European Commission

Renewal Assessment Report of the Inclusion of the Active Substance in Annex I of the Regulation (EC) 1107/2009

Oxamyl 10SL

Volume 3 (CP)
ANNEX B.6
Toxicology and metabolism data and assessment of risks for humans

Rapporteur Member State: Italy
Co-Rapporteur Member State: France

December 2017

VERSION HISTORY

Date	Data points containing amendments or additions	Document identifier or version number
May 2016	First RAR of Italy	
December 2017	Revised RAR after comment CoRMS (France)	Yellow highlighted

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

Introduction

Oxamyl 10SL was not the representative formulation for the first EU approval review of oxamyl.

This document addresses the CP 7 data requirements (mammalian toxicology) related to Oxamyl 10SL.

Test substance specification can be determined from the test substance code which is a research and development code number given to a specific batch of produced material (either technical or formulated). The approximate composition of the material(s) used in the various tests is/are given in Table 1.

Table 1 Test substance specification

Test substance	Lot/Batch code	Type	Composition
2015 Submission			
Oxamyl 10SL	D1410-368	Soluble liquid formulation (SL)	100 g oxamyl/L
Oxamyl 10SL	D1410-381	Soluble liquid formulation (SL)	100 g oxamyl/L
Oxamyl 10SL	D1410-381B	Soluble liquid formulation (SL)	100 g oxamyl/L

The composition of Oxamyl 10SL used in the toxicological studies is provided in Oxamyl RAR vol. 4

Unless specifically indicated, all reports in this section are submitted to address mandatory data requirements for the approval of active substance.

Unless specifically indicated, all tests submitted in this section, which involve vertebrate animals, address mandatory data requirements which could not be met with alternative methods. Studies were conducted according to prescribed guidelines.

Unless specifically indicated, this section does not contain reports of studies duplicating previous tests on vertebrate animals.

B.6.1 **Acute toxicity of plant protection product**

Acute toxicity studies were conducted with Oxamyl 10SL. Summaries of these studies are presented below.

B.6.1.1 Oral toxicity

Study submitted to the EU for the first time in this submission.

B.6.1.1/01

Reference CP 7.1.1/01	Report:	[redacted] (1999); Vydate 10L: Acute oral toxicity study in male and female rats DuPont Report No.: DuPont-2140 Guidelines: EEC Method B.1. (1992), OECD 401 (1987), U.S. EPA 81-1 (1984), 59 NohSan No. 4200 (1985) Deviations: None Testing Facility: [redacted] Testing Facility Report No.: DuPont-2140 GLP: Yes Certifying Authority: Laboratories in the USA are not certified by any governmental agency, but are subject to regular inspections by the U.S. EPA.

Executive summary:

Oxamyl 10SL was mixed with deionised water and administered by single-dose oral gavage to fasted male and female rats (5/sex/dose) at doses of 22, 35, or 47 mg/kg body weight. Surviving animals were observed for clinical signs of toxicity, body weight effects, and mortality for up to 14 days after dosing. All rats were examined for gross pathological changes.

Oral LD_{50}	Males	=	41 mg/kg bw
	Females	=	38 mg/kg bw
	Sexes Combined	=	39 mg/kg bw

Mortality occurred in the 35 and 47 mg/kg groups. All deaths occurred on the day of dosing (Table 2). Clinical signs most often observed included tremors, muscle fasciculations, salivation, ocular discharge, wet perineum, and staining of various body parts. Other clinical signs included gasping, lethargy, alopecia, lung noise, hunched over posture, and diarrhoea. With the exception of alopecia and staining and one rat that exhibited ocular discharge through study termination, no clinical signs were observed after Test Day 3. No test substance-related weight loss occurred in male or female rats dosed at 22 or 47 mg/kg bw. Two males and one female dosed at 35 mg/kg bw exhibited weight loss of approximately 3 or 9% of the fasted body weight up to Test Day 3. No test substance-related gross lesions were observed at necropsy. A Category 2 classification, H300 Fatal if swallowed is applicable in accordance to Annex I - Part 3 - points 3.1.3 to 3.1.3.6.2.3 of Regulation (EC) No. 1272/2008 and its corresponding ATPs.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Oxamyl 10SL
   Lot/Batch #: D1410-381
   Purity: 100 g a.s./L
   Description: Green liquid
   Stability of test compound: Not determined
2. Vehicle and/or positive control: Deionised water
3. Test animals
   Species: Rat
   Strain: Crl:CD®(SD)IGS BR
   Age at dosing: 57 or 59 days (males); 78 or 80 days (females)
   Weight at dosing: 210.0-260.1 g for males; 193.6-218.4 g for females
   Source: [redacted]
   Acclimation period: 6 days
   Diet: PMI® Nutrition International, LLC Certified Rodent LabDiet® (#5002), *ad libitum*
   Water: Tap water, *ad libitum*
   Housing: Animals were housed singly in stainless steel, wire-mesh cages suspended above cage boards.
4. Environmental conditions
   Temperature: 22–24°C
   Humidity: 40–60%
   Air changes: Not recorded
   Photoperiod: Alternating 12-hour light and dark cycles

B. STUDY DESIGN AND METHODS

1. In-life initiated/completed

   08-January-1999 to 27-January-1999

2. Animal assignment and treatment

   Doses of 22, 35, or 47 mg/kg bw were selected. Following an overnight fast (approximately 17 hours), rats were given a single dose of Oxamyl 10SL by gavage. The test substance was mixed with deionised water and administered at volumes of approximately 4.4, 7.0, and 9.4 mL/kg bw. Animals were observed for mortality and signs of illness, injury, or abnormal behaviour daily. The animals were observed for clinical signs daily (weekends excluded unless warranted by the condition of the rats). The animals were weighed daily until no significant weight loss was present and on Test Days 8 and 15. On Test Day 15, surviving animals were euthanised and all animals were necropsied to detect grossly observable evidence of organ or tissue damage or dysfunction.

3. Statistics

   The data did not warrant statistical analysis.

II. RESULTS AND DISCUSSION

A. MORTALITY

All deaths occurred on the day of dosing. Details are provided in Table 2.

Table 2 Acute oral toxicity of Oxamyl 10SL: Doses, mortality/animals treated, oral LD_{50}

Dose (mg/kg bw)	Males[a]	Females[a]	Sexes Combined
22	0/5	0/5	0/10
35	1/5	2/5	3/10
47	4/5	4/5	8/10
Oral LD_{50}:	**41 mg/kg bw**	**38 mg/kg bw**	**39 mg/kg bw**

[a] number of animals died/number of animals in dose group

B. CLINICAL OBSERVATIONS

Clinical signs most often observed included tremors, muscle fasciculations, salivation, ocular discharge, wet perineum, and staining of various body parts. Other clinical signs included gasping, lethargy, alopecia, lung noise, hunched over posture, and diarrhoea. With the exception of alopecia and staining and one rat that exhibited ocular discharge through study termination, no clinical signs were observed after Test Day 3.

C. BODY WEIGHT

No test substance-related weight loss occurred in male or female rats dosed at 22 or 47 mg/kg bw. Weight loss of approximately 4% of the fasted body weight occurred in one male rat dosed at 22 mg/kg bw. This weight loss was attributed to food inadvertently not being returned to this rat until approximately 24 hours after dosing. Two males and one female dosed at 35 mg/kg bw exhibited weight loss of approximately 3 or 9% of the fasted body weight up to Test Day 3.

D. NECROPSY AND GROSS PATHOLOGY

No gross lesions attributed to treatment were present in the rats at necropsy.

III. CONCLUSIONS

The acute oral LD_{50} for Oxamyl 10SL in fasted rats was 41 and 38 mg/kg of body weight for males and females, respectively. A Category 2 classification, H300 Fatal if swallowed is applicable in accordance to Annex I - Part 3 - points 3.1.3 to 3.1.3.6.2.3 of Regulation (EC) No. 1272/2008 and its corresponding ATPs.

RMS comments and conclusion for the renewal

The study is acceptable as a key study.

It is noted that the OECD TG used has been replaced and is no more valid; however this was in 2001, after the completion of this study, which is therefore acceptable.

B.6.1.2Dermal toxicity

Study submitted to the EU for the first time in this submission.

B.6.1.2/01

Reference CP 7.1.2/01	Report:	Report: [redacted] (1999); Vydate 10L: Acute dermal toxicity study in rats DuPont Report No.: DuPont-2130 Guidelines: U.S. EPA 81-2 (1984), OECD 402 (1987), EEC Method B.3. (1992), 59 NohSan No. 4200 (1985) Deviations: None Testing Facility: [redacted] Testing Facility Report No.: DuPont-2130 GLP: Yes Certifying Authority: Laboratories in the USA are not certified by any governmental agency, but are subject to regular inspections by the U.S. EPA.

Executive summary:

A single dose of Oxamyl 10SL was applied to the shaved, intact skin of 5 male and 5 female rats at a dose of 5000 mg/kg body weight. The application site covered approximately 10% of each animal's body surface area. The application site was semi-occluded for 24 hours after which the test substance was removed. The rats were observed for clinical signs, body weight effects, and mortality for up to 14 days following application. All animals were examined for gross pathological changes.

Dermal LD_{50}	Males	=	>5000 mg/kg bw
	Females	=	>5000 mg/kg bw
	Combined	=	>5000 mg/kg bw

No mortalities were observed (Table 3). No clinical signs of toxicity were noted associated with test substance treatment. There were no test substance-related body weight effects noted. No test substance-related gross lesions were observed at necropsy. In accordance with the provisions of Regulation (EC) No. 1272/2008 for classification criteria, classification of Oxamyl 10SL by the dermal route is not required.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material: Oxamyl 10SL
   Lot/Batch #: D1410-381
   Purity: 100 g a.s./L
   Description: Green liquid
   Stability of test compound: Not determined.
2. Vehicle and/or positive control: Test material dosed as received.
3. Test animals
   Species: Rat
   Strain: Crl:CD®(SD)IGS BR
   Age at dosing: 9 weeks (males); 12 weeks (females)
   Weight at dosing: 297.1–328.9 g for males; 217.3–251.6 g for females
   Source: [redacted]
   Acclimation period: 6 days
   Diet: PMI® Nutrition International, LLC Certified Rodent LabDiet® (#5002), *ad libitum*
   Water: Tap water, *ad libitum*
   Housing: Animals were housed singly in stainless steel, wire-mesh cages suspended above cage boards.
4. Environmental conditions
   Temperature: 22-24°C
   Humidity: 40-60%
   Air changes: Not recorded
   Photoperiod: Alternating 12-hour light and dark cycles

B. STUDY DESIGN AND METHODS

1. In-life initiated/completed

   12-January-1999 to 26-January-1999

2. Animal assignment and treatment

   A dose of 5000 mg/kg body weight was selected for this study. Approximately 24 hours before dosing, the fur of each animal was closely shaved to expose the back from the scapular to the lumbar region (approximately 10% of each animal's body surface area). A single dose of Oxamyl 10SL was applied to the intact skin of 5 males and 5 females per dose group. The application site was covered with a porous gauze dressing. After 24 hours, excess test substance was washed from the dorsal skin of each animal with warm water and the skin was dried with a paper towel. Animals were observed for mortality and signs of illness, injury, or abnormal behaviour daily. The animals were observed for clinical signs daily (weekends excluded). Observations for dermal irritation were made daily. Dermal effects were scored according to the Draize Scale. The animals were weighed on Test Days 0, 1, 2, 8 and 15. On Test Day 15, surviving animals were euthanised and all animals were necropsied to detect grossly observable evidence of organ or tissue damage or dysfunction.

3. Statistics

   The data did not warrant statistical analysis.

II. RESULTS AND DISCUSSION

A. MORTALITY

No mortalities occurred. Details are provided in Table 3.

Table 3 Acute dermal toxicity of Oxamyl 10SL: Doses, mortality/animals treated, dermal LD_{50}

Dose (mg/kg bw)	Males[a]	Females[a]	Combined[a]
5000	0/5	0/5	0/10
Dermal LD_{50}:	**>5000 mg/kg bw**	**>5000 mg/kg bw**	**>5000 mg/kg bw**

[a] number of animals died/number of animals in dose group

B. CLINICAL OBSERVATIONS

No clinical signs of toxicity or dermal irritation were noted associated with test substance treatment.

C. BODY WEIGHT

There were no test substance-related body weight effects noted.

D. NECROPSY AND GROSS PATHOLOGY

No gross lesions were present in the rats at necropsy.

III. CONCLUSIONS

The dermal LD_{50} for Oxamyl 10SL was greater than 5000 mg/kg body weight for both male and female rats. In accordance with the provisions of Regulation (EC) No. 1272/2008 for classification criteria, classification of Oxamyl 10SL by the dermal route is not required.

RMS comments and conclusion for this renewal

The study is acceptable as a key study.

B.6.1.3Inhalation toxicity

Study submitted to the EU for the first time in this submission.

B.6.1.3/01

Reference CP 7.1.3/01	Report:	[redacted] (1998); Oxamyl 10% (non voc) liquid formulation: Inhalation median lethal concentration (LC50) study in rats DuPont Report No.: HL-1998-01611 Guidelines: U.S. EPA 81-3 (1984), 59 Nohsan No. 4200 (1985), EEC Method B.2. (1992), OECD 403 (1981) Deviations: None Testing Facility: [redacted] Testing Facility Report No.: HL-1998-01611 GLP: Yes Certifying Authority: Laboratories in the USA are not certified by any governmental agency, but are subject to regular inspections by the U.S. EPA.

Executive summary:

Oxamyl 10SL (100 g a.s./L), suspended in air, was administered as a single four-hour, nose-only, aerosol exposure to rats. Five groups of 5 male and 5 female rats were exposed to 0.30, 0.32, 0.51, 0.56, or 0.66 mg/L of

the test substance. Animals were observed for clinical signs of toxicity, body weight effects and mortality for up to 14 days after dosing. All animals were examined for gross pathological changes.

Inhalation LD_{50} Combined = 0.62 mg/L

Mortalities occurred in the 0.51, 0.56, or 0.66 mg/L groups. All mortalities occurred during the exposure period, with the exception of one female at 0.66 mg/L that died by Test Day 3 (Table 5). Clinical signs of toxicity immediately following the exposure and during the 14-day recovery period included hunched posture, gasping, irregular respiration, tremors, muscle fasciculation, abnormal gait/mobility, immobility, nasal/ocular discharge, corneal opacity, diarrhoea, and salivation. Surviving rats exhibited slight to severe body weight loss up to 3 days following exposure but experienced an overall weight gain by the end of the 14-day recovery period. No test substance-related gross lesions were observed at necropsy. In accordance with the provisions of inhalation Category 3 is applicable in accordance to Annex I - Part 3 points 3.1.3 to 3.1.3.6.2.3 of Regulation (EC) No. 1272/2008 and its corresponding ATPs for classification criteria, Oxamyl 10SL is classified as H331 toxic if inhaled.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:	Oxamyl 10SL
Lot/Batch #:	D1410-368
Purity:	100 g a.s./L
Description:	Clear liquid
Stability of test compound:	Not determined.
2. Vehicle and/or positive control:	Oxamyl 10SL was suspended in air.
3. Test animals	
Species:	Rat
Strain:	Crl:CD®(SD)IGS BR
Age at dosing:	Approximately 8 weeks old
Weight at dosing:	235–294 g for males; 172–204 g for females
Source:	[redacted]
Acclimation period:	6 days
Diet:	PMI® Nutrition International, LLC Certified Rodent LabDiet® (#5002), *ad libitum*
Water:	Tap water, *ad libitum*
Housing:	Animals were housed singly in stainless steel, wire-mesh cages suspended above cage boards.
4. Environmental conditions	
Temperature:	22-24°C
Humidity:	40-60%
Air changes:	Not recorded
Photoperiod:	Alternating 12-hour light and dark cycles

B. STUDY DESIGN AND METHODS

1. In-life initiated/completed

13-April-1998 to 12-May-1998

2. Animal assignment and treatment

Five groups of 5 male and 5 female rats each were exposed to 0.30, 0.32, 0.51, 0.56, or 0.66 mg/L of the test substance suspended in air for a single 4-hour period. During exposure, animals were individually restrained in perforated stainless steel cylinders with conical nose pieces. The restrainers were inserted into a polymethylmethacrylate faceplate attached to the exposure chamber so that the nose of each animal extended into the exposure chamber. Animals were observed for mortality and response to alerting stimuli during the exposure and observed for mortality and clinical signs of toxicity immediately after they were removed from the restrainers following exposure. During a 14-day post exposure period, all surviving rats were observed each day for mortality, and were weighed and

observed for clinical signs of toxicity 5 to 7 times per week. At the end of the 14-day recovery period, all surviving animals were necropsied and all animals were examined for gross pathological changes.

3. Generation of the test atmosphere/chamber description

The test substance was metered into a Spraying Systems nebuliser with a Harvard Apparatus Model 22 syringe infusion pump. Filtered, high-pressure air was metered into the nebuliser and carried the resulting atmosphere into the 29-L exposure chamber. The atmospheric concentration of Oxamyl 10SL was determined by gravimetric analysis at approximately 30-minute intervals during the exposure period. HPLC analysis was performed on 3 of the samples collected for gravimetric analysis per dose level. The filters were desorbed by sonication in acetonitrile and analysed using a Zorbax RX-C8 column and a diode array detector. Samples to determine particle size distribution were taken during the exposure with a Sierra® Series 210 cyclone pre-separator/cascade impactor and Sierra® Series 110 constant flow air sampler.

Table 4 Acute inhalation toxicity of Oxamyl 10SL: Exposure atmosphere characteristics

Parameter	Value
Flow rate	35 L/min
Nominal concentration(s)[a]	Analytical concentration(s)[b]
1.13 mg/L	0.30 ± 0.054 mg/L
0.83 mg/L	0.32 ± 0.057 mg/L
1.5 mg/L	0.51 ± 0.089 mg/L
1.2 mg/L	0.56 ± 0.11mg/L
1.7 mg/L	0.66 ± 0.087mg/L
Particle size MMAD[c]/GSD[d]	1.6-2.7 µm/2.0-2.3
Particles <1 µm (% w/w)	11-24%
Particles <3 µm (% w/w)	54-83%
Particles <10 µm (% w/w)	94 to >99%

[a] Theoretical atmospheric concentration calculated when the total amount of test substance delivered to the chamber is divided by the total airflow for the exposure.

[b] Mean ± standard deviation of analytically determined concentrations by gravimetric analyses from chamber samples.

[c] MMAD = mass median aerodynamic diameter

[d] GSD = geometric standard deviation

4. Statistics

The data did not warrant statistical analysis.

II. RESULTS AND DISCUSSION

A. MORTALITY

All mortalities occurred during the exposure period, with the exception of one female at 0.66 mg/L that died by Test Day 3. Details are provided in Table 5.

Table 5 Acute inhalation toxicity of Oxamyl 10SL: Doses, mortality/animals treated, inhalation LC_{50}

Dose (mg/L)	Males[a]	Females[a]	Combined[a]
0.30	0/5	0/5	0/10
0.32	0/5	0/5	0/10
0.51	0/5	1/5	1/10
0.56	3/5	1/5	4/10
0.66	2/5	4/5	6/10
Inhalation LC_{50}:	0.69 mg/L	0.61 mg/L	**0.62 mg/L**

[a] number of animals died/number of animals in dose group

B. CLINICAL OBSERVATIONS

Clinical signs of toxicity immediately following the exposure and during the 14-day recovery period included hunched posture, gasping, irregular respiration, tremors, muscle fasciculation, abnormal gait/mobility, immobility, nasal/ocular discharge, corneal opacity, diarrhoea, and salivation.

C. BODY WEIGHT

Surviving rats exhibited slight to severe body weight loss up to 3 days following exposure but experienced an overall weight gain by the end of the 14-day recovery period.

D. NECROPSY AND GROSS PATHOLOGY

No gross lesions were present in the rats at necropsy.

III. CONCLUSIONS

The acute inhalation LC_{50} for Oxamyl 10SL in rats was 0.62 mg/L for males and females combined. Looking at the separate values for the two sexes, the lowest one is that obtained for females (0.61 mg/L), which is very similar to the combined one. In accordance with the provisions of inhalation Category 3 is applicable in accordance to Annex I - Part 3 points 3.1.3 to 3.1.3.6.2.3 of Regulation (EC) No. 1272/2008 and its corresponding ATPs for classification criteria, Oxamyl 10SL is classified as H331 toxic if inhaled.

RMS comments and conclusion for this renewal

The study is acceptable as a key study.

B.6.1.4 Skin irritation

Study submitted to the EU for the first time in this submission.

B.6.1.4/01

Reference CP 7.1.4/01	Report:	[redacted] (1999); Vydate 10L: Primary dermal irritation study in rabbits DuPont Report No.: DuPont-2024 Guidelines: U.S. EPA 81-5 (1984), OECD 404 (1992), 59 NohSan No. 4200 (1985), EEC Method B.4. (1992) # Deviations: None Testing Facility: [redacted] Testing Facility Report No.: DuPont-2024 GLP: Yes Certifying Authority: Laboratories in the USA are not certified by any governmental agency, but are subject to regular inspections by the U.S. EPA.

Executive summary:

Oxamyl 10SL was applied as a single 0.5 mL dermal dose to the shaved intact skin of 6 male rabbits. The rabbits were exposed to the test substance for 4 hours after which the test substance was removed. Test sites were evaluated by Draize (1959) for signs of dermal irritation 1, 22, 48, and 72 hours after test substance removal.

Although the skin of the rabbits was stained by the test substance, the test sites could be evaluated for erythema. No dermal irritation was observed in two rabbits. Of the remaining 4 rabbits, at 1 hour and 22 hours, no dermal irritation was observed in 1 rabbit, and well-defined erythema was observed in 3 rabbits. At 48 hours, very slight erythema was observed in 1 rabbit; the remaining 3 rabbits exhibited no dermal irritation. No dermal irritation was observed at 72 hours. No oedema or clinical signs of toxicity were observed. Based on the mean degree of skin reaction observed at 22 to 72 hours, and according to the provisions of Regulation (EC) No. 1272/2008 for classification criteria, classification of Oxamyl 10SL as a skin irritant is not required.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:	Oxamyl 10SL
Lot/Batch #:	D1410-381
Purity:	100 g a.s./L
Description:	Green liquid
Stability of test compound:	Not determined.
2. Vehicle and/or positive control:	Test material dosed as received.
3. Test animals	
Species:	Rabbit
Strain:	New Zealand White
Age at dosing:	Young adult
Weight at dosing:	2208–2538 g for males
Source:	[redacted]
Acclimation period:	14 days
Diet:	PMI® Nutrition International, LLC Certified Rabbit LabDiet® (#5322), approximately 125 g per day
Water:	Tap water, *ad libitum*
Housing:	Animals were housed singly in stainless steel, wire-mesh cages suspended above cage boards.
4. Environmental conditions	
Temperature:	19-21°C
Humidity:	40-60%
Air changes:	Not recorded
Photoperiod:	Alternating 12-hour light and dark cycles

B. STUDY DESIGN AND METHODS

1. In-life start/completion

07-January-1999 to 10-January-1999

2. Animal assignment and treatment

Oxamyl 10SL was applied as a single 0.5 mL dermal dose to the shaved intact skin of 6 male young adult New Zealand White rabbits. The test substance was applied to a 6 cm^2 area of skin. The application area was covered with a 1-inch, 2-ply gauze square that was held in place with non-irritating tape and covered with rubber sheeting for a semi-occlusive dressing. The rabbits were exposed to the test substance for 4 hours after which the test substance was removed. Test sites were evaluated by Draize (1959) for signs of dermal irritation 1, 22, 48, and 72 hours after test substance removal.

II. RESULTS AND DISCUSSION

Although the skin of the rabbits was stained by the test substance, the test sites could be evaluated for erythema. No dermal irritation was observed in two rabbits. Of the remaining 4 rabbits, at 1 hour and 22 hours, no dermal irritation was observed in 1 rabbit, and well-defined erythema was observed in 3 rabbits. At 48 hours, very slight erythema was observed in 1 rabbit; the remaining 3 rabbits exhibited no dermal irritation. No dermal irritation was observed at 72 hours. No oedema or clinical signs of toxicity were observed.

Table 6 Individual and mean dermal irritation scores according to Draize (1959)

	Time	Erythema						Oedema				
	33346[a]	33347[a]	33348[a]	33350[a]	33352[a]	33353[a]	33346[a]	33347[a]	33348[a]	33350[a]	33352[a]	33353[a]
1 h	0	0	2	2	0	2	0	0	0	0	0	0
22h	0	0	2	2	2	0	0	0	0	0	0	0
48 h	0	0	0	0	1	0	0	0	0	0	0	0
72 h	0	0	0	0	0	0	0	0	0	0	0	0
Mean scores 22-72 h	0.39						0.00					
Additional criteria specified in Directive 93/21/EEC Point 3.2.6.1 fulfilled: Yes												

[a] Animal number

III. CONCLUSIONS

Based on the mean degree of skin reaction observed at 22 to 72 hours, and according to the provisions of Regulation (EC) No. 1272/2008 for classification criteria, classification of Oxamyl 10SL as a skin irritant is not required.

RMS comments and conclusion for this renewal

The study is acceptable as a key study.

B.6.1.5 Eye irritation

Study submitted to the EU for the first time in this submission.

B.6.1.5/01

Reference CP 7.1.5/01	Report:	[redacted] (1999); Vydate 10L: Primary eye irritation study in rabbits DuPont Report No.: DuPont-2040 Guidelines: U.S. EPA 81-4 (1984), OECD 405 (1987), EEC Method B.5. (1992), 59 NohSan No. 4200 (1985) Deviations: None Testing Facility: [redacted] Testing Facility Report No.: DuPont-2040 GLP: Yes Certifying Authority: Laboratories in the USA are not certified by any governmental agency, but are subject to regular inspections by the U.S. EPA.

Executive summary:

A single dose of 0.1 mL of Oxamyl 10SL was administered into the lower conjunctival sac of the right eye of 6 male young adult New Zealand White rabbits. The pH of the test substance was determined to be 2.55. Because of anticipated clinical signs of toxicity and since marked effects were expected due to the low pH of the test material, 1 rabbit was initially treated. The remaining 5 rabbits were treated the following day when it was

apparent the test substance was not a severe eye irritant. The eyes remained unwashed after treatment. The conjunctiva, iris, and cornea of each treated eye were evaluated for evidence of irritation approximately 1, 24, 48, and 72 hours following administration of the test substance.

The pupil of the treated eye of all rabbits was constricted on the day of treatment. The pupils were normal by the day after treatment. Oxamyl 10SL produced conjunctival redness (score of 1) in the treated eye of all of the rabbits. In addition, iritis (score of 1) was observed in the treated eye of 2 rabbits, and conjunctival chemosis (score of 1) was observed in the treated eye of 1 rabbit. The treated eye of 1 rabbit was normal by 24 hours, 3 were normal by 48 hours, and 2 were normal by 72 hours. One rabbit pawed its treated eye after instillation. Based on the mean degree of eye irritation observed at 24 to 72 hours, and according to the provisions of Regulation (EC) No. 1272/2008 for classification criteria, classification of Oxamyl 10SL as an eye irritant is not required.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:	Oxamyl 10SL
Lot/Batch #:	D1410-381B
Purity:	100 g a.s./L
Description:	Green liquid
Stability of test compound:	Not determined.
2. Vehicle and/or positive control:	Test material dosed as received.
3. Test animals	
Species:	Rabbit
Strain:	New Zealand White
Age at dosing:	Young adult
Weight at dosing:	2189–2463 g for males
Source:	[redacted]
Acclimation period:	14 days
Diet:	PMI® Nutrition International, LLC Certified Rabbit LabDiet® (#5322), approximately 125 g per day
Water:	Tap water, *ad libitum*
Housing:	Animals were housed singly in stainless steel, wire-mesh cages suspended above cage boards.
4. Environmental conditions	
Temperature:	19-21°C
Humidity:	40-60%
Air changes:	Not recorded
Photoperiod:	Alternating 12-hour light and dark cycles

B. STUDY DESIGN AND METHODS

1. In-life start/completion

11-January-1999 to 15-January-1999

2. Animal assignment and treatment

A single dose of 0.1 mL of Oxamyl 10SL was administered into the lower conjunctival sac of the right eye of 6 male young adult New Zealand White rabbits. The pH of the test substance was determined to be 2.55. Because of anticipated clinical signs of toxicity and since marked effects were expected due to the low pH of the test material, 1 rabbit was initially treated. The remaining 5 rabbits were treated, as there was no severe irritant response in the first animal. The eyes were not rinsed after introduction of the test substance. The conjunctiva, iris, and cornea of each treated eye were evaluated for evidence of irritation approximately 1, 24, 48, and 72 hours following administration of the test substance using the Draize scale.

II. RESULTS AND DISCUSSION

The pupil of the treated eye of all rabbits was constricted on the day of treatment. The pupils were normal by the day after treatment. Oxamyl 10SL produced conjunctival redness (score of 1) in the treated eye of all of the

rabbits. In addition, iritis (score of 1) was observed in the treated eye of 2 rabbits, and conjunctival chemosis (score of 1) was observed in the treated eye of 1 rabbit. The treated eye of 1 rabbit was normal by 24 hours, 3 were normal by 48 hours, and 2 were normal by 72 hours. One rabbit pawed its treated eye after instillation. Weight loss of approximately 3% of initial body weight was observed in 1 rabbit by study termination (72 hours).

Table 7 Individual and mean eye irritation scores according to Draize (1959)

Cornea						
Animal no.	33349	33363	33364	33365	33356	33357
1 hour	0[a]	0[a]	0[a]	0[a]	0[a]	0[a]
24 hours	0	0	0	0	0	0
48 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0
Overall Average of Means (24-72 h): 0.00						
Iris						
Animal no.	33349	33363	33364	33365	33356	33357
1 hour	1	0	0	1	0	0
24 hours	0	0	0	0	0	0
48 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0
Overall Average of Means (24-72 h): 0.00						
Conjunctiva-redness						
Animal no.	33349	33363	33364	33365	33356	33357
1 hour	1	1	1	1	1	1
24 hours	1	0	1	1	1	1
48 hours	0	0	1	1	0	0
72 hours	0	0	0	0	0	0
Overall Average of Means (24-72 h): 0.39						
Conjunctiva-chemosis						
Animal no.	33349	33363	33364	33365	33356	33357
1 hour	0	0	0	0	1	0
24 hours	0	0	0	0	0	0
48 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0
Overall Average of Means (24-72 h): 0.00						
Additional criteria specified in Directive 93/21/EEC Point 3.2.6.2 fulfilled: Yes						

[a] The pupil of the treated eye was constricted

III. CONCLUSIONS

Based on the mean degree of eye irritation observed at 24 to 72 hours, and according to the provisions of Regulation (EC) No. 1272/2008 for classification criteria, classification of Oxamyl 10SL as an eye irritant is not required.

RMS comments and conclusion for this renewal

The study is acceptable as a key study.

B.6.1.6Skin sensitisation

Study submitted to the EU for the first time in this submission.

B.6.1.6/01

Reference CP 7.1.6/01	Report:	[redacted] [redacted] (1999); Vydate 10L: Evaluation of the potential dermal sensitization in the guinea pig (modified Buehler method) DuPont Report No.: DuPont-2016 Guidelines: 59 NohSan No. 4200 (1985), OECD 406 (1992), EEC Method B.6. (1992), U.S. EPA 81-6 (1984) Deviations: None Testing Facility: [redacted] Testing Facility Report No.: 99881 GLP: Yes Certifying Authority: Laboratories in the USA are not certified by any governmental agency, but are subject to regular inspections by the U.S. EPA.

Executive summary:

The dermal sensitisation potential of Oxamyl 10SL was evaluated by the Modified Buehler method in male albino guinea pigs. Twenty animals were topically induced with 0.5 mL of the test substance. This procedure was performed once a week for three weeks (3 six-hour applications). After the third induction application, animals were rested for 15 days before receiving a challenge concentration of 0.5 mL of the test substance on the clipped, naive, right flank. Approximately 24 and 48 hours after challenge application, the test sites were evaluated for dermal irritation or elicited sensitisation. No contemporaneous positive control was evaluated; however, α-hexylcinnamaldehyde is periodically tested in order to document the effect of a known sensitiser in this test system.

No test substance-related dermal irritation was observed following the induction or challenge phases. The percentage of sensitisation at 24 and/or 48 hours for the test article animals was 0%. No responses were noted in the vehicle control. Appropriate historical control data using α-hexylcinnamaldehyde demonstrated a positive response. According to the classification criteria under Regulation (EC) No. 1272/2008, classification is not required.

I. MATERIALS AND METHODS

A. MATERIALS

1. Test material:	Oxamyl 10SL
Lot/Batch #:	D1410-381
Purity:	100 g a.s./L
Description:	Green liquid
Stability of test compound:	Not determined.
2. Vehicle and/or positive control:	Normal saline
3. Test animals	
Species:	Guinea pig
Strain:	Hartley albino
Age at dosing:	Young adult
Weight at dosing:	325 – 455 g for males
Source:	[redacted]
Acclimation period:	6 or 13 days
Diet:	Purina Certified Guinea Pig diet (#5026), *ad libitum*
Water:	Tap water, *ad libitum*
Housing:	Animals were group housed in stainless steel cages with wire-mesh floors suspended above cage boards
4. Environmental conditions	
Temperature:	19-26°C
Humidity:	2-82%
Air changes:	Not recorded
Photoperiod:	Alternating 12-hour light and dark cycles

B. STUDY DESIGN AND METHODS

1. Experimental start/completion

26-January-1999 to 05-March-1999

2. Animal assignment and treatment

Range-finding study: Preliminary irritation was evaluated by exposing a group of 4 animals to 0.5 mL of two concentrations of test substance (undiluted and a 50% dilution) to determine the appropriate concentration of the test substance for topical induction and challenge. Since no dermal irritation was observed at any concentration tested, 0.5 mL of the undiluted test material was selected for topical induction and challenge.

Main study: Twenty male guinea pigs were topically induced with 0.5 mL of the test substance on the left flank of each animal. This procedure was performed once a week for three weeks (3 six-hour applications). After the third induction application, animals were rested for 15 days before receiving a challenge concentration of 0.5 mL of the test substance on the clipped, naive, right flank. Approximately 24 and 48 hours after induction treatments, the test sites were evaluated for dermal irritation and signs of elicited sensitisation. Very faint redness (usually non-confluent, score of 0.5) was not considered a positive dermal reaction. Scores of 1 (faint redness, usually confluent) or greater were required to be indicative of sensitisation. Vehicle control animals were challenged with both Oxamyl 10SL and normal saline. No contemporaneous positive control was evaluated; however α-hexylcinnamaldehyde is periodically tested in order to document the effect of a known sensitiser in this test system.

II. RESULTS AND DISCUSSION

No test substance-related dermal irritation was observed during the induction or challenge phases. The percentage of sensitisation at 24 and/or 48 hours for the test article animals was 0%. No responses were noted in the vehicle control animals. Appropriate historical control data using α-hexylcinnamaldehyde demonstrated a positive response. No test substance-related clinical signs of toxicity or body weight effects were observed.

Table 8 Modified Buehler test with Oxamyl 10SL: Dermal response to challenge

Group	24 hours	48 hours
Oxamyl 10SL	0/20[a]	0/20
Normal saline	0/10	0/10
Positive control	9/20	

[a] number of animals with positive dermal response/number of animals in dose group

III. CONCLUSIONS

Oxamyl 10SL does not possess skin sensitising potential under the conditions of the Modified Buehler test. According to the classification criteria under Regulation (EC) No. 1272/2008, classification is not required.

RMS comments and conclusion for this renewal

The study is acceptable as a key study

B.6.1.7 Supplementary studies on the plant protection product

No supplementary studies are required to satisfy the data requirements for registration of Oxamyl 10SL.

B.6.1.8 Supplementary studies for combinations of plant protection products

No supplementary studies are required to satisfy the data requirements for registration of Oxamyl 10SL.

B.6.1.9 Summary of acute toxicity

Table 9 Summary of acute toxicity data for Oxamyl 10SL

Type of study	Species	Results	Reference
Acute oral LD_{50}	Rat	LD_{50} = 38 mg/kg	DuPont-2140
Acute dermal LD_{50}	Rat	LD_{50} =>5000 mg/kg	DuPont-2130
Acute inhalation LC_{50} (4 h)	Rat	LC_{50} = 0.62 mg/L	HL-1998-01611
Skin irritation	Rabbit	Not irritating	DuPont-2024
Eye irritation	Rabbit	Not irritating	DuPont-2040
Skin sensitisation (Buehler test)	Guinea Pig	Not sensitising	DuPont-2016

Oxamyl 10SL was highly toxic by the oral route of exposure with an LD_{50} of 38 mg/kg bw. It was also found to be toxic by the inhalation route with an LC_{50} of 0.62 mg/L. In contrast, by the dermal route of exposure it was not toxic as the LD_{50} was found to be >5000 mg/kg bw. Oxamyl 10SL was not irritating to the eyes or skin of rabbits and was found not to be a sensitiser in a modified Buehler study which was conducted in lieu of the Guinea Pig Maximization study as the material is highly toxic if dosed systemically.

In accordance with Regulation (EC) No. 1272/2008, classification of Oxamyl 10SL for acute oral and inhalation toxicity is required. Acute oral Category 2 is applicable in accordance to Annex I - Part 3 - points 3.1.3 to 3.1.3.6.2.3 of Regulation (EC) No. 1272/2008 and its corresponding ATPs. Acute inhalation Category 3 is applicable in accordance to Annex I - Part 3 points 3.1.3 to 3.1.3.6.2.3 of Regulation (EC) No. 1272/2008 and its corresponding ATPs. Therefore, hazard statements, H300 Fatal if swallowed and H331 Toxic if inhaled apply to Oxamyl 10SL. Classification for acute dermal, skin and eye irritation, and dermal sensitisation is not required.

There is evidence that absorption of the material through the eyes can result in neurotoxic symptoms (pupil constriction) characteristic of the carbamates. Also in extreme exposure cases this could be fatal.

B.6.2 **Dermal absorption**

Although Oxamyl 10SL was not the representative formulation supporting the authorisation of oxamyl in the EU in the first approval review, the extent of absorption of Oxamyl 10SL concentrate through skin was assessed in an *in vivo* dermal absorption study in rats and in a comparative *in vitro* dermal absorption study using rat and human skin. All relevant data were included in the Oxamyl DAR and are considered adequate. These studies were reviewed by the RMS at the time of Annex 1 renewal in the EU Dossier in 2003.

B.6.2.1 Dermal absorption, *in vivo* in the rat

Study submitted in the EU Dossier in 2003 and included in the first EU approval review.

B.6.2.1/01

Reference --	Report:	[redacted] (2002b); Oxamyl (DPX-D1410) 10SL: In vivo dermal absorption of [1-14C]oxamyl in the rat DuPont Report No.: DuPont-6366 Guidelines: OECD 427 (draft, 2000) Testing facility: [redacted] GLP: Yes Certified Laboratory: No. Laboratories in the USA are not certified by any governmental agency, but are subject to regular inspections by the US EPA. Guidelines: OECD Draft Guideline 427, Skin Absorption: in vivo Method **Deviations:** Based on OECD draft test guideline 427, no guideline deviations were identified. However. only the undiluted product was tested

I. MATERIALS AND METHODS:

This study was designed to measure the absorption of Oxamyl in rats following dermal exposure to the radiolabelled active substance incorporated into the liquid, soluble concentrate formulation, Oxamyl 10SL. The test material, Oxamyl (DPX-D1410) 10SL, contains the active substance Oxamyl at 100 g/L. The dose application rate was approximately 10 µl/cm^2.

The radiochemical purity of [1-^{14}C]-Oxamyl was > 95%; the non-radiolabelled technical grade Oxamyl had a chemical purity of > 97%.

Young adult male Crl:CD®(SD)IGS BR rats aged approximately 6-8 weeks were used. Four groups of 4 rats each (total of 16 rats) were exposed to a single topical application of the prepared formulation for 6 hours. After 6 hours, the application site was washed. One group of 4 rats was sacrificed immediately after the exposure period. Of the remaining three groups of 4 rats each, one group was sacrificed 6 hours post-exposure, one group at 18 hours post- exposure, and the remaining group at 66 hours post-exposure. Samples of urine and faeces were collected for all rats in all groups. Residual feed and cage washings were collected from all animals following sacrifice.

II. RESULTS

Following the single exposure, an average of 6.51% (681.03 µg Oxamyl equivalents) of the applied dose had been absorbed by 6 hours (the value was obtained summing up the amount systemically available and the residue in the skin at the application site).

Post exposure, the mean amount of radioactivity eliminated via the urine and faeces was low (≤ 0.43%). Depletion of radioactivity from the dosed skin, which contained an average of 5.91% of the applied dose, was not observed up to 66 hours post exposure, thus indicating that the systemically-absorbed dose was no greater than the difference between the absorbed doses at 6 and 66 hours (6.51 and 5.91% = 0.59%). This represents

approximately 62.01 µg equivalents of the applied dose. Therefore, following a 6-hour exposure approximately 5.91 µg equiv/cm^2 was absorbed (Table B.6.12.4.1).

Table 10 Systemically-absorbed dose following a single topical application of Oxamyl 10SL

	Hours post exposure				
	0	**6**	**18**	**66**	**Average**
Total dose absorbed - %	6.57	5.18	6.15	8.12	6.51
Dose skin - %	5.81	4.82	5.81	7.21	5.91
Systemically absorbed dose (%)[a]	0.76	0.36	0.34	0.91	0.58
Total amount systemically absorbed (µg equiv)[b]	79.54	37.68	35.58	95.24	62.01
Amount absorbed per area (µg equiv/cm^2)	7.58	3.59	3.39	9.07	5.91

[a] Total dose absorbed – dose skin,[b] 10466 µg applied x (systemically-absorbed dose ÷100), [c] Total amount systemically absorbed ÷10.5 cm^2

III. Conclusions

Following exposure to a single topical application of undiluted **Oxamyl 10SL, 6.51% of the applied dose was absorbed by 6 hours**. Of the total percent absorbed, a significant portion was contained in the dosed skin at the end of the 6-hour exposure period. However, depletion of the absorbed radioactivity from the application skin site was not observed up to 66 hours post-exposure. Based on these findings, the percent of the applied dose that was systemically absorbed was approximately 0.58%.

RMS comments and conclusion for this renewal

The study is acceptable as a key study. However it is noted that only the undiluted formulation was tested and therefore no information is available on the in use dilution.

B.6.2.2 Comparative dermal absorption, *in vitro* using rat and human skin

Study submitted in the EU Dossier in 2003 and included in the first EU approval review.

5.6.2.2/01

Reference	Report:	Fasano, W. J. (2002a); Oxamyl (DPX-D1410) 10SL: *In vitro* dermal kinetics of [1-^{14}C]oxamyl in rat, human and rabbit skin DuPont Report No.: DuPont-6823 Guidelines: OECD 428 (draft, 2000)
--		

1. Test material: [1-^{14}C]oxamyl
(uniformly blended into the Oxamyl 10SL formulation prior to application)
Lot/Batch #: HOTC 567
Radiochemical purity: >95%

I. MATERIALS AND METHODS

This study was designed to determine the *in vitro* penetration kinetics and the distribution of ^{14}C-Oxamyl in rat, human and rabbit skin during and following a 6-hour exposure to a single, topical application of Oxamyl (DPX-D1410) 10SL soluble concentrate formulation. This was applied as an undiluted concentrate at 100 g Oxamyl/L. The formulated product was applied at a rate of 10 µL/cm^2 and remained in contact with the skin for 6 hours. Following exposure, the skin surface was washed and depletion of skin residues monitored until 18 hours post-exposure. The amount of active substance applied per area of skin was approximately 1000 µg/cm^2.

The radiochemical purity of [1-^{14}C]-Oxamyl was > 95%; the non-radiolabelled technical grade Oxamyl had a chemical purity of > 97%.

Rat skin used was from female Crl:CD®(SD)IGS BR rats; human skin was obtained post- mortem from the lateral thigh of donors aged 49-80 years; rabbit skin was obtained from the dorsal surface of adult male New Zealand rabbits aged approximately 5 months. Twelve skin preparations per species were tested. The exposure period was 6 hours for each skin preparation.

Three exposure groups (each one consisting of n=4 skin preparations) were used:

1) 0-hour post-exposure group: skins washed and processed immediately following the 6- hour exposure period to determine initial distribution of the applied dose and establish skin residue levels.

2) 6-hour post-exposure group: skins washed immediately following the 6-hour exposure period, held for 6 hours and then processed to determine the final distribution of the applied dose and skin depletion rate.

3) 18-hour post-exposure group: skins washed immediately following the 6-hour exposure period, held for 18 hours and then processed to determine the final distribution of the applied dose and skin depletion rate.

Findings:

The measurement of the dermal penetration and absorption of Oxamyl *in vitro* through rat, human, and rabbit skin was to aid in the extrapolation of *in vitro* data to the *in vivo* situation.

During the initial 6-hour exposure period, ^{14}C-Oxamyl penetrated through rat skin (3.28 µg equivalents/cm^2/hr) 4- and 1.6-fold faster than through human (0.81 µg equivalents/cm^2/hr) and rabbit skin (2.07 µg equivalents/cm^2/hr), respectively (Table 11). However, total absorption from the 100 g/L undiluted concentrate, expressed as an average of mean data from the 0-, 6-, and 18-hour post-exposure groups, was greatest for rabbit skin (28.8%), compared to rat (7.11%) and human skin (1.99%) (Table 12).

Penetration of radiolabelled Oxamyl continued following washing of the skin surface at 6 hours in all three species.

Table 11 Summary of observed penetration rate data (µg equivalents/cm^2/hr) for Oxamyl 10SL

	Rat	Human	Rabbit
0-6 hr penetration rate[a]	3.28	0.81	2.07
0-6 hr post-exposure penetration rate[b]	0.41	0.12	1.10
6-18 hr post-exposure penetration rate[c]	0.14	0.09	0.86

[a] Average of 0-6 hour mean data from the 0-, 6-, and 18-hour post-exposure groups
[b] Average of 6-hour post-exposure mean data from the 6-, and 18-hour post-exposure groups
[c] 18-hour post-exposure group data only

Table 12 Summary of recovery data for Oxamyl 10SL (% of applied dose)

	Rat	Human	Rabbit
Total absorbed	7.11	1.99	28.8
Skin wash	85.9	92.7	67.1
Total unabsorbed	86.4	92.9	68.6
Total recovery	92.3	95.6	97.4

[a] Average of mean data from the 0-, 6- and 18-hour post-exposure groups

III. CONCLUSIONS

The results of this study demonstrate that the penetration rate and total absorption of ^{14}C- Oxamyl from the Oxamyl 10SL formulation was lowest for human skin compared to rabbit and rat skin.

RMS comments and conclusion for this renewal

The study is acceptable as a key study. However, the dermal absorption value of 0.2% does not take into account the EFSA Guidance on Dermal Absorption, (EFSA Journal 2012;10(4):2665). Therefore, a reassessment of the studies and re-calculation of the dermal absorption value is necessary. It has been carried out and reported in the following.

A number of items were identified from the oxamyl studies that were conducted in 2002 and used to determine the dermal absorption factor. Data on rat and human skin preparations were reported for comparison in Table 13

Table 13 Oxamyl (DPX-D1410) 10SL: *In vitro* dermal kinetics of [1-^{14}C]oxamyl in rat and human skin (n=4)

	0 hour post exposure				6 hour post exposure				18 hour post exposure			
	Rat[a]		Human		Rat[b]		Human		Rat		Human[b]	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Receptor fluid	3.35	2.27	0.55	0.06	1.19	0.09	0.69	0.18	1.68	0.48	0.81	0.08
Skin	5.53	6.14	1.17	0.40	2.59	0.71	1.67	0.85	1.33	0.34	1.08	0.34
Absorbed dose	8.89	8.41	1.72	0.45	**3.7**	**0.80**	**2.37**	**1.03**	3.01	0.69	1.89	0.31
Skin wash	83.50	10.90	95.80	1.69	82.70	16.30	93.30	1.58	91.40	1.03	89.10	11.80
Donor chamber	1.23	1.68	0.10	0.13	0.38	0.74	0.19	0.23	0.01	0.01	0.10	0.16
Unabsorbed dose	84.70	9.25	95.90	1.67	83.10	15.50	93.50	1.53	91.40	1.03	89.20	11.60
Total dose recovered	**90.10**	**5.54**	**97.60**	**1.63**	**92.50**	**4.26**	**96.30**	**1.70**	**94.40**	**0.53**	**92.80**	**9.88**

[a] N=2; two samples were excluded.

[b]N=3: one sample was excluded being an outlier (not representative of the other 3 samples)

It is evident that the values identified for rat (7.11%) and human (1.99%) skins do not meet the criteria described the EFSA Guidance on Dermal Absorption, (EFSA Journal 2012;10(4):2665). First of all, data obtained with rat skin preparation at 0 hrs post dosing are extremely variable. It has to be noted that at that time point two skin preparations were excluded from the calculation: data were paired and the two higher values were not considered. Although the choice was in a way arbitrary, the reported values are consistent with the ones measured at longer time points (the 4 samples all together would have given rise to an absorbable dose of 21.76 ± 17.34%).

Values obtained at 6 hrs post exposure represent the worst case, giving rise to the highest level of absorption: those values were used for the derivation of the in vitro dermal absorption in rat and human. The values were obtained by summing up the absorbed dose detected in the receptor fluid to the amount detected in the skin : this is a conservative approach since the tape stripping was not carried out, therefore also the amount in the *stratum corneum* was included.

Recovery of applied radioactivity was sufficiently high (>90%); therefore, no correction for recovery is needed.

A correction for high variability is needed for the human value as the relative standard deviation was ≥25%. Therefore, to be in compliance with the EFSA guidance on dermal absorption, the estimated total absorbed dose should be the sum of the mean and the standard deviation.

On this basis **the total absorbable dose in rat and human skin in vitro is 3.7% and 3.4%, respectively**.

B.6.2.3 Summary of dermal absorption

The dermal absorption of oxamyl was investigated *in vivo* conditions in the rat and *in vitro* using rat and human skin. Tests were done with the undiluted formulations. For the current use this product is applied *via* a drip irrigation system. Since this application method does not generate a spray, typical applicator exposure *via* airborne droplets is not a source of exposure. Once the concentrated product is loaded it is introduced directly to the soil by drip irrigation. Therefore only the undiluted formulations has the opportunity to be absorbed through the skin of the operators, during mixing and loading.

The measurement of the dermal penetration and absorption of oxamyl *in vitro* through rat, human, and rabbit skin was conducted to aid in the extrapolation of *in vitro* data to the *in vivo* situation. During the initial 6-hour exposure period, [^{14}C]oxamyl penetrated through rat skin (3.28 µg equivalents/cm^2/hr) 4- and 1.6-fold faster than through human (0.81 µg equivalents/cm^2/hr) and rabbit skin (2.07 µg equivalents/cm^2/hr), respectively. However, total absorption from the 100 g/L undiluted concentrate, expressed as an average of mean data from the 0-, 6-, and 18-hour post-exposure groups, was greatest for rabbit skin, compared to rat and human skin. Penetration of radiolabelled oxamyl continued following washing of the skin surface at 6 hours in all three species. The results of this study demonstrate that the penetration rate and total absorption of [^{14}C]oxamyl from the Oxamyl 10SL formulation was lowest for human skin compared to rabbit and rat skin. The values for in vitro dermal absorption, were derived according to the indications contained in the EFSA Guidance (EFSA Journal 2012;10(4):2665) for human and rat skin, since the latter can be used for an in vivo/in vitro comparison, and were 3.4% and 3.7%, respectively. According to EFSA guidance on dermal absorption in vitro human dermal absorption study should be used at first tier, for this reason the proposed value for dermal absorption is 3.4%.

Further an *in vivo* dermal absorption study was designed and conducted to measure the absorption of oxamyl in rats following dermal exposure to the radiolabelled active substance incorporated into the liquid, soluble concentrate formulation, Oxamyl 10SL. The study conclusions indicate that following exposure to a single topical application of Oxamyl 10SL, 6.51% of the applied dose was absorbed by 6 hours. Of the total percent absorbed, a significant portion was contained in the dosed skin at the end of the 6-hour exposure period. However, depletion of the absorbed radioactivity from the application skin site was not observed up to 66 hours post-exposure (Table 14): it is therefore reasonable not to include the residue in the skin, which seems not to be bioavailable. Based on these findings, the highest percent value of the applied dose that was systemically absorbed was at 6 hour post exposure and accounting for high variability (standard deviation >25%) the % absorbed dose = 0.75 + 0.81 = 1.56%

Table 14 Oxamyl (DPX-D1410) 10SL: *In vivo* dermal absorption of [1-^{14}C]oxamyl in the rat

	Percent of applied dose							
	Hours post exposure							
	0		6		18		66	
Sample	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Urine	0.26	0.40	0.11	0.08	0.15	0.05	0.43	0.16
Faeces	0.00	0.00	0.00	0.00	0.01	0.00	0.04	0.03
Residual feed	N.A.[a]	N.A.	N.A.	N.A.	N.A.	N.A.	0.03	0.01
Cage wash	0.26	0.38	0.09	0.01	0.08	N.A.	0.19	0.11
Carcass	0.29	0.18	0.19	0.06	0.21	0.04	0.26	0.05
Whole blood	0.01	0.01	0.01	0.00	0.01	0.01	0.01	0.00
RBC	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Plasma	0.00	0.00	0.00	0.00	N.A.	N.A.	0.00	0.00
Systemic dose	0.75	0.81	0.36	0.17	0.34	0.19	0.91	0.28
Dosed skin	5.81	1.76	4.82	1.67	5.81	2.48	7.21	1.09
Non-dosed skin	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
Potentially absorbed dose	6.57	1.51	5.18	1.62	6.15	2.65	8.12	1.29
Body wrap	1.06	1.94	0.92	1.64	0.08	0.02	0.11	0.02
Mesh cover	0.88	0.84	1.40	1.94	0.58	1.12	2.40	3.10
Skin wash	90.50	4.10	89.12	6.85	90.31	2.21	81.59	9.72
O-ring	0.71	0.20	1.71	2.26	0.59	0.20	5.41	5.70
Total dose recovered	**99.72**	**1.36**	**98.34**	**2.05**	**97.71**	**1.59**	**97.61**	**2.03**

[a] Samples were below the limit of detection (<LOD) or limit of quantitation (<LOQ)

Being available data on in vitro absorption in human skin and in vivo and in vitro dermal absorption in rat, it is possible to apply the triple pack approach to extrapolate to the in vivo situation in human.

Triple pack values

Rat	*in vivo*	1.56 %
Rat	*in vitro*	3.7 %
Human	*in vitro*	3.4 %

Absorbed dose	**1.4 %**	**(Rat *in vivo*) × (human *in vitro*)/(rat *in vitro*) (1.56%) × (3.4%)/(3.7%)**

Accordingly, a dermal absorption value of 1.4% was obtained.

Since the value obtained by using the human in vitro data is more conservative, and considering the high variability of in vitro rat data (two samples were excluded), it is proposed to use 3.4% .

B.6.3 Available toxicological data relating to co-formulants

Safety data sheets (SDS) for each co-formulant can be found in Document H, and are contained within Oxamyl 10SL EU Renewal Dossier, Document J, Part 3, DuPont-42121 EU. Additional data to that contained on the safety data sheets is not currently available to the applicant.

B.6.4 Exposure data

B.6.4.1 Operator exposure

B.6.4.1.1 Estimation of operator exposure

Estimation of operator exposure assuming personal protective equipment is not used

Exposure models used

German model: *Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protection): Mitteilungen aus der Biologischen Bundesanstalt fur Land- und Forstwirtschaft, Berlin-Dahlem, no. 277, 1992*

UK model: *Predictive Operator Exposure Model (POEM), UK MAFF, 1992, (revised 2007)*

Usage information pertinent to operator exposure is summarised in Table 13.

Table 135 Summary of critical use patterns (*i.e.*, worst-case)

Crop (greenhouses)	Application rate (kg a.s./ha)	Spray dilution (L product/ha)	Application equipment	Number applications
Soil bed preparation [solarisation] in greenhouses designated for the growing of: Tomato, cucurbits edible peel, cucurbits inedible peel, pepper, aubergine, plant nurseries	5.5	Not applicable-product applied by drip line	Irrigation drip line covered with plastic film	1

The estimates of total systemic exposure of oxamyl predicted by the German model and the UK model were calculated as a proportion of the AOEL. A systemic AOEL of 0.01 mg/kg bw/day is proposed for oxamyl based on the NOAEL of 0.1 mg/kg bw where cholinesterase inhibition and decreased body weight were observed at doses >0.1 mg/kg bw from a rat acute neurotoxicity study with a 10-fold safety factor proposed based on the observations from human studies that indicate the human LOAEL for cholinesterase inhibition is 0.15 mg/kg b.w (full discussion presented in Oxamyl EU Renewal Dossier, Document M-CA, Section 5, DuPont-40932 EU) A dermal penetration factor of 1.4% is proposed for the Oxamyl 10SL formulation based on the result of an *in vivo* dermal absorption study with a correction based on *in vitro* results.[1] A default assumption of 100% retention and absorption of inhaled product was used to model exposure by inhalation. Exposure estimates were calculated using the maximum use rate. The estimates of total oxamyl exposure (expressed as the systemically absorbed dose) predicted by the German model and UK model were calculated as a proportion of the proposed systemic AOEL and are summarised in the table below.

Table 146 Operator exposure as a proportion of the AOEL – no protective clothing or equipment used

Application method	Operator total systemic exposure (mg/kg bw/day)		% of AOEL	
	German model	UK model	German model	UK model
Drip irrigation - solarization	0.0028	0.0026	28	26

The calculations show that the estimated exposure is less than the AOEL using both the German model and the UK POEM.

Oxamyl 10SL is a soluble liquid concentrate containing a nominal concentration of 100 g oxamyl a.s./L which is packaged in five-litre containers. For the current use this product is applied *via* a drip irrigation system. Since this application method does not generate a spray, typical applicator exposure *via* airborne droplets is not a source of exposure.

Once the concentrated product is loaded it is introduced directly to the soil by drip irrigation. Therefore, contaminated plant surfaces are also not of concern as an exposure source. Adequate PPE must be used to prevent exposure during adjustments for repairs to equipment.

The margins of safety for operators to Oxamyl 10SL exposures were determined with the UK and German models. Calculations of operator exposure were based on the assumption that operators wore no personal protective clothing or equipment.

[1] EFSA Scientific Report (2005) 26, 1-78, Conclusion on the peer review of oxamyl, page 13

Additional assumptions/data utilised in the models are as follows:

Area treated in one day:	1 ha
Application rate (maximum):	5.5 kg a.s./ha
Packaging:	5 L container
Application volume:	Drip irrigation – applied with irrigation water

Calculations

The actual calculations of the estimations of operator exposure for the German and UK models, with no protective clothing or equipment worn, are provided in Appendix 1. Mixer/loader exposure only was considered for drip irrigation. This is appropriate because the product is introduced directly into the soil in irrigation water on bare soil for bed preparation.

Conclusion

Exposure to Oxamyl 10SL during loading, and application does not involve a significant risk to the health of operators according to both the German model and UK POEM, assuming personal protective equipment is not used.

Operator exposure as a proportion of the AOEL – no protective clothing or equipment used – assuming dermal absorption of 0.8%

Application method	Operator total systemic exposure (mg/kg bw/day)		% of AOEL	
	German model	UK model	German model	UK model
Drip irrigation - solarization	0.0028	0.0026	28	26

RMS comments and conclusion for this renewal

A justification to use 1ha for the surface of area treated in one day should be provided**.**

B.6.4.1.2 Measurement of operator exposure

The risk assessment detailed above (Point B.6.4.1.1) indicates that exposures to Oxamyl 10SL through agricultural use represent an acceptable level of risk to the operator. Therefore, no actual measurement of field operator exposure was done.

B.6.4.2 Bystander and resident exposure

The very low vapour pressure and high water solubility of oxamyl preclude significant vapour concentration, and its direct incorporation into soil and indoor application *via* drip irrigation will result in no generation of spray droplets, therefore, no inhalation or dermal exposure to bystanders and residents is anticipated.

B.6.4.2.1 Estimation of bystander and resident exposure

Due to the physical/chemical properties of oxamyl and the nature of the application technique, drip irrigation, exposure to bystanders and residents is anticipated to be negligible.

B.6.4.2.2 Measurement of bystander and resident exposure

Due to negligible anticipated exposure to potential bystanders/residents, no measurement of exposure was done.

B.6.4.3 Worker exposure

Since Oxamyl 10SL is applied directly to soil and there is negligible likelihood of worker exposure by contact with crop foliage, estimating exposure based on soil residue rather than foliar residue is presented here.

B.6.4.3.1 Estimation of worker exposure

Estimation of worker exposure assuming personal protective equipment is not used

A conservative exposure estimate can be made using the approach in the EUROPOEM II report[2]. Potential dermal exposure (PDE) can be calculated as follows:

$$PDE = C \times DA \times SA \times T$$

Where:

C = concentration of active substance in soil (0.0055 mg/cm³)
DA = adherence of soil to skin (0.00029 cm³/cm²)
SA = exposed skin surface area (820 cm²)
T = percent of soil residue transferred to skin (100%)

The value for C is based on the maximum drip irrigation application rate of 5500 g of oxamyl/ha (55 L of 100 g a.s./L formulated product) and assuming it is uniformly distributed in the soil to a depth of 10 cm. This is the worst-case soil concentration; equivalent to 5.5 g a.s./m^3 or 0.0055 mg a.s./cm^3. DA is based on the EUROPOEM cited value of 0.44 mg soil/cm² of skin surface area and assumed soil bulk density of 1.5 g/cm^3. SA is based on the surface area of the hands assumed to be 820 cm^2. T is assumed to be 100% as a conservative figure.

$$PDE = 0.0055 \text{ mg/cm}^3 \times 0.00029 \text{ cm}^3\text{/cm}^2\text{/day} \times 820 \text{ cm}^2 \times 1 = 0.0013 \text{ mg a.s./day}$$

Assuming 60 kg body weight and 1.4% dermal absorption gives a systemic dose equivalent to <1% of the AOEL of 0.01 mg/kg/day.

This is a conservative assessment since residue transfer to skin is assumed to be 100%. In addition, oxamyl degrades in soil and the application is made at planting time when no re-entry work is likely to occur for some time.

Conclusion

The risk assessment detailed above indicates that it is unlikely that exposures to Oxamyl 10SL through agricultural use will result in exceedance of the AOEL for oxamyl.

Comments

Estimated worker exposure due to contact with treated soil remains well below the AOEL assuming 1.4% dermal absorption.

B.6.4.3.2 Measurement of worker exposure

The risk assessment detailed above (Point B.6.4.3.1) indicates that exposures to Oxamyl 10SL through agricultural use represent an acceptable level of risk to field workers. Therefore, no actual measurement of exposure was done.

B.6.5 Exposure and risk assessment

Please refer to B.6.4 and appendix 1.

2 EUROPOEM II (2002) Report of the Re-Entry Working Group – Post-Application Exposure of Workers to Pesticides in Agriculture. EUROPOEM II Project FAIR3-CT96-1406, December, 2002.

B.6.6 **References relied on**

List of information, tests and studies which are considered as relied upon by the RMS for the evaluation with a view to the approval of the active substance.

Studies marked in yellow are submitted for the first time.

Sorted by Annex Point

Data Requirement No., Reference No.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data Protection Y/N	Justification if data protection is claimed	Owner
B.6.1.1/01	[redacted]	1999	Vydate 10L: Acute oral toxicity study in male and female rats [redacted] DuPont-2140 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont
B.6.1.2/01	[redacted]	1999	Vydate 10L: Acute dermal toxicity study in rats [redacted] DuPont-2130 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont
B.6.1.3/01	[redacted]	1998	Oxamyl 10% (non voc) liquid formulation: Inhalation median lethal concentration (LC_{50}) study in rats [redacted] HL-1998-01611 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont

Data Requirement No., Reference No.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data Protection Y/N	Justification if data protection is claimed	Owner
B.6.1.4/01	[redacted]	1999	Vydate 10L: Primary dermal irritation study in rabbits [redacted] DuPont-2024 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont
B.6.1.5/01	[redacted]	1999	Vydate 10L: Primary eye irritation study in rabbits [redacted] DuPont-2040 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont
B.6.1.6/01	[redacted]	1999	Vydate 10L: Evaluation of the potential dermal sensitization in the guinea pig (modified Buehler method) [redacted] DuPont-2016 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont

Data Requirement No., Reference No.	**Author(s)**	**Year**	**Title Source Company Report No. GLP or GEP Status (where relevant) Published or not**	**Vertebrate study Y/N**	**Data Protection Y/N**	**Justification if data protection is claimed**	**Owner**
B.6.2.1/01	[redacted]	2002b	Oxamyl (DPX-D1410) 10SL: *In vivo* dermal absorption of [1-^{14}C]oxamyl in the rat [redacted] DuPont-6366 Previously submitted and included in the first EU approval review. Published: No	Y	N	DuPont	
B.6.2.2/01	Fasano, W.J.	2002a	Oxamyl (DPX-D1410) 10SL: *In vitro* dermal kinetics of [1-^{14}C]oxamyl in rat, human and rabbit skin DuPont Haskell Laboratory DuPont-6823 Previously submitted and included in the first EU approval review. Published: No	N	N	DuPont	

Sorted by Author

Data Requirement No., Reference No.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data Protection Y/N	Justification if data protection is claimed	Owner
B.6.2.1/01	[redacted]	2002b	Oxamyl (DPX-D1410) 10SL: *In vivo* dermal absorption of [1-^{14}C]oxamyl in the rat [redacted] DuPont-6366 Previously submitted and included in the first EU approval review. Published: No	Y	N	DuPont	
B.6.2.2/01	Fasano, W.J.	2002a	Oxamyl (DPX-D1410) 10SL: *In vitro* dermal kinetics of [1-^{14}C]oxamyl in rat, human and rabbit skin DuPont Haskell Laboratory DuPont-6823 Previously submitted and included in the first EU approval review. Published: No	N	N	DuPont	
B.6.1.1/01	[redacted]	1999	Vydate 10L: Acute oral toxicity study in male and female rats [redacted] DuPont-2140 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont

Data Requirement No., Reference No.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data Protection Y/N	Justification if data protection is claimed	Owner
B.6.1.2/01	[redacted]	1999	Vydate 10L: Acute dermal toxicity study in rats [redacted] DuPont-2130 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont
B.6.1.4/01	[redacted]	1999	Vydate 10L: Primary dermal irritation study in rabbits [redacted] DuPont-2024 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont
B.6.1.5/01	[redacted]	1999	Vydate 10L: Primary eye irritation study in rabbits [redacted] DuPont-2040 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont

Data Requirement No., Reference No.	Author(s)	Year	Title Source Company Report No. GLP or GEP Status (where relevant) Published or not	Vertebrate study Y/N	Data Protection Y/N	Justification if data protection is claimed	Owner
B.6.1.6/01	[redacted]	1999	Vydate 10L: Evaluation of the potential dermal sensitization in the guinea pig (modified Buehler method) [redacted] DuPont-2016 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont
B.6.1.3/01	[redacted]	1998	Oxamyl 10% (non voc) liquid formulation: Inhalation median lethal concentration (LC_{50}) study in rats [redacted] HL-1998-01611 GLP: Yes Published: No	Y	Y	Data protection on a MS by MS basis. The study provides additional data for the regulatory decision, conducted according to GLP and has not previously been protected or submitted in all MS.	DuPont

APPENDIX 1
GERMAN MODEL AND UK POEM MODEL ESTIMATIONS OF OPERATOR EXPOSURE ASSUMING NO PPE

Oxamyl 10SL German Model operator exposure estimation: Solarisation, no PPE

THE GERMAN MODEL (GEOMETRIC MEAN VALUES)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles						
Product	**Oxamyl 10SL**			Active substance		**Oxamyl**	
Formulation type	Liquid			a.s. concentration		**100**	g/l
Dermal absorption from product	**1,4**	%		Dermal absorption from spray		**0**	%
RPE during mix/loading	None			RPE during application		None	
PPE during mix/loading	None						
PPE during application: Head	None		Hands	None	Body	None	
Dose	**55**	l product/ha		Work rate/day		**1**	ha

DERMAL EXPOSURE DURING MIXING AND LOADING

Hand contamination/kg a.s.	2,4	mg/kg a.s.
Hand contamination/day	13,2	mg/day
Protective clothing	none	
Transmission to skin	100	%
Dermal exposure to a.s.	13,2	mg/day

INHALATION EXPOSURE DURING MIXING AND LOADING

Inhalation exposure/kg a.s.	0,0006	mg/kg a.s.
Inhalation exposure/day	0,0033	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0,0033	mg/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique: Tractor-mounted/trailed boom sprayer: hydraulic nozzles

	Head	Hands	Rest of body	
Dermal contamination/kg a.s.	0,06	0,38	1,6	
Dermal contamination/day	0,33	2,09	8,8	
Protective clothing	none	none	none	
Transmission to skin	100	100	100	%
Total dermal exposure to a.s.	11,22	mg/day		

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure/kg a.s.	0,001	mg/kg a.s.
Inhalation exposure/day	0,0055	mg/day
RPE	none	
Transmission through RPE	100	%
Inhalation exposure to a.s.	0,0055	mg/day

ABSORBED DOSE

	Mix/load		Application	
Dermal exposure to a.s.	13,2	mg/day	11,22	mg/day
Percent absorbed	1,4	%	0	%
Absorbed dose (dermal route)	0,1848	mg/day	0	mg/day
Inhalation exposure to a.s.	0,0033	mg/day	0,0055	mg/day
Total systemic exposure	0,1881	mg/day	0,0055	mg/day

PREDICTED EXPOSURE

Total systemic exposure	0,1936	mg/day
Operator body weight	70	kg
Operator exposure	0,002765714	mg/kg bw/day

Oxamyl 10SL UK POEM operator exposure estimation: Solarisation, no PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM)

Application method	Tractor-mounted/trailed boom sprayer: hydraulic nozzles				
Product	**Oxamyl 10SL**		Active substance	**Oxamyl**	
Formulation type	water-based		a.s. concentration	**100**	mg/ml
Dermal absorption from product	**1,4**	%	Dermal absorption from spray	**0**	%
Container	5 litres 45 or 63 mm closure				
PPE during mix/loading	None		PPE during application	None	
Dose	**55**	l/ha	Work rate/day	**1**	ha
Application volume	**55**	l/ha	Duration of spraying	**6**	h

EXPOSURE DURING MIXING AND LOADING

Container size	5	litres
Hand contamination/operation	0,01	ml
Application dose	55	litres product/ha
Work rate	1	ha/day
Number of operations	11	/day
Hand contamination	0,11	ml/day
Protective clothing	None	
Transmission to skin	100	%
Dermal exposure to formulation	0,11	ml/day

DERMAL EXPOSURE DURING SPRAY APPLICATION

Application technique	Tractor-mounted/trailed boom sprayer: hydraulic nozzles			
Application volume	55	spray/ha		
Volume of surface contamination	10	ml/h		
Distribution	Hands	Trunk	Legs	
	65%	10%	25%	
Clothing	None	Permeable	Permeable	
Penetration	100%	5%	15%	
Dermal exposure	6,5	0,05	0,375	ml/h
Duration of exposure	6	h		
Total dermal exposure to spray	41,55	ml/day		

ABSORBED DERMAL DOSE

	Mix/load		Application	
Dermal exposure	0,11	ml/day	41,55	ml/day
Concen. of a.s. product or spray	100	mg/ml	100	mg/ml
Dermal exposure to a.s.	11	mg/day	4155	mg/day
Percent absorbed	1,4	%	0	%
Absorbed dose	0,154	mg/day	0	mg/day

INHALATION EXPOSURE DURING SPRAYING

Inhalation exposure	0,01	ml/h
Duration of exposure	6	h
Concentration of a.s. in spray	100	mg/ml
Inhalation exposure to a.s.	6	mg/day
Percent absorbed	100	%
Absorbed dose	0	mg/day

PREDICTED EXPOSURE

Total absorbed dose	0,154	mg/day
Operator body weight	60	kg
Operator exposure	0,002566667	mg/kg bw/day