish the degradation pathway and the rate of degradation of cymoxanil in soil, is a black andosol originating from Japan. This soil, which was investigated twice in two separate studies (using the same soil batch), exhibited the most pronounced metabolite pattern of all soils investigated. This soil type may be considered at least partly relevant for the EU region since andosols are also found in (formally active) volcanic areas in the EU (e.g. central France, central Italy including Sardinia and Sicily). Therefore, this soil was included into the overall environmental risk assessment for conservative reasons. However, before onset of the second study this soil was stored outdoors over a period of 2 years. In comparison with the first study using freshly sampled soil, the microbial activity of the soil was likely to be severely comprised by the long storage time. Therefore, results on degradation rates of cymoxanil and metabolites (including

maximum occurrence of metabolites) obtained in the second study were omitted from the final risk assessment.

2.5.2.1 Route of degradation

The **aerobic route of soil degradation** of cymoxanil was investigated in total 6 soils (4 studies) with a representative range of properties (pH, organic carbon, texture, origin), at varying temperature (20 and 25 °C) and varying incubation conditions (viable and sterile) using cyanoacetamide-2 labelled cymoxanil.

The degradation of cymoxanil under **aerobic, viable conditions** is characterized by an extensive mineralization to CO₂, which has to be considered the major degradation product of cymoxanil in aerobic, viable soils. After an incubation period of 10 days, 17.0 – 53.0 % of AR (*n* = 4) was found to be released as ¹⁴CO₂. Two of these studies were conducted for a longer time period, levels of released ¹⁴CO₂ steadily increased towards study termination (56.7 and 60.4 % of AR by 90 and 92 DAT, respectively). In two further (degradation rate) experiments, conducted for only 3 days and 1 day, formation of ¹⁴CO₂ was pronounced, too, accounting for 28.7 and 45.7 % of AR (!), respectively.

In soil degradation experiments, which allowed to adequately account for the maximum formation (*n* = 3), peak levels of NER were observed in a range of 36.8 – 50.8 % of AR, occurring by 2 DAT and decreasing thereafter until study termination. In 3 further experiments, maximum formation of NER was observed by study termination (i.e. 10, 3 and 1 DAT) with levels of 35.6, 43.5 and 30.3 % of AR, respectively.

Once in contact with soil water (soil moisture and pore water) at neutral and alkaline conditions, cymoxanil undergoes rapid hydrolysis by (partly reversible) cyclisation processes, leading to the highly transient metabolites IN-U3204 (six-member ring system) and IN-JX915 (five-member ring system), and by cleavage (hydrolysis) of the parent leading to equimolare release of IN-W3595 and ethyl urea (Fig. 2.5.2.1-1). Ethyl urea was never quantified in soil degradation studies, since the labelling of the parent (cyanoacetamide-2 position) did not allow to follow the fate of this cleavage product. However, according to SANCO/221/2000, rev. 10 (2003), ethyl urea and further degradation products of ethyl urea are considered compounds of no concern. Metabolite IN-U3204 is highly unstable in soil, rapidly degrading into IN-KP533, IN-T4226 and IN-KQ960. IN-T4226 is a further transient metabolite rapidly degrading into IN-KP533 by ring cleavage. The highly transient metabolite IN-JX915 further degrades into IN-KQ960 and IN-R3273, which in turn degrade to IN-T4226. The hydrolysis end products IN-W3595, IN-KQ960, IN-R3273 and IN-KP533 are considered rather stable under sterile soil conditions (as demonstrated in one study) but are extensively degraded further in viable soils owing to soil microbial activity into oxamic acid (IN-18474), oxalic acid and, finally, CO₂.

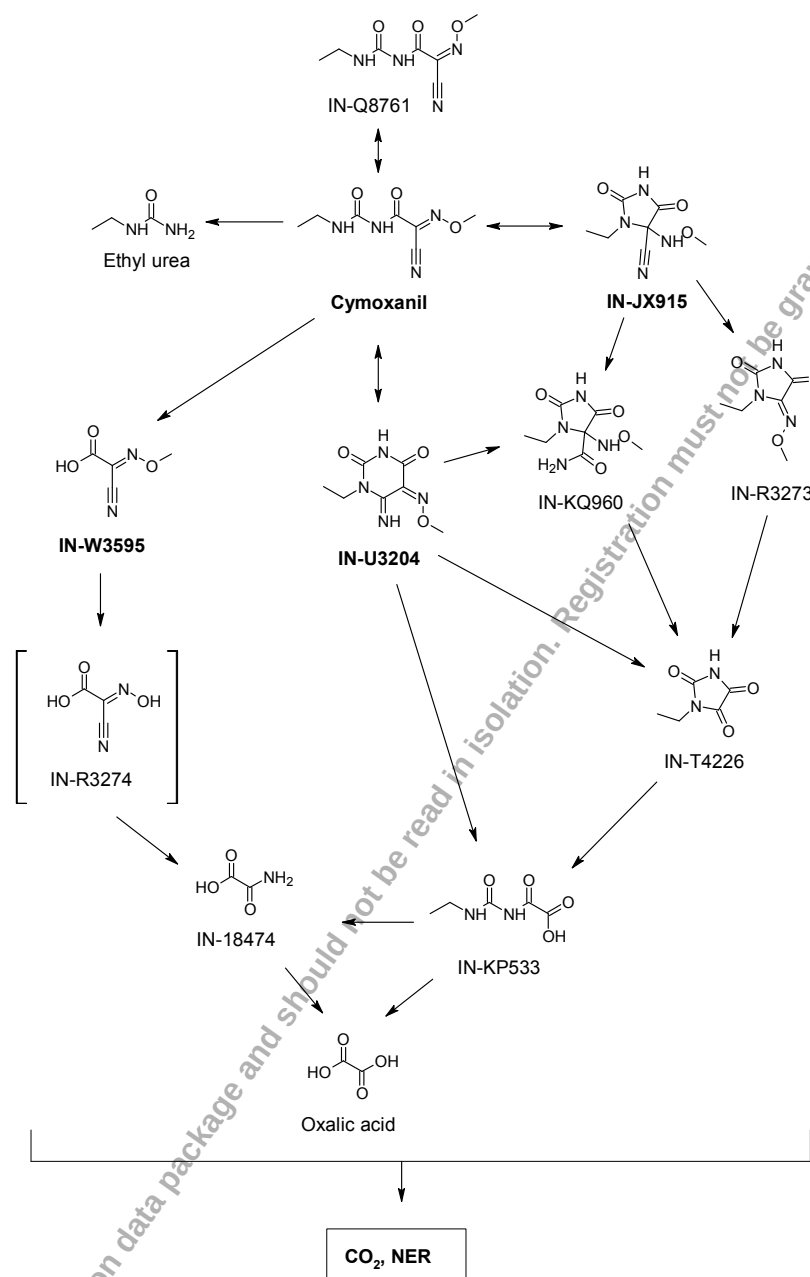


Figure 2.5.2.1-1: Proposed aerobic and photolytic degradation pathway of cymoxanil in soil (metabolites in bold exceed 10 % of AR).

Formation of the Z-isomer of cymoxanil (IN-Q8761, observed only in the soil photolysis study, minor amounts in irradiated and dark control samples, Berg, 1996) could not be linked to any environmental impact. Therefore, IN-Q8761 is considered of no concern in the environmental fate assessment.

Under **dark aerobic viable conditions** two metabolites have to be considered as major metabolites (> 10 % of AR): IN-U3204 (maximum occurrence 24.7 % of AR) and IN-W3595 (maximum 10.1 % of AR). Under the reasonable assumption that the unidentified metabolite

fraction Met IV (observed in a degradation rate study, Melkebeke, 1999) is at least partly identical to IN-U3204, this highly transient metabolite was observed > 10 % of AR in 4 of 9 soil (route and rate) degradation studies. Metabolite IN-W3595 was only observed in the Japanese 'Black Andosol' (study with freshly sampled soil) slightly above 10 % of AR and > 5 % of AR in 'Sermoise' soil. On the basis of available data, IN-W3595 is not considered to exceed 5 % of AR in any other soil tested.

The highly transient metabolite IN-JX915 (maximum occurrence 7.6 % of AR in the Japanese 'Black Andosol') exceeded 5 % of AR in 2 of 9 soils degradation studies. Metabolite IN-KQ960 was only found > 5 % of AR in the Japanese 'Black Andosol' (maximum 6.3 % of AR), IN-KQ960 is not considered to exceed 5 % of AR in any other soil tested.

Metabolite IN-18474 (oxamic acid, maximum occurrence of 7.8 % of AR) is a naturally occurring molecule and, based on molecular structure, a degradation product of no concern (SANCO/221/2000, rev. 10, 2003).

No other metabolite or metabolite fraction exceeded 5 % of AR under aerobic, viable conditions.

No data are available on the **route of degradation under anaerobic conditions**.

Degradation under anaerobic conditions is not considered relevant for cymoxanil owing to its use pattern in lettuce and potatoes. Cymoxanil degrades so fast in an aerobic environment that it would not persist long enough to be exposed to extensive anaerobic conditions.

One experiment on the **aerobic degradation under sterile conditions** is available, conducted with the Japanese 'Black Andosol'. Under sterile conditions, mineralization of cymoxanil to CO₂ was found to be negligible. Formation of NER was distinct slower than under viable conditions accounting for 48.7 % of AR by 15 DAT (study termination). However, rapid degradation of cymoxanil occurred owing to abiotic hydrolysis processes. In fact, the metabolite pattern formed was almost identical to the metabolite pattern observed in sterile hydrolysis studies. Metabolite IN-U3204 peaked with 22.7 % of AR, decreasing thereafter rapidly. Metabolites IN-W3595, IN-KQ960 and IN-R3273 were observed at maximum levels of 28.4, 19.0 and 6.5 % of AR, respectively, slowly decreasing thereafter in case of IN-R3273 and IN-KQ960.

Under **conditions of soil photolysis**, metabolite pattern formed was similar to dark conditions. However, the degradation pathway is shifted to almost exclusive formation of the common photolysis metabolite IN-JX915 (the degradation pathway via IN-JX915 is also most pronounced during photolysis in sterile water), which has to be considered major in soil photolysis (maximum occurrence 10.9 % of AR). However, IN-JX915, a highly transient metabolite in moist and viable soils, is unlikely to reach this level under real outdoor conditions even under the impact of irradiation. Cymoxanil is applied post emergence (BBCH

40 for lettuce and BBCH 21 for potatoes) and any soil surface photolysis will be significantly reduced due to the presence of crop canopy. In this respect, photolysis may be considered a minor route of degradation for cymoxanil in soil. However, IN-JX915 is included into the list of 'major' soil metabolites for conservative reasons.

2.5.2.2 Rate of degradation

The **laboratory soil degradation rate** of cymoxanil was investigated in total 9 soils (5 studies) with a representative range of properties (pH, organic carbon, texture, origin), at varying temperature (10, 20 and 25 °C) and varying incubation conditions (viable and sterile) using cyanoacetamide-2 labelled cymoxanil:

- pH: 4.3 – 7.8
- Organic carbon: 0.5 – 2.1 %
- Clay content: 8.8 – 32.3 %
- Origin: EU, USA, Japan
- Temperature: 10, 20 and 25 °C
- Incubation conditions: Aerobic viable and aerobic sterile

Under **aerobic and viable conditions** and temperatures of 20 – 25 °C cymoxanil rapidly degraded with a half-life time in a range of 0.1 – 4.3 days (based on best fit, $n = 9$, $R^2 \geq 0.86$, χ^2 error ≤ 17.6 %) with a geometric mean of 0.8 days. Respective DT_{90} values were in a range of 0.5 – 33.3 days with a geometric mean of 4.3 days. Degradation of cymoxanil mainly followed FOMC kinetics.

No impact of the microbial biomass on the degradation rate could be observed at all. However, since degradation of cymoxanil is mainly driven by pH depending hydrolysis, a significant impact ($p < 0.05$) of the soil pH on the degradation rate could be obtained (at lower pH values degradation of cymoxanil was less rapid). In addition, degradation of cymoxanil has to be considered to slow down at higher application rates.

Since degradation of cymoxanil mainly follows FOMC kinetics, normalization of the DT_{50} was based on the re-calculated SFO- DT_{50} obtained from the FOMC- DT_{90} by division with 3.32 in order to derive adequate modelling endpoints (SANCO/10058/2005, ver. 1.0). Normalized re-calc. SFO- DT_{50} values were in a range of 0.1 – 7.3 days with a geometric mean of 1.0 days. This geometric mean was considered appropriate for groundwater risk assessment. Nevertheless, to account for the impact of the soil pH on the degradation rate of cymoxanil, additional groundwater modellings were performed using the maximum re-calc. SFO- DT_{50} of cymoxanil observed in acidic soils (7.3 days). Soil risk assessment was based on the worst-case normalized re-calc. SFO- DT_{50} of 7.3 days.

At 10 °C degradation half life of cymoxanil in one soil was 1.4 days ($n = 1$) following SFO kinetics ($R^2 = 1.00$, χ^2 error = 2.8 %). Respective DT_{90} was 4.7 days.

Soil degradation studies, which were characterized by significant formation of metabolites (in particularly 'Black Andosol' and 'Sermoise' soil), were subjected to multi-compartment modelling analysis to obtain reliable degradation half-lives for major (> 10 % of AR) metabolites and metabolites considered relevant for groundwater risk assessment (> 10 % of AR, 2 consecutive samples > 5 % of AR or steady increase).

The highly transient major soil metabolite IN-U3204 (which is considered identical to the metabolite fraction Met IV in the study from Melkebeke, 1999), resulting from a (partly reversible) cyclisation of the parent, showed DT_{50} values in a range of 0.2 – 0.6 days ($n = 3$, all compartments SFO kinetics, $R^2 \geq 0.88$, χ^2 error ≤ 26.2 %) with a formation fraction in a range of 0.24 – 0.48 (arithmetic mean 0.36). Following normalization, DT_{50} of IN-U3204 was in a range of 0.1 – 0.7 days with a geometric mean of 0.2 days.

The degradation rate of the major metabolite IN-W3595 (observed in only one soil slightly > 10 % of AR) could only be determined in two soils. Directly linked to the parent, the DT_{50} of IN-W3595 was in a range of 1.7 – 2.8 days ($n = 2$, all compartments SFO kinetics, $R^2 \geq 0.60$, χ^2 error ≤ 69.3 %) with a formation fraction of 0.07 – 0.15. Statistical fit parameters (R^2 and χ^2 error) were rather bad in one of the two soils. However, based on visual assessment the modelling was considered acceptable. Following normalization, DT_{50} of IN-W3595 was in a narrow range of 2.1 – 2.2 days.

Based on the overall degradation pathway of cymoxanil in soil, degradation of IN-KQ960, a minor metabolite in soil but considered relevant for groundwater risk assessment, was calculated using a multi-compartment model (parent, IN-U3204 and IN-KQ960 in series, all SFO kinetics). Since IN-KQ960 was only observed in the Japanese 'Black Andosol' soil above the trigger (2 consecutive samples > 5 % of AR), only one reliable DT_{50} could be

obtained, i.e. 7.6 days ($n = 1$, $R^2 = 0.84$, χ^2 error = 19.2 %) with a formation fraction of 0.16 (from IN-U3204), following normalization DT_{50} was 9.3 days.

The photolysis metabolite IN-JX915, which was shown to exceed 10 % of AR under conditions of soil photolysis but not in dark incubated soils, has to be considered as a highly transient metabolite with a $DT_{50} \leq 0.6$ days (formation fraction from parent 0.10). Following normalization, DT_{50} of IN-JX915 was determined to be 0.7 days.

Under **aerobic sterile conditions** (study conducted only with the 'Black Andosol' soil, Japan, at 25 °C) cymoxanil rapidly degraded according to abiotic hydrolysis with a half-life of 0.9 days (SFO kinetics, $R^2 = 1.98$, χ^2 error = 8.6 %) and a DT_{90} of 2.8 days. In contrast to viable conditions, formation of metabolites was more pronounced, the transient metabolite IN-U3204 degraded with a DT_{50} of 0.7 days, IN-R3273 degraded with a DT_{50} of 20 days, IN-W3595 and IN-KQ960 were almost stable under sterile conditions. In general, under sterile soil conditions degradation of cymoxanil and formation of metabolites closely follows hydrolysis observed in sterile water.

No data are available on the **anaerobic degradation rate** of cymoxanil. However, cymoxanil is not intended to be used in soil with extensive anaerobic conditions. In the eventuality that cymoxanil will be subjected to temporarily or local anaerobic conditions, it is likely that cymoxanil will rapidly degrade owing to hydrolysis (at least under neutral and alkaline conditions) and during aerobic conditions.

Under conditions of **photolysis on the soil surface** (one valid study conducted with air dried soil), cymoxanil degraded with an experimental half-life of 14.1 days (SFO kinetics, $R^2 = 0.90$, χ^2 error = 6.4 %) on a soil of pH 6.4. Based on the degradation rate of cymoxanil in the dark control samples of 38.5 days, a net soil photolysis of 22.1 days could be obtained. Taking into account that cymoxanil will degrade rapidly in moist and viable soils, photolysis on the soil surface is considered to be of minor impact onto the overall dissipation of cymoxanil under environmental conditions.

2.5.2.3 Mobility in soil

Reasonable adsorption/desorption coefficients according to Freundlich isotherms (K_{FOC} , $1/n$ values) were determined for cymoxanil in soil batch experiments using 4 soils (3 EU, 1 USA) with a representative spectrum of soil properties. Owing to the high instability of cymoxanil in soil studies, time for adsorption had to be restricted to 3 hrs. Resulting K_{FOC} values of cymoxanil were in a range of 15.1 – 87.1 L kg⁻¹ with an arithmetic mean of 43.6 L kg⁻¹. Arithmetic mean $1/n$ value was 0.86. No impact of soil pH on the adsorption could be found.

Metabolites IN-U3204, IN-W3595, IN-R3273, IN-JX915 and IN-KQ960 were investigated in batch equilibrium experiments (only one concentration tested) using 4 soil (all US) with a representative spectrum of soil properties. Owing to the high instability of IN-U3204 in aqueous solutions, no reliable K_{OC} value could be stated for this metabolite. K_{OC} values for IN-JX915, also instable in aqueous solutions (data corrected for degradation), were in a range of 5.4 – 34.4 L kg⁻¹, with an arithmetic mean of 16.3 L kg⁻¹. Metabolite IN-R3273 was stable during equilibration time, K_{OC} values were calculated to be in a range of 25.7 – 49.5 L kg⁻¹, arithmetic mean 41.9 L kg⁻¹. Adsorption of IN-R3273 is considered to be lower in more acidic soils. Adsorption of IN-W3595, an acidic compound which was stable during the test, was strongly depending on soil pH likely owing to dissociation processes under more alkaline conditions. K_{OC} values were in a range of 2.3 – 27.4 L kg⁻¹ (arithmetic mean 9.2 L kg⁻¹) with lowest adsorption found in the most alkaline soil (pH 7.8). This behaviour of the major soil metabolite IN-W3595 was adequately taken into account for groundwater risk assessment. In case of IN-KQ960 (virtually no adsorption observed, compound partly instable during the test) no reliable K_{OC} value could be stated owing to analytical reasons. Since no Freundlich isotherms could be calculated owing to the test design, 1/n values were set to the FOCUS default value of 0.9 for all metabolites.

In an additional study, metabolites IN-U3204 (unstable under conditions of soil batch experiments), IN-KQ960 (no reliable K_{OC} could be calculated in the batch experiment), IN-T4226, IN-W3595 and IN-KP533 were investigated in a HPLC method according to OECD guideline 121. On the basis of their retention times in comparison to the reference substances cymoxanil, atrazine, saccharin, IN-R3273 and IN-JX915, the K_{OC} values of IN-U3204, IN-KQ960, IN-T4226, IN-W3595 and IN-KP533 were estimated to be 27.9, 21.6, 17.7, 13.8 and 12.9 L kg⁻¹, respectively. 1/n values were set to the FOCUS default value of 0.9.

In a **field lysimeter study**, conducted in Lower Saxony, Germany, cyanoacetamide-2-¹⁴C labelled cymoxanil, formulated as Curzate 50 WP, was applied three times at 320 g ai ha⁻¹ (7 day interval) onto a loamy sand soil with a pH of 5.4 in the top soil layer. At application, lysimeter were planted with potatoes (flowering stage), application was repeated in one of the two lysimeter in the second year.

In respect to the lysimeter soil pH and the application rate, the lysimeter study is considered a worst-case situation.

Cymoxanil was never found in leachate samples > LOQ (i.e. 0.01 µg L⁻¹).

A significant fraction of radioactivity found in the leachates could be attributed to polar compounds, which were detected with a maximum annual mean concentration of 0.15 µg ai equiv. L⁻¹. This polar fraction was shown to comprise oxalic acid at maximum annual mean amounts of 0.03 µg L⁻¹ and metabolite IN-R3274 at maximum annual mean amounts of 0.02

$\mu\text{g L}^{-1}$. However, the majority of polars remained unidentified with a maximum annual mean concentration of $0.11 \mu\text{g ai equiv. L}^{-1}$. From the chromatographic behaviour and from the low molecular weight of polar metabolites, it is unlikely that unidentified polar compounds exceeded $0.1 \mu\text{g L}^{-1}$ individually. None of the other investigated, less polar metabolites (IN-U3204, IN-T4226 and IN-R3273) exceeded $0.05 \mu\text{g L}^{-1}$ individually.

The great majority (approx. 85 %) of radioactivity found in the leachates, accounting for a maximum annual mean concentration of $0.46 \mu\text{g ai equiv. L}^{-1}$, could not be identified. This amount results from loss of radioactivity during work-up before HPLC (maximum $0.13 \mu\text{g ai equiv. L}^{-1}$), unidentified radioactivity distributed over the HPLC chromatogram (maximum $0.22 \mu\text{g ai equiv. L}^{-1}$) and unidentified polars (maximum $0.11 \mu\text{g L}^{-1}$).

2.5.3.4 PEC_s calculations

PEC_s calculations were based on worst case laboratory degradation rates for cymoxanil and metabolites.

Formulation TANOS 50 WG (DuPont):

Maximum (initial) PEC_s calculated were 0.24, 0.029, 0.009 and 0.013 mg kg^{-1} for cymoxanil, IN-U3204, IN-W3595 and IN-JX915, respectively.

Formulation CYMOXANIL 50 % WP (Oxon):

Maximum (initial) PEC_s calculated were 0.18, 0.024, 0.007 and 0.010 mg kg^{-1} for cymoxanil, IN-U3204, IN-W3595 and IN-JX915, respectively (maximum PEC_s observed for application in lettuce).

2.5.3 Fate and behaviour in water

2.5.3.1 Hydrolysis

Hydrolysis of cymoxanil was investigated in sterile buffer solutions at pH 4, 5, 7 and 9 in two independent studies (DuPont and Oxon), which gave consistent results.

Once in contact with (sterile) buffer solutions, cymoxanil undergoes extensive hydrolysis strongly depending on the pH of the solution, leading to the formation of numerous metabolites. Cymoxanil is considered stable at a pH of 4 (and below); half-life times at pH 5, 7 and 9 were 144, 1.1 and 0.02 days at 25 °C. At 20 °C half-life times at pH 7 and 9 were determined to be 2.1 and 0.04 days.

Hydrolysis of cymoxanil is driven by three main processes (Figure 2.5.3.1-1):

- partly reversible cyclisation into IN-U3204 (six-member ring system) – major process

- partly reversible cyclisation into IN-JX915 (five-member ring system) – minor process
- cleavage of the parent to release IN-W3595 and ethyl urea – major process

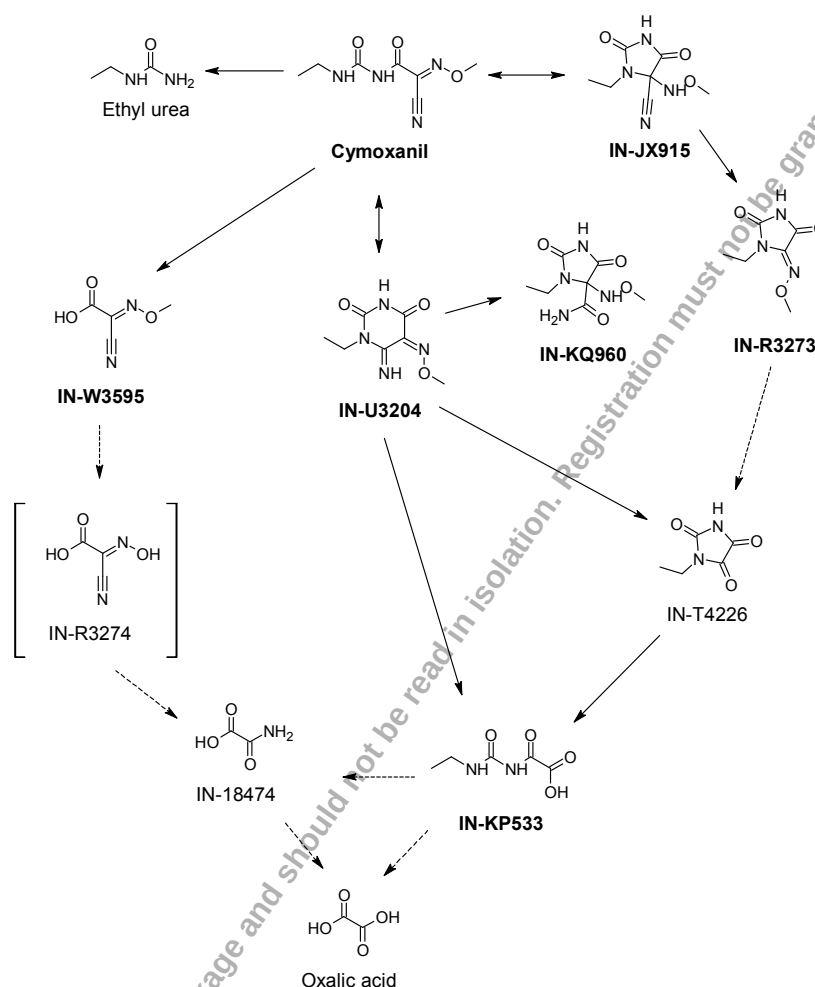


Figure 2.5.3.1-1: Proposed hydrolytic degradation pathway of cymoxanil in sterile water (metabolites in bold exceed 10 % of AR at a pH of 7 or 9).

Metabolite **IN-U3204** is highly unstable in aqueous solutions, rapidly degrading into **IN-KP533**, **IN-T4226** and **IN-KQ960**. **IN-T4226** is a further transient hydrolysis metabolite rapidly degrading into **IN-KP533** by ring cleavage; **IN-KQ960** and **IN-KP533** have to be considered stable under the conditions of sterile hydrolysis.

Metabolite **IN-JX915** rapidly further degrades into **IN-R3273**, which in turn slowly degrades into **IN-T4226**.

The parent cleavage product **IN-W3595** is considered rather stable under the conditions of hydrolysis in sterile buffer solutions. **Ethyl urea**, which is likely to be formed together with **IN-W3595**, was never quantified in environmental fate studies, since the labelling of the parent (cyanoacetamide position) does not allow to follow the fate of this cleavage product.

Nevertheless, ethyl urea has to be considered a major degradation product of the hydrolysis of cymoxanil in sterile buffer solutions at neutral and alkaline pH, too. According to SANCO/221/2000, rev. 10 (2003), guidance document on the relevance of metabolites in groundwater, ethyl urea and its degradation products are considered compounds of no concern and therefore not further considered in the environmental risk assessment.

Hydrolysis half-life of the transient metabolites IN-U3204, IN-JX915 and IN-T4226 at pH 7 and pH 9 were estimated to be 2.5 and 0.5 days, 0.7 and 1.7 days, and 7.2 and 2.0 days, respectively. The metabolites IN-W3595, IN-KQ960, IN-R3273 and IN-KP533 have to be considered rather stable under the conditions of sterile hydrolysis at each pH, their amounts remained almost stable once the hydrolysis process has finished (which occurred by approx. 15 DAT at pH 7 and by 7 DAT at pH 9).

Under conditions of sterile hydrolysis, the following metabolites were observed > 10 % of AR (at pH 7 or pH 9): IN-U3204 (maximum of 60.8 % of AR), IN-JX915 (11.0 % of AR), IN-W3595 (41.5 % of AR), IN-KP533 (57.4 % of AR), IN-R3273 (10.2 % of AR) and IN-KQ916 (14.1 % of AR). In the Oxon study (Slangen and Willams, 2003) several degradation products, not exceeding 10 % of AR individually, remained unidentified.

2.5.3.2 Photolysis

Photolysis of cymoxanil in sterile buffer solution was investigated at pH 5 (where cymoxanil is considered to be almost stable) in two independent studies (DuPont and Oxon), which gave consistent results.

Under the impact of irradiation, degradation of cymoxanil owing to photolysis is strongly driven by formation of the cyclisation metabolite IN-JX915 (five-member ring system, maximum occurrence 52.6 % of AR), which rapidly further degrades to IN-R3273 (maximum occurrence 35.4 % of AR by study termination). No other major metabolites were observed. This pathway is clearly the major degradation route of cymoxanil in acidic solutions exposed to irradiation. The alternative hydrolysis processes (cyclisation to IN-U3204 and cleavage of the parent to form IN-W3595) were almost negligible at the investigated pH value. In the dark control samples almost no degradation of cymoxanil was observed.

Net photolysis half-life time of cymoxanil in sterile buffer solution at pH 5 was calculated to be 1.7 and 3.0 days (DuPont and Oxon study, respectively). The experimental net photolysis of cymoxanil corresponds to 4.3 and 12.1 days (DuPont and Oxon study, respectively) under environmental conditions (midsummer day, approx. 40 °N). Additional calculations with GC-SOLAR yielded a theoretical half-life of cymoxanil of 5.2 and 17.3 days (DuPont and OXON study, respectively) in the top layer of an aqueous system integrated over a full day in the summer at 40 °N (at pH 5.0).

As demonstrated in one additional experiment, conducted in non-sterile pond water at pH 7.0, the impact of irradiation on the overall dissipation of cymoxanil in aquatic ecosystems loses its significance at neutral and alkaline conditions owing to the extensive abiotic hydrolysis of cymoxanil at higher pH values.

Quantum yield (Φ) of cymoxanil was calculated to be 0.0052 (DuPont) and 0.00058 (Oxon).

The DT_{50} of IN-JX915, owing to the influence of photolysis and hydrolysis, was calculated to be approx. 6.6 days at the investigated pH of 5.0 (DuPont and Oxon study). However, owing to the highly transient character of IN-JX915 during hydrolysis under neutral and alkaline conditions (hydrolysis $DT_{50} < 2$ days) it is expected that levels of photolytically formed IN-JX915 will be significantly lower in aquatic systems under environmental conditions (without considering biotic degradation). Based on GC-SOLAR modelling, DT_{50} of IN-JX915 under environmental conditions (pH 5) was estimated to be 21.2 days.

Degradation half-life of IN-R3273 at pH 5.0, owing to the influence of photolysis and hydrolysis, was calculated to be 32.7 days in the DuPont study, in the Oxon study, no reliable half-life time could be calculated for IN-R3273. Based on GC-SOLAR modelling, DT_{50} of IN-R3273 under environmental conditions (pH 5) was estimated to be 4.7 days.

Further minor photolysis products ($< 10\%$ of AR) were IN-T4226 and IN-KP533 which derive from the degradation of IN-JX915 and IN-R3273.

2.5.3.3 Biological degradation

Results of a **readily biodegradability study** indicate that cymoxanil can not be considered readily biodegradable.

The fate and behaviour of cymoxanil in **water/sediment systems** was investigated in four contrasting test systems ('Brandywine Creek', 'Lums Pond', 'OVP' and 'SW') with a representative range of properties in the water and sediment layer.

- 'Brandywine Creek': Sand, 0.8 % organic C, pH_{water} 7.4, pH_{sed} 7.0
- 'Lums Pond': Sand, 0.1 % organic C, pH_{water} 5.3, pH_{sed} 5.1
- 'OVP': Silty clay loam, 4.7 % organic C, pH_{water} 8.3, pH_{sed} 7.5
- 'SW': Silty loam, 4.9 % organic C, pH_{water} 8.3, pH_{sed} 7.5

Dissolved oxygen contents and redox potential values in the water layer indicated aerobic conditions the water layer of all test systems. Anaerobic (reducing) conditions were found in the sediment layers of all systems.

Formation of CO₂ accounted for approx. 41 % of AR by 99 DAT in test systems 'Brandywine creek' and 'Lums Pond', both poor in organic C and microbial activity. Owing to the reductive conditions in these test systems, a significant formation of organic volatiles, likely to be methane, could be demonstrated. In the test systems 'OVP' and 'SW', both with a high amount of organic C in the sediment, formation of CO₂ accounted for 75.5 and 68.5 % of AR by 100 DAT, respectively.

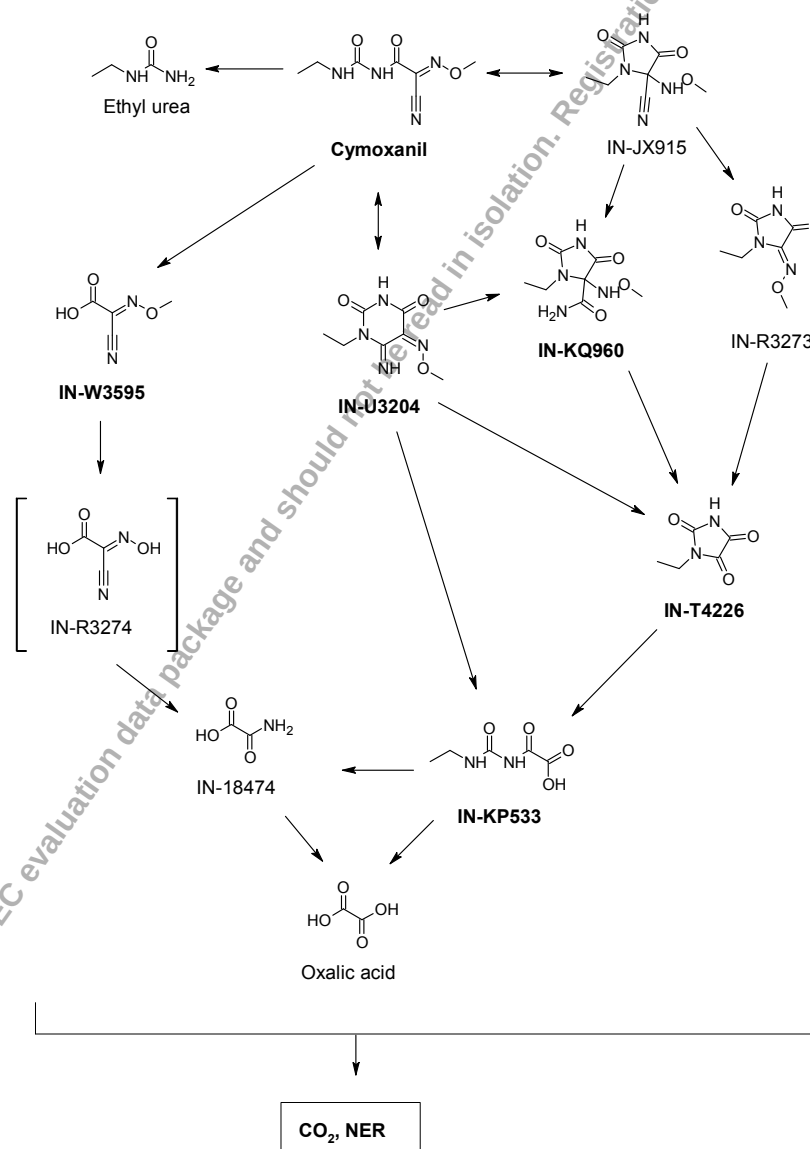


Figure 2.5.3.3-1: Proposed degradation pathway of cymoxanil in water/sediment systems (metabolites in bold exceed 10 % of AR).

Maximum formation of NER accounted for 22.5 – 35.2 % of AR, with the maximum amount occurring around 28/30 DAT. By 100 DAT, NER have decreased to amounts in a range of 17.9 – 25.6 % of AR.

Degradation of cymoxanil in the entire system was fast with a DegT_{50} values in a range of 0.1 – 1.5 days following SFO kinetics ($R^2 \geq 0.99$) with a geometric mean of 0.3 days. Respective DT_{90} values were in a range of 0.2 – 5.0 days, geometric mean 1.0 days. Since transfer of cymoxanil into the sediment layer was negligible, dissipation in the water layer is almost consistent to degradation in the entire system. In accordance to hydrolysis, degradation of cymoxanil in the water/sediment system strongly depends on the water pH with slower degradation observed under more acidic conditions. However, likely owing to non-sterile conditions, degradation of cymoxanil in the rather acidic 'Lums Pond' system (pH in water 5.3) was much faster than expected from hydrolysis alone (conducted under sterile conditions).

Degradation of cymoxanil in the water/sediment system is driven by hydrolysis and microbial turnover. In this respect, formation and occurrence of metabolites is similar to the pattern observed in the hydrolysis study. However, owing to the microbial activity, all metabolites observed to be rather stable under conditions of sterile hydrolysis were rapidly degraded further.

Based on the entire system, the following metabolites are considered major (> 10 % of AR): IN-U3204 (maximum occurrence 24.7 % of AR by 0.1 DAT), IN-W3595 (27.5 % of AR by 0.3 DAT), IN-KQ960 (14.3 % of AR by 3 DAT), IN-T4226 (12.0 % of AR by 3 DAT), metabolite fraction M5 (22.9 % of AR by 1 DAT) and IN-KP533 (26.0 % of AR by 10 DAT). IN-KP533 is included by the RMS into the list of major water/sediment metabolites owing to conservative reasons. IN-KP533 is part of the polar HPLC fraction M1, observed in one water/sediment study (Slangen and Willems, 2000) with a maximum occurrence of 35.0 % of AR. Metabolite fraction M1 additionally comprises IN-W3595, IN-R3274, oxamic acid (IN-18474) and oxalic acid. IN-W3595 could be adequately separated by an additional TLC system, the individual amounts of the remaining polars contributing to the remaining fraction of M1 (maximum 26.0 % of AR) are not known. In the water/sediment study from Trabue and Lydick, 2001, IN-KP533 was observed with maximum amounts of 8.0 % of AR in the entire system. However, formation of polars was generally smaller in this study in comparison to the water/sediment study from Slangen and Willems (2000). For conservative reasons, the sum of the remaining polars (including IN-KP533) is attributed to IN-KP533. Under conditions of sterile hydrolysis, IN-KP533 was observed up to 57.4 % of AR (at pH 7.0).

No metabolite or metabolite fraction was observed > 10 % of AR in the sediment phases of all test systems investigated.

None of the observed metabolites in the water/sediment studies was persistent. Based on the entire system, geometric mean DegT₅₀ values for the metabolites IN-U3204, IN-W3595, IN-T4226, IN-JX915, IN-KP533 and the metabolite fraction M5 were calculated to be 0.4, 3.0, 4.6, 1.7, 2.6 and 1.4 days, respectively. IN-R3273 and IN-KQ960 degraded slower with geometric mean DegT₅₀ values of 6.3 and 47.4 days, respectively.

2.5.3.4 Predicted environmental concentrations in surface water, sediment and groundwater (PEC_{SW}, PEC_{SED} and PEC_{GW})

Surface water

The major routes of entry to surface water are likely to be via spray drift and runoff/drainage for the parent and metabolites IN-U3204, IN-W3595, IN-KQ960, IN-T4226, IN-KP533, IN-JX915 and IN-R3273 (the two latter major in soil and water photolysis only). Since metabolite fraction M5 was not observed in soil, only formation via drift of the parent is considered relevant. PEC_{SW} and PEC_{SED} were calculated for the single and split application using FOCUS surface water STEPS 1 & 2.

Neither cymoxanil nor any degradate was observed > 10 % of AR in the sediment phase.

Formulation TANOS 50 WG (DuPont):

Maximum PEC_{SW} for cymoxanil and metabolites IN-U3204, IN-W3595, IN-KQ960, IN-T4226, IN-JX915, IN-R3273, IN-KP533 and metabolite fraction M5 (considering single and multiple application) were calculated to be 1.61, 0.40, 0.33, 2.12, 1.15, 0.85, 2.11, 2.04 and 0.37 µg L⁻¹ at FOCUS surface water STEP 2, respectively.

Formulation CYMOXANIL 50 % WP (Oxon):

Maximum PEC_{SW} for cymoxanil and metabolites IN-U3204, IN-W3595, IN-KQ960, IN-T4226, IN-JX915, IN-R3273, IN-KP533 and metabolite fraction M5 (considering single and multiple application) were calculated to be 2.21, 0.55, 0.39, 1.50, 0.44, 1.16, 1.06, 0.74 and 0.51 µg L⁻¹ at FOCUS surface water STEP 2, respectively.

Groundwater

Groundwater risk assessment for cymoxanil and metabolites was based on laboratory degradation data using the leaching models FOCUS PEARL 3.3.3 and FOCUS PELMO 3.3.2.

In groundwater cymoxanil and metabolites are considered non-relevant as predicted 80th percentile annual average concentrations were clearly < 0.1 µg L⁻¹ in all FOCUS scenarios for all intended uses (TANOS 50 WG in potatoes and CYMOXANIL 50 % WP in potatoes and lettuce).

Groundwater modelling results are confirmed by a representative lysimeter study conducted in Germany.

2.5.4 Fate and behaviour in air

Neither cymoxanil nor any of its environmental relevant metabolites have significant volatility. The vapour pressure of cymoxanil was 1.5×10^{-4} Pa at 20 °C. There is no guidance available for conducting meaningful studies regarding the potential breakdown of cymoxanil or its relevant metabolites in air. Furthermore, the Henry's law constant of cymoxanil is less than 3.8×10^{-5} Pa m³ mol⁻¹, suggesting little potential for volatilisation in the environment.

2.6 Effects on non-target organisms

2.6.1 Effects on terrestrial vertebrates

2.6.1.1 Birds:

The relevant toxicity endpoints of Cymoxanil to birds are as follows:

Acute toxicity (a.s.): LD₅₀ > 2000 mg/kg bw (bobwhite quail, mallard duck)

Acute toxicity (Cymoxanil 50 WP): LD₅₀ > 2000 mg form./kg bw (japanese quail)

Short-term dietary toxicity: LD₅₀ > 260 mg/kg bw (mallard duck)

Reproductive toxicity: NOEL = 14.9 mg/kg bw (mallard duck)

The exposure assessment is based on recommendations in the Guidance Document for Risk Assessment of Birds and Mammals (SANCO/4145/2000, Sept. 2002). The major exposure route of cymoxanil to wild birds is assumed to be via intake of foliage and arthropods contaminated after spray treatment. In the first tier of the assessment, realistic worst case exposure scenarios are selected with regard to the intended application rate and relevant bird indicator species. The estimated tier 1 TER-figures are presented in the table below. Estimations relate to the intended use of 4 x 240 g ai/ha in lettuce and 8 x 175 g ai/ha in potatoes for medium herbivorous and insectivorous birds.

TER calculations for acute, short- and long-term exposure of birds to Cymoxanil (tier 1)

Time scale	Scenario	TER lettuce	TER potaoes
Acute (a.s.)	medium herbivorous bird	> 70	> 86
	insectivorous bird	> 154	> 211
Acute (50 WP)	medium herbivorous bird	> 35	/
	insectivorous bird	> 127	/
Short-term	medium herbivorous bird	16	19.6
	insectivorous bird	36	49.3
Long-term	medium herbivorous bird	1.7	2.1
	insectivorous bird	2.1	2.8

On the acute and short-term time scale, according to the resulting TER figures the risk can be considered as low. However, a potential high risk was identified in the first tier long-term risk assessment and a refined risk assessment was conducted.

In order to refine the risk to herbivores, measured data on the residue decline of cymoxanil on plant foliage were taken into account. A worst case estimate of the DT_{50} was used and the MAF was set to 1 as it was shown that due to rapid decline no accumulation of residues occurred.

The resulting refined TERIt figures for herbivores are 5.4 for lettuce and 7.5 for potatoes. Refinement for insectivorous species: For lettuce the Yellow Wagtail was chosen as focal species. Based on literature data, the diet of the Yellow Wagtail consists of 80 % large arthropods and 20 % small arthropods. In potatoes two focal species are considered as relevant: the Yellowhammer and Yellow Wagtail. The Yellowhammer is assumed to feed on 82 % large arthropods and 12 % small arthropods, and to spend 50 % of its time in the treated crop, which is based on public domain literature. The diet of the Yellow Wagtail was refined as for lettuce.

The resulting refined TERIt figures for insectivores are in lettuce 6.9 for the Yellow Wagtail, and in potatoes 28 for the Yellowhammer and 9.5 for the Yellow Wagtail.

The exposure via drinking water was also assessed and revealed acceptable TERs. No metabolites of ecotoxicological concern were identified and the risk of bioaccumulation is low. All resulting TER figures are above the respective trigger values given in Annex VI of directive 91/414 and indicate that the risk to wild birds after application of cymoxanil according to GAP is low.

2.6.1.2 Mammals:

The ecotoxicologically relevant toxicity endpoints for cymoxanil are as follows:

Acute toxicity: $LD_{50} = 760 / 1200$ mg/kg bw (a.s., m / f rat)
 $LD_{50} = 1200$ mg/kg bw (Cymoxanil 50 WP, rat)
 $LD_{50} = 1732 / 566$ mg/kg bw (Tanos, m / f rat)

Reproductive toxicity: NOAEL = 10.5 mg/kg bw (rat, two-generation)

The overall NOAEL of 10.5 mg/kg bw from two two-generation reproduction studies in rats is considered conservative and appropriate for risk assessment. It's based on reduced pup weight and viability at the next higher dose level.

The exposure assessment is based on recommendations of the Guidance Document for Risk Assessment of Birds and Mammals (SANCO/4145/2000, Sept. 2002). The major exposure route of cymoxanil to wild mammals is assumed to be via intake of contaminated plant material. In the first tier of the assessment, realistic worst case exposure scenarios are selected with regard to the intended application rate and relevant mammalian indicator species. For TERIt / Tier 1 estimations, a default half-life of cymoxanil of 10 days was assumed. The estimated tier 1 TER-figures for medium herbivores are presented in the table

below. Estimations relate to the intended use of 4 x 240 g ai/ha in lettuce and 8 x 175 g ai/ha in potatoes.

TER calculations for acute and long-term exposure of mammals to cymoxanil (tier 1)

Time scale	Scenario	TER lettuce	TER potatoes
Acute (a.s.)	medium herbivorous mammal	72	89
	insectivorous mammal	359	492
Acute (Cym 50 WP)	medium herbivorous mammal	57	/
	insectivorous mammal	285	/
Acute (Tanos)	medium herbivorous mammal	/	17
	insectivorous mammal	/	92
Long-term	medium herbivorous mammal	3.3	4
	insectivorous mammal	14	19

All acute TER's and the long-term TER's for insectivores indicate an acceptable risk.

However, a refined risk assessment is required for medium herbivores.

In order to refine the risk to herbivores, measured data on the residue decline of cymoxanil on plant foliage were taken into account. A worst case estimate of the DT₅₀ was used and the MAF was set to 1 as it was shown that due to rapid decline no accumulation of residues occurred. Furthermore in potatoes the scenario of herbivores is considered not relevant, as potato foliage is unpalatable to mammals.

The resulting refined TER's are 10 and 14 for lettuce and potatoes, respectively, and indicate a low risk.

The exposure via drinking water was also assessed and revealed acceptable TERs. No metabolites of ecotoxicological concern were identified and the risk of bioaccumulation is low. In conclusion, the risk for wild mammals after the use of cymoxanil according to the GAP appears low.

2.6.2 Effects on aquatic species

A risk assessment for aquatic organisms was performed according to the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001).

TER calculations:

Active substance: Generally for the groups fish, invertebrates, algae and aquatic macrophytes the respective toxicity value for the most sensitive species was used for TER calculations. Toxicity values for the active substance cymoxanil were compared to maximal PEC_{sw} values from FOCUS step 1 and 2 modelling derived for the "worst case" intended uses for the formulations Tanos and Cymoxanil 50 % WP.

Plant protection products: For the formulations Cymoxanil 50 % WP (Oxon) and Tanos (DuPont) toxicity data for fish, daphnids and algae are available. However, the formulation Tanos contains as a second active substance famoxadone. The toxicity of famoxadone was not evaluated during this review report.

To assess the potential risk from the exposure of aquatic organisms to Cymoxanil 50 % WP (only cymoxanil as active substance) the toxicity of the formulation was expressed as active substance and then compared to PEC_{sw} values for the active substance.

The risk from the plant protection product Tanos (two active ingredients) was assessed by comparing toxicity values for the product (expressed as product concentration) to PEC_{sw} water values for the product (assuming only spray drift input into surface waters based on Ganzelmeier drift values).

Risk to aquatic organisms from exposure to cymoxanil

All acute and chronic/long-term TER values for fish, invertebrates, algae and macrophytes were above the respective triggers set in Annex VI of Directive 91/414/EEC when calculated with PEC_{sw} values from FOCUS step 2 modelling (based on "worst case" intended uses for both plant protection products: Cymoxanil 50 % WP and Tanos).

Risk to aquatic organisms from exposure to metabolites of cymoxanil

In section 'Fate and Behaviour' the metabolites IN-U3204, IN-W3595, IN-KQ960, IN-T4226, IN-JX915, IN-R3273, IN-KP533 and the metabolite fraction M5 were considered relevant for the environment. Respective PEC_{sw} values were calculated with FOCUS step 1 and step 2 modelling for the intended uses of the plant protection products Cymoxanil 50 % WP and Tanos.

Acute risk:

Fish: Acceptable studies on the acute toxicity of the metabolites IN-T4226, IN-W3595, IN-KQ960 and IN-U3204 to fish were submitted. Respective TER values (based on PEC_{sw} from FOCUS step 2) are above the triggers set in Annex VI of Directive 91/414/EEC. In an additional static acute study on the toxicity of cymoxanil to fish metabolites arising from the mainly abiotic degradation of cymoxanil under test conditions were identified and quantified (in parallel test solutions without fish). The PEC_{sw} values (FOCUS step 2) for the metabolites IN-JX915, IN-R3273, IN-KP533 and the metabolite fraction M5 are clearly lower (one to three orders of magnitude) than the concentrations at which no fish had died in the mentioned study. Therefore the risk to fish from these metabolites is considered to be low.

Aquatic invertebrates: Acceptable studies on the acute toxicity of the metabolites IN-T4226, IN-W3595, IN-KQ960 and IN-U3204 to daphnids were submitted. Respective TER values are above the triggers set in Annex VI of Directive 91/414/EEC when calculated with FOCUS step 2 PEC_{sw} values. For the metabolites IN-JX915, IN-R3273, IN-KP533 and the metabolite fraction M5 no toxicity information on daphnids is available. However, if the toxicity of these metabolites to daphnids would be by a factor of 100 higher than the toxicity of the active substance, TER values would still be above the respective Annex VI trigger. This is an indication that the risk to aquatic invertebrates from exposure to these metabolites is low. Looking at the whole toxicity profile of cymoxanil and its metabolites and taking into account that the metabolites IN-JX915, IN-R3273, IN-KP533 and the metabolite fraction M5 are not highly toxic to fish, and PEC_{sw} values for these products are likely to be overestimated (see

section fate and behaviour) the RMS is of the opinion, that the risk to invertebrates from these degradation products is low.

Algae: For the metabolites IN-T4226 and IN-W3595 acceptable toxicity estimates for algae are available and respective TER values were above the triggers set in Annex VI of Directive 91/414/EEC. For the metabolites IN-KQ960, IN-U3204, IN-JX915, IN-R3273, IN-KP533 and the metabolite fraction M5 no valid toxicity data are available for algae. However, all studies with algae were performed under static conditions at relatively high pH levels. At alkaline pH levels the degradation of cymoxanil is mainly driven by abiotic processes (basically hydrolysis) which is well understood. Hence from fate and behaviour information on cymoxanil it is reasonable that the metabolites IN-KQ960, IN-U3204, IN-JX915, IN-R3273, IN-KP533 and the metabolite fraction M5 have been present in the test solutions. Therefore the risk to aquatic algae from exposure to these metabolites is considered to be low.

Chronic risk:

According to SANCO/3268/2001 long-term/chronic tests should only be required if the metabolite is more acutely toxic than the active substance. The only metabolite for which this trigger is clearly given is IN-KQ960 (daphnids). A chronic daphnid study with this metabolite was submitted. The respective TER value is above the trigger of 10 set in Annex VI of Directive 91/414/EEC.

Risk to aquatic organisms from exposure to the products Cymoxanil 50 % WP and Tanos

TER values for the plant protection product Cymoxanil 50 % WP indicate a low risk from acute exposure to the formulation (based on PEC_{sw} values for the active substance derived with FOCUS step 1 and 2).

TER values for the product Tanos indicate a low acute risk to aquatic organisms from exposure to the formulation provided that appropriate risk mitigation measures are implemented (based on PEC_{sw} values assuming only drift input in surface waters).

Risk to sediment dwelling organisms:

Since the active substance and its metabolites are not likely to partition into sediments (see section fate and behaviour), no PEC_{sed} values are presented here and no risk assessment for sediment dwelling organisms is demanded.

Bioconcentration in fish:

The log Pow of cymoxanil was found to be 0.67 - 0.59 at 20 °C. Hence no bioconcentration study is demanded.

No experimentally derived log Pow values are available for metabolites of cymoxanil. The RMS estimated log Pow values with the software KOWWIN v1.67 (software developed by US Environmental Protection Agency) for the metabolites IN-KQ960, IN-U3204, IN-T4226, IN-JX915, IN-R3273 and IN-KP533 and IN-W3595 (see table B.9.2.3-1).

For the metabolites IN-KQ960, IN-U3204, IN-T4226, IN-JX915, IN-R3273 and IN-KP533 modelled log Pow values were below the trigger of 3 and hence no fish bioconcentration studies are demanded for these degradation products. For IN-W3595 a log Pow of 4.27 was

derived with KOWWIN. IN-W3595 is an organic acid and the software estimates the log Pow for the non dissociated form of the acid. However, in aquatic environments the substance is partly dissociated and it was shown to be highly water soluble. Taking this information into account it is unlikely that it will accumulate in fat tissue (for which the log Pow is an indication). Therefore no bioconcentration study in fish with the metabolite IN-W3595 is considered necessary.

2.6.3 Effects on bees and other arthropod species

Honey-bees:

Cymoxanil is of low toxicity to bees, the LD₅₀-value for the active substance for contact toxicity is > 100 µg ai/bee and for oral toxicity > 85 µg ai/bee. Cymoxanil/Famoxadone 52.5WG showed a contact LD₅₀ > 200 µg form./bee and an oral LD₅₀ of > 186 µg form./bee. Based on these data hazard quotients (HQ's) have been calculated for oral and for contact exposure for both application scenarios. The resulting HQ's are < 3 and therefore below the relevant trigger, which indicates a low risk to honeybees. Hence, it is concluded that after application of cymoxanil under conditions of the intended representative use the risk to honey-bees is low.

Non-target arthropods:

Laboratory studies with different cymoxanil containing formulations and eight species of non-target arthropods, among them the two indicator species, have been used for the risk assessment.

A LR₅₀ of > 480 g a.s./ha is indicated for both *Aphidius rhopalosiphi* and *Typhlodromus pyri* based on laboratory data with Cymoxanil 50 WP.

A risk assessment for non-target arthropods was performed according to the recommendations of ESCORT II. Hazard quotients were calculated for exposure in in-field and off-field areas for both indicator species and are shown in the table below.

Hazard Quotient (HQ) calculations for the indicator species in lettuce and potatoes in-field

Test substance	Species	Application rate (AR)	MAF	LR ₅₀ (g a.s./ha)	HQ in-field	HQ off-field
lettuce						
Cymoxanil 50 WP	<i>Typhlodromus pyri</i>	4 x 240 g a.s./ha	2.7	> 480	< 1.35	< 0.02
	<i>Aphidius rhopalosiphi</i>			> 480	< 1.35	< 0.02
potato 1						
Cymoxanil 50 WP	<i>Typhlodromus pyri</i>	5 x 120 g a.s./ha	3	> 480	< 0.75	< 0.01
	<i>Aphidius rhopalosiphi</i>			> 480	< 0.75	< 0.01
potato 2						
Cymoxanil/Famoxadone 50WG	<i>Typhlodromus pyri</i>	8 x 175 g a.s./ha	3.5	> 480	< 1.28	< 0.02
	<i>Aphidius rhopalosiphi</i>			> 480	< 1.28	< 0.02

All HQ-values for *Typhlodromus pyri* and *Aphidius rhopalosiphi* indicate an acceptable risk for the in- and off-field area.

In two laboratory studies with *T. pyri* a complete inhibition of reproduction was observed.

However, in two field studies and up to 6 applications only transient reductions in the abundance of mites and eggs were noted and it can be concluded that under field conditions no long-term impact also on reproduction will occur.

Additional laboratory, extended laboratory and semi-field studies with foliage- and ground dwelling arthropods showed a low risk.

The results of many first- and higher tier studies with several species and different cymoxanil containing products support the assumption that at drift rates there will be no adverse effects on non-target arthropod populations.

It is concluded that both in- and off-field exposure to from the intended use does not cause unacceptable effects to populations of terrestrial non-target arthropods.

2.6.4 Effects on earthworms and other soil macro-organisms

Acute toxicity:

Acute toxicity studies with *Eisenia foetida* with cymoxanil, the 50 WP formulation and the formulation Cymoxanil/Famoxadone 52.5 WP (containing 22.7 % cymoxanil) revealed LC₅₀ values of > 1000 mg a.s./kg soil dw, > 1000 mg product/kg soil dw and 989 mg product/kg soil dw, respectively. At lower concentration levels some effects on the body weight were observed and resulted in a NOEC of 309 mg/kg dw for cymoxanil and 556 mg product/kg soil dw for the 50WP, whereas no NOEC could be determined for the combi-formulation. In general the combination with famoxadone poses a higher risk to earthworms than the active substance or single formulation. However all calculated TER values are >1000, well above the trigger of 10, and the acute risk to earthworms is acceptable for all GAP's.

Metabolites:

Based on the rapid degradation of the a.s. and because the major metabolites IN-U3204, IN-W3595 and IN-JX915 can be assumed to have occurred during the 14-day incubation of cymoxanil in artificial soil, soil metabolites of cymoxanil pose no unacceptable risk to earthworms.

Sublethal/reproductive toxicity:

Due to the multiple use scenarios a sublethal / reproduction test was performed with the Cymoxanil/Famoxadone 50 WG formulation (Tanos). As a data requirement according to the Sanco/10329/2002 document a sublethal study is required for the DuPont use in potatoes (> 6 applications) only. Since no effects occurred up to and including the highest concentration applied, the issue of whether to attribute impact to either one or both active substances does not arise. The calculated TER value for this long term exposure is significantly above the trigger value of 5. Therefore the long term risk for earthworms after the application of cymoxanil according to GAP is considered low.

2.6.5 Effects on soil micro-organisms

Active substance and formulation Cymoxanil/Famoxadone 20SC:

Cymoxanil and Cymoxanil/Famoxadone 20SC did not significantly affect the activity of the soil micro-flora under laboratory test conditions. The tests were performed at rates of 1.6 mg a.s./kg soil dw (corresponding to 1.2 kg a.s./ha) and 0.016 mL formulation/kg soil dw (corresponding to 1.44 kg a.s./ha).

Conclusion: Neither respiration nor nitrogen mineralisation of soils treated with cymoxanil up to rates that correspond with all intended multiple use scenarios differed from untreated soils by greater than 25 % after 28 days. The maximum PEC_{soil} for cymoxanil is significantly below the highest test concentration with no lasting effects greater than 25 %.

Hence cymoxanil is not expected to cause any significant effects on soil microbial populations when applied according to GAP.

Metabolites:

Based on the rapid degradation of the a.s. and because the major metabolites IN-U3204, IN-W3595 and IN-JX915 can be assumed to have occurred during the 28-day studies, soil metabolites of cymoxanil pose no unacceptable risk to soil microbes.

2.6.6 Effects on other non-target organisms (flora and fauna)

Non-target plants:

The most sensitive species determined in a vegetative vigour test was *Allium cepa* which showed a reduction of shoot biomass of 44.77 % at a rate of 240 g cymoxanil/ha. The relevant endpoint for risk assessment is a $EC_{50} > 240$ g a.s./ha.

A quantitative risk assessment approach was taken according to the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002). TER's were determined based on drift deposition at 1 m from the edge of the field considering a multiple application factor (MAF)

and the worst case application scenario for the crops lettuce and potatoes.

The resulting TER's exceed the trigger for all intended GAPs and indicate that at a distance of 1 m to the edge of the field no significant damage will occur to non-target terrestrial plants.

This is based on the effects of the "single formulation" Cymoxanil 50WP and also covers the cymoxanil component of the formulation TANOS.

The submitted studies on terrestrial plants and the calculated TER-values indicate that the risk for non-target plants after the use of cymoxanil according to GAP is low at a distance of 1 m to the treated area.

2.6.7 Effects on biological methods of sewage treatment

In a test with activated sludge from a sewage treatment system an EC_{50} of > 19.4 mg a.s./L was determined. It can be assumed that no undue effects to sewage treatment will occur, when cymoxanil is applied according to the GAP.

Overall Conclusions, including a listing of critical end points

recommended restrictions/conditions with regard to physical and chemical properties and analytical methods	None
recommended restrictions/conditions with regard to toxicity and metabolism findings	Appropriate PPE (gloves during mixing and loading as well as during application and overall during application) has to be considered for the operator
recommended restrictions/conditions with regard to residues and risks for consumers	None
recommended restrictions/conditions with regard to fate and behaviour in the environment	Degradation of cymoxanil in soil and in the water phase is considered to significantly depend on the pH with slower degradation rate in more acidic systems. In this respect, MS should pay particular attention to the aquatic risk assessment when assessing application for national authorisations in acidic soils and surface water.
recommended restrictions/conditions with regard to ecotoxicological findings	Plant protection product Tanos: Appropriate risk mitigation measures (e.g. buffer zones) are necessary to protect aquatic organisms.

Appendix 1

Standard Terms and Abbreviations

Part 1 Technical Terms

A	Ampere
ACh	Acetylcholine
AChE	Acetylcholinesterase
ADI	acceptable daily intake
ADP	adenosine diphosphate
AFID	alkali flame-ionization detector of detection
A/G	albumin/globulin ratio
ai	active ingredient
ALD ₅₀	approximate median lethal dose, 50 %
ALT	alanine aminotransferase (SGPT)
AMD	automatic multiple development
ANOVA	analysis of variance
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
approx.	Approximate
as	active substance
AST	aspartate aminotransferase (SGOT)
ASV	air saturation value
ATP	adenosine triphosphate
BCF	bioconcentration factor
bfa	body fluid assay
BOD	biological oxygen demand
bp	boiling point
BSAF	biota-sediment accumulation factor
BSE	bovine spongiform encephalopathie
BSP	bromosulfophthalein
Bt	bacillus thuringiensis
Bti	bacillus thuringiensis israelensis
Btk	bacillus thuringiensis kurstaki
Btt	bacillus thuringiensis tenebrionis
BUN	blood urea nitrogen
bw	body weight
c	centi- (x 10 ⁻²)
°C	degree Celsius (centigrade)
CA	controlled atmosphere
CAD	computer aided design
CBI	confidential business information
cd	candela
CDA	controlled drop(let) application
cDNA	complementary DNA
CEC	cation exchange capacity
cf	confer, compare to
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CL	confidence limits
cm	centimetre
CNS	central nervous system
COD	chemical oxygen demand
CPK	creatine phosphatase
cv	coefficient of variation

Cv	ceiling value
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DES	diethylstilboestrol
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic Acid
dna	designated national authority
DO	dissolved oxygen
DOC	dissolved organic carbon
dpi	days post inoculation
DT ₅₀	period required for 50 percent dissipation (define method of estimation)
DT ₉₀	period required for 90 percent dissipation (define method of estimation)
dw	dry weight
DWQG	drinking water quality guidelines
ε	decadic molar extinction coefficient
EC ₅₀	median effective concentration
ECD	electron capture detector
ECU	European currency unit
ED ₅₀	median effective dose
EDI	estimated daily intake
ELISA	enzyme linked immunosorbent assay
e-mail	electronic mail
EMDI	estimated maximum daily intake
EPMA	electron probe micro analysis
ERC	environmentally relevant concentration
ERL	extraneous residue limit
F ₀	parental generation
F ₁	filial generation, first
F ₂	filial generation, second
FIA	fluorescence immuno assay
FID	flame ionization detector
FOB	functional observation battery
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography
g	gram
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionization detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GEP	good experimental practice
GFP	good field practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract
GL	guideline level
GLC	gas liquid chromatography
GLP	good laboratory practice
GMM	genetically modified micro-organism
GMO	genetically modified organism
GPC	gel-permeation chromatography
GPPP	good plant protection practice
GPS	global positioning system
GSH	glutathion
GV	granulosevirus

h	hour(s)
H	Henry's Law constant (calculated as a unitless value), (see also K)
ha	hectare
Hb	haemoglobin
HCG	human chorionic gonadotropin
Hct	haemocrit
HEED	high energy electron diffraction
HID	helium ionization detector
hl	hectolitre
hma	host-mediated assay
HPAEC	high performance anion exchange chromatography
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography -mass spectroscopy
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HRGC	high resolution gas chromatography
H _s	Shannon-Weaver index
Ht	haematocrit
I ₅₀	inhibitory dose, 50 %
IC ₅₀	median immobilization concentration
ICM	integrated crop management
ID	ionization detector
IEDI	international estimated daily intake
IGR	insect growth regulator
im	intramuscular
inh	inhalation
ip	intraperitoneal
IPM	integrated pest management
IR	infrared
ISBN	international standard book number
ISSN	international standard serial number
iv	intravenous
IVF	in vitro fertilization
k	kilo
K	Kelvin or Henry's Law constant (in atmospheres per cubic meter per mole) (see also H)
K _{ads}	adsorption constant
K _{des}	apparent desorption coefficient
kg	kilogram
K _{oc}	organic carbon adsorption coefficient
K _{om}	organic matter adsorption coefficient
kg	kilogram
L	litre
LAN	local area network
LASER	light amplification by stimulated emission of radiation
LBC	loosely bound capacity
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC ₅₀	lethal concentration, median
LCA	life cycle analysis
LC _{Lo}	lethal concentration low
LD ₅₀	lethal dose, median; dosis letalis media
LD _{Lo}	lethal dose low
LDH	lactate dehydrogenase
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LOD	limit of detection

LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
LOQ	limit of quantification (determination)
LPLC	low pressure liquid chromatography
LSC	liquid scintillation counting or counter
LSD	least squared denominator multiple range test
LSS	liquid scintillation spectrometry
LT	lethal threshold
m	metre
M	molar
µm	micrometer (micron)
MAF	multiple application factor
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MDL	method detection limit
MFO	mixed function oxidase
mg	milligram
µg	microgram
MHC	moisture holding capacity
min	minute(s)
mL	millilitre
MLD	minimum lethal dose
MLT	median lethal time
mm	millimetre
mo	month(s)
mol	Mole(s)
MOS	margin of safety
mp	melting point
MRE	maximum residue expected
MRL	maximum residue level
mRNA	messenger ribonucleic acid
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
n	normal (defining isomeric configuration) or number of observations
NAEL	no adverse effect level
nd	not detected
NEDI	no effect daily intake (mg/kg body wt/day)
NEL	no effect level
NERL	no effect residue level
ng	nanogram
nm	nanometer
NMR	nuclear magnetic resonance
no	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NOIS	notice of intent to suspend
NPD	nitrogen-phosphorus detector of detection
NPV	nuclear polyhedrosis virus
NR	not reported
nse	non standard exposure
NTE	neurotoxic target esterase
OC	organic carbon content
ODP	ozone-depleting potential

ODS	ozone depleting substances
OM	organic matter content
op	organophosphorous pesticide
Pa	Pascal
PAD	pulsed amperometric detection
2-PAM	2-pralidoxime
pc	paper chromatography
PCV	haematocrit (packed corpuscular volume)
PEC	predicted environmental concentration
PEC _A	predicted environmental concentration in air
PEC _{GW}	predicted environmental concentration in ground water
PEC _s	predicted environmental concentration in soil
PEC _{SW}	predicted environmental concentration in surface water
PED	plasma-emissions-detector
pH	pH-value
PHI	pre-harvest interval
PIC	prior informed consent
pic	phage inhibition capacity
pic	phage inhibitory capacity
PIXE	proton induced X-ray emission
pKa	negative logarithm (to the base 10) of the dissociation constant
PNEC	predicted no effect concentration
po	by mouth
PPE	Personal protective equipment
P _{OW}	partition coefficient between n-octanol and water
POP	persistent organic pollutants
ppb	parts per billion (10 ⁻⁹)
ppm	parts per million (10 ⁻⁶)
ppp	plant protection products
ppq	parts per quadrillion (10 ⁻²⁴)
ppt	parts per trillion (10 ⁻¹²)
PSP	phenolsulfophthalein
PrT	prothrombin time
PRL	practical residue limit
PT	prothrombin time
PTDI	provisional tolerable daily intake
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r	correlation coefficient
r ²	coefficient of determination
RBC	red blood cell
REI	restricted entry interval
Rf	ratio of fronts
RfD	reference dose
RH	relative humidity
RL ₅₀	residual lifetime
RNA	ribonucleic acid
RP	reversed phase
rpm	rotations per minute
rRNA	ribosomal ribonucleic acid
RRT	relative retention time
s	seconds
SAC	strong adsorption capacity
SAP	serum alkaline phosphatase
SAR	structure/activity relationship
SBLC	shallow bed liquid chromatography
sc	subcutaneous
sce	sister chromatid exchange

SD	standard deviation
SE	standard error
se	standard error
SEM	standard error of the mean
SEP	standard evaluation procedure
SF	safety factor
SFC	supercritical fluid chromatography
SFE	supercritical fluid extraction
SIMS	secondary ion mass spectroscopy
SOP	standard operating procedures
sp	species (only after a generic name)
SPE	solid phase extraction
SPF	specific pathogen free
spp	subspecies
sq	square
SSD	sulphur specific detector
SSMS	spark source mass spectrometry
STEL	short term exposure limit
STMR	supervised trials median residue
t	tonne (metric ton)
t _{1/2}	half-life (define method of estimation)
T ₃	tri-iodothyroxine
T ₄	thyroxine
TADI	temporary acceptable daily intake
TBC	tightly bound capacity
TCD	thermal conductivity detector
TC _{Lo}	toxic concentration, low
TD _{Lo}	toxic dose low
TDR	time domain reflectrometry
TER	Toxicity Exposure Ratio
TER _i	toxicity exposure ratio for initial exposure
TER _{LT}	toxicity exposure ratio following chronic exposure
TER _{ST}	toxicity exposure ratio following repeated exposure
tert	tertiary (in a chemical name)
TEP	typical end-use product
TGGE	temperature gradient gel electrophoresis
TID	thermionic detector, alkali flame detector
TLC	thin layer chromatography
Tlm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRC	theoretical maximum residue contribution
TMRL	temporary maximum residue limit
TOC	total organic carbon
Tremcard	Transport emergency card
tRNA	transfer ribonucleic acid
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
ULV	ultra low volume
UV	ultraviolet
v/v	volume ratio (volume per volume)
WBC	white blood cell
wk	week
wt	weight
w/v	weight per volume

w/w	weight per weight
ww	wet weight
XRFA	X-ray fluorescence analysis
yr	year
≤	less than or equal to
≥	greater than or equal to
<	less than
>	greater than

Part 2 Organisations and Publications

ASTM	American Society for Testing and Materials
BA	Biological Abstracts (Philadelphia)
BART	Beneficial Arthropod Registration Testing Group
CA	Chemical Abstracts
CAB	Centre for Agriculture and Biosciences International
CAC	Codex Alimentarius Commission
CAS	Chemical Abstracts Service
CCFAC	Codex Committee on Food Additives and Contaminants
CCGP	Codex Committee on General Principles
CCPR	Codex Committee on Pesticide Residues
CE	Council of Europe
CIPAC	Collaborative International Pesticides Analytical Council Ltd
COREPER	Comite des Representants Permanents
EC	European Commission
ECB	European Chemical Bureau
ECCA	European Crop Care Association
ECDIN	Environmental Chemicals Data and Information Network of the European Communities
ECDIS	European Environmental Chemicals Data and Information System
ECE	Economic Commission for Europe
ECETOC	European Chemical Industry Ecology and Toxicology Centre
ECLO	Emergency Centre for Locust Operations
ECMWF	European Centre for Medium Range Weather Forecasting
ECPA	European Crop Protection Association
EDEXIM	European Database on Export and Import of Dangerous Chemicals
EHC	Environmental Health Criteria (number)
(number)	
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMIC	Environmental Mutagens Information Centre
EPA	Environmental Protection Agency
EPO	European Patent Office
EPPO	European and Mediterranean Plant Protection Organization
ESCORT	European Standard Characteristics of Beneficials Regulatory Testing
EU	European Union
EUPHIDS	European Pesticide Hazard Information and Decision Support System
EUROPOEM	European Predictive Operator Exposure Model
FAO	Food and Agriculture Organization of the UN
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use

GATT	General Agreement on Tariffs and Trade
GAW	Global Atmosphere Watch
GCOS	Global Climate Observing System
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GEDD	Global Environmental Data Directory
GEMS	Global Environmental Monitoring System
GIEWS	Global Information and Early Warning System for Food and Agriculture
GIFAP	Groupeement International des Associations Nationales de Fabricants de Produits Agrochimiques
GRIN	Germplasm Resources Information Network
HRAC	Herbicide Resistance Action Committee
IARC	International Agency for Research on Cancer
IATS	International Academy of Toxicological Science
IBT	Industrial Bio-Test Laboratories
ICBB	International Commission of Bee Botany
ICBP	International Council for Bird Preservation
ICES	International Council for the Exploration of the Seas
ICPBR	International Commission for Plant-Bee Relationships
ILO	International Labour Organisation
IMO	International Maritime Organisation
IOBC	International Organization for Biological Control of Noxious Animals and Plants
IPCS	International Programme on Chemical Safety
IRAC	Insecticide Resistance Action Committee
IRC	International Rice Commission
ISCO	International Soil Conservation Organization
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
JECFA	FAO/WHO Joint Expert Committee on Food Additives
JFCMP	Joint FAO/WHO Food and Animal Feed Contamination Monitoring Programme
JMP	Joint Meeting on Pesticides (WHO/FAO)
JMPR	Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
NAFTA	North American Free Trade Agreement
NATO	North Atlantic Treaty Organisation
NCI	National Cancer Institute (USA)
NCTR	National Center for Toxicological Research (USA)
NGO	non-governmental organization
NTP	National Toxicology Programme (USA)
OECD	Organization for Economic Cooperation and Development
OLIS	On-line Information Service of OECD
PAN	Pesticide Action Network
RNN	Re-registration Notification Network
RTECS	Registry of Toxic Effects of Chemical Substances (USA)
SCPH	Standing Committee on Plant Health
SETAC	Society of Environmental Toxicology and Chemistry
SI	Système International d'Unites
SITC	Standard International Trade Classification
Toxline	Toxicology Information On-line
UN	United Nations
UNEP	United Nations Environment Programme

WCDP	World Climate Data Programme
WCP	World Climate Programme
WCRP	World Climate Research Programme
WFP	World Food Programme
WHO	World Health Organization
WTO	World Trade Organization
WWF	World Wildlife Fund

Part 3 Preparation (Formulation) Types and Codes *

Code	Description	Definition
AB	Grain bait	Special forms of bait.
AE	Aerosol dispenser	A container-held preparation which is dispersed generally by a propellant as fine droplets/particles upon actuation of a valve.
AL	Other liquids to be applied undiluted	Self defining.
BB	Block baits	Special forms of bait.
BR	Briquette	Solid block designed for controlled release of active ingredient into water.
CB	Bait concentrate	A solid or liquid intended for dilution before use as a bait.
CG	Encapsulated granule	A granule with a protective or release controlling coating.
CS	Capsule suspension	A stable suspension of capsules in a fluid normally intended for dilution with water before use.
DC	Dispersible concentrate	A liquid homogeneous preparation to be applied as a solid dispersion after dilution in water.
DP	Dustable powder	A free-flowing powder suitable for dusting.
DS	Powder for dry seed treatment	A powder for application in the dry state directly to seed.
EC	Emulsifiable concentrate	A liquid, homogenous preparation to be applied as an emulsion after dilution in water.
ED	Electrochargeable liquid	Special liquid preparation for electrostatic (electrodynamic) spraying.
EO	Emulsion, water in oil	A fluid, heterogeneous preparation consisting of a dispersion of fine globules of pesticide in water in a continuous organic liquid phase.
ES	Emulsion for seed treatment	A stable emulsion for application to the seed either directly or after dilution.
EW	Emulsion, oil in water	A fluid, heterogeneous preparation consisting of a dispersion of fine globules of pesticide in an organic liquid in a continuous water phase.
FD	Smoke tin	Special form of smoke generator.
FG	Fine granule	A granule in the particle size range from 300 to 2500µ.
FK	Smoke candle	A smoke generator in the form of a candle.
FP	Smoke cartridge	Special form of smoke generator.
FR	Smoke rodlet	Special form of smoke generator.
FS	Flowable concentrate for seed treatment	A stable suspension for application to the seed either directly or after dilution.
FT	Smoke tablet	Special form of smoke generator.
FU	Smoke generator	A combustible preparation generally solid, which upon ignition releases the active substances in the form of a smoke.
FW	Smoke pellet	Special form of smoke generator.
GA	Gas	A gas packed in pressure bottle or pressure tank.
GB	Granular bait	Special forms of bait.
GE	Gas generating product	A preparation which generates a gas by chemical reaction.
GG	Macrogranule	A granule in the particle size range from 2000 to 6000 µ.
GP	Flo-dust	Very fine dustable powder for pneumatic application in glass-houses.
GR	Granule	A free-flowing solid preparation of a defined granule size range

* based upon the catalogue of Pesticide Formulation types and International Coding Systems, developed by GIFAP in co-operation with the German working group on documentaion questions (Arbeitsgruppe EDV Pflanzenschutz Versuchswesen). GIFAP Technical Monograph No 2, 1989.

Code	Description	Definition
GS	Grease	ready for use.
HN	Hot fogging concentrate	Very viscous preparation based on oil or fat.
KN	Cold fogging concentrate	A preparation suitable for application by fogging equipment either directly or after dilution.
LA	Lacquer	A preparation suitable for application by cold fogging equipment, either directly or after dilution.
LS	Solution for seed treatment	A solvent based film-forming preparation.
MG	Microgranule	A solution for application to the seed either directly or after dilution.
OF	Oil miscible flowable (=oil active substances in a miscible suspension)	A granule in the particle size range from 100 to 600 µ.
OL	Oil miscible liquid	A stable suspension of concentrate fluid intended for dilution in an organic liquid before use.
OP	Oil dispersible powder	A liquid, homogenous preparation to be applied as a homogenous liquid after dilution in an organic liquid.
PA	Paste	A powder preparation to be applied as a suspension after dispersion in an organic liquid.
PB	Plate bait	A water based film forming preparation.
PC	Gel or paste concentrate	Special forms of bait.
PR	Plant rodlet	A solid preparation to be applied as a gel or a paste after dilution with water.
PS	Seed coated with a pesticide	A small rodlet, usually a few centimetres in length and a few millimetres in diameter containing active substance.
RB	Bait (ready for use)	Self defining.
SB	Scrap bait	A preparation designed to attract and be eaten by the target species.
SC	Suspension concentrate (= flowable concentrate)	Special forms of bait.
SE	Suspo-emulsion	A stable suspension of active substance(s) in a fluid intended for dilution with water before use.
SG	Water soluble granules	A fluid, heterogeneous preparation consisting of a stable dispersion of active substance(s) in the form of solid particles and of fine globules in a continuous water phase.
SL	Soluble concentrate	A preparation consisting of granules to be applied as a true solution of active substance after dissolution in water but may contain insoluble inert ingredients.
SO	Spreading oil	A liquid homogenous preparation to be applied as a true solution of the active substance after dilution with water.
SP	Water soluble powder	A preparation designed to form a surface layer on application to water.
SS	Water soluble powder for seed treatment	A powder preparation to be applied as a true solution of the active substance after solution in water but which may contain insoluble inert ingredients.
SU	Ultra low volume (ULV) suspension	A powder to be dissolved in water before application to the seed.
TB	Tablet	A suspension ready for use through ULV equipment.
TP	Tracking powder	Solid preparation in the form of small, flat plates for dissolution in water.
UL	Ultra low volume (ULV) liquid	A rodenticidal contact preparation in powder form.
VP	Vapour releasing product	A homogenous liquid ready for use through ULV equipment.
WG	Water dispersible	A preparation containing one or more volatile ingredients, the vapours of which are released into the air. Evaporation rate normally is controlled by using suitable preparations and/or dispensers.
WP	Wettable powder	A preparation granule consisting of granules to be applied after disintegration and dispersion in water.
WS	Water dispersible powder for slurry seed treatment	A powder preparation to be applied as a suspension after dispersion in water.
XX	Others	A powder to be dispersed at high concentration in water before application as a slurry to the seed.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Appendix 2

Specific Terms and Abbreviations

Physical chemical properties

ECD	Electrochemical detector
NPD	Nitrogen-phosphorous detector
IEC	Ion exchange chromatography
ILV	Independent laboratory validation
RSD	Relative standard deviation

Residue

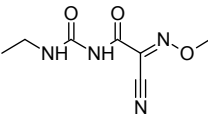
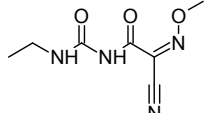
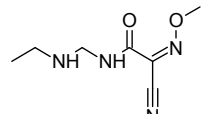
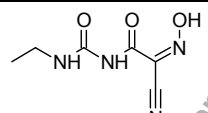
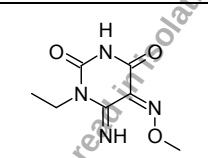
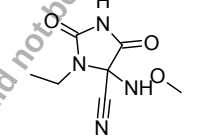
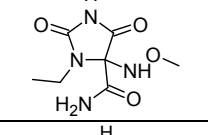
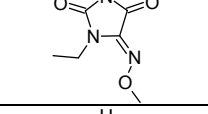
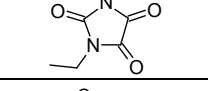
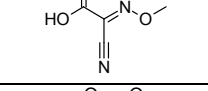
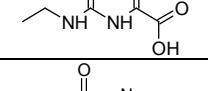
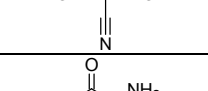
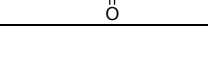
RCI rotational crop interval

DASST days after single soil treatment

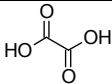
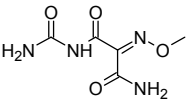
‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

List of metabolites of cymoxanil found in different matrices

Code	Chemical name	Chemical structure	Mole mass [g mol ⁻¹]	Occurrence
Cymoxanil, DPX-T3217 (parent compound)	2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide (E-configuration)		198.2	Parent
IN-Q8761	2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide (Z-configuration)		198.2	-
Metabolite A	2-cyano-N-[(ethylamino)methyl]-2-(methoxyimino)acetamide (E-configuration)		184.2	Rat
Metabolite 4 (oxime)	2-cyano-N-[(ethylamino)carbonyl]-2-(hydroxyimino)acetamide (E-configuration)		184.2	Rat
IN-U3204	1-ethyl-6-iminodihydropyrimidine-2,4,5(3H)-trione 5-(O-methyloxime) (E-configuration)		198.2	Rat Soil, aerobic Water/sediment, water phase
IN-JX915	3-ethyl-4-(methoxyamino)-2,5-dioximidazolidine-4-carbonitrile (stereomer racemate)		198.2	Soil, aerobic, photolysis Water, photolysis
IN-KQ960	3-ethyl-4-(methoxyamino)-2,5-dioximidazolidine-4-carboxamide (stereomer racemate)		216.2	Rat Plant (lettuce) Soil, aerobic Water/sediment, water phase
IN-R3273	1-ethylimidazolidine-2,4,5-trione 5-(O-methyloxime) (E-configuration)		171.2	Water, photolysis
IN-T4226	1-ethylimidazolidine-2,4,5-trione		142.1	Rat Water/sediment, water phase
IN-W3595	Cyano(methoxyimino)acetic acid (E-configuration)		128.1	Rat Plant (lettuce) Soil, aerobic Water/sediment, water phase
IN-KP533	{[(ethylamino)carbonyl]amino}(oxo)acetic acid		160.1	Plant (lettuce) Water/sediment, water phase
IN-R3274	Cyano(hydroxyimino)acetic acid		114.1	-
IN-18474	Amino(oxo)acetic acid, oxamic acid		89.1	Soil, aerobic

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Code	Chemical name	Chemical structure	Mole mass [g mol ⁻¹]	Occurrence
Oxalic acid	Oxalic acid		90.0	-
Metabolite fraction M5 ^a	N-(aminocarbonyl)-2-(methoxyimino)malonamide (E-configuration)		188.1	Water/sediment, water phase

^a Metabolite fraction M5 comprises at least 2 compounds, one is considered to be represented by the structure shown in the table, the other compound(s) is/are unknown

Appendix 3

List of endpoints

based on EPCO Manual E4 - rev. 4 (September 2005)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Chapter: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Cymoxanil
Function (e.g. fungicide)	Fungicide
Rapporteur Member State	Austria
Co-rapporteur Member State	none

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	1-(2-cyano-2-methoxyiminoacetyl)-3-ethylurea
Chemical name (CA) ‡	2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide
CIPAC No ‡	419
CAS No ‡	57966-95-7
EC No (EINECS or ELINCS) ‡	261-043-0
FAO Specification (including year of publication) ‡	Not less than 970 g/kg 419/TC (April 2005)
Minimum purity of the active substance as manufactured ‡	970 g/kg (both notifiers)
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	No relevant impurities present
Molecular formula ‡	C ₇ H ₁₀ N ₄ O ₃
Molecular mass ‡	198.2 g/mol
Structural formula ‡	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	161 to 162 °C (99.2% to 99.6%)
Boiling point (state purity) ‡	Cymoxanil did not boil below its decomposition/sublimation temperature
Temperature of decomposition (state purity)	Cymoxanil is thermally stable (99.2% to 99.6%). No decomposition or chemical transformation observed through the melting point (162 °C).
Appearance (state purity) ‡	white crystalline solid or pale peach to pale pink, powdery, crystalline solid (98.8% to 99.6 %).
Vapour pressure (state temperature, state purity) ‡	1.50×10^{-4} Pa (20 °C, 99.9%)
Henry's law constant ‡	3.3×10^{-5} Pa.m ³ .mol ⁻¹ at pH 5 3.8×10^{-5} Pa.m ³ .mol ⁻¹ at pH 7 (Cymoxanil hydrolyses rapidly at pH 9, so water solubility and hence Henry's law constant cannot be determined at an alkaline pH)
Solubility in water (state temperature, state purity and pH) ‡	890 mg/L (20 °C, pH 5, 99.9%) 780 mg/L (20 °C, pH 7, 99.9%) 782 mg/L (20 °C, unbuffered, pH 5.68, 99.9%)
Solubility in organic solvents ‡ (state temperature, state purity)	n-Hexane: 0.037 g/L Toluene: 5.29 g/L Acetonitrile: 57.0 g/L Ethyl-acetate: 27.9 -28.8 g/L 1-Octanol: 1.43 g/L Methanol: 22.9 - 29.0 g/L Acetone: 62.4 - 68.2 g/L Dichloromethane: 133.2 g/L n-Heptane: 0.017 g/L Xylene: 7.6 g/L Methylene chloride: 58.4 g/L (Purity 97.4% to 99.1% at 20 °C)
Surface tension ‡ (state concentration and temperature, state purity)	68.7 mN/m at 19 °C (90 % saturated solution, 98.8%)
Partition co-efficient ‡ (state temperature, pH and purity)	log P _{OW} = 0.64 at 20 °C pH (unbuffered, 99.1%) log P _{OW} = 0.59 at 20 °C, pH 5 (99.9%) log P _{OW} = 0.67 at 20 °C, pH 7 (99.9%)
Dissociation constant (state purity) ‡	pKa = 9.0 - 9.7 at 20°C (99.1% to 99.9%)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

UV/VIS absorption (max.) incl. ϵ ‡ (state purity, pH)	ϵ in [L.mol ⁻¹ .cm ⁻¹], Purity 99.6% (Applicant A): λ_{max} [nm]: 244, ϵ = 9333.20 (25° C, pH 1.5) λ_{max} [nm]: 244, ϵ = 9296.80 (25° C, pH 6.9) ϵ in [L.mol ⁻¹ .cm ⁻¹], Purity 99.1% (Applicant B): λ_{max} [nm]: 240, ϵ = 9287.6 (acid conditions) λ_{max} [nm]: 240, ϵ = 9419.3 (neutral conditions) λ_{max} [nm]: 240, ϵ = 7739.7 (alkaline conditions)
Flammability ‡ (state purity)	Not classified as highly flammable (97.8% to 98.8%)
Explosive properties ‡ (state purity)	Not explosive (97.8% to 98.8%)
Oxidising properties ‡ (state purity)	Not oxidizing (97.8% to 98.8%). Additional data required.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be made on the basis of this document.

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Summary of representative uses evaluated (name of active substance or the respective variant)*

Crop and/or situation	Member state or Country (a)	Product Name (b)	F G or I (c)	Pests or Groups of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks (e)
					Type	Conc. of as	method kind	growth stage (d)	Number min max	Interval between application	kg as/ha min max	water l/ha min max	kg as/ha min max		
Lettuce	South	CYM 50	F	<i>Bremia lactucae</i>	WP	500 g/kg	Spray	40-49	3-4	7	0.03-0.048	500-800	0.240	10	Oxon
Potato	North	CYM 50	F	<i>Phytophthora infestans</i>	WP	500 g/kg	Spray	21-95	4	7-10	0.026-0.060-	200-450	0.120	7	Oxon
	South	CYM 50			WP	500 g/kg	Spray	21-95	5	7	0.012-0.024	500-1000	0.120	7	Oxon
	North	Tanos	F	<i>Phytophthora infestans</i>	WG	250g/kg	Spray	21-95	6-8	7-10	0.029-0.058	300-600	0.175	14	DuPont
	South														
(a) Southern Europe (South) Northern Europe (North).															
(b) CYM 50 = Cymoxanil 50 %WP; Tanos = Cymoxanil/Famoxadone 250:250g/kg.															
(c) Outdoor or field use (F), glasshouse application (G) or indoor application (I).															
(d) Growth stage at the first application according to BBCH system for a uniform coding of phenologically similar growth stages of all mono- and dicotyledonous plant species.															
(e) GAP for products supported by Oxon or DuPont.															

* End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Methods of Analysis

Chapter: Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	HPLC- UV
Impurities in technical as (analytical technique)	HPLC-UV
Plant protection product (analytical technique)	HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin	Cymoxanil
Food of animal origin	Not applicable
Soil	Cymoxanil
Water surface	Cymoxanil
drinking/ground	Cymoxanil
Air	Cymoxanil
Body fluids and tissues (analytical technique and LOQ)	Not applicable

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	GC-NPD: LOQ = 0.05 mg/kg in commodities with high water, high acid content and dry crops
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	No residue definition is proposed, therefore no analytical method is required
Soil (analytical technique and LOQ)	HPLC-UV: LOQ = 0.01 mg/kg
Water (analytical technique and LOQ)	HPLC-UV: LOQ = 0.10 µg/L (drinking and surface water)
Air (analytical technique and LOQ)	HPLC-UV: LOQ = 0.46 µg/m ³
Body fluids and tissues (analytical technique and LOQ)	Cymoxanil is not classified as toxic or highly toxic, therefore no analytical method is required

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	none

Impact on Human and Animal Health

Chapter: Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	Rapid (T_{max} 0.5 – 3 h in plasma) but limited 76.0 to 81.1 % within 48 h (based on urinary and biliary excretion + carcass) after single low dose in rats
Distribution ‡	Widely distributed; highest residues in liver and kidneys
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	Rapid and extensive (≥ 80 %) within 48 h, mainly via urine (60 – 70 %)
Metabolism in animals ‡	Extensively metabolised (> 95 %); all metabolites identified are intermediates leading to the formation of glycine used for incorporation and conjugation
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound
Toxicologically relevant compounds ‡ (environment)	With respect to groundwater contamination, no metabolites of concern have been identified (i.e. > 0.1 µg/L)

Acute toxicity (Annex IIA, point 5.2)

Rat LD ₅₀ oral ‡	960 mg/kg bw	R22
Rat LD ₅₀ dermal ‡	> 2000 mg/kg bw	
Rat LC ₅₀ inhalation ‡	> 5.6 mg/L air/4h (nose only)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Slightly irritating (no classification required)	
Skin sensitisation ‡	Sensitising (M & K)	R43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	<u>Testes</u> (organ weight, macroscopic and microscopic changes), <u>epididymides</u> (macroscopic and microscopic changes), <u>liver</u> (organ weight, histology), kidney (organ weight) and thymus (histology)	R48/22
Relevant oral NOAEL ‡	1-year dog: 2.8 mg/kg bw/day 90-day rat: 6.5 mg/kg bw/day	
Relevant dermal NOAEL ‡	28 day, rat: > 1000 mg/kg bw/day	
Relevant inhalation NOAEL ‡	No data, not relevant	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Impact on Human and Animal Health

Genotoxicity ‡ (Annex IIA, point 5.4)

Equivocal results <i>in vitro</i> ; negative <i>in vivo</i> overall no genotoxic/mutagenic potential	
---	--

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Macroscopic as well as histological alterations in several organs (lungs, testes, retina, liver, pancreas, sciatic nerve, rectum, stomach, epididymides, duodenum, uterus)
Relevant NOAEL ‡	2-year rat: 4.08 mg/kg bw/day 18-month, mouse: 4.19 mg/kg bw/day
Carcinogenicity ‡	No evidence of a cancerogenic potential

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	<u>Parental</u>: body weight and weight gain; increased relative testis weight <u>Reproductive</u>: reduced live pups born, reduced number of corpora lutea and implantations, and increase of post implantation loss at parental toxic dose levels) <u>Offspring</u>: Reduced viability and litter survival at parental toxic dose levels; reduced pup weight	
Relevant parental NOAEL ‡	10.5 mg/kg bw/day (150 ppm)	
Relevant reproductive NOAEL ‡	31.6 mg/kg bw/day (450 ppm)	
Relevant offspring NOAEL ‡	10.5 mg/kg bw/day (150 ppm)	

Developmental toxicity

Developmental target / critical effect ‡	<u>Rat</u>: increased incidences of <u>malformations</u> (hemi vertebra, exencephaly and fused ribs) at maternal toxic doses (clinical observations, reduced body weight and food consumption); increased incidences of variants (incomplete/poor ossification) and minor anomalies at the lowest dose tested without maternal toxicity	R63
--	--	------------

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Impact on Human and Animal Health

	Rabbit: increased incidences of <u>skeletal malformations</u> (vertebra and/or rib alterations linked with scoliosis) at maternal toxic dose levels (clinical observations, reduced body weight gain); <u>hydrocephaly</u> and <u>cleft palates</u> ; increased incidences of <u>visceral malformations</u> (dilation of heart ventricles) at maternal toxic dose levels (reduced body weight gain and food consumption)	
Relevant maternal NOAEL ‡	Rat: 10 mg/kg bw/day Rabbit: 8 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 10 mg/kg bw/day Rabbit: 8 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data available – not required (no concern from other studies)	
Repeated neurotoxicity ‡	90-day rat : no evidence of neurotoxic effects up to 224 mg/kg bw/day	
Delayed neurotoxicity ‡	No data available – not required	
Developmental neurotoxicity ‡	Rats: no evidence of developmental neurotoxic effects up to 100 mg/kg bw/day	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No evidence of immunotoxicity in 28 day studies in rats and mice	
Studies performed on metabolites/impurities ‡	Metabolite IN-3204 (3-ethyl-4-(methoxyimino)-2,5-dioxo-4-imidazolidine-carboxamide): LD ₅₀ > 7500 mg/kg bw	

Medical data ‡ (Annex IIA, point 5.9)

No evidence of adverse effects to workers of manufacturing plants; no clinical cases and poisoning incidents related to the agricultural use of cymoxanil containing plant protection products have been reported
--

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Impact on Human and Animal Health

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.03 mg/kg bw/day	Dog, 1-year study [DuPont, OXON]	100
AOEL ‡	0.02 mg/kg bw/day	Dog, 1-year study [DuPont, OXON]	100 + enteral absorption of 75 %
ARfD ‡	0.08 mg/kg bw/day	Rabbit, teratogenicity study [DuPont]	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation "Cymoxanil 50 % WP", [OXON]

75 % (default value)

Formulation "TANOS", [DuPont]

Concentrate: 0.05 %; Spray dilutions: 2.2 % based on *in vivo* rat and comparative *in vitro* (human/rat skin)

Exposure scenarios (Annex IIIA, point 7.2)

Operator

"Cymoxanil 50 % WP", [OXON]:
(lettuce: 0.24 kg a.i./ha; potatoes: 0.12 kg a.i./ha)

BBA model:

tractor mounted equipment, without PPE:
2091.8 % of AOEL (lettuce), 1045.9 % of AOEL (potatoes)

tractor mounted equipment, with PPE (gloves and coverall):
76.8 % of AOEL (lettuce), 38.4 % of AOEL (potatoes)

POEM model:

tractor mounted equipment, without PPE:
8979.9 % of AOEL (lettuce), 5426.6 % of AOEL (potatoes)

tractor mounted equipment, with PPE (gloves):
273.2 % of AOEL (lettuce), 283.5 % of AOEL (potatoes)

"TANOS", [DuPont]:
(potatoes: 0.175 kg a.i./ha).

BBA model:

tractor mounted equipment, without PPE:
13.7 % of AOEL (potatoes)

POEM model:

tractor mounted equipment, without PPE:
56.5 % of AOEL (potatoes)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Impact on Human and Animal Health

Workers

Not relevant since re-entry is not considered necessary shortly after spraying

Bystanders

No risk identified

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

Substance classified (name)

RMS proposal

Xn "harmful"

Xi "irritant"

R22 "Harmful if swallowed"

R43 "May cause skin sensitisation by skin contact"

R48/22 "Harmful: danger of serious damage to health by prolonged exposure if swallowed"

R63 "Possible risk of harm to the unborn child"

Residues

Chapter: Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	leaf vegetables (lettuce, lactuca sativa), root and tuber vegetables (potato); spray application for both crops
Rotational crops	leaf vegetables (lettuce, lactuca sativa), sugar plants (sugar beet), cereals (spring wheat). A "non residue" situation in rotational crops is established, therefore no further investigations were done on these crops.
Metabolism in rotational crops similar to metabolism in primary crops?	yes
Processed commodities	not applicable ("non residue" situation in lettuce or potato; human TMDI < 10% of ADI, no processing studies are regarded necessary)
Residue pattern in processed commodities similar to residue pattern in raw commodities?	not applicable
Plant residue definition for monitoring	cymoxanil (parent compound only)
Plant residue definition for risk assessment	cymoxanil (parent compound only)
Conversion factor (monitoring to risk assessment)	---

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	lactating goat
Time needed to reach a plateau concentration in milk and eggs	goat was daily oral dosed with 15 mg ¹⁴ C-cymoxanil over 3 consecutive days; after 24 hours a plateau concentration (0.27 - 0.33 mg eq/L) in the milk could be assessed
Animal residue definition for monitoring	not regarded necessary ("non residue" situation in potato tubers and in goat tissues); cymoxanil provisionally
Animal residue definition for risk assessment	not regarded necessary ("non residue" situation in potato tubers and in goat tissues); cymoxanil provisionally
Conversion factor (monitoring to risk assessment)	---
Metabolism in rat and ruminant similar (yes/no)	yes

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Residues

Fat soluble residue: (yes/no)

no (log $P_{o/w}$ of cymoxanil: < 1.0 at pH 5 or 7, 20 °C).
Additionally, no evidence of fat soluble residues with regard to animal metabolism (i.e. fat tissue of goat) is identifiable.

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

The application onto bar soil is equivalent to 1.212 kg labelled as/ha (1.3 N - intended lettuce use by Oxon; 0.9 to 2.0 N - intended potato uses by DuPont or Oxon); the rotational crop interval (RCI) was 30 (120) days, the detected TRR values of commodities are given below:

lettuce head (mature)	<0.01 (<0.01) mg eq/kg
sugar beet foliage	0.02 (<0.01) mg eq/kg
sugar beet roots	0.01 (<0.01) mg eq/kg
spring wheat forage	0.07 (0.01) mg eq/kg
spring wheat straw	0.14 (0.12) mg eq/kg
spring wheat grain	0.04 (0.05) mg eq/kg

Note: No cymoxanil or structurally related metabolites were identified in any analysed lettuce, sugar beet or spring wheat sample.

No evidence of relevant residues in succeeding crops is identifiable.

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Storage conditions: about -20 °C, darkness.

Cymoxanil residues in homogenised lettuce/whole lettuce were stable for 30 days/12 months at least.

Cymoxanil residues in homogenised potato tuber were stable for 12.5 months at least.

Note: A storage period for whole potato was not tested.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Residues

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)

Potential for accumulation (yes/no):

Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)

Muscle

Liver

Kidney

Fat

Milk

Eggs

The trigger value of ≥ 0.1 mg residue/kg diet (dry weight) is reached for beef and pig formally. Nevertheless, feeding studies are regarded as not necessary, because a "non residue" situation (< 0.05 mg cymoxanil/kg) on potato (relevant feedingstuff) is established. Additionally, according to the goat metabolism study no cymoxanil (< 0.05 mg/kg) or structurally related metabolites were detected in any got tissue (e.g. milk, liver, kidney, muscles or fat).		
Ruminant:	Poultry:	Pig:
Conditions of requirement of feeding studies		
0.1 mg/kg dry mass	< 0.1 mg/kg dry mass	0.1 mg/kg dry mass
no	no	no
no	no	no
Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant)		
Residue levels in matrices : Mean (max) mg/kg		
not applicable	not applicable	not applicable
not applicable	not applicable	not applicable
not applicable	not applicable	not applicable
not applicable	not applicable	not applicable
not applicable		
	not applicable	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Residues

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use (b)	HR (b), (c)	STMR (b), (d)
Lettuce (<i>lactuca sativa</i>)	Southern Europe	6x <0.05 mg cymoxanil/kg	residue trials submitted by Oxon only	0.05* mg/kg	0.05* mg/kg	0.05* mg/kg
Potato	Northern Europe	6x <0.05 mg cymoxanil/kg 4x <0.05 mg cymoxanil/kg	residue trials submitted by DuPont residue trials submitted by Oxon	0.05* mg/kg	0.05* mg/kg	0.05* mg/kg
Potato	Southern Europe	6x <0.05 mg cymoxanil/kg 15x <0.05 mg cymoxanil/kg	residue trials submitted by DuPont residue trials submitted by Oxon	0.05* mg/kg	0.05* mg/kg	0.05* mg/kg

(a) Numbers of trials in which particular residue levels were reported e.g. 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17

(b) Expressed as mg cymoxanil/kg. Asterix on figure indicates LOQ (= 0.05 mg/kg) of cymoxanil in/on lettuce or potato matrix.

(c) Highest residue

(d) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Residues

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI

TMDI (% ADI) according to WHO European diet, adult

TMDI (% ADI) according to German diet model, VELS model, child

TMDI (% ADI) according to UK (PSDs) diet model, 10 consumer groups

0.03 mg/kg bw/day		
adult 60.0 kg bw	0.013465 mg/person/day	0.7 % of ADI
child 16.15 kg bw	0.002140 mg/person/day	0.4 % of ADI
adult 76.0 kg bw	0.00019 mg/person/day	0.6 % of ADI
infant 8.7 kg bw	0.00058 mg/person/day	1.9 % of ADI
toddler 14.5 kg bw	0.00050 mg/person/day	1.6 % of ADI
4-6 year old child 20.5 kg bw	0.00044 mg/person/day	1.5 % of ADI
7-10 year old child 30.9 kg bw	0.00039 mg/person/day	1.3 % of ADI
11-14 year old child 48.0 kg bw	0.00029 mg/person/day	0.9 % of ADI
15-18 year old child 63.8 kg bw	0.00025 mg/person/day	0.8 % of ADI
vegetarian 66.7 kg bw	0.00022 mg/person/day	0.7 % of ADI
elderly - own home 70.8 kg bw	0.00019 mg/person/day	0.6 % of ADI
elderly - residential 61.6 kg bw	0.00017 mg/person/day	0.5 % of ADI
0.08 mg/kg bw/day		
child 16.15 kg bw	lettuce: 0.0008071 potato: 0.0023492 mg/kg bw/day	1.0 % of ARfD 2.9 % of ARfD
adult 76.0 kg bw	lettuce: 0.00049 potato: 0.00120 mg/kg bw/day	0.6 % of ARfD 1.5 % of ARfD
infant 8.7 kg bw	lettuce: 0.00063 potato: 0.00769 mg/kg bw/day	0.8 % of ARfD 9.6 % of ARfD
toddler 14.5 kg bw	lettuce: 0.00060 potato: 0.00532 mg/kg bw/day	0.8 % of ARfD 6.6 % of ARfD
4-6 year old child 20.5 kg bw	lettuce: 0.00089 potato: 0.00400 mg/kg bw/day	1.1 % of ARfD 5.0 % of ARfD
7-10 year old child 30.9 kg bw	lettuce: 0.00067 potato: 0.00275 mg/kg bw/day	0.8 % of ARfD 3.4 % of ARfD

ARfD

NESTI (% ARfD) according to large portions of German diet model, VELS model, child

NESTI (% ARfD) according to large portions of UK (PSDs) diet model, 10 consumer groups

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Residues

	11-14 year old child 48.0 kg bw lettuce: potato:	0.00042 0.00195 mg/kg bw/day	0.5 % of ARfD 2.4 % of ARfD
	15-18 year old child 63.8 kg bw lettuce: potato:	0.00040 0.00145 mg/kg bw/day	0.5 % of ARfD 1.8 % of ARfD
	vegetarian 66.7 kg bw lettuce: potato:	0.00055 0.00149 mg/kg bw/day	0.7 % of ARfD 1.9 % of ARfD
	elderly - own home 70.8 kg bw lettuce: potato:	0.00035 0.00119 mg/kg bw/day	0.4 % of ARfD 1.5 % of ARfD
	elderly - residential 61.6 kg bw lettuce: potato:	0.00020 0.00130 mg/kg bw/day	0.2 % of ARfD 1.6 % of ARfD
Factors included in NESTI ---			

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
---	---	---	---	---

No processing studies are required, since human TMDI accounts for less than 10 % of ADI.

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Proposed MRLs

.....

lettuce (lactuca sativa): 0.05* mg cymoxanil/kg
potatoes: 0.05* mg cymoxanil/kg

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Chapter: Fate and Behaviour in the Environment**Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)**

Mineralization after 100 days ‡

45.7, 28.7, 53.0, 28.6, 56.7 and 60.4 % AR
after 1, 3, 10, 15, 90 and 92 days, respectively

(Sterile conditions: Mineralization negligible)

Non-extractable residues after 100 days ‡

30.3, 43.5, 35.6, 47.0, 38.7 and 22.1 % AR
after 1, 3, 10, 15, 90 and 92 days, respectively

(Sterile conditions: 48.7 % of AR by 15 DAT)

Metabolites requiring further consideration ‡
- name and/or code, % of applied (range and maximum)**Soil risk assessment:**

IN-U3204: 4.0 – 24.7 % AR (n = 5)

IN-W3595: 7.4 – 10.1 % AR (n = 2)

Groundwater risk assessment:

IN-U3204: 4.0 – 24.7 % AR (n = 5)

IN-W3595: 7.4 – 10.1 % AR (n = 2)

IN-KQ960: 0.6 – 6.3 % AR (n = 2)

IN-JX915: 1.3 – 7.6 % of AR (n = 3)

Route of degradation in soil – Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days

No data available, not considered relevant

Non-extractable residues after 100 days

No data available, not considered relevant

Metabolites that may require further consideration
for risk assessment – name and/or code, % of
applied (range and maximum)

No data available, not considered relevant

Soil photolysis ‡

Metabolites that may require further consideration
for risk assessment – name and/or code, % of
applied (range and maximum)**Soil risk assessment:**

IN-JX915: 10.9 % AR (n = 1)

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

Cymoxanil	Aerobic conditions						
Soil type	pH	t. °C / % MWHC	DT ₅₀ /DT ₉₀ (d)	SFO-DT ₅₀ ^a (d) 20 °C pF2/10kPa	r ²	χ ² error (%)	Method of calculation ^b
Sandy loam, UK	6.0	20 °C / 40 % MWHC	0.1 / 0.5	0.1	1.00	1.6	FOMC
Sandy loam, US	6.4	25 °C / 75 % 1/3 bar	1.2 / 18.8	5.8	0.86	17.6	FOMC

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

Sandy clay loam, J	6.8	25 °C / 50 % MWHC	0.2 / 0.8	0.4	0.98	5.9	FOMC
Sandy loam, DE	6.5	20 °C / 50 % MWHC	2.3 / 13.1	3.1	0.99	6.9	FOMC
Sandy loam, F	7.8	20 °C / 50 % MWHC	0.7 / 2.3	0.6	0.95	16.7	FOMC
Sandy clay loam, UK	5.7	20 °C / 50 % MWHC	2.5 / 33.3	7.3	0.98	6.5	FOMC
Silt loam, UK	4.3	20 °C / 40 % MWHC	4.3 / 25.2	5.1	0.97	4.4	FOMC
Silt loam, UK	6.4	20 °C / 40 % MWHC	0.9 / 3.1	0.5	1.00	2.6	SFO
Clay loam, UK	7.5	20 °C / 40 % MWHC	0.2 / 0.8	0.1	0.98	5.7	SFO
Geometric mean			0.8 / 4.3	1.0	-	-	-

^a SFO-DT₅₀ re-calculated from FOMC-DT₅₀ by division with 3.32

^b Best fit

IN-U3204		Aerobic conditions						
Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. (from parent)	DT ₅₀ (d) 20 °C pF2/10kPa	r ²	χ ² error (%)	Method of calculation
Sandy clay loam, J	6.8	25 °C / 50 % MWHC	0.6 / 1.9	0.48	0.7	0.93	11.0	P _{SFO} →M _{SFO}
Silt loam, UK	6.4	20 °C / 40 % MWHC	0.4 / 1.3	0.24	0.2	0.88	26.2	P _{SFO} →M _{SFO}
Clay loam, UK	7.5	20 °C / 40 % MWHC	0.2 / 0.6	0.36	0.1	0.95	12.2	P _{SFO} →M _{SFO}
Geometric mean			0.4 / 1.1	-	0.2	-	-	-
Arithmetic mean			- / -	0.36	-	-	-	-

IN-W3595		Aerobic conditions						
Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. (from parent)	DT ₅₀ (d) 20 °C pF2/10kPa	r ²	χ ² error (%)	Method of calculation
Sandy clay loam, J	6.8	25 °C / 50 % MWHC	1.7 / 5.5	0.15	2.1	0.85	14.5	P _{SFO} →M _{SFO}
Sandy loam, F	7.8	20 °C / 50 % MWHC	2.8 / 9.4	0.07	2.2	0.60	69.3	P _{SFO} →M _{SFO}
Worst case			2.8 / 9.4	-	2.2	-	-	-
Arithmetic mean			- / -	0.11	-	-	-	-

IN-KQ960		Aerobic conditions						
Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. (from IN- U3204)	DT ₅₀ (d) 20 °C pF2/10kPa	r ²	χ ² error (%)	Method of calculation
Sandy clay loam, J	6.8	25 °C / 50 % MWHC	7.6 / 25.2	0.16	9.3	0.84	19.2	P _{SFO} →M1 _{SFO} →M2 _{SFO} ^a

^a M1 = IN-U3204, M2 = IN-KQ960

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Cymoxanil - Appendix 3: list of endpoints
Fate and Behaviour in the Environment

June 2007

IN-JX915		Aerobic conditions						
Soil type	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. (from parent)	DT ₅₀ (d) 20 °C pF2/10kPa	r ²	χ ² error (%)	Method of calculation
Sandy clay loam, J	6.8	25 °C / 50 % MWHC	0.6 / 1.9	0.10	0.7	0.73	27	P _{SFO} → M _{SFO}

Field studies ‡

Cymoxanil	No data available, not triggered
------------------	----------------------------------

pH dependence ‡
(yes / no) (if yes type of dependence)

Cymoxanil: Soil DT₅₀ significantly ($p < 0.05$) depending
on soil pH (lower under acidic conditions)

Soil accumulation and plateau concentration ‡

Not expected to occur.

Laboratory studies ‡

Cymoxanil		Soil photolysis (net, converted to environmental midsummer days, approx. 40 °N)					
Soil type	pH	t. °C / % MWHC	Conditions	DT ₅₀ / DT ₉₀ (d)	DT ₅₀ (d) 20 °C pF2/10kPa	r ²	Method of calculation
Sandy loam, USA	6.4	25 °C / air dried	Irradiated	14.1 / 46.7	-	0.90	SFO
		25 °C / air dried	Dark	38.5 / 128	-	0.87	SFO
		25 °C / air dried	Net, lab	22.1 / 73.6	-	-	-
		-	Net, environment	64.5 / 214	-	-	-

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Cymoxanil ‡								
Soil Type	OC %	Soil pH (H ₂ O)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n	
Silt loam, DE	0.59	6.9	-	-	0.090	15.1	0.88	
Sandy loam, US	1.0	5.7	-	-	0.910	87.1	0.87	
Loamy sand, UK	1.6	8.1	-	-	0.462	28.9	0.81	
Clay, UK	2.0	7.2	-	-	0.856	43.4	0.87	
Arithmetic mean			-	-	-	43.6	0.86	
pH dependence, Yes or No			No					

IN-W3595 ‡								
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

Loamy sand, US	2.3	4.6	0.63	27	-	-	-
Sandy loam, US	0.99	7.6	0.026	2.6	-	-	-
Silt loam, US	3.2	7.8	0.074	2.3	-	-	-
Sandy loam, US	0.46	6.4	0.020	4.3	-	-	-
Arithmetic mean			-	9.1	-	-	0.9^a
K _{OC-acid}		-		33.3			
K _{OC-base}		-		2.3			
pK _a		5.2		-			
pH dependence (yes or no)			Yes				

^a FOCUS default value

IN-R3273 ‡							
Soil Type	OC %	Soil pH	K _d (mL/g)	K _{oc} (mL/g)	K _f (mL/g)	K _{foc} (mL/g)	1/n
Loamy sand, US	2.3	4.6	0.59	25.7	-	-	-
Sandy loam, US	0.99	7.6	0.49	49.5	-	-	-
Silt loam, US	3.2	7.8	1.5	46.9	-	-	-
Sandy loam, US	0.46	6.4	0.21	45.7	-	-	-
Arithmetic mean			-	41.9	-	-	0.9^a
pH dependence (yes or no)			Yes				

^a FOCUS default value

IN-JX915 ‡							
Soil Type	OC %	Soil pH	K _d (mL/g)	K _{oc} (mL/g)	K _f (mL/g)	K _{foc} (mL/g)	1/n
Loamy sand, US	2.3	4.6	0.13	5.4	-	-	-
Sandy loam, US	0.99	7.6	0.34	34.3	-	-	-
Silt loam, US	3.2	7.8	0.66	20.6	-	-	-
Sandy loam, US	0.46	6.4	0.021	4.4	-	-	-
Arithmetic mean			-	16.3	-	-	0.9^a
pH dependence (yes or no)			No				

^a FOCUS default value

IN-U3204 ‡							
Soil Type	OC %	Soil pH (CaCl ₂)	K _d (mL/g)	K _{oc} (mL/g)	K _f (mL/g)	K _{foc} (mL/g)	1/n
HPLC method	-	-	-	27.9	-	-	0.9^a
pH dependence (yes or no)			?				

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

^a FOCUS default value

IN-KQ960 ‡							
Soil Type	OC %	Soil pH (CaCl ₂)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
HPLC method	-	-	-	21.6	-	-	0.9^a
pH dependence (yes or no)			?				

^a FOCUS default value

IN-T4226 ‡							
Soil Type	OC %	Soil pH (CaCl ₂)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
HPLC method	-	-	-	17.7	-	-	0.9^a
pH dependence (yes or no)			?				

^a FOCUS default value

IN-KP533 ‡							
Soil Type	OC %	Soil pH (CaCl ₂)	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
HPLC method	-	-	-	12.9	-	-	0.9^a
pH dependence (yes or no)			?				

^a FOCUS default value

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡

Not studied - no data requested

Aged residues leaching ‡

Not studied - no data requested

Lysimeter/ field leaching studies ‡

One lysimeter study conducted in Lower Saxony, Germany

Two soil monoliths (1 m², 1.2 m soil depth):
0 – 30 cm: sand 75.2 %, silt 21.2 %, clay 3.6 %, C_{org} 1.29 %, pH (CaCl₂) 5.4

Application (as Curzate 50 WP) onto potatoes:

Lys1: 3 x 320 g ai/ha, June 30, July 6, July 14, 1993
3 x 320 g ai/ha, June 30, July 7, July 14, 1994

Lys2: 3 x 320 g ai/ha, June 30, July 6, July 14, 1993

Crop cover: potatoes, winter rye (1st year),
potatoes, winter barley (2nd year)

Precipitation: 1171 mm (1st year), 1176 mm (2nd year),

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

	850 mm (3rd year) Mean annual temperature: 11.9 °C (1st year), 9.9 °C (2nd year), 8.5 °C (3rd year) Leachate (mean of both lysimeter): 894 mm (1st year), 738 mm (2nd year), 497 mm (3rd year) Annual mean concentrations in leachates: Total radioactivity in leachates: Lys1: 0.27, 0.56 and 0.19 µg ai equiv./L (1st, 2nd, 3rd year) Lys2: 0.26, 0.11 µg ai equiv./L (1st, 2nd year) Unidentified radioactivity in leachates (owing to loss during work-up, unidentified radioactivity of RP-C8 HPLC, unidentified polars): Lys1: 0.23, 0.46 and 0.16 µg ai equiv./L (1st, 2nd, 3rd year) Lys2: 0.21, 0.10 µg ai equiv./L (1st, 2nd year) Maximum annual mean concentration in leachates: Cymoxanil: < LOQ IN-U3204: < 0.01 µg L⁻¹ (Lys2, 2nd year) IN-T4226: 0.02 µg L⁻¹ (Lys1, 2nd year) IN-R3273: 0.01 µg L⁻¹ (Lys1, 2nd year) IN-R3274: 0.02 µg L⁻¹ (Lys1, 2nd year) Oxamic acid (IN-18474): < LOQ Oxalic acid: 0.03 µg L⁻¹ (Lys1, 2nd year) LOQ = 0.01 µg L⁻¹
--	--

PEC (soil) (Annex IIIA, point 9.1.3)

Cymoxanil
Method of calculation

DT₅₀ (d): 7.3
Kinetics: SFO
(SFO-DT₅₀ re-calculated from lab FOMC-DT₉₀ by division with 3.32, normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2)
Representative worst-case from lab studies,
representative worst-case for acidic soils

IN-U3204
Method of calculation

DT₅₀ (d): 0.7
Kinetics: SFO
(normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2)
Representative worst case from lab studies
Max. occurrence: 24.7 % (lab)
Molar ratio: 198.2/198.2 = 1.00

IN-W3595
Method of calculation

DT₅₀ (d): 2.2
Kinetics: SFO
(normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2)
Representative worst case from lab studies
Max. occurrence: 10.1 % (lab)
Molar ratio: 128.1/198.2 = 0.646

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Cymoxanil - Appendix 3: list of endpoints
Fate and Behaviour in the Environment

June 2007

IN-JX915 Method of calculation Application data	DT ₅₀ (d): 0.7 Kinetics: SFO <i>(normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2)</i> Representative worst case from lab studies Max. occurrence: 10.9 % (soil photolysis) Molar ratio: 198.2/198.2 = 1.00																																									
	<table> <tr> <td>Notifier:</td><td>DuPont</td></tr> <tr> <td>Crop:</td><td>Potatoes</td></tr> <tr> <td>Application rate(s):</td><td>175 g ai/ha</td></tr> <tr> <td>Number of applications:</td><td>8</td></tr> <tr> <td>Interval (d):</td><td>7</td></tr> <tr> <td>% plant interception:</td><td>50 (average canopy)</td></tr> <tr> <td>Notifier:</td><td>Oxon</td></tr> <tr> <td>Crop:</td><td>Potatoes</td></tr> <tr> <td>Application rate(s):</td><td>120 g ai/ha</td></tr> <tr> <td>Number of applications:</td><td>4 (North EU) 5 (South EU)</td></tr> <tr> <td colspan="2"><i>(calculated with 5 applications, worst-case)</i></td></tr> <tr> <td>Interval (d):</td><td>7</td></tr> <tr> <td>% plant interception:</td><td>50 (average canopy)</td></tr> <tr> <td>Notifier:</td><td>Oxon</td></tr> <tr> <td>Crop:</td><td>Lettuce</td></tr> <tr> <td>Application rate(s):</td><td>240 g ai/ha</td></tr> <tr> <td>Number of applications:</td><td>4</td></tr> <tr> <td>Interval (d):</td><td>7</td></tr> <tr> <td>% plant interception:</td><td>70 (full canopy)</td></tr> <tr> <td>Depth of soil layer:</td><td>5 cm</td></tr> <tr> <td>Soil bulk density:</td><td>1.5 g/cm³</td></tr> </table>	Notifier:	DuPont	Crop:	Potatoes	Application rate(s):	175 g ai/ha	Number of applications:	8	Interval (d):	7	% plant interception:	50 (average canopy)	Notifier:	Oxon	Crop:	Potatoes	Application rate(s):	120 g ai/ha	Number of applications:	4 (North EU) 5 (South EU)	<i>(calculated with 5 applications, worst-case)</i>		Interval (d):	7	% plant interception:	50 (average canopy)	Notifier:	Oxon	Crop:	Lettuce	Application rate(s):	240 g ai/ha	Number of applications:	4	Interval (d):	7	% plant interception:	70 (full canopy)	Depth of soil layer:	5 cm	Soil bulk density:
Notifier:	DuPont																																									
Crop:	Potatoes																																									
Application rate(s):	175 g ai/ha																																									
Number of applications:	8																																									
Interval (d):	7																																									
% plant interception:	50 (average canopy)																																									
Notifier:	Oxon																																									
Crop:	Potatoes																																									
Application rate(s):	120 g ai/ha																																									
Number of applications:	4 (North EU) 5 (South EU)																																									
<i>(calculated with 5 applications, worst-case)</i>																																										
Interval (d):	7																																									
% plant interception:	50 (average canopy)																																									
Notifier:	Oxon																																									
Crop:	Lettuce																																									
Application rate(s):	240 g ai/ha																																									
Number of applications:	4																																									
Interval (d):	7																																									
% plant interception:	70 (full canopy)																																									
Depth of soil layer:	5 cm																																									
Soil bulk density:	1.5 g/cm ³																																									

PEC_(s)
(mg/kg)

Potatoes (DuPont)				
<u>Cymoxanil</u>				
	Single application	Single application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Initial	0.117		0.239	
Short term 24 h	0.106	0.111	0.217	0.228
2 d	0.096	0.106	0.198	0.218
4 d	0.080	0.097	0.164	0.200
Long term 7 d	0.060	0.086	0.123	0.176
14 d	0.031	0.065	0.063	0.134
21 d	0.016	0.051	0.033	0.105
28 d	0.008	0.042	0.017	0.085

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

PEC _(s) (mg/kg)	Potatoes (DuPont)			
	<u>Cymoxanil</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
50 d	0.001	0.025	0.002	0.051
100 d	0.000	0.013	0.000	0.026
Plateau concentration	Not expected to occur		Not expected to occur	

PEC _(s) (mg/kg)	Potatoes (Oxon)			
	<u>Cymoxanil</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.080		0.159	
Short term 24 h	0.073	0.076	0.144	0.152
2 d	0.066	0.073	0.131	0.145
4 d	0.055	0.067	0.109	0.133
Long term 7 d	0.041	0.059	0.082	0.117
14 d	0.021	0.045	0.042	0.089
21 d	0.011	0.035	0.022	0.070
28 d	0.006	0.029	0.011	0.057
50 d	0.001	0.017	0.001	0.034
100 d	0.000	0.009	0.000	0.017
Plateau concentration	Not expected to occur		Not expected to occur	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

PEC _(s) (mg/kg)	Lettuce (Oxon)			
	<u>Cymoxanil</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.096		0.184	
Short term 24 h	0.087	0.092	0.167	0.176
2 d	0.079	0.088	0.152	0.168
4 d	0.066	0.080	0.126	0.153
Long term 7 d	0.049	0.070	0.095	0.135
14 d	0.025	0.054	0.049	0.103
21 d	0.013	0.042	0.025	0.081
28 d	0.007	0.034	0.013	0.066
50 d	0.001	0.021	0.002	0.039
100 d	0.000	0.010	0.000	0.020
Plateau concentration	Not expected to occur		Not expected to occur	

PEC _(s) (mg/kg)	Potatoes (DuPont)			
	<u>IN-U3204</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.029		0.029	
Short term 24 h	0.011	0.020	0.011	0.020
2 d	0.004	0.014	0.004	0.015
4 d	0.001	0.009	0.001	0.009
Long term 7 d	0.000	0.006	0.000	0.006
14 d	0.000	0.003	0.000	0.003
21 d	0.000	0.002	0.000	0.002
28 d	0.000	0.002	0.000	0.002
50 d	0.000	0.001	0.000	0.001
100 d	0.000	0.000	0.000	0.000
Plateau concentration	Not expected to occur		Not expected to occur	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

PEC _(s) (mg/kg)	Potatoes (Oxon)			
	<u>IN-U3204</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.020		0.020	
Short term 24 h	0.007	0.014	0.007	0.014
2 d	0.003	0.010	0.003	0.010
4 d	0.000	0.006	0.000	0.006
Long term 7 d	0.000	0.004	0.000	0.004
14 d	0.000	0.002	0.000	0.002
21 d	0.000	0.001	0.000	0.001
28 d	0.000	0.001	0.000	0.001
50 d	0.000	0.001	0.000	0.001
100 d	0.000	0.000	0.000	0.000
Plateau concentration	Not expected to occur		Not expected to occur	

PEC _(s) (mg/kg)	Lettuce (Oxon)			
	<u>IN-U3204</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.024		0.024	
Short term 24 h	0.009	0.016	0.009	0.016
2 d	0.003	0.012	0.003	0.012
4 d	0.000	0.007	0.000	0.008
Long term 7 d	0.000	0.005	0.000	0.005
14 d	0.000	0.003	0.000	0.003
21 d	0.000	0.002	0.000	0.002
28 d	0.000	0.001	0.000	0.001
50 d	0.000	0.001	0.000	0.001
100 d	0.000	0.000	0.000	0.000

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

PEC_(s) (mg/kg)	Lettuce (Oxon)			
	<u>IN-U3204</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Plateau concentration	Not expected to occur		Not expected to occur	

PEC_(s) (mg/kg)	Potatoes (DuPont)			
	<u>IN-W3595</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.008		0.009	
Short term 24 h	0.006	0.007	0.006	0.007
2 d	0.004	0.006	0.005	0.006
4 d	0.002	0.004	0.002	0.005
Long term 7 d	0.001	0.003	0.001	0.004
14 d	0.000	0.002	0.000	0.002
21 d	0.000	0.001	0.000	0.001
28 d	0.000	0.001	0.000	0.001
50 d	0.000	0.001	0.000	0.001
100 d	0.000	0.000	0.000	0.000
Plateau concentration	Not expected to occur		Not expected to occur	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

PEC _(s) (mg/kg)	Potatoes (Oxon)			
	<u>IN-W3595</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.005		0.006	
Short term 24 h	0.004	0.004	0.004	0.005
2 d	0.003	0.004	0.003	0.004
4 d	0.001	0.003	0.002	0.003
Long term 7 d	0.001	0.002	0.001	0.002
14 d	0.000	0.001	0.000	0.001
21 d	0.000	0.001	0.000	0.001
28 d	0.000	0.001	0.000	0.001
50 d	0.000	0.000	0.000	0.000
100 d	0.000	0.000	0.000	0.000
Plateau concentration	Not expected to occur		Not expected to occur	

PEC _(s) (mg/kg)	Lettuce (Oxon)			
	<u>IN-W3595</u>			
	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.006		0.007	
Short term 24 h	0.005	0.005	0.005	0.006
2 d	0.003	0.005	0.004	0.005
4 d	0.002	0.004	0.002	0.004
Long term 7 d	0.001	0.003	0.001	0.003
14 d	0.000	0.002	0.000	0.002
21 d	0.000	0.001	0.000	0.001
28 d	0.000	0.001	0.000	0.001
50 d	0.000	0.000	0.000	0.001
100 d	0.000	0.000	0.000	0.000
Plateau concentration	Not expected to occur		Not expected to occur	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

PEC_(s) (mg/kg)		Potatoes (DuPont)			
		IN-JX915			
		Single application	Single application	Multiple application	Multiple application
		Actual	Time weighted average	Actual	Time weighted average
Initial		0.013		0.013	
Short term	24 h	0.005	0.009	0.005	0.009
	2 d	0.002	0.006	0.002	0.006
	4 d	0.000	0.004	0.000	0.004
Long term	7 d	0.000	0.003	0.000	0.003
	14 d	0.000	0.001	0.000	0.001
	21 d	0.000	0.001	0.000	0.001
	28 d	0.000	0.001	0.000	0.001
	50 d	0.000	0.000	0.000	0.000
	100 d	0.000	0.000	0.000	0.000
Plateau concentration		Not expected to occur		Not expected to occur	

PEC_(s) (mg/kg)		Potatoes (Oxon)			
		IN-JX915			
		Single application	Single application	Multiple application	Multiple application
		Actual	Time weighted average	Actual	Time weighted average
Initial		0.009		0.009	
Short term	24 h	0.003	0.006	0.003	0.006
	2 d	0.001	0.004	0.001	0.004
	4 d	0.000	0.003	0.000	0.003
Long term	7 d	0.000	0.002	0.000	0.002
	14 d	0.000	0.001	0.000	0.001
	21 d	0.000	0.001	0.000	0.001
	28 d	0.000	0.000	0.000	0.000
	50 d	0.000	0.000	0.000	0.000
	100 d	0.000	0.000	0.000	0.000

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

PEC _(s) (mg/kg)	Potatoes (Oxon)			
	<u>IN-JX915</u>			
	Single application	Single application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Plateau concentration	Not expected to occur		Not expected to occur	

PEC _(s) (mg/kg)	Lettuce (Oxon)			
	<u>IN-JX915</u>			
	Single application	Single application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Initial	0.010		0.010	
Short term 24 h	0.004	0.007	0.004	0.007
2 d	0.001	0.005	0.001	0.005
4 d	0.000	0.003	0.000	0.003
Long term 7 d	0.000	0.002	0.000	0.002
14 d	0.000	0.001	0.000	0.001
21 d	0.000	0.001	0.000	0.001
28 d	0.000	0.001	0.000	0.001
50 d	0.000	0.000	0.000	0.000
100 d	0.000	0.000	0.000	0.000
Plateau concentration	Not expected to occur		Not expected to occur	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Route and rate of degradation in water (Annex IIA. point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡

Cymoxanil:

DT₅₀: pH 4: Stable (20 °C)
pH 5: 144 days (25 °C)
pH 7: 1.1 days (25 °C), 2.1 days (20 °C)
pH 9: 0.02 days (25 °C), 0.04 days (20 °C)

Metabolites > 10 %:

IN-U3204 (pH 7 max. 52.7 % AR, pH 9 max. 60.8 % AR)
DT₅₀ (pH 7) = 2.6 days (25 °C), 2.3 days (20 °C)
DT₅₀ (pH 9) = 0.4 days (25 °C), 0.5 days (20 °C)
IN-JX915 (pH 7 max. 7.2 % AR, pH 9 max. 11.0 % AR)
DT₅₀ (pH 7) = 1.1 days (25 °C), 0.5 days (20 °C)
DT₅₀ (pH 9) = 1.7 days (25 °C), 1.7 days (20 °C)
IN-W3595 (pH 7 max. 22.6 % AR, pH 9 max. 41.5 % AR)
Stable at pH 7 and 9
IN-KP533 (pH 7 max. 57.4 % AR, pH 9 max. 34.4 % AR)
Stable at pH 7 and 9
IN-R3273 (pH 7 max. 10.2 % AR, pH 9 max. 7.2 % AR)
Stable at pH 7 and 9
IN-KQ960 (pH 7 max. 9.0 % AR, pH 9 max. 14.1 % AR)
Stable at pH 7 and 9

Photolytic degradation of active substance and metabolites above 10 % ‡

Cymoxanil:

Sterilized buffer solution, pH 5.0, 25 °C:

Net photolysis DT₅₀ = 1.7 / 3.0 days (n = 2)

Converted to natural summer light (approx. 40 °N):

Net photolysis DT₅₀ = 4.3 / 12.1 days (n = 2)

Non-sterile pond water, pH 7.0:

Net photolysis DT₅₀ = 0.42 days

Converted to natural summer light (38 °N):

Net photolysis DT₅₀ = 1.1 days

Metabolites > 10 % AR:

IN-JX915 (pH 5 max. 52.6 % AR)
DT₅₀ (pH 5, hydrolysis/photolysis):
6.7 / 6.5 days (n = 2)
IN-R3273 (pH 5 max. 35.4 % of AR)
DT₅₀ (pH 5, hydrolysis/photolysis):
32.7 days / stable (n = 2)

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

WARNING: This document forms part of an EC evaluation data package and should not be used for any other purpose without the written consent of the European Commission.

Fate and Behaviour in the Environment

Quantum yield of direct photo-transformation in water at $\Sigma > 290$ nm	Cymoxanil: $\Phi = 0.0052 / 0.00058$ (n = 2) GC-SOLAR: DT_{50} (natural summer light, pH 5, 40 °N): 5.2 / 17.3 days (n = 2) Metabolites: GC-SOLAR: IN-JX915: $\Phi = 0.000504$ DT_{50} (natural summer light, pH 5, 40 °N): 21.2 days IN-R3273: $\Phi = 0.0000241$ DT_{50} (natural summer light, pH 5, 40 °N): 4.7 days
Readily biodegradable ‡ (yes/no)	Not readily biodegradable (based on data)

Degradation in water / sediment

Cymoxanil	Distribution (max. in sediment 3.9 % AR after 1 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50} / DT_{90} (d) whole sys.	r^2	DT_{50} / DT_{90} (d) water	r^2	DT_{50} / DT_{90} (d) sed	r^2	Method of calculation
Sand	7.4	7.0	20	0.5 / 1.7	1.00	0.5 / 1.7	1.00	Nc	-	P_{SFO}
Sand	5.3	5.1	20	1.6 / 5.3	0.99	1.5 / 5.0	0.99	Nc	-	P_{SFO}
Silty clay loam	8.3	7.5	20	0.1 / 0.2	1.00	0.1 / 0.2	1.00	Nc	-	P_{SFO}
Silt loam	8.3	7.5	20	0.2 / 0.5	1.00	0.2 / 0.5	1.00	Nc	-	P_{SFO}
Geometric mean				0.3 / 1.0		0.3 / 1.0		Nc		

IN-U3204	Distribution (max. in water 24.7 % AR after 0.13 d, max. in sediment 0.5 % AR after 3 d)									
Water / sediment system (aerobic)	pH water phase	pH sed	t. °C	DT_{50} / DT_{90} (d) whole sys.	r^2	DT_{50} / DT_{90} (d) water	r^2	DT_{50} / DT_{90} (d) sed	r^2	Method of calculation
Sand	7.4	7.0	20	0.6 / 2.0	0.92	Nc	-	Nc	-	$P_{SFO} \rightarrow M_{SFO}$
Silty clay loam	8.3	7.5	20	0.2 / 0.5	0.98	Nc	-	Nc	-	$P_{SFO} \rightarrow M_{SFO}$
Silt loam	8.3	7.5	20	0.5 / 1.7	0.96	Nc	-	Nc	-	$P_{SFO} \rightarrow M_{SFO}$
Geometric mean				0.4 / 1.2		Nc		Nc		-

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

IN-W3595 Distribution (max. in water 26.1 % AR after 0.25 d, max. in sediment 2.3 % AR after 1 d)										
Water / sediment system (aerobic)	pH water phase	pH sed	t. °C	DT ₅₀ / DT ₉₀ (d) whole sys.	r ²	DT ₅₀ / DT ₉₀ (d) water	r ²	DT ₅₀ / DT ₉₀ (d) sed	r ²	Method of calculation
Sand	7.4	7.0	20	3.6 / 12.1	0.95	Nc	-	Nc	-	P _{SFO} →M _{SFO}
Silty clay loam	8.3	7.5	20	2.7 / 9.0	0.99	Nc	-	Nc	-	P _{SFO} →M _{SFO}
Silt loam	8.3	7.5	20	2.7 / 8.9	0.98	Nc	-	Nc	-	P _{SFO} →M _{SFO}
Geometric mean				3.0 / 9.9		Nc		Nc		-

IN-KQ960 Distribution (max. in water 13.0 % AR after 1 d, max. in sediment 5.5 % AR after 30 d)										
Water / sediment system (aerobic)	pH water phase	pH sed	t. °C	DT ₅₀ / DT ₉₀ (d) whole sys.	r ²	DT ₅₀ / DT ₉₀ (d) water	r ²	DT ₅₀ / DT ₉₀ (d) sed	r ²	Method of calculation
Sand	7.4	7.0	20	154 / 521	0.76	Nc	-	Nc	-	M _{SFO}
Sand	5.3	5.1	20	45.4 / 151	0.97	Nc	-	Nc	-	M _{SFO}
Silt loam	8.3	7.5	20	15.2 / 50.5	0.98	Nc	-	Nc	-	M _{SFO}
Geometric mean				47.4 / 158		Nc		Nc		-

IN-T4226 Distribution (max. in water 11.1 % AR after 3 d, max. in sediment 1.0 % AR after 8 d)										
Water / sediment system (aerobic)	pH water phase	pH sed	t. °C	DT ₅₀ / DT ₉₀ (d) whole sys.	r ²	DT ₅₀ / DT ₉₀ (d) water	r ²	DT ₅₀ / DT ₉₀ (d) sed	r ²	Method of calculation
Sand	7.4	7.0	20	3.9 / 12.9	0.99	Nc	-	Nc	-	M _{SFO}
Sand	5.3	5.1	20	5.4 / 17.9	0.91	Nc	-	Nc	-	M _{SFO}
Geometric mean				4.6 / 15.2		Nc		Nc		-

IN-JX915 Distribution (max. in water 7.2 % AR after 1 d, max. in sediment 1.2 % AR after 1 d)										
Water / sediment system (aerobic)	pH water phase	pH sed	t. °C	DT ₅₀ / DT ₉₀ (d) whole sys.	r ²	DT ₅₀ / DT ₉₀ (d) water	r ²	DT ₅₀ / DT ₉₀ (d) sed	r ²	Method of calculation
Sand	7.4	7.0	20	2.5 / 8.3	0.79	Nc	-	Nc	-	P _{SFO} →M _{SFO}
Sand	5.3	5.1	20	1.1 / 3.7	0.96	Nc	-	Nc	-	P _{SFO} →M _{SFO}
Silty clay loam	8.3	7.5	20	2.1 / 7.1	0.88	Nc	-	Nc	-	P _{SFO} →M _{SFO}
Silt loam	8.3	7.5	20	1.5 / 5.1	0.97	Nc	-	Nc	-	P _{SFO} →M _{SFO}
Geometric mean				1.7 / 5.8		Nc		Nc		-

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Fate and Behaviour in the Environment

IN-R3273 Distribution (max. in water 5.0 % AR after 3 d, max. in sediment 0.5 % AR after 3 d)										
Water / sediment system (aerobic)	pH water phase	pH sed	t. °C	DT ₅₀ / DT ₉₀ (d) whole sys.	r ²	DT ₅₀ / DT ₉₀ (d) water	r ²	DT ₅₀ / DT ₉₀ (d) sed	r ²	Method of calculation
Sand	7.4	7.0	20	6.0 / 19.9	0.93	Nc	-	Nc	-	M _{SFO}
Sand	5.3	5.1	20	6.7 / 22.2	0.98	Nc	-	Nc	-	M _{SFO}
Geometric mean				6.3 / 21.0		Nc		Nc		-

IN-KP533 Distribution (max. in water 20.5 % AR after 10 d, max. in sediment 6.5 % AR after 1 d) ^a										
Water / sediment system (aerobic)	pH water phase	pH sed	t. °C	DT ₅₀ / DT ₉₀ (d) whole sys.	r ²	DT ₅₀ / DT ₉₀ (d) water	r ²	DT ₅₀ / DT ₉₀ (d) sed	r ²	Method of calculation
Sand	7.4	7.0	20	2.3 / 7.5	0.96	Nc	-	Nc	-	M _{SFO}
Sand	5.3	5.1	20	3.0 / 10.0	0.97	Nc	-	Nc	-	M _{SFO}
Geometric mean				2.6 / 8.7		Nc		Nc		-

^a Worst-case assessment, individual amounts of IN-KP533 in two of four water/sediment systems not known (in two systems maximal 8.0 % of AR in the entire system)

Metabolite fraction M5 Distribution (max. in water 22.9 % AR after 1 d, max. in sediment 0.0 % AR)										
Water / sediment system (aerobic)	pH water phase	pH sed	t. °C	DT ₅₀ / DT ₉₀ (d) whole sys.	r ²	DT ₅₀ / DT ₉₀ (d) water	r ²	DT ₅₀ / DT ₉₀ (d) sed	r ²	Method of calculation
Silty clay loam	8.3	7.5	20	1.2 / 4.0	1.00	Nc	-	Nc	-	M _{SFO}
Silt loam	8.3	7.5	20	1.6 / 5.2	1.00	Nc	-	Nc	-	M _{SFO}
Geometric mean				1.4 / 4.6		Nc		Nc		-

Mineralization and non extractable residues						
Water / sediment system (aerobic)	pH water phase	pH sed	Mineralization (end of study)	Non-extractable residues in sed.	Non-extractable residues in sed. (end of the study)	
Sand	7.4	7.0	45.6 % ^a after 127 d	27.4 % after 28 d	23.1 % after 127 d	
Sand	5.3	5.1	39.6 % ^a after 70 d	35.2 % after 15 d	22.8 % after 70 d	
Silty clay loam	8.3	7.5	75.5 % after 100 d	22.5 % after 30 d	17.9 % after 100 d	
Silt loam	8.3	7.5	68.5 % after 100 d	29.7 % after 30 d	25.6 % after 100 d	

^a Not including significant formation of non trapped volatiles, likely to be methane

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

PEC (surface water) and PEC sediment (Annex IIIA. point 9.2.3)

Cymoxanil

Parameters used in FOCUSsw step 1 and 2

Version control no. of FOCUS calculator:	1.1
Molecular weight (g/mol):	198.2
Water solubility (mg/L):	783
K _{FOC} (L/kg):	43.6
DT ₅₀ soil (d):	1.0
<i>(geometric mean, lab, normalized, SFO-DT₅₀ re-calculated from FOMC-DT₉₀ / 3.32)</i>	
DT ₅₀ water/sediment system (d):	0.3
DT ₅₀ water (d):	0.3
DT ₅₀ sediment (d):	0.3

IN-U3204

Parameters used in FOCUSsw step 1 and 2

Molecular weight (g/mol):	198.2
Water solubility (mg/L):	783
Soil or water metabolite:	Soil/water
K _{OC} (L/kg):	27.9
DT ₅₀ soil (d):	0.2
<i>(geometric mean of normalized lab data, SFO)</i>	
DT ₅₀ water/sediment system (d):	0.4
DT ₅₀ water (d):	0.4
DT ₅₀ sediment (d):	0.4
Maximum occurrence observed (% molar basis with respect to the parent):	
Soil:	24.7
Water:	24.7
Sediment:	0.5
Total system:	24.7

IN-W3595

Parameters used in FOCUSsw step 1 and 2

Molecular weight (g/mol):	128.1
Water solubility (mg/L):	783
Soil or water metabolite:	Soil/water
K _{OC} (L/kg):	9.2
DT ₅₀ soil (d):	2.2
<i>(worst case of normalized lab data)</i>	
DT ₅₀ water/sediment system (d):	3.0
DT ₅₀ water (d):	3.0
DT ₅₀ sediment (d):	3.0
Maximum occurrence observed (% molar basis with respect to the parent):	
Soil:	10.1
Water:	26.1
Sediment:	2.3
Total System:	27.5

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Cymoxanil - Appendix 3: list of endpoints
Fate and Behaviour in the Environment

June 2007

IN-KQ960 Parameters used in FOCUSsw step 1 and 2	<table> <tr><td>Molecular weight (g/mol):</td><td>216.2</td></tr> <tr><td>Water solubility (mg/L):</td><td>783</td></tr> <tr><td>Soil or water metabolite:</td><td>Soil/water</td></tr> <tr><td>K_{OC} (L/kg):</td><td>21.6</td></tr> <tr><td>DT₅₀ soil (d):</td><td>9.3</td></tr> <tr><td colspan="2"><i>(worst case of normalized lab data)</i></td></tr> <tr><td>DT₅₀ water/sediment system (d):</td><td>47.4</td></tr> <tr><td>DT₅₀ water (d):</td><td>47.4</td></tr> <tr><td>DT₅₀ sediment (d):</td><td>47.4</td></tr> <tr><td colspan="2">Maximum occurrence observed (% molar basis with respect to the parent):</td></tr> <tr><td>Soil:</td><td>6.3</td></tr> <tr><td>Water:</td><td>13.0</td></tr> <tr><td>Sediment:</td><td>5.5</td></tr> <tr><td>Total System:</td><td>14.3</td></tr> </table>	Molecular weight (g/mol):	216.2	Water solubility (mg/L):	783	Soil or water metabolite:	Soil/water	K _{OC} (L/kg):	21.6	DT ₅₀ soil (d):	9.3	<i>(worst case of normalized lab data)</i>		DT ₅₀ water/sediment system (d):	47.4	DT ₅₀ water (d):	47.4	DT ₅₀ sediment (d):	47.4	Maximum occurrence observed (% molar basis with respect to the parent):		Soil:	6.3	Water:	13.0	Sediment:	5.5	Total System:	14.3						
Molecular weight (g/mol):	216.2																																		
Water solubility (mg/L):	783																																		
Soil or water metabolite:	Soil/water																																		
K _{OC} (L/kg):	21.6																																		
DT ₅₀ soil (d):	9.3																																		
<i>(worst case of normalized lab data)</i>																																			
DT ₅₀ water/sediment system (d):	47.4																																		
DT ₅₀ water (d):	47.4																																		
DT ₅₀ sediment (d):	47.4																																		
Maximum occurrence observed (% molar basis with respect to the parent):																																			
Soil:	6.3																																		
Water:	13.0																																		
Sediment:	5.5																																		
Total System:	14.3																																		
IN-T4226 Parameters used in FOCUSsw step 1 and 2	<table> <tr><td>Molecular weight:</td><td>142.1</td></tr> <tr><td>Water solubility (mg/L):</td><td>783</td></tr> <tr><td>Soil or water metabolite:</td><td>Water</td></tr> <tr><td>K_{OC} (L/kg):</td><td>17.7</td></tr> <tr><td>DT₅₀ soil (d):</td><td>1000</td></tr> <tr><td colspan="2"><i>(degradation in soil unknown)</i></td></tr> <tr><td>DT₅₀ water/sediment system (d):</td><td>4.6</td></tr> <tr><td>DT₅₀ water (d):</td><td>4.6</td></tr> <tr><td>DT₅₀ sediment (d):</td><td>4.6</td></tr> <tr><td colspan="2">Maximum occurrence observed (% molar basis with respect to the parent):</td></tr> <tr><td>Soil:</td><td>1.7</td></tr> <tr><td>Water:</td><td>11.1</td></tr> <tr><td>Sediment:</td><td>1.0</td></tr> <tr><td>Total System:</td><td>12.0</td></tr> </table>	Molecular weight:	142.1	Water solubility (mg/L):	783	Soil or water metabolite:	Water	K _{OC} (L/kg):	17.7	DT ₅₀ soil (d):	1000	<i>(degradation in soil unknown)</i>		DT ₅₀ water/sediment system (d):	4.6	DT ₅₀ water (d):	4.6	DT ₅₀ sediment (d):	4.6	Maximum occurrence observed (% molar basis with respect to the parent):		Soil:	1.7	Water:	11.1	Sediment:	1.0	Total System:	12.0						
Molecular weight:	142.1																																		
Water solubility (mg/L):	783																																		
Soil or water metabolite:	Water																																		
K _{OC} (L/kg):	17.7																																		
DT ₅₀ soil (d):	1000																																		
<i>(degradation in soil unknown)</i>																																			
DT ₅₀ water/sediment system (d):	4.6																																		
DT ₅₀ water (d):	4.6																																		
DT ₅₀ sediment (d):	4.6																																		
Maximum occurrence observed (% molar basis with respect to the parent):																																			
Soil:	1.7																																		
Water:	11.1																																		
Sediment:	1.0																																		
Total System:	12.0																																		
IN-JX915 Parameters used in FOCUSsw step 1 and 2	<table> <tr><td>Molecular weight:</td><td>198.2</td></tr> <tr><td>Water solubility (mg/L):</td><td>783</td></tr> <tr><td>Soil or water metabolite:</td><td>Soil/water</td></tr> <tr><td>K_{OC} (L/kg):</td><td>16.3</td></tr> <tr><td>DT₅₀ soil (d):</td><td>0.7</td></tr> <tr><td colspan="2"><i>(worst case of normalized lab data)</i></td></tr> <tr><td>DT₅₀ water/sediment system (d):</td><td>1.7</td></tr> <tr><td>DT₅₀ water (d):</td><td>1.7</td></tr> <tr><td>DT₅₀ sediment (d):</td><td>1.7</td></tr> <tr><td colspan="2">Maximum occurrence observed (% molar basis with respect to the parent):</td></tr> <tr><td>Soil:</td><td>10.9</td></tr> <tr><td colspan="2"><i>(value from soil photolysis used, worst-case assessment)</i></td></tr> <tr><td>Water:</td><td>7.2</td></tr> <tr><td>Sediment:</td><td>1.2</td></tr> <tr><td>Total System:</td><td>8.5</td></tr> <tr><td>Photolysis in sterile water, pH 5:</td><td>52.6</td></tr> <tr><td colspan="2"><i>(value from photolysis used, worst-case assessment)</i></td></tr> </table>	Molecular weight:	198.2	Water solubility (mg/L):	783	Soil or water metabolite:	Soil/water	K _{OC} (L/kg):	16.3	DT ₅₀ soil (d):	0.7	<i>(worst case of normalized lab data)</i>		DT ₅₀ water/sediment system (d):	1.7	DT ₅₀ water (d):	1.7	DT ₅₀ sediment (d):	1.7	Maximum occurrence observed (% molar basis with respect to the parent):		Soil:	10.9	<i>(value from soil photolysis used, worst-case assessment)</i>		Water:	7.2	Sediment:	1.2	Total System:	8.5	Photolysis in sterile water, pH 5:	52.6	<i>(value from photolysis used, worst-case assessment)</i>	
Molecular weight:	198.2																																		
Water solubility (mg/L):	783																																		
Soil or water metabolite:	Soil/water																																		
K _{OC} (L/kg):	16.3																																		
DT ₅₀ soil (d):	0.7																																		
<i>(worst case of normalized lab data)</i>																																			
DT ₅₀ water/sediment system (d):	1.7																																		
DT ₅₀ water (d):	1.7																																		
DT ₅₀ sediment (d):	1.7																																		
Maximum occurrence observed (% molar basis with respect to the parent):																																			
Soil:	10.9																																		
<i>(value from soil photolysis used, worst-case assessment)</i>																																			
Water:	7.2																																		
Sediment:	1.2																																		
Total System:	8.5																																		
Photolysis in sterile water, pH 5:	52.6																																		
<i>(value from photolysis used, worst-case assessment)</i>																																			

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

IN-R3273 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 171.2 Water solubility (mg/L): 783 Soil or water metabolite: Water K_{OC} (L/kg): 41.9 DT₅₀ soil (d): 1000 (<i>degradation in soil unknown</i>) DT₅₀ water/sediment system (d): 6.3 DT₅₀ water (d): 6.3 DT₅₀ sediment (d): 6.3 Maximum occurrence observed (% molar basis with respect to the parent): Soil: 2.4 Water: 5.0 Sediment: 0.5 Total System: 5.0 Photolysis in sterile water, pH 5: 35.4 (<i>value from photolysis used, worst-case assessment</i>)
IN-KP533 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 160.1 Water solubility (mg/L): 783 Soil or water metabolite: Water K_{OC} (L/kg): 12.9 DT₅₀ soil (d): 1000 (<i>degradation in soil unknown</i>) DT₅₀ water/sediment system (d): 2.6 DT₅₀ water (d): 2.6 DT₅₀ sediment (d): 2.6 Maximum occurrence observed (% molar basis with respect to the parent): Soil: 2.7 Water: 20.5 Sediment: 6.5 Total System: 26.0 (<i>maximum occurrence in water/sediment system worst-case, individual amounts in two of four water/sediment studies not known, in two studies max. 8.0 % of AR in the entire system</i>)
Metabolite fraction M5 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 198.2 (<i>unknown, value of parent used</i>) Water solubility (mg/L): 783 Soil or water metabolite: Water K_{OC} (L/kg): 9.2 (<i>K_{OC} unknown, value of IN-W3595 used</i>) DT₅₀ soil (d): 1000 (<i>degradation in soil unknown</i>) DT₅₀ water/sediment system (d): 1.4 DT₅₀ water (d): 1.4 DT₅₀ sediment (d): 1.4 Maximum occurrence observed (% molar basis with respect to the parent): Soil: 0.0 Water: 22.9 Sediment: 0.0 Total System: 22.9

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Application rate	Notifier:	DuPont
	Crop:	Potatoes
	Application rate(s):	175 g as/ha
	Number of applications:	8
	Interval (d):	7
	Crop interception:	50 % (average)
	Application window:	March – May
	Scenarios:	South/North EU
	Notifier:	Oxon
	Crop:	Potatoes
	Application rate(s):	120 g as/ha
	Number of applications:	4 (North EU), 5 (South EU)
	Interval (d):	7
	Crop interception:	50 % (average)
	Application window:	June – September
	Scenarios:	South/North EU
	Notifier:	Oxon
	Crop:	Lettuce
	Application rate(s):	240 g as/ha
	Number of applications:	4
	Interval (d):	7
	Crop interception:	70 % (full)
	Application window:	June – September
	Scenarios:	South EU

FOCUS STEP 1 Scenario	Potatoes (DuPont)		
	Substance	PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum
-	Cymoxanil	56.7	24.0
	IN-U3204	14.3	3.88
	IN-W3595	32.4	2.77
	IN-KQ960	33.2	7.05
	IN-T4226	6.66	1.01
	IN-JX915	7.07	1.01
	IN-R3273	13.1	4.84
	IN-KP533	12.7	1.29
	Metabolite fraction M5	0.37	0.02
FOCUS STEP 1 Scenario	Potatoes (Oxon)		
	Substance	PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum
North EU	Cymoxanil	38.9	16.5
	IN-U3204	9.80	2.66
	IN-W3595	11.1	0.95

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Cymoxanil - Appendix 3: list of endpoints
Fate and Behaviour in the Environment

June 2007

	IN-KQ960	11.4	2.42
	IN-T4226	2.28	0.35
	IN-JX915	4.85	0.70
	IN-R3273	4.49	1.66
	IN-KP533	4.36	0.44
	Metabolite fraction M5	0.25	0.01
South EU	Cymoxanil	38.9	16.5
	IN-U3204	9.80	2.66
	IN-W3595	13.9	1.19
	IN-KQ960	14.2	3.02
	IN-T4226	2.86	0.43
	IN-JX915	4.85	0.70
	IN-R3273	5.61	2.07
	IN-KP533	5.45	0.55
	Metabolite fraction M5	0.25	0.01
FOCUS STEP 1 Scenario	Lettuce (Oxon)		
	Substance	PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum
-	Cymoxanil	77.8	33.0
	IN-U3204	19.6	5.32
	IN-W3595	22.2	1.90
	IN-KQ960	22.7	4.83
	IN-T4226	4.57	0.69
	IN-JX915	9.70	1.39
	IN-R3273	8.98	3.32
	IN-KP533	8.72	0.89
	Metabolite fraction M5	0.51	0.03

FOCUS STEP 2 Scenario	Potatoes (DuPont)				
	Substance	Single application		Multiple application	
		PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum	PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum
North EU	Cymoxanil	1.61	0.15	0.88	0.15
	IN-U3204	0.40	0.01	0.22	0.01
	IN-W3595	0.29	0.02	0.20	0.02

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Cymoxanil - Appendix 3: list of endpoints
Fate and Behaviour in the Environment

June 2007

	IN-KQ960	0.52	0.11	1.42	0.30
	IN-T4226	0.14	0.02	0.61	0.10
	IN-JX915	0.85	0.06	0.49	0.03
	IN-R3273	0.49	0.16	1.21	0.46
	IN-KP533	0.34	0.03	1.06	0.13
	Metabolite fraction M5	0.37	0.01	0.21	0.01
South EU	Cymoxanil	1.61	0.30	0.88	0.30
	IN-U3204	0.40	0.01	0.22	0.01
	IN-W3595	0.33	0.03	0.32	0.03
	IN-KQ960	0.81	0.17	2.12	0.45
	IN-T4226	0.21	0.03	1.15	0.20
	IN-JX915	0.85	0.06	0.49	0.03
	IN-R3273	0.53	0.20	2.11	0.84
	IN-KP533	0.36	0.04	2.04	0.26
	Metabolite fraction M5	0.37	0.01	0.21	0.01
FOCUS STEP 2 Scenario	Potatoes (Oxon)				
	Substance	Single application		Multiple application	
		PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum	PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum
North EU	Cymoxanil	1.10	0.10	0.74	0.10
	IN-U3204	0.27	0.01	0.18	0.01
	IN-W3595	0.20	0.01	0.16	0.01
	IN-KQ960	0.36	0.08	0.79	0.17
	IN-T4226	0.10	0.01	0.24	0.04
	IN-JX915	0.58	0.04	0.42	0.03
	IN-R3273	0.34	0.11	0.56	0.21
	IN-KP533	0.23	0.02	0.40	0.05
	Metabolite fraction M5	0.25	0.01	0.18	0.01
South EU	Cymoxanil	1.10	0.15	0.72	0.16
	IN-U3204	0.27	0.01	0.18	0.01
	IN-W3595	0.20	0.01	0.19	0.02
	IN-KQ960	0.45	0.10	1.10	0.23
	IN-T4226	0.12	0.02	0.40	0.07
	IN-JX915	0.58	0.04	0.40	0.03
	IN-R3273	0.34	0.12	0.83	0.31

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

	IN-KP533	0.23	0.02	0.70	0.09
	Metabolite fraction M5	0.25	0.01	0.17	0.01
FOCUS STEP 2 Scenario	Lettuce (Oxon)				
	Substance	Single application		Multiple application	
		PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum	PEC _{SW} (µg/L) global maximum	PEC _{SED} (µg/kg) global maximum
South EU	Cymoxanil	2.21	0.19	1.49	0.19
	IN-U3204	0.55	0.02	0.37	0.01
	IN-W3595	0.39	0.02	0.33	0.02
	IN-KQ960	0.67	0.14	1.50	0.32
	IN-T4226	0.19	0.03	0.44	0.07
	IN-JX915	1.16	0.08	0.83	0.06
	IN-R3273	0.67	0.21	1.06	0.40
	IN-KP533	0.46	0.03	0.74	0.09
	Metabolite fraction M5	0.51	0.02	0.35	0.01

PEC (ground water) (Annex IIIA. point 9.2.1)

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)

Modelling using FOCUS models, with appropriate FOCUSgw scenarios, according to FOCUS guidance

Model(s) used: PEARL 3.3.3
FOCUS PELMO 3.3.2
Scenarios (list of names): All if appropriate
Crops: Potatoes (DuPont)
Potatoes (Oxon)
Lettuce (Oxon)

Cymoxanil:

Geometric mean SFO-DT_{50lab, norm.}: 1.0 d
(re-calculated from lab FOMC-DT₉₀ / 3.32, normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2, n = 9)

K_{FOC}: 43.6 L/kg (arithmetic mean, n = 4)

¹I_n = 0.86 (arithmetic mean, n = 4)

Plant uptake: 0.5

IN-U3204:

Geometric mean DT_{50lab, norm.}: 0.2 d
(normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2)

K_{OC}: 27.9 L/kg (HPLC, n = 1)

¹I_n = 0.9 (default value)

Maximum occurrence in soil: 24.7 %

Plant uptake: 0.0

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

IN-W3595

Worst case DT_{50lab, norm.}: 2.2 d
(normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2)
K_{OC}: pH depending (batch, n = 4)
PEARL: K_{OC-acid} = 33.3, K_{OC-base} = 2.3,
pK_a = 5.2
PELMO: Scenario specific, individual K_F value
for each soil depth depending on soil pH
¹/_n = 0.9 (default value)
Maximum occurrence in soil: 10.1 %
Plant uptake: 0.0

IN-JX915:

Worst case DT_{50lab, norm.}: 0.7 d
(normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2)
K_{OC}: 16.1 kg/L (batch, n = 4)
¹/_n = 0.9 (default value)
Maximum occurrence in soil: 10.9 % (soil photolysis)
Plant uptake: 0.0

IN-KQ960:

Worst case DT_{50lab, norm.}: 9.3 d
(normalisation to 10 kPa or pF2, 20 °C with Q₁₀ of 2.2)
K_{OC}: 21.6 kg/L (HPLC, n = 1)
¹/_n = 0.9 (default value)
Maximum occurrence in soil: 6.3 %
Plant uptake: 0.0

Application rate

Notifier:	DuPont
Crop:	Potatoes
Application rate:	175 g/ha
Number of applications:	8
Interval (d):	7
% crop interception:	50 (1 st – 4 th application) 80 (5 th – 8 th application)
Time of 1 st application:	7 days after leaf emergence
Notifier:	Oxon
Crop:	Potatoes
Application rate:	120 g/ha
Number of applications:	4 (North EU), 5 (South EU)
Interval (d):	7
% crop interception:	50 (1 st – 3 th application) 80 (4 th – 5 th application)
Time of 1 st application:	28 days pre harvest (North EU) 35 days pre harvest (South EU)
Notifier:	Oxon
Crop:	Lettuce
Application rate:	240 g/ha
Number of applications:	4
Interval (d):	7
% crop interception:	70

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Time of 1st application: 31 days pre harvest

PEC(gw) - FOCUS modelling results (80th percentile annual average concentration at 1 m)

FOCUS PELMO 3.3.2	Scenario	Cymoxanil (µg/L)	Metabolite (µg/L)			
			IN-U3204	IN-W3595	IN-JX915	IN-KQ960
Potatoes (DuPont)	Chateaudun (C)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Hamburg (H)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Jokioinen (J)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Kremsmünster (K)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Okehampton (N)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Piacenza (P)	< 0.001	< 0.001	< 0.001	< 0.001	0.001
	Porto (O)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla (S)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva (T)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Potatoes (Oxon)	Chateaudun (C)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Hamburg (H)	< 0.001	< 0.001	< 0.001	< 0.001	0.001
	Jokioinen (J)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Kremsmünster (K)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Okehampton (N)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Piacenza (P)	< 0.001	< 0.001	< 0.001	< 0.001	0.006
	Porto (O)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla (S)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva (T)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Lettuce (Oxon)	Piacenza (P)	No cabbage (used as surrogate for lettuce)				
	Porto (O)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla (S)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva (T)	< 0.001	< 0.001	0.001	< 0.001	< 0.001

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Cymoxanil - Appendix 3: list of endpoints
Fate and Behaviour in the Environment

June 2007

PEARL 3.3.3	Scenario	Cymoxanil (µg/L)	Metabolite (µg/L)			
			IN-U3204	IN-W3595	IN-JX915	IN-KQ960
Potatoes (DuPont)	Chateaudun (C)	< 0.001	< 0.001	< 0.001	< 0.001	0.004
	Hamburg (H)	< 0.001	< 0.001	< 0.001	< 0.001	0.009
	Jokioinen (J)	< 0.001	< 0.001	< 0.001	< 0.001	0.001
	Kremsmünster (K)	< 0.001	< 0.001	< 0.001	< 0.001	0.004
	Okehampton (N)	< 0.001	< 0.001	< 0.001	< 0.001	0.007
	Piacenza (P)	< 0.001	< 0.001	< 0.001	< 0.001	0.014
	Porto (O)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla (S)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva (T)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Potatoes (Oxon)	Chateaudun (C)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Hamburg (H)	< 0.001	< 0.001	< 0.001	< 0.001	0.006
	Jokioinen (J)	< 0.001	< 0.001	< 0.001	< 0.001	0.002
	Kremsmünster (K)	< 0.001	< 0.001	< 0.001	< 0.001	0.001
	Okehampton (N)	< 0.001	< 0.001	< 0.001	< 0.001	0.003
	Piacenza (P)	< 0.001	< 0.001	< 0.001	< 0.001	0.012
	Porto (O)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla (S)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva (T)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Lettuce (Oxon)	Piacenza (P)	No cabbage (used as surrogate for lettuce)				
	Porto (O)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Sevilla (S)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	Thiva (T)	< 0.001	< 0.001	0.002	< 0.001	0.011

Fate and behaviour in air (Annex IIA. point 7.2.2. Annex III. point 9.3)

Direct photolysis in air ‡

Quantum yield of direct photo-transformation

Photochemical oxidative degradation in air ‡

Volatilisation ‡

Metabolites

Not studied - no data requested
0.0052 / 0.00058 (n = 2)
DT ₅₀ of 21.3 hrs derived by the Atkinson model (version 1.91), OH ⁻ concentration (12-hrs day) assumed = 1.5 × 10 ⁶ cm ⁻³
Not studied – no data requested
Not studied – no data requested
Not studied – no data requested

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

PEC (air)

Method of calculation

Expert judgement, based on vapour pressure and dimensionless Henry's Law Constant

PEC_(a)

Maximum concentration

Negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology)

Soil: Cymoxanil, IN-U3204, IN-W3595, IN-JX915 (the latter from soil photolysis)

Surface Water: Cymoxanil, IN-U3204, IN-W3595, IN-KQ960, IN-T4226, IN-KP533, metabolite fraction M5, IN-JX915, IN-R3273 (the two latter from water photolysis)

Sediment: Cymoxanil

Groundwater: Cymoxanil

Air: Cymoxanil

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)

No monitoring data

Surface water (indicate location and type of study)

No monitoring data

Ground water (indicate location and type of study)

No monitoring data

Air (indicate location and type of study)

No monitoring data

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Not readily biodegradable

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Chapter: Ecotoxicology

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
<i>Colinus virginianus</i>	a.s.	Acute	LD ₅₀ > 2000	/
<i>Coturnix c. japonica</i>	Cymoxanil 50 WP	Acute	LD ₅₀ > 2000	/
<i>Anas platyrhynchos</i>	a.s.	Short-term	LD ₅₀ > 260*	2945
<i>Anas platyrhynchos</i>	a.s.	Long-term	NOAEL 14.9	100
Mammals ‡				
<i>Rattus norvegicus</i>	a.s.	Acute	LD ₅₀ (m) 760	/
<i>Rattus norvegicus</i>	Cymoxanil 50 WP	Acute	LD ₅₀ 1200	/
<i>Rattus norvegicus</i>	Tanos	Acute	LD ₅₀ (f) 566	/
<i>Rattus norvegicus</i>	a.s.	Long-term	NOEL 10.5	150
Additional higher tier studies ‡				
Not required				

* Since food consumption was reduced at dietary concentrations above and below the LC₅₀ value, it is not possible to convert the LC₅₀ to a reliable daily dose estimate. The highest sub-LC₅₀ dietary concentration that caused no significant impact on food consumption was 625 ppm, corresponding to 260 mg a.s./kg bw/day.

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Lettuce, 4 x 240 g a.s./ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
medium herbivorous	Acute a.s.	29	> 70	10
insectivorous	Acute a.s.	13	> 154	10
medium herbivorous	Acute Cym 50WP	29	> 35	10
insectivorous	Acute Cym 50WP	13	> 127	10
medium herbivorous	Short-term	16	16	10
insectivorous	Short-term	7	36	10
medium herbivorous	Long-term	9	1.7	5
insectivorous	Long-term	2	2.1	5
Higher tier refinement (Birds): actual residues + decline considered for herbivores; focal species considered for insectivores: Yellow Wagtail: feeding on 80 % large + 20 % small insects				
medium herbivorous	Long-term	2.8	5.4	10
insectivorous	Long-term	2.2	6.9	5
Tier 1 (Mammals)				
medium herbivorous	Acute a.s.	11	72	10
insectivorous	Acute a.s.	2	359	10

Ecotoxicology

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
medium herbivorous	Acute Cym 50WP	11	57	10
insectivorous	Acute Cym 50WP	2	285	10
medium herbivorous	Long-term	3.2	3.3	5
insectivorous	Long-term	0.8	14	5
Higher tier refinement (Mammals): actual residues + decline considered				
medium herbivorous	Long-term	1	10	5

Potatoes, 8 x 175 g a.s./ha

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
medium herbivorous	Acute a.s.	23	> 86	10
insectivorous	Acute a.s.	10	> 211	10
medium herbivorous	Short-term	13	20	10
insectivorous	Short-term	5	49	10
medium herbivorous	Long-term	7	2.1	5
insectivorous	Long-term	5	2.8	5
Higher tier refinement (Birds): actual residues + decline considered for herbivores; focal species considered for insectivores: Yellowhammer: feeding on 82 % large + 12 % small insects, PT 0.5; Yellow Wagtail: feeding on 80 % large + 20 % small insects				
medium herbivorous	Long-term	2	7.5	10
Insectivorous 1: Yellowh.	Long-term	0.53	28	5
Insectivorous 2: Y. Wagtail	Long-term	1.57	9.5	5
Tier 1 (Mammals)				
medium herbivorous	Acute a.s.	9	89	10
insectivorous	Acute a.s.	2	492	10
medium herbivorous	Acute Tanos	9	17	10
insectivorous	Acute Tanos	2	92	10
medium herbivorous	Long-term	3	4	5
insectivorous	Long-term	2	19	5
Higher tier refinement (Mammals): actual residues + decline considered				
medium herbivorous	Long-term	0.7	14	5

WARNING: This document forms part of an EC evaluation data package and should not be used in isolation. Registration must not be granted on the basis of this document.

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Test substance	Test organism	Test system / Duration	Endpoints	NOEC [mg/L]	LC ₅₀ [mg/L]	Nominal/mean meas. ^a
Cymoxanil	<i>Lepomis macrochirus</i>	s / 96 h	Mortality Subleth. effects	17	29	mm
	<i>Cyprinodon variegatus</i>	f / 36 d	Growth Fry surviv.	0.0581	-	mm
IN-T4226	<i>Oncorhynchus mykiss</i>	ss / 96 h	Mortality Subleth. effects	111	> 111	mmL
IN-KQ960	<i>Oncorhynchus mykiss</i>	s / 96 h	Mortality Subleth. effects	120	> 120	nL
IN-U3204	<i>Oncorhynchus mykiss</i>	ss / 96 h	Mortality Subleth. effects	97	> 97	mmL
IN-W3595	<i>Oncorhynchus mykiss</i>	s / 96 h	Mortality Subleth. effects	130	> 130	mmL
Cymoxanil 50 % WP	<i>Oncorhynchus mykiss</i>	ss / 96 h	Mortality	36 prod 18.2 a.s.	120 prod 60.6 a.s.	n
Tanos	<i>Oncorhynchus mykiss</i>	f / 96 h	Mortality Subleth. effects	0.014 prod	0.0287 prod	n
Cymoxanil	<i>Daphnia magna</i>	s / 48 h	Immobility	15	27	mm
	<i>Daphnia magna</i>	ss / 21 d	Mortality Reproduction	0.067	-	mm
IN-T4226	<i>Daphnia magna</i>	ss / 48 h	Immobility sublethal effects	116	> 116	mm
IN-KQ960	<i>Daphnia magna</i>	s / 48 h	Immobility sublethal effects	n.d.	0.8	mm
	<i>Daphnia magna</i>	ss / 21 d	Mortality Reproduction	0.302	-	mm
IN-U3204	<i>Daphnia magna</i>	ss / 48 h	Immobility sublethal effects	53	100	mm
IN-W3595	<i>Daphnia magna</i>	s / 48 h	Immobility sublethal effects	126	> 126	mm
Cymoxanil 50 % WP	<i>Daphnia magna</i>	ss / 48 h	Immobility	200 prod. 101 a.s.	> 200 prod. > 101 a.s.	nL
Tanos	<i>Daphnia magna</i>	f / 48 h	Immobility sublethal effects	0.014 prod.	0.0555 prod.	n
Cymoxanil	<i>Anabaena flos-aquae</i>	s / 96 h	Growth rate Biomass	0.0652 0.034	0.254 0.122	im
IN-T4226	<i>Anabaena flos-aquae</i>	s / 96 h	Growth rate Biomass	20 20	35.9 25.8	n
IN-W3595	<i>Anabaena flos-aquae</i>	s / 96 h	Growth rate Biomass	5	19.9 12.7	n
Cymoxanil 50 % WP	<i>Pseudokirchneriella subcapitata</i>	s / 72 h	Growth rate Biomass	0.11 ai 0.196 ai	0.41 ai ^b 0.11 ai	twa
DPX-KX007	<i>Pseudokirchneriella subcapitata</i>	s / 72 h	Growth rate Biomass	1.25 prod	11.0 prod 4.2 prod	n
Cymoxanil	<i>Lemna gibba</i>	s / 14 d	Growth rate Biomass	0.7 0.7	> 0.7 > 0.7	im

f...flow through, im...initial measured, mm...mean measured, mmL...mean measured/limit test, n...nominal, n.d....not derived, nL...nominal/limit test, s...static, ss....semi-static, twa...time weighted average concentration.

^a This column states if toxicity estimates are based on nominal or measured concentrations.

^b For classification and labelling of the plant protection product an E_rC₅₀ of 4.72 mg Product/L based on nominal concentrations was used.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

Plant protection product Cymoxanil 50 % WP, FOCUS step 1 and step 2

GAP: Lettuce, 4 x 240 g ai/ha (interval between applications: 7 d), South EU. This GAP is worst case compared to the intended use of Cymoxanil 50 % WP in lettuce in North EU or to the use in potatoes.

Test substance	Test organism	Toxicity estimate	Toxicity [mg ai/L]	PEC _{sw} [mg ai/L]		TER		Annex VI trigger
				Step 1	Step 2	Step 1	Step 2	
Cymoxanil	<i>Lepomis macrochirus</i>	LC ₅₀ (96 h)	29	0.0778	0.00221	373	13122	100
	<i>Cyprinodon variegatus</i>	NOEC (36 d)	0.0581	0.0778	0.00221	0.7	26	10
IN-T4226	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	> 111	0.00457	0.00044	>24289	252273	100
IN-KQ960	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	> 120	0.0227	0.00150	>5286	80000	100
IN-U3204	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	> 97	0.0196	0.00055	>4949	176364	100
IN-W3595	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	> 130	0.0222	0.00039	>5856	333333	100
Cymoxanil 50 % WP	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	60.6	0.0778	0.00221	779	27421	100
Cymoxanil	<i>Daphnia magna</i>	EC ₅₀ (48 h)	27	0.0778	0.00221	347	12217	100
	<i>Daphnia magna</i>	NOEC (21 d)	0.067	0.0778	0.00221	1	30	10
IN-T4226	<i>Daphnia magna</i>	EC ₅₀ (48 h)	> 116	0.00457	0.00044	25383	263636	100
IN-KQ960	<i>Daphnia magna</i>	EC ₅₀ (48 h)	0.8	0.0227	0.00150	35	533	100
	<i>Daphnia magna</i>	NOEC (21 d)	0.302	0.0227	0.00150	13	201	10
IN-U3204	<i>Daphnia magna</i>	EC ₅₀ (48 h)	100	0.0196	0.00055	5102	181818	100
IN-W3595	<i>Daphnia magna</i>	EC ₅₀ (48 h)	> 126	0.0222	0.00039	5676	323077	100
Cymoxanil 50 % WP	<i>Daphnia magna</i>	EC ₅₀ (48 h)	101	0.0778	0.00221	1298	45701	100
Cymoxanil	<i>Anabaena flos-aquae</i>	E _r C ₅₀ (96 h)	0.254	0.0778	0.00221	3	115	10
		E _b C ₅₀ (96 h)	0.122			2	55	
IN-T4226	<i>Anabaena flos-aquae</i>	E _r C ₅₀ (96 h)	35.9	0.00457	0.00044	7856	81591	10
		E _b C ₅₀ (96 h)	25.8			5646	58636	
IN-W3595	<i>Anabaena flos-aquae</i>	E _r C ₅₀ (96 h)	19.9	0.0222	0.00039	896	51026	10
		E _b C ₅₀ (96 h)	12.7			572	32564	
Cymoxanil 50 % WP	<i>Pseudokirchneriella subcapitata</i>	E _r C ₅₀ (72 h)	0.41	0.0778	0.00221	5	186	10
		E _b C ₅₀ (72 h)	0.11			1	50	
Cymoxanil	<i>Lemna gibba</i>	E _r C ₅₀ (14 d) E _b C ₅₀ (14 d)	> 0.7 > 0.7	0.0778	0.00221	9	317	10

Plant protection product Tanos, FOCUS step 1 and step 2

GAP: Potatoes, 8 x 175 g ai/ha (interval between applications: 7 d), South EU. This GAP is worst case compared to the intended use of Tanos in North EU.

TER values for the active substance:

Test substance	Test organism	Toxicity estimate	Toxicity [mg ai/L]	PEC _{SW} [mg ai/L]		TER		Annex VI trigger
				Step 1	Step 2	Step 1	Step 2	
Cymoxanil	<i>Lepomis macrochirus</i>	LC ₅₀ (96 h)	29	0.0567	0.00161	511	18012	100
	<i>Cyprinodon variegatus</i>	NOEC (36 d)	0.0581	0.0567	0.00161	1.0	36	10
IN-T4226	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	> 111	0.00666	0.00115	>1666 7	96522	100
IN-KQ960	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	> 120	0.0332	0.00212	>3614	56604	100
IN-U3204	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	> 97	0.0143	0.00040	>6783	242500	100
IN-W3595	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	> 130	0.0324	0.00033	>4012	393939	100
Cymoxanil	<i>Daphnia magna</i>	EC ₅₀ (48 h)	27	0.0567	0.00161	476	16770	100
	<i>Daphnia magna</i>	NOEC (21 d)	0.067	0.0567	0.00161	1	42	10
IN-T4226	<i>Daphnia magna</i>	EC ₅₀ (48 h)	> 116	0.00666	0.00115	17417	100870	100
IN-KQ960	<i>Daphnia magna</i>	EC ₅₀ (48 h)	0.8	0.0332	0.00212	24	377	100
	<i>Daphnia magna</i>	NOEC (21 d)	0.302	0.0332	0.00212	9	142	10
IN-U3204	<i>Daphnia magna</i>	EC ₅₀ (48 h)	100	0.0143	0.00040	6993	250000	100
IN-W3595	<i>Daphnia magna</i>	EC ₅₀ (48 h)	> 126	0.0324	0.00033	3889	381818	100
IN-JX915 ^a	<i>Daphnia magna</i>	EC ₅₀ (48 h)	0.27	0.00707	0.00085	38	318	100
IN-R3273 ^a	<i>Daphnia magna</i>	EC ₅₀ (48 h)	0.27	0.0131	0.00211	21	128	100
IN-KP533 ^a	<i>Daphnia magna</i>	EC ₅₀ (48 h)	0.27	0.0127	0.00204	21	132	100
Metabolite fraction M5 ^a	<i>Daphnia magna</i>	EC ₅₀ (48 h)	0.27	0.00037	0.00037	730	730	100
Cymoxanil	<i>Anabaena flos-aquae</i>	E _r C ₅₀ (96 h)	0.254	0.0567	0.00161	4	158	10
		E _b C ₅₀ (96 h)	0.122			2	76	
IN-T4226	<i>Anabaena flos-aquae</i>	E _r C ₅₀ (96 h)	35.9	0.00666	0.00115	5390	31217	10
		E _b C ₅₀ (96 h)	25.8			3874	22435	
IN-W3595	<i>Anabaena flos-aquae</i>	E _r C ₅₀ (96 h)	19.9	0.0324	0.00033	614	60303	10
		E _b C ₅₀ (96 h)	12.7			392	38485	
Cymoxanil	<i>Lemna gibba</i>	E _r C ₅₀ (14 d)	> 0.7	0.0567	0.00161	12	435	10
		E _b C ₅₀ (14 d)	> 0.7			12	435	

WARNING: This document forms part of the evaluation data for the active substance and should not be used for the registration of this document.

Ecotoxicology

Ganzelmeier drift input of the plant protection product Tanos:

TER values for the active substance:

Test substance	Test organism	Toxicity estimate	Toxicity [mg prod./L]	Buffer zone	Drift [%]	PEC _{sw} [mg prod./L]	TER	Annex VI trigger
Tanos	<i>Oncorhynchus mykiss</i>	LC ₅₀ (96 h)	0.0287	0 m	2.77	0.006463	4.4	100
				20 m	0.15	0.000350	82	
				30 m	0.10	0.000233	123	
	<i>Daphnia magna</i>	EC ₅₀ (48 h)	0.0555	0 m	2.77	0.006463	9	100
				20 m	0.15	0.000350	159	
DPX-KX007	<i>Pseudokirchneriella subcapitata</i>	NOEC	1.25	0 m	2.77	0.006463	193	10

Bioconcentration		
logP _{OW}	Active substance	log P _{OW} = 0.59-0.67 at 20 °C
	IN-KQ960	-1.64 (KOWWIN)
	IN-U3204	0.39 (KOWWIN)
	IN-T4226	0.16 (KOWWIN)
	IN-JX915	-0.37 (KOWWIN)
	IN-R3273	2.07 (KOWWIN)
	IN-KP533	-1.29 (KOWWIN)
	IN-W3595	4.27 (KOWWIN)
Bioconcentration factor (BCF) ¹ ‡		Not demanded
Annex VI Trigger for the bioconcentration factor		
Clearance time (days) (CT ₅₀)		
(CT ₉₀)		
Level and nature of residues (%) in organisms after the 14 day depuration phase		

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD ₅₀ µg/bee)	Acute contact toxicity (LD ₅₀ µg/bee)
a.s. ‡	> 85.29	> 100
Preparation Cymoxanil/Famoxadone 52.5WG	> 186 [formulation] > 55.5 [a.s.]	> 200 [formulation] > 60 [a.s.]
Field or semi-field tests		
not required		

Hazard quotients for honey bees (Annex IIIA, point 10.4)

lettuce, 4 x 240 g a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	< 2.8	50
a.s.	oral	< 2.4	50

potatoes, 8 x 175 g a.s./ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	< 2.1	50
a.s.	oral	< 1.8	50

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR ₅₀)
<i>Typhlodromus pyri</i> ‡	Cymoxanil 50 WP	Mortality	> 480 g a.s./ha
<i>Aphidius rhopalosiphi</i> ‡	Cymoxanil 50 WP	Mortality	> 480 g a.s./ha

lettuce, 4 x 240 g a.s./ha

Test substance	Species	Effect (LR ₅₀ g/ha)	HQ in-field	HQ off-field ¹	Trigger
Cymoxanil 50 WP	<i>Typhlodromus pyri</i>	> 480 [a.s.]	< 1.35	< 0.02	2
Cymoxanil 50 WP	<i>Aphidius rhopalosiphi</i>	> 480 [a.s.]	< 1.35	< 0.02	2

¹ indicate distance assumed to calculate the drift rate

potatoes, 8 x 175 g a.s./ha

Test substance	Species	Effect (LR ₅₀ g/ha)	HQ in-field	HQ off-field ¹	Trigger
Cymoxanil 50 WP	<i>Typhlodromus pyri</i>	> 480 [a.s.]	< 1.28	< 0.02	2
Cymoxanil 50 WP	<i>Aphidius rhopalosiphi</i>	> 480 [a.s.]	< 1.28	< 0.02	2

¹ 1 m distance

Ecotoxicology

Further laboratory, extended laboratory and semi-field studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ha) 1	End point	% effect ³	Trigger value
<i>Aphidius rhopalosiphi</i>	adults	extended lab, Cymoxanil/F 20SC, leaves 48 h + 10 d	264 3 x 264 6 x 264	mortality fecundity mortality fecundity mortality fecundity	0 34 33 35 25 23	50 %
<i>Aphidius colemani</i>	adults	semi-field, 12 d Cymoxanil/F 50WG, potato leaves	179 3 x 179 6 x 179 9 x 179	parasitism parasitism parasitism parasitism	-7 25 / 26 ² 5 / 52 ² -43	50 %
<i>Trichogramma cacoeciae</i>	adults	extended lab, Cymoxanil/F 52. 5WG, grape leaves 8 d	120 3 x 120 6 x 120 9 x 120 12 x 120	reproduction reproduction reproduction reproduction reproduction	-11.7 -50.5 13.1 8.1 -5.6	50 %
<i>Typhlodromus pyri</i>	protonymphs	lab, 21 d Cymoxanil/F 20SC, glass plate	132	mortality reproduction	98.9 100	50 %
<i>Typhlodromus pyri</i>	protonymphs	extended lab, Cymoxanil/F 20SC, leaves 14 d	120 3 x 120 6 x 120 9 x 120 12 x 120	mortality benef.capacity mortality benef.capacity mortality benef.capacity mortality benef.capacity mortality benef.capacity	22.5 24.8 40 28.6 37.5 27.5 23.9 23.9 21.2 16.5	50 %
<i>Typhlodromus pyri</i>	protonymphs	extended lab, Cymoxanil/F 20SC, leaves 14 d	1-6 x 159	mortality benef.capacity	25.3 65-89	50 %
<i>Typhlodromus pyri</i>	protonymphs	extended lab, Cymoxanil/F 52. 5WG, leaves 14 d	1-6 x 134 1-6 x 268	mortality benef.capacity mortality benef.capacity	34.7 85-100 42.4 100	50 %
<i>Chrysoperla carnea</i>	larvae	lab, 9 w Cymoxanil 50WP glass plate	480	mortality fecundity	7.1 9	50 %
<i>Chrysoperla carnea</i>	larvae	lab, 21+28 d Cymoxanil/F 20SC, glass plate	132	mortality fecundity	-7.3 17.3	50 %
<i>Chrysoperla carnea</i>	larvae	lab, 21+28 d Cymoxanil/F 50WG, glass plate	186	mortality fecundity	-8.4 4.1	

Ecotoxicology

Species	Life stage	Test substance, substrate and duration	Dose (g a.s./ha) ¹	End point	% effect ³	Trigger value
<i>Chrysoperla carnea</i>	larvae	extended lab, Cymoxanil/F 50 WG leaves 10 d	179 3 x 179 6 x 179	mortality mortality mortality	23 0 13	50 %
<i>Episyrphus balteatus</i>	larvae to adults	lab, 22 d Cymoxanil/F 50WG, glass plate	186	mortality fecundity	1.2 33.5	50 %
<i>Episyrphus balteatus</i>	larvae to adults	extended lab, Cymoxanil/F 20SC, leaves 3 w	289 3 x 289 6 x 289	mortality fecundity mortality fecundity mortality fecundity	1.1 33.4 -3.4 26.3 -0.3 23.2	50 %
<i>Episyrphus balteatus</i>	larvae to adults	extended lab, Cymoxanil/F 50 WG leaves 4 w	3 x 186 6 x 186	mortality fecundity mortality fecundity	0 69 7 50	50 %
<i>Episyrphus balteatus</i>	larvae to adults	semi-field, 14 d Cymoxanil/F 50WG, buck-wheat plants	181 363	mortality reproduction mortality reproduction	-1.3 -58.1 2.8 -94.6	50 %
<i>Poecilus cupreus</i>	adults	lab, 14 d Cymoxanil 50WP, glass plate	480	mortality	0	50 %
<i>Poecilus cupreus</i>	adults	lab, 14 d Cymoxanil/F 20SC, glass plate	132	mortality	0	50 %
<i>Poecilus cupreus</i>	adults	lab, 14 d Cymoxanil/F 50WG, glass plate	186	mortality	0	50 %
<i>Poecilus cupreus</i>	adults	extended lab, Cymoxanil/F 50 WG, soil 7 d	186 4 x 186 6 x 186 9 x 186	mortality mortality mortality mortality	0 0 0 0	50 %
<i>Poecilus cupreus</i>	adults	semi-field, 7 d Cymoxanil/F 20SC, silty sand soil	289 3 x 289 6 x 289	mortality mortality mortality	11.3 18.9 7.5	50 %
<i>Aleochara bilineata</i>	larvae to adults	lab, 10 w Cymoxanil/F 50WG, quartz sand	186	mortality parasitic capacity	7.5 2.6	50 %

F = Famoxadone

¹ initial residues

² site 1/site 2

³ positive percentages relate to adverse effects

Ecotoxicology

Field tests
<i>Typhlodromus pyri</i> : treatment of 6 x 120 – 168 g a.s./ha (Cymoxanil/F 52.5WG), vineyard: transient reductions in abundance (mites + eggs), no long-term effect
<i>Typhlodromus pyri</i> : treatment of 5 x 240 or 4 x 480 g a.s./ha (Cymoxanil/F 50WP), vineyard: no adverse effects on abundance (mites + eggs)

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point ¹
Earthworms			
<i>Eisenia foetida</i>	a.s. ‡	Acute 14 days	LC ₅₀ > 1000 mg a.s./kg d.w.soil
<i>Eisenia foetida</i>	Preparation Cymoxanil 50 WP	Acute	LC ₅₀ > 505 mg a.s./kg d.w.soil
<i>Eisenia foetida</i>	Preparation Cymoxanil/Famoxadone 52.5 WP	Acute	LC ₅₀ 297 mg a.s./kg d.w.soil
<i>Eisenia foetida</i>	Preparation Cymoxanil/Famoxadone 50 WG	Chronic	NOEC 6.6 mg a.s./kg soil dw
Other soil macro-organisms			
Soil mite	a.s. ‡		
/	Preparation		
Collembola			
/	a.s. ‡	Chronic	NOEC mg a.s./kg d.w.soil (mg a.s./ha)
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡		- 8.4 % effect at day 28 at 1.6 mg a.s./kg d.w.soil (1.2 kg a.s./ha)
	Cymoxanil/Famoxadone 20SC		- 0.3 % effect at day 28 at 0.016 mL prod./kg d.w.soil (1.44 kg a.s./ha)
Carbon mineralisation	a.s. ‡		- 15.5 % effect at day 28 at 1.6 mg a.s./kg d.w.soil (1.2 kg a.s./ha)
	Cymoxanil/Famoxadone 20SC		- 10 % effect at day 28 at 0.016 mL prod./kg d.w.soil (1.44 kg a.s./ha)
Field studies ²			
not required			

¹ indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})

² litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

Toxicity/exposure ratios for soil organisms

Lettuce, 4 x 240 g a.s./ha

Test organism	Test substance	Time scale	Soil PEC ² (mg/kg)	TER	Trigger
Earthworms					
<i>Eisenia foetida</i>	a.s. ‡	Acute	0.184	> 5435	10
<i>Eisenia foetida</i>	Cymoxanil 50 WP	Acute	0.184	> 2745	10
<i>Eisenia foetida</i>	Cymoxanil/Famoxadone 50 WG	Chronic	0.184	36	5
Other soil macro-organisms: no studies required					
Soil mite	a.s. ‡			/	
Collembola	a.s. ‡			/	

Potatoes, 5 x 120 g a.s./ha (Oxon)

Test organism	Test substance	Time scale	Soil PEC ² (mg/kg)	TER	Trigger
Earthworms					
<i>Eisenia foetida</i>	a.s. ‡	Acute	0.159	> 6289	10
<i>Eisenia foetida</i>	Cymoxanil 50 WP	Acute	0.159	> 3176	10
<i>Eisenia foetida</i>	Cymoxanil/Famoxadone 50 WG	Chronic	0.159	42	5
Other soil macro-organisms: no studies required					
Soil mite	a.s. ‡			/	
Collembola	a.s. ‡			/	

Potatoes, 8 x 175 g a.s./ha (DuPont)

Test organism	Test substance	Time scale	Soil PEC ² (mg/kg)	TER	Trigger
Earthworms					
<i>Eisenia foetida</i>	a.s. ‡	Acute	0.239	> 4184	10
<i>Eisenia foetida</i>	Cymoxanil/Famoxadone 52.5 WP	Acute	0.239	1241	10
<i>Eisenia foetida</i>	Cymoxanil/Famoxadone 50 WG	Chronic	0.239	28	5
Other soil macro-organisms: no studies required					
Soil mite	a.s. ‡			/	
Collembola	a.s. ‡			/	

Ecotoxicology

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Preliminary screening data

Not required

Laboratory dose response tests

Most sensitive species	Test substance	ER ₅₀ (g/ha) vegetative vigour	ER ₅₀ (g/ha) emergence	Exposure ¹ (g/ha)	TER	Trigger
lettuce						
<i>Allium cepa</i>	Cymoxanil 50 WP	> 240 g [a.s.]	/	18 [a.s.]	> 13	5
potatoes						
<i>Allium cepa</i>	Cymoxanil 50 WP	> 240 g [a.s.]	/	17 [a.s.]	> 14	5

¹ based on Ganzelmeier drift data at 1 m distance

Additional studies (e.g. semi-field or field studies)

not required

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	end point
Activated sludge	19.4 mg a.s./L

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	Parent (state name), Metabolite 1 (state name)
water	Parent (state name)
sediment	Metabolite 2 (state name)
groundwater	Parent (state name)

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

Active substance

RMS/peer review proposal

Preparation

RMS/peer review proposal

Level 3

Cymoxanil

Proposed Decision with Respect to the Application
for Inclusion of the Active Substance in Annex I

3 Proposed decision with respect to the application for inclusion of the active substance in Annex I

3.1 Background to the proposed decision

Physical and chemical properties

Concerning physical and chemical properties all studies required by Directive 91/414/EEC are available and were conducted according to Guideline requirements and GLP regulations. Cymoxanil acts as a fungicide for the control of *Phytophthora infestans* in potato and *Bremia lactucae* in lettuce. It works by contact and protectively and needs to be applied before the disease attack in a concentration of max. 240 g as/ha for lettuce and max. 175 g as/ha for potatoes.

Cymoxanil is formulated as a water dispersible granules or wettable powder and registered in several European countries using various trade names. A maximum number of 4 applications are recommended for lettuce and 10 for potatoes. Spraying is achieved by using standard equipment for field crops, like tractor mounted hydraulic field sprayer. The typical spray volumes are ranging between 500 L/ha to 800 L/ha for lettuce and 200 L/ha up to 1000 L/ha for potatoes, depending on the cultivated area in Europe (South, North).

Analytical methodology is available for the determination of the active substance in the technical material as well as in the formulated product. The methods are sufficiently validated.

The analytical method for residues in food/feed of plant origin is successfully validated since the LOQ's enable the enforcement of the relevant residue limits (at the time of evaluation). Methods for the determination of residues in soil, water and air are validated successfully. Confirmatory techniques for each matrix confirm the validity of the applied methods.

Mammalian toxicology

The available data on mammalian toxicology, mutagenicity and animal metabolism for the active substance are considered to adequately support the risk evaluation of cymoxanil in humans. Concerning toxicology and metabolism, all studies required by directive 91/414/EEC are available and are conducted according to guideline requirements; the majority of the studies submitted meets GLP regulations.

Cymoxanil was found to be harmful after oral ingestion; the active substance is of low acute toxicity when tested dermally or by the inhalation route. It is not irritating to skin and only slight irritating to eyes; classification and labelling with respect to possible skin sensitisation is considered necessary based on a positive M&K-test. Effects with regard to testes and

Ecotoxicology

epididymides observed in subchronic studies submitted (macroscopic changes and histological alterations) justify corresponding classification and labelling (R48/22). Concerning teratogenicity, cymoxanil has to be classified with R 63 ("Possible risk of harm to the unborn child"). No genotoxic, cancerogenic and fertility disturbing properties can be attributed to the test substance.

Harmful effects on the health of operators, bystanders, workers or consumers are not to be expected when the plant protection product is used in accordance with good plant protection practice and with regard to the intended uses.

Residues

The joint submitted Annex II studies by DuPont and Oxon offered principally the evaluation on residue data of cymoxanil with respect to the intended uses (lettuce, potato). The plant metabolism of cymoxanil investigated on lettuce heads and potato tubers showed an extensive and rapid degradation of cymoxanil in plant matrix (intermediates detected in lettuce only were IN-W3595, IN-KQ960 and IN-KP533; no intermediates could be identified in potato tubers) and led to natural products (i.e. mainly glycine, which was further conjugated/incorporated with/in carbohydrates and others). A small amount of cymoxanil was identified in lettuce metabolism studies only (DuPont: 2.1 % of TRR in lettuce surface wash; Oxon: 1.4 % of TRR in unwashed lettuce foliage). "No residue" of cymoxanil (<0.05 mg/kg) or structurally relevant metabolites were identified in/on lettuce or potato (supervised residue trials), rotational crops or in goat tissues or milk (ruminant metabolism). The chronic and acute risk assessment for human consumers on cymoxanil with regard to the intended GAP for lettuce (Oxon) and potato (DuPont/Oxon) show no unacceptable risk on long or short term intake of both commodities. The theoretical maximum intake (TMDI) accounted for 0.7 % of ADI (WHO, European diet, adult 60.0 kg bw) or 0.4 % of ADI (German VELs model, child, 16.15 kg bw) or 0.5 to 1.9 % of ADI (UK model, elderly-residential to infant, 61.6 to 8.7 kg bw). The large portion intake of lettuce and potato tubers amounted to 1.0 and 2.9 % of AfRD (German VELs model, child, 16.15 kg bw), respectively. Using the UK model, max. 1.1 % of AfRD for lettuce (4-6 year old child) and max. 9.6 % of AfRD for potato (infant) were calculated.

Fate and behaviour in the environment

Analysis of cymoxanil and metabolites in various soil degradation experiments allows for the conclusion that neither the parent nor the metabolites of cymoxanil are persistent in soil. The soil degradation rate of cymoxanil depends on the soil pH with slower rates under more acidic conditions. Neither cymoxanil nor its metabolites are expected to accumulate in soil under the conditions of intended uses. The 80th percentile annual concentration in leachates leaving the top 1 m soil layer for cymoxanil and soil metabolites were predicted to be less

Ecotoxicology

than $0.1 \mu\text{g L}^{-1}$ in all FOCUS scenarios. The low risk of cymoxanil and metabolites to leach into shallow groundwater is supported by a representative lysimeter study. In surface water cymoxanil and several metabolites were present $> 10 \%$, in the great majority owing to extensive hydrolysis of the parent. None of these compounds is persistent. It is considered that the major entry routes for the parent and almost all metabolites are likely to be via drift and soil runoff/drainage. In air cymoxanil shows a short half life and a low vapour pressure. Therefore, cymoxanil is unlikely to be subjected to long range transport.

Effects on non-target organisms

The available data on ecotoxicology are considered adequate to allow for a risk evaluation of cymoxanil and its metabolites with regard to non-target organisms.

Cymoxanil is of low toxicity to terrestrial vertebrates and soil organisms.

The toxicity of the active substance to fish and aquatic invertebrates is also low. Cymoxanil is very toxic to algae. However, the risk assessment for aquatic organisms demonstrated that the risk from exposure to cymoxanil applied with the plant protection product Cymoxanil 50 % WP is low. The risk to aquatic organisms from a use of Cymoxanil with the plant protection product Tanos is low provided that appropriate risk mitigation measures are implemented.

Cymoxanil is of low toxicity to bees and non-target arthropods. In conclusion, no unacceptable effects on terrestrial vertebrates, bees, non-target arthropods, non target terrestrial plants, soil organisms and water organisms are expected if the plant protection product is used in accordance with good plant protection practice with regard to the intended use and if appropriate risk mitigation measures are implemented.

3.2 Proposed decision concerning inclusion in Annex I

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

The information in section 3.2 has been removed upon request by the EU Commission as it relates to risk management recommendations or proposals.

-
- 3.3 Rational for the postponement of the decision to include the active substance in Annex I, or for the conditions and restrictions to be associated with a proposed inclusion in Annex I, as appropriate**

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

Level 4

Cymoxanil

Demand for Further information

WARNING: This document forms part of an EC evaluation data package and should not be used for registration. Registration must not be granted on the basis of this document.

4 Further information to permit a decision to be made, or to support a review of the conditions and restrictions associated with the proposed inclusion in Annex I

4.1 Identity of the active substance

See point 4.5 (Analytical methods for the determination of impurities)

4.2 Physical and chemical properties of the active substance

Oxidizing properties:

The test method for oxidizing properties of Cymoxanil is considered invalid, due to the fact that the reference mixture for an oxidizer failed to burn. Moreover the test results by both applicants are contradictory and inconclusive. The study should be repeated in an inert atmosphere.

4.3 Data on application and further information

No further data requirements.

4.4 Classification, packaging and labelling

No further data requirements.

4.5 Methods of analysis

Analytical methods for the determination of active ingredient and impurities:

Analytical methods for the determination of active ingredient

No further data requirements.

Analytical methods for the determination of impurities:

Applicant A (DuPont):

According to SANCO 3030/99 point 3.1.3 (*Confirmation of analyte identification*) to demonstrate specificity, information must be given on how the identity of the impurities was confirmed (spectroscopic methods).

Applicant B (Oxon):

According to SANCO 3030/99 point 3.1.3 (*Confirmation of analyte identification*) to demonstrate specificity, information must be given on how the identity of the impurities was confirmed (spectroscopic methods).

Analytical methods for the determination of the active ingredient in the formulation:

No further data requirements.

Analytical methods (residue) for plants and plant products:

No further data requirements.

Analytical methods (residue) for soil, water, air:

No further data requirements.

4.6 Toxicology and metabolism

No further data requirements.

4.7 Residue data

No further data requirements.

4.8 Environmental fate and behaviour

No further data requirements.

4.9 Ecotoxicology

No further data requirements.

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.