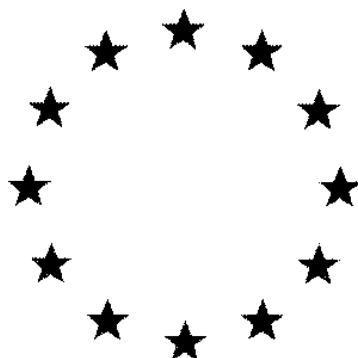


European Commission



**Draft (Renewal) Assessment Report prepared
according to the Commission Regulation (EC) No
1107/2009**

**Daminozide (ISO); 4-(2,2-
dimethylhydrazino)-4-oxobutanoic
acid; *N*-dimethylaminosuccinamic
acid**

Volume 3 – B.6 (PPP) – Dazide Enhance

Rapporteur Member State: Czech Republic
Co-Rapporteur Member State: Hungary

Version history page:

| Date | Version | Reason for revision |
|--------------|----------------|--------------------------------------------|
| March 2018 | Version 1 | First draft |
| October 2018 | Version 2 | Notifier's + Co-RMS comments |
| June 2019 | Version 3 | Update following the ECHA accordance check |

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B.6 TOXICOLOGY AND METABOLISM

INTRODUCTION

Dazide Enhance (also Dazide 85) is a water soluble granule formulation (SG) containing 850 g/kg Daminozide (ISO); 4-(2,2-dimethylhydrazino)-4-oxobutanoic acid; N-dimethylaminosuccinamic acid ('hereafter referred to as 'daminozide') active substance, 85% w/w which was included into Annex I of Directive 91/414 (Inclusion Directive 2005/53/EC). The product is a plant growth regulator intended for use on indoor and outdoor ornamental plants. The mode of action is through interference with gibberellic acid biosynthesis. It is absorbed by the leaves and translocated throughout the treated plant. As a result more compact plants (by inhibition of intermodal elongation) are produced. The representative uses applied are a maximum of 5 applications to ornamental crops grown either indoors or in the field.

This document presents data and information on the metabolism and toxicology of daminozide and is submitted in support of the renewal of approval for daminozide under Regulation (EC) 1107/2009. Most of the data presented here were included in the submission that was made to secure the first inclusion of daminozide in Annex I to Directive 91/414/EEC.

The original submission was determined to be complete and enabled the setting of appropriate reference doses. The evaluation of the original RMS (The Netherlands) is set out in the Monograph of June 1999 and its addenda in June 2002, June 2003 and September 2004. The critical end points relating to this section, for use in risk assessments, were published in the Review Report for daminozide; SANCO/3043/99 final, 15 February 2005.

The RMS for this renewal of daminozide is the Czech Republic. All studies previously relied upon for Annex I listing are briefly summarised below.

Bridging principle

Both preparations ALAR and DAZIDE ENHANCE are mainly similar, presented by same EU Daminozide Task Force, as a minor change in wetting agent, which is considered to be of no toxicological relevance in the actual concentration, thus it is reasonable to assume that the toxicological profile of ALAR represents a realistic worst case for the related DAZIDE ENHANCE allowing bridging of the toxicological properties.

For studies that have not been previously reviewed, the following statement will precede each summary:

| | |
|---------------------|----------------------------------------------------|
| Previous evaluation | None; submitted for the purpose of Annex I renewal |
|---------------------|----------------------------------------------------|

Dazide Enhance**Pure active substance**

| | | |
|-------------------------------------------|-----------------|-------------------|
| content of pure active substance : | 850 g/kg | (85% w/w) |
| limits : ± 25 g/kg | 825 – 875 g/kg | 82.5 – 87.5 % w/w |

Technical active substance

| | | |
|------------------------------------------------|--------------------|---------------------|
| content of technical active substance : | 858.6 g/kg | (85.86% w/w) |
| limits : ± 25 g/kg | 833.6 – 883.6 g/kg | 83.36 – 88.36 % w/w |

| |
|-----------------------------------------------------------------------|
| at a minimum purity of the technical active substance of 99 %. |
|-----------------------------------------------------------------------|

The following information is based on the evaluation contained in the Monograph and relevant addenda, together with new data generated to supplement and elaborate the original dossier.

This dossier is submitted to support the renewal of the approval of daminozide under Regulation (EC) 1107/2009. The submission is made in accordance with Commission Regulation (EU) No 844/2012 of 18 September 2012, setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.

Dossier for the renewal of daminozide is submitted by the

EU Daminozide Task Force

The EU Daminozide Task Force is an equal partnership between:

Fine Agrochemicals Limited

Hill End House
Whittington,
Worcester
WR5 2RQ,
UK
And

Arysta LifeScience Benelux SPRL (formerly: Chemtura Europe Limited and MacDermid Agricultural Solutions Incorporated)
rue de Renory 26/1
B-4102 Ougrée
Belgium

All data are jointly owned unless indicated otherwise.

A representative label for the Fine Agrochemicals product 'DAZIDE ENHANCE' is presented.

Plant protection product:

| | |
|-----------------------------------------------------------------|-----------------------------------------------|
| Trade name: | Dazide Enhance |
| Alternative names and company code numbers used in the dossier: | Dazide 85 WSG, Dazide WG, Dazide SG, FAL 2400 |

B.6.1 Acute toxicity

The preparation DAZIDE 85 WSG: needs no classification for acute oral and dermal toxicity or for eye or skin irritation. The acute inhalation toxicity study with DAZIDE 85 was not considered suitable for evaluation. DAZIDE 85 WSG does not need to be classified for skin sensitization. The DAZIDE 85 WSG formulation is considered to be sufficiently comparable to the DAZIDE ENHANCE formulation such that the DAZIDE 85 WSG data can be extrapolated to support DAZIDE ENHANCE.

Table B.6.1-1: Summary of acute toxicity, irritation and skin sensitisation studies

The results of all the acute toxicity studies performed with the formulation are summarized in the following table:

| Type of study | Species | Results | Ref |
|---------------------------------------------------------------------|-----------|---------------------------------|-----------------|
| Acute oral / Dazide 85 WSG CP 7.1.1/01 | Rat(F) | LD ₅₀ >5000 mg/kg bw | ██████ 2003a * |
| Acute dermal / Dazide 85 WSG CP 7.1.2/01 | Rat(M+F) | LD ₅₀ >5000 mg/kg bw | ██████ 2003b) * |
| Acute skin irritation/ Dazide 85 WSG CP 7.1.4/01 | Rabbit(F) | Not irritating | ██████ 2002a * |
| Acute eye irritation / Dazide 85 WSG CP 7.1.5/01 | Rabbit | Not irritating | ██████ 2002b * |
| Skin sensitization (dermal LLNA)) / Dazide 85 WSG CP 7.1.6/01 | Mice(F) | Non sensitizing | ██████ 2003c * |

* New studies : New data for Dazide 85 WSG - AIR3 renewal, Owner: Fine Agrochemicals Ltd.

B.6.1.1 Oral toxicity**Dazide 85 WSG: Acute Oral Toxicity Study in the Female Rat**

| | |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reference: | CP 7.1.1/01 ██████ (2003a)) Dazide 85 WSG: Acute Oral Toxicity Study in the Female Rat (Acute Toxic Class) ██████ 2242/004 Fine Agrochemicals Limited – 28th April 2015 Document ID: M-CP 7 |
| Report No.: | Fine Agrochemicals Ltd. Report No: FAL REF 265 |
| Guideline: | OECD 423 (2001),US EPA OPPTS 870.1100 (2002) |
| GLP: | Yes |
| Previous evaluation | None; submitted for the purpose of AIR III renewal |

Executive Summary

In an acute oral toxicity study, Dazide 85 WSG (Dazide Enhance) was administered by gavage to fasted female Wistar rats dispersed in 1% w/v methylcellulose at the limit dose of 5000 mg/kg bw and at an application volume of 20 mL/kg bw.

No mortality occurred. There were no clinical signs of reaction to treatment and all animals gained weight throughout the observation period. No macroscopic abnormalities were observed for animals killed on day 15.

The acute oral median lethal dose (LD50) for Dazide 85 WSG (Dazide Enhance) in female rats was > 5000 mg/kg bw.

I. MATERIAL AND METHODS**A. MATERIALS**

1. Test Material:
Dazide 85 WSG
Description: White solid
Lot/Batch: 4190802 II-NF-2
Active substance content
(nominal): 85.9%
Stability: Expiry date: 30 September 2004
2. Vehicle and/or positive
Control : 1% methylcellulose / no positive control required
3. Test Animals
Species: Rat
Strain: Wistar [REDACTED]: WI(Glx/BRL/Han)IGSBR
Age: 10 to 13 weeks at the start of the study
Weight at dosing: 181 to 198 g
Source: [REDACTED]
Acclimation period: 15 to 22 days
Diet: SQC(E) Rat and Mouse diet No. 1 (Special Diets Service Ltd) ad libitum,
with the exception overnight prior to and approx. 3 hrs after dosing
Water: Drinking water ad libitum
Housing: Animals were accommodated in cages that conformed to the 'Code of
Practice for Housing and Care of Animals Used in Scientific Procedures'.
Environmental Conditions
Temperature: 19-25°C – Any slight deviations that may have occurred had no impact on the study.
Humidity: 40-70% – Any slight deviations that may have occurred had no impact on the study.
Air changes: at least 15 per hour
Photoperiod: 12 hrs of artificial light in each 24-h period

B. STUDY DESIGN AND METHODS**1. In-life dates**

20 August to 10 September 2003

2. Animal assignment and treatment

The rats were allocated without conscious bias to cages within the treatment group. Dazide 85 WSG was administered dispersed in 1% w/v methylcellulose at a volume of 20 mL/kg bw by oral gavage using a plastic syringe and a rubber catheter. The day of dosing was designated day 1.

3. Statistics

None required.

II. RESULTS AND DISCUSSION

A. MORTALITY

No mortality occurred in the study.

B. CLINICAL OBSERVATIONS

No clinical signs were observed throughout the study

Results are summarised in Table 6.1.1-1.

Table 6.1.1/01-1: Acute oral toxicity of Dazide 85 WSG to rats

| Dose (mg/kg bw) | Toxicological results* | Duration of signs | LD50 (mg/kg bw) |
|--------------------|------------------------|-------------------|--------------------|
| 5000 | 0/0/3 | - | >5000 |

* number of animals which died/number of animals with clinical signs/number of animals used

C. BODY WEIGHT

All animals gained weight throughout the observation period

D. NECROPSY

No macroscopic abnormalities were observed for animals killed on day 15.

E. DEFICIENCIES

None.

III. CONCLUSION

Dazide 85 WSG is of low acute oral toxicity to rats. The acute oral median lethal dose (LD50) for Dazide 85 WSG in female rats is > 5000 mg/kg bw.

| | |
|-----------------------|------------------------------------------------------------------------------------------------------------------|
| RMS comments | The study is valid for the risk assessment |
| Endpoint / conclusion | Acute oral LD ₅₀ > 5 000 mg/kg bw in the rat; classification for acute oral toxicity is not required. |

B.6.1.2 DERMAL TOXICITY

B.6.1.2/01 Dazide 85 WSG: Acute Dermal Toxicity Study in the Rat

| | |
|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reference: | CP 7.1.2/01 [REDACTED] (2003b) Dazide 85 WSG: Acute Dermal Toxicity Study in the Rat [REDACTED], 2242/005 Fine Agrochemicals Ltd. Report No: FAL REF 264 |
| Report No | Fine Agrochemicals Ltd. Report No: FAL REF 264 |
| Guideline: | OECD 402 (1987), US EPA OPPTS 870.1200 (2002) |
| GLP: | Yes |

| | |
|----------------------|----------------------------------------------------|
| Previous evaluation: | None; submitted for the purpose of AIR III renewal |
|----------------------|----------------------------------------------------|

Executive Summary

In an acute dermal toxicity study, Dazide 85 WSG was applied to the moistened skin of group of five male and five female Wistar rats as supplied at the limit dose of 5000 mg/kg bw. The treated areas of dorsum were covered by a semi-occlusive dressing for 24h. All animal were killed on Day 15 and subsequently underwent a full necropsy.

No mortality occurred and no clinical signs or dermal responses were observed during the study. One male and one female lost body weight during the first week and gained weight during the second week. All other rats achieved anticipated body weight gains throughout the study. Upon macroscopic examination three males rats revealed slight or moderate pelvic dilatation, the significance of which is equivocal. No other macroscopic abnormalities were observed-

The acute dermal median lethal dose (LD50) for Dazide 85 WSG in male and female rats was > 5000 mg/kg bw.

I. MATERIAL AND METHODS

A. MATERIALS

1. **Test Material:** Dazide 85 WSG

Description: White solid

Lot/Batch: 4190802 II-NF-2

Active substance content

(nominal): 85.9%

Stability: Expiry date: 30 September 2004

2. **Vehicle and/or positive**

control: None, administered as supplied / no positive control required

3. **Test Animals**

Species: Rat

Strain: Wistar (■■■■)WI(Glx/BRL/Han)IGSBR)

Age: 10 to 11 weeks

Weight at dosing: 201 to 238 g (females); 326 to 352 g (males)

Source: ■■■■■■■■■■

Acclimation period: 22 days

Diet: SQC(E) Rat and Mouse Diet No. 1 (Special Diets Service Ltd) *ad libitum*

Water: Drinking water *ad libitum*

Housing: Individually in cages that conformed to the 'Code of Practice for Housing and Care of Animals Used in Scientific Procedures'

Environmental Conditions

Temperature: 19-25°C – Any slight deviations that may have occurred had no

impact on the study

Air changes: at least 15 per hour

Photoperiod: 12 hrs of artificial light in each 24-h period

B. STUDY DESIGN AND METHODS

1. In-life dates

27 August to 10 September 2003

2. Animal assignment and treatment

The rats were allocated without conscious bias to cages within the treatment group. On the day prior to treatment hair was removed from the dorsum region of each rat with electric clippers exposing an area approximately 6×8 cm. The dermal test site was an area approximately 5×5 cm (equivalent to approx 10% of the total body surface). Dazide 85 WSG in form of powder was applied uniformly to the clipped dorsum that had been moistened with approximately 0.2 mL of purified water immediately before application of the test material. The treated area was covered with a dense gauze patch which was held in place with an elasticated, open weave, adhesive compression bandage. At the end of the 24 hour exposure period, the dressings were removed and the treated area of skin was swabbed with water-moistened cotton wool. The day of dosing was designated day 1

3. Statistics

None required.

II. RESULTS AND DISCUSSION

A. MORTALITY

No mortality occurred during the study.

B. CLINICAL OBSERVATIONS

No clinical signs were observed during the study.

C. BODY WEIGHT

One male and one female lost body weight during the first week and gained weight during the second week. All other rats achieved anticipated body weight gains throughout the study.

D. DERMAL IRRITATION

No dermal responses were observed during the study.

E. NECROPSY

No macroscopic abnormalities were observed for the majority of animals killed on day 15. Terminal examination revealed unilateral pelvic dilation in three male rats. The degree of severity was slight in two of the animals and moderate in the third. The significance of this finding is equivocal.

F. DEFICIENCIES

None.

III. CONCLUSION

Dazide 85 WSG is of low acute dermal toxicity to rats. The acute dermal median lethal dose (LD50) for Dazide 85 WSG in male and female rats is > 5000 mg/kg bw.

| | |
|-----------------------|---------------------------------------------|
| RMS comments | The study is valid for the risk assessment |
| Endpoint / conclusion | Dermal LD50 is > 5,000 mg/kg bw in the rat. |

B.6.1.3 Inhalation toxicity

Justification for non-submission of data

Under Regulation EC No. 1272/2008, in the absence of study data, preparations may be classified for acute lethal effects using the conventional means/acute toxicity estimates (ATE).

Details of the product composition are presented in Document J. Dazide Enhance contains no compounds classified as Category 1-4 via inhalation.

In accordance with Regulation EC No. 1272/2008, 'In order to ensure that classification of the mixture is accurate, and that the calculation need only be performed once for all systems, sectors, and categories, the ATE of ingredients shall be considered'. Classification of the product using the ATE of the product should include ingredients with a known acute toxicity, which fall into any of the acute toxicity categories but ignore ingredients if the oral limit test does not show acute toxicity at 2,000 mg/kg bodyweight. As none of the components of the product are classified for acute toxicity, an appropriate ATE cannot be calculated but would be greater than the upper limit for classification as Category 4 for acute toxicity.

Furthermore, classification of a non-gaseous product is only considered if a substances classified for acute toxicity is present at concentrations greater than or equal to the applicable concentrations defined in table 1.1 in Annex I of Regulation EC No. 1272/2008. The product contains no components classified for inhalation toxicity at concentration greater than the concentration limit defined in the above table.

It is therefore not necessary to classify this product as acutely toxic via inhalation. A study is not required nor considered an appropriate use of animals.

| | |
|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RMS comments | Agree with applicant's proposed classification and labelling of Dazide Enhance for acute inhalation toxicity. Since the product is a water soluble granule (SG), data requirement would be to provide an acute inhalation study unless no exposure can be demonstrated. Based on the information from the MCP2, the product is nearly dust-free and high attrition-resistance is shown. Therefore, the exposure via inhalation route will be negligible. No acute inhalation study was submitted according to Regulation (EU) No 284/2013, no acute inhalation study is required. The formulation does not contain any formulants classified for acute inhalation toxicity. |
| Endpoint / conclusion | The classification for acute inhalation toxicity is not required in accordance with Regulation (EC) No 1272/2008 as amended. |

B.6.1.4 Skin Irritation

B.6.1.4/01 Dazide WSG (New Formulation) Skin Irritation to the Rabbit

| | |
|---------------------|-------------------------------------------------------------------------------------------------------|
| Reference: | CP 7.1.4/01 [REDACTED] (2002a) Dazide WSG (New Formulation) Skin Irritation to the Rabbit |
| Report No.: | [REDACTED] Report No. FNA 106/022932 Fine Agrochemicals Ltd. Report No. FAL 211 Report No. FAL 211 |
| Guideline: | OECD 404 (1992), US EPA FIFRA 81-5 (1984) |
| GLP: | Yes |
| Previous evaluation | None; submitted for the purpose of AIR III renewal |

Executive summary

The primary skin irritation potential of Dazide WSG was evaluated in three male rabbits. 0.5 g of Dazide WSG was spread on a gauze patch (2.5 × 2.5 cm) and the patch was applied for 4 hours under semi-occlusive bandage to clipped intact dorsal skin. Dazide WSG was judged to be non-irritating based on the absence of any skin irritation reaction in any animal.

I. MATERIALS AND METHODS**A. MATERIALS:**

| | |
|-------------------------------------------|----------------------------------------------------------------|
| 1. Test material: | Dazide WSG |
| Description | White free flowing powder |
| Lot/Batch # | PW 1805 |
| Purity: | Not stated |
| Stability of the test compound | 3 years |
| 2. Vehicle and or positive control | The test material was used as supplied. There was no vehicle. |
| 3. Test animals | |
| Species: | Rabbit |
| | New Zealand White |
| Age at dosing | At least 8 weeks |
| Weight at dosing | 3.17 to 3.32 kg |
| Source | [REDACTED] |
| Acclimation period: | At least 18 days |
| Diet: | Special Diet Services STANRAB (P) SQC pellet <i>ad libitum</i> |
| | Tap water <i>ad libitum</i> |
| Housing: | Individually in stainless steel cages with perforated floors. |
| Environmental conditions | |
| Temperature: | 15 - 23°C |
| Humidity: | 40 - 79% |
| Air change: | Not stated |
| Photoperiod: | 12 hr light / 12 hr dark |

B. STUDY DESIGN AND METHOD

1. In-life dates

12 April 2002 – 24 April 2002

2. Animal assignment and treatment

On the day prior to application of the test material, hair was clipped from the dorso-lumbar area of the rabbits using clippers. The treatment site was ‘wetted’ with 0.5 mL of reverse osmosis water and approximately 0.5 g of test material was applied under a two-ply 25 mm × 25 mm porous gauze pad to intact skin sites on the test animals. An additional site was similarly treated with the exception of the test material to act as a control. A single animal received three exposures (three minutes, one hour and four hours duration) in a step-wise manner and acted as a preliminary screen. In the absence of a severe effect on removal of the dressings, the next exposure was initiated. For exposures of one hour or more, each treatment site was covered with an elasticated bandage dressing for the duration of the exposure period. The animals were returned to their cages immediately after treatment. At the end of the exposure period, the semi-occlusive dressing and gauze pad were removed and the treatment site was washed with lukewarm water to remove any residual test material. Examination of the treated skin was made approximately 1, 24, 48 and 72 h later. Only the data for the 4h exposure were reported. Animals were observed daily for signs of ill health or toxicity and skin reactions assessed using the Draize scale.

II. RESULTS AND DISCUSSION**A. FINDINGS**

No signs of toxicity or ill health were observed in any of the animals.

No dermal irritation was observed, as shown in Table 6.1.4/01-1

Table 6.1.4/01-1: Summary of irritant effects on the skin (Exposure: 4 hours)

| Animal | | 24 hours | 48 hours | 72 hours | Mean scores |
|--------|-----------------------------------------|----------|----------|----------|-------------|
| 1 | Erythema (redness) and Eschar formation | 0 | 0 | 0 | 0 |
| | Oedema Formation | 0 | 0 | 0 | 0 |
| 2 | Erythema (redness) and Eschar formation | 0 | 0 | 0 | 0 |
| | Oedema Formation | 0 | 0 | 0 | 0 |
| 3 | Erythema (redness) and Eschar formation | 0 | 0 | 0 | 0 |
| | Oedema Formation | 0 | 0 | 0 | 0 |

B. DEFICIENCIES

None.

III. CONCLUSION

In an acceptable dermal irritation test, Dazide WSG was not found to be irritating to the rabbit skin

| | |
|-----------------------|--------------------------------------------------------------------------------------------------------------------|
| RMS comments | The study is valid for the risk assessment |
| Endpoint / conclusion | The classification for skin irritation is not required in accordance with Regulation (EC) No 1272/2008 as amended. |

B.6.1.5 Eye Irritation**B.6.1.5/01 Dazide WSG (New Formulation) Eye Irritation to the Rabbit**

| | |
|-------------|----------------------------------------------------------------------------------|
| Reference: | CP 7.1.5/01 (2002b) Dazide WSG (new formulation) Eye Irritation to the Rabbit |
| Report No.: | Report No. FNA 107/023169 |

| | |
|---------------------|-----------------------------------------------------------------------|
| Guideline: | Fine Agrochemicals Ltd. Report No. FAL 216 |
| GLP: | OECD 405 (1987), EC No. 440/2008 method B5 (2008), EPA OPPTS 870.2400 |
| Previous evaluation | Yes |
| Previous evaluation | None; submitted for the purpose of AIR III renewal |

Executive summary

Dazide WSG was tested for primary eye irritation potential in four rabbits. A volume of 0.1 mL of test material was placed into the conjunctival sac of one eye of each animal and animals observed for 22 days. Injection of the conjunctival blood vessels or a crimson-red conjunctival appearance was evident in the treated eye of each animal in the first week after treatment resolving on one animal by day 15 and all animals by day 22. Very-slight or slight chemosis and very-slight to moderate discharge were apparent in the first 48 hours after treatment, in one case very-slight discharge was still evident after 72 hours. Small amounts of mucus were apparent up to 48 hours after treatment. Scattered or diffuse areas of opacity covering one quarter of the corneal surface were apparent in one animal throughout the first 48 hours of observations. On the basis of these observations, Dazide WSG does not require classification for eye irritancy.

I. MATERIALS AND METHODS

A. MATERIALS:

- Test material:

| | |
|--------------------------------|---------------------------|
| Description | Dazide WSG |
| Lot/Batch | White free flowing powder |
| Purity: | # PW 1805 |
| Stability of the test compound | Not stated |
- Vehicle and/or positive control The test material was used as supplied. There was no vehicle.
- Test animals

| | |
|---------------------|--------------------------------------------------------------|
| Species: | Rabbit |
| Strain: | New Zealand White |
| Age at dosing | At least 8 weeks |
| Weight at dosing | 3.34 to 3.44 kg |
| Source | |
| Acclimation period: | At least six days |
| Diet: | Special Diet Services STANRAB (P) SQC ad libitum |
| Water: | Tap water ad libitum |
| Housing: | Individually in stainless steel cages with perforated floors |

Environmental

conditions

| | |
|--------------|-------------------------|
| Temperature: | 15 - 23°C |
| Humidity: | 40 - 70% |
| Air change: | Not stated |
| Photoperiod: | 12 hr light /12 hr dark |

B. STUDY DESIGN AND METHOD

- In-life dates 18 April 2002 – 22 May 2002

2. Animal assignment and treatment

The eyes of each animal were examined prior to the application of the test material to ensure that there was no pre-existing corneal damage, iridial inflammation or conjunctival irritation. A preliminary irritation screen was carried out using a single animal treated with 0.1 mL of test material with duration of exposure limited to 30 seconds by

irrigation of the treated eye. The behaviour of this animal was observed to allow assessment of the initial pain response. Since a moderate pain response was observed in this animal, all subsequent animals were received local anaesthesia (1% amethocaine hydrochloride) to both eyes prior to instillation of the test material. The test material was applied to the right eye and the eyelids were gently held together for one second before releasing; the left eye remained untreated. The animals were returned to their cages and observed for the first hour after dosing and at regular intervals throughout the day to determine whether there were any severe injuries. Ocular reactions to treatment were assessed at 1, 24, 48 and 72 hours after treatment according to the Draize scale.

II. RESULTS AND DISCUSSION

No clinical signs or toxicity were observed in any of the animals during the experimental period.

Injection of the conjunctival blood vessels and very-slight chemosis and discharge were apparent in the preliminary irritation screen animal one hour after instillation. The chemosis and discharge resolved with the next day with the conjunctival injection persisting until 72 hours after instillation.

Injection of the conjunctival blood vessels or a crimson-red conjunctival appearance was evident in the treated eye of each animal in the first week after treatment resolving on one animal by day 15 and all animals by day 22. Very-slight or slight chemosis and very-slight to moderate discharge were apparent in the first 48 hours after treatment, in one case very-slight discharge was still evident after 72 hours. Small amounts of mucus were apparent up to 48 hours after treatment. Scattered or diffuse areas of opacity covering one quarter of the corneal surface were apparent in one animal throughout the first 48 hours of observations.

Results of the eye irritation test are presented in Tables 6.1.5/01-1 to 6.1.5/01-4.

Table 6.1.5/01-1: Mean values for ocular lesions followed by irrigation

| Animal number and sex | Corneal opacity | Iridial lesions | Redness of Conjunctiva | Chemosis |
|-----------------------|-----------------|-----------------|------------------------|----------|
| 3923 M | 0.0 | 0.0 | 1.0 | 0.0 |

Table 6.1.5/01-2: Mean values for ocular lesions

| Animal number and sex | Corneal opacity | Iridial lesions | Redness of Conjunctiva | Chemosis |
|-----------------------|-----------------|-----------------|------------------------|----------|
| 3924 M | 0.0 | 0.0 | 2.0 | 0.0 |
| 3925 M | 0.0 | 0.0 | 1.7 | 0.7 |
| 3927 M | 0.7 | 0.3 | 1.7 | 1.0 |

Table 6.1.5/01-3: Grades for ocular irritation responses followed by irrigation (animal number 3923M)

| Region of the eye | Response | Grade of response at time after instillation (hours) | | | | |
|-------------------|-----------|------------------------------------------------------|----|----|----|-------|
| | | 1 | 24 | 48 | 72 | Day 8 |
| Cornea | Opacity | 0 | 0 | 0 | 0 | 0 |
| Iris | Value | 0 | 0 | 0 | 0 | 0 |
| Conjunctiva | Redness | 1 | 1 | 1 | 1 | 0 |
| | Chemosis | 1 | 0 | 0 | 0 | 0 |
| | Discharge | 1 | 0 | 0 | 0 | 0 |

Table 6.1.5/01-4: Grades for ocular irritation response

| Region of the eye | Response | Grade of response at time after instillation | | | | | | |
|-------------------|-----------|----------------------------------------------|------|------|------|-----|------|------|
| | | 1 h | 24 h | 48 h | 72 h | 8 d | 15 d | 22 d |
| Animal 3924 M | | | | | | | | |
| Cornea | Opacity | 0 | 0F- | 0 | 0 | 0 | 0 | 0 |
| Iris | Value | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Conjunctiva | Redness | 2 | 2 | 2 | 2 | 1 | 1 | 0 |
| | Chemosis | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| | Discharge | 2 | 0 B | 1 | 1 | 0 | 0 | 0 |
| Animal 3925 M | | | | | | | | |
| Cornea | Opacity | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Iris | Value | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| Conjunctiva | Redness | 2 | 2 | 2 | 1 | 1 | 1 | 0 |
| | Chemosis | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| | Discharge | 2 | 1 | 1 B | 0 | 0 | 0 | 0 |
| Animal 3927 M | | | | | | | | |
| Cornea | Opacity | 1 | 1 F+ | 1 F+ | 0 F- | 0 | 0 | 0 |
| Iris | Value | 1 | 1 | 0 | 0 | 0 | 0 | 0 |
| Conjunctiva | Redness | 1 | 2 | 2 | 1 | 1 | 0 | 0 |
| | Chemosis | 1 | 2 | 1 | 0 | 0 | 0 | 0 |
| | Discharge | 2 | 3 B | 2 B | 0 | 0 | 0 | 0 |

B: mucus present on eye, eye flushed with 30 mL saline

F-: fluorescein negative

F+: fluorescein positive

III. CONCLUSION

In an acceptable ocular irritation test, Dazide WSG give a slight irritancy response, however the test material was not classifiable as irritant in line EU criteria.

| | |
|-----------------------|--------------------------------------------------------------------------------------------------------|
| RMS comments | The study is valid for the risk assessment |
| Endpoint / conclusion | The test substance is not considered an eye irritant according to criteria in Regulation 1272/2008/EC. |

B.6.1.6 Skin Sensitization

B.6.1.6/01 Dazide WSG Skin sensitization to the mouse (LLNA)

| | |
|---------------------|-----------------------------------------------------------------------------------------------|
| Reference: | CP 7.1.6/01 (2003c) Dazide 85 WSG: Local Lymph Node Assay in the Mouse (Individual Method) |
| Report No.: | Report No. 2242//06 Fine Agrochemicals Limited. Report No. FAL 266 |
| Guideline: | OECD 429, EPA OPPTS 870.2600 |
| GLP: | Yes |
| Previous evaluation | None; submitted for the purpose of AIR III renewal |

Executive Summary

The potential for skin sensitisation of Dazide 85 WSG was evaluated in mice using the Local Lymph Node Assay. Groups of five female mice were subjected to topical applications of vehicle control (dimethyl sulphoxide - DMSO) or one of the test formulations (2.5, 5 or 10% in DMSO) to the outer aspect of the auditory pinnae once daily on days 1, 2 and 3. On day 6, a 20 µCi dose of titrated thymidine was injected intravenously into each animal.

Five hours later the auricular lymph nodes were recovered from each animal and processed through a scintillation counter. Test results are expressed in terms of Stimulation Indices with the threshold level to be considered a positive indicator of the potential to cause skin sensitisation being 3.0. Periodic positive control assays gave an appropriate positive response. All results were <3.0 and based on these results, Dazide 85 WSG is not considered to be a skin sensitiser.

I. MATERIALS AND METHODS

A. MATERIALS:

| | |
|--------------------------|-----------------|
| 1. Test material: | Dazide 85 WSG |
| Description: | White solid |
| Lot/Batch: | 4190802 II-NF-2 |
| Purity: | 85.9% w/w |
| CAS#: | 1596-84-5 |

Stability: Analytically determined (Test compound considered stable for the duration of the study)

2. Vehicle and/or positive control: Vehicle: dimethyl sulphoxide
Positive control: α -hexylcinnamaldehyde and mercaptobenzothiazole

3. Test animals:

| | |
|----------------------------------|-----------------------------------------------|
| Species: | Mouse |
| Strain: | ■:CBA/CA Cru.BR |
| Age: | Not stated |
| Weight at dosing: | 16 to 21 g on the day before dosing |
| Source: | ■ |
| Acclimation period: | 15 days |
| Diet: | SQC(E) Rat and Mouse Maintenance Diet No 1 |
| Water: | Mains water <i>ad libitum</i> |
| Housing: | Individually in cages |
| Environmental conditions: | |
| Temperature: | 19-25 °C |
| Humidity: | 49-75% |
| Air changes: | At least 15 ACH |
| Photoperiod: | 12 hours light / 12 hours dark |

B. STUDY DESIGN AND METHODS:

1. In life dates:
21st – 27th August 2003

2. Animals assignment and treatment

Each mouse was manually restrained with both auditory pinnae left free. The outer aspect of both pinnae of each mouse was treated by direct application of the appropriate test or control formulation (0.025 mL/pinna). The four groups of five female mice were subjected to application of the vehicle control or one of the test formulations to the outer aspect of the auditory pinnae on days 1, 2 and 3.

On day 6, 0.25 mL phosphate buffered saline incorporating 20 µCi of methyl-3H thymidine into a tail vein of each mouse by slow bolus injection. Approximately five hours after the intravenous injections of the titrated thymidine, all mice were killed with no more than fifteen minutes between death and the recovery of the auricular lymph nodes.

The lymph nodes were processed and then measured by liquid scintillation counting as disintegrations per minute.

3. Statistics

Statistical differences in DPM values between test groups and the vehicle control group were determined

II. RESULTS AND DISCUSSION

A. FINDINGS

All animals survived treatment and there were no clinical signs indicative of a systemic effect of treatment among mice treated with any of the controls or test formulations. The vehicle and test formulation application sites remained free of irritation. There was no indication of treatment-related effect on body weight.

Test results are expressed in terms of Stimulation Indices; the ratio of the scintillation count per lymph node obtained from a test group relative to the scintillation counts from controls. The threshold level for the Stimulation Index to be considered a positive indicator of the potential to cause skin sensitisation is 3.0.

Table 6.1.6/01 DPM and Stimulation index (SI)

| Concentration of test article in applied formulation (% m/v) | Control | 2.5% | 5% | 10% |
|--------------------------------------------------------------|---------|------|------|------|
| Stimulation Index (SI) | N/A | 1.36 | 1.14 | 0.90 |
| Mean DPM values* | 1085 | 1476 | 1239 | 979 |

*The data from scintillation counter (disintegrations per minute during a ten minute period). To calculate SI the mean DPM value for each tested group was divided by the mean DPM for the control group.

B. DEFICIENCIES

None.

III. CONCLUSION

The Local Lymph Node Assay demonstrated that Dazide 85 WSG does not have the potential to cause skin sensitisation. Periodic positive control assays gave an appropriate positive response. The test material did not meet the criteria for classification as a skin sensitiser.

| | |
|-----------------------|--------------------------------------------------------------------------------------|
| RMS comments | The study is valid for the risk assessment |
| Endpoint / conclusion | The test material did not meet the criteria for classification as a skin sensitiser. |

| | |
|--|--|
| | |
|--|--|

B.6.1.7 Supplementary Studies On The Plant Protection Product

No supplementary studies were performed.

B.6.1.8 Supplementary Studies For Combinations of Plant Protection Products

No supplementary studies for combinations of plant protection products were conducted

B.6.2 Dermal Absorption

No dermal penetration studies were carried out for the first inclusion of Daminozide, a dermal penetration of 13% (default value) was assumed *(Sanco/3043/99 final, 15 February 2005 from the Review Report)

Human in vitro dermal absorption data have been generated for daminozide/Dazide Enhance since the previous EC review of daminozide. These data, reported in Section CP 7.3, have been performed with the product formulation and support values of 0.2% for the product concentrate, 1% for a spray concentration of 0.425 g a.s./L and 2% for a spray concentration of 5.1 g/L. A dermal absorption value of 0.9% is used for the worker exposure assessment which is based on a concentration for skin loading appropriate to the predicted levels of worker exposure (1125 µg daminozide/cm²).

For UDMH, values of 10.7% (0.15% solution), 20.1% (1.5% solution) and 24.5% (15% solution) have previously been agreed (Review Report for Daminozide, SANCO/3043/99). Given that the spray concentrations recommended for Dazide Enhance are at a lower concentration of UDMH than the dermal absorption value provides a precautionary value to use for the risk assessment. The 10.7% value for UDMH is assumed for the risk assessment as this is considered the most representative concentration tested (0.15% solution) for in-use spray dilutions.

| | |
|-----------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RMS comments | <ul style="list-style-type: none"> The recalculation for human in vitro dermal absorption data for Dazide Enhance (850 g/kg SG) was done by RMS according EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873). The values of dermal absorption for UDMH were previously agreed during the first re-evaluation of daminozid and are still relevant |
| Endpoint / conclusion | <ul style="list-style-type: none"> The application of the template calculator provided by EFSA as supportive information resulted in the following values for daminozide: <ul style="list-style-type: none"> 0.2 % for the concentrate 1.9 % for the spray dilution 1 (0.425 g/L) 1.2 % for the spray dilution 2 (5.1 g/L) 0.97 % for the highest re-entry product dilution (112 g/L) 0.77 % for the lowest re-entry product dilution (11.2 g/L) For UDMH the lowest value of 10.7% (at 0.116 µg/cm²) could be used in risk assessment of Dazide Enhance, 850 SG (20.1% at 1.13 µg/cm² and 24.5 % at 12.5 µg/cm²) - Review Report for Daminozide, SANCO/3043/99 |

B.6.2.1 Dermal Absorption, *in vivo*

No study available.

a) Dermal absorption of daminozide

No study available.

B.6.2.2 Dermal Absorption, *in vitro*

B.6.2.2/01 Dermal absorption of daminozide, *in vitro* study using human skin

| | |
|---------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reference: | Blackstock, C. (2012) Daminozide: The <i>In Vitro</i> Percutaneous Absorption of Radiolabelled Daminozide in the Water Soluble Granule (SG) Concentrate, Two In-Use Spray Dilutions and Two Test Preparations Representing Re-Entry Scenarios Through Human Skin |
| Report No. | Charles River., UK, Test Facility Study No. 790977 Fine Agrochemicals Limited, Report No.: 32807 Chemtura Corporation |
| Guideline: | OECD 428 (2004) and EFSA Panel on Plant Protection Product and their Residues (PPR); Guidance on Dermal Absorption (2012) |
| GLP: | Yes |
| Previous evaluation | None; submitted for the purpose of AIR III renewal |

Executive Summary

The absorption and distribution of daminozide from an 85% daminozide SG formulation was measured *in vitro* through human dermatomed skin membranes at five dose levels: 212.5 g/kg, corresponding to the concentrate commercial formulation, and 5.1 g/L, 0.425 g/L, 112 g/L and 11.2 g/L, corresponding two in-use spray dilutions and two test preparations representing worker re-entry scenarios, respectively. The concentrate and dilutions was applied to the surface of 10 skin samples from at least 5 donors at a rate of 20 mg/cm² and 10 µL/cm² respectively. Application residue was washed off the skin surface after 8 hours, with the absorption of daminozide through the skin being assessed over an observation period of 24 h. At the end of the experiment, the distribution of daminozide in the test system was assessed, which included a tape stripping technique to determine its absorption into the stratum corneum and a 24 h absorption profile was determined. All samples were analysed for radioactivity by liquid scintillation counting (LSC).

The vast majority of the **concentrate** commercial formulation applied daminozide (98.70%) was washed off the skin at 8 h, with only small residues being removed at the 24 h wash (0.15%). A small proportion of the applied dose was recovered from the entire *stratum corneum* and unexposed skin (0.11% and 0.03%, respectively). The mean absorbed amount over the entire study period was 0.13 %.

For the **highest in-use spray dilution** the vast majority of the dilution applied daminozide (101.03%) was washed off the skin at 8 h, with only small residues being removed at the 24 h wash (0.29%). A small proportion of the applied dose was recovered from the entire *stratum corneum* and unexposed skin (0.98% and 0.13%, respectively). The mean absorbed amount over the entire study period was 1.26%.

For the **low in-use spray dilution** the vast majority of the dilution applied daminozide (98.89%) was washed off the skin at 8 h, with only small residues being removed at the 24 h wash (0.02%). A small proportion of the applied

dose was recovered from the entire *stratum corneum* (0.83%). The mean absorbed amount over the entire study period was 0.93%.

For the **highest re-entry dilution** the vast majority of the dilution applied daminozide (99.99%) was washed off the skin at 8 h, with only small residues being removed at the 24 h wash (0.33%). A small proportion of the applied dose was recovered from the entire *stratum corneum* and unexposed skin (0.30% and 0.05%, respectively). The mean absorbed amount over the entire study period was 0.61 %.

For the **lowest re-entry dilution** the vast majority of the dilution applied daminozide (100.2%) was washed off the skin at 8 h, with only small residues being removed at the 24 h wash (0.26%). A small proportion of the applied dose was recovered from the entire *stratum corneum* and unexposed skin (0.27% and 0.01%, respectively). The mean absorbed amount over the entire study period was 0.55 %.

I. MATERIAL AND METHODS

A. MATERIALS

1a. Test Material - Radiolabelled [1(4)-14C]N,N-Dimethylaminosuccinamic acid

Description: White solid. The structure and site of labelling (*) of [14C]-Daminozide are shown below.

Lot/Batch: 4593FDG007-8

Radiochemical Purity: 98.3% (determined at the testing facility by HPLC)

Specific Activity: 56.90 mCi/mmol (351.3 µCi/mg)

1b. Test Material – Non-Radiolabelled

Description: Pure white powder

Lot/Batch: 2010-08-05

Purity: 99.70%

Stability: November 2012

1c. Blank formulation

Description: Dazide Enhance blank formulation

Lot/Batch: 4190911+XII-NF1

2. Test System

Human skin samples were obtained from the male and female donors from NHS Lothian, St John's Hospital, Livingston, UK and Biopredic tissue bank, 8-18 Rue Jean Pecker, 3500 Rennes, France. Subcutaneous fat and connective tissue was removed and the samples were then stored frozen, at -20°C, on aluminium foil until required for use. The source and identity of the skin samples were considered confidential and not reported; the sex, anatomical location, age of donor and storage information were documented in the performing laboratory's records. Split-thickness skin membranes were cut from the samples at a thickness setting of 200-400 µm using an electric dermatome and frozen at -20°C.

3. Preparation of dose solutions

Concentrate commercial formulation (Test Preparation 1): 8.5 mL radiodiluted daminozide was transferred into a vial and the deionised water was evaporated. 149.98 mg of Dazide Enhance Blank Formulation and 2.5075 g of artificial sweat solution were added and then the solution vortex mixed, mixed, and sonicated. Radioactivity was subsequently determined by LSC.

Highest in-use spray dilution (Test Preparation 2): 200 µL of [14C]-daminozide was added to a flask and the methanol evaporated. 11.14 mg of daminozide technical was added with a solution of blank formulation in water and the contents mixed and vortex mixed. Radioactivity was determined by LSC. The radioactivity concentration was too high and so an aliquot of blank formulation in water was added and the contents mixed. This was repeated once more until a suitable concentration was obtained.

Lowest in-use spray dilution (Test Preparation 3): 160 µL of [14C]-daminozide was added to a flask and the methanol evaporated. Blank formulation in water was added to the 2 mL line in a volumetric flask and the contents mixed and vortex mixed. Radioactivity was determined by LSC. The radioactivity concentration was too high and so an aliquot of blank formulation in water was added and the contents mixed. A suitable concentration was subsequently obtained.

Highest re-entry dilution (Test Preparation 4): 150 µL of [14C]-daminozide was added to a flask and the solvent evaporated. 223.91 mg daminozide technical was added and artificial sweat solution added to the 2 mL line in a volumetric flask. The contents were mixed and vortex mixed and radioactivity subsequently determined by LSC.

Lowest re-entry dilution (Test Preparation 5): 150 µL of [14C]-daminozide was added to a flask and the solvent evaporated. 22.13 mg daminozide technical was added and artificial sweat solution added to the 2 mL line in a volumetric flask. The contents were mixed and vortex mixed and radioactivity subsequently determined by LSC. The artificial sweat solution was prepared in accordance with EU standard EN 1811. Sodium chloride (0.5%, w/v), urea (0.1% w/v) and lactic (0.1%, v/v) were dissolved in water and the pH of the solution adjusted to pH 6.6 using ammonium hydroxide.

4. Diffusion cells and receptor fluid

An automated flow-through diffusion cell apparatus was used. The flow-through diffusion cells were placed in a manifold heated via a circulating water bath to maintain a skin surface temperature of $32 \pm 1^\circ\text{C}$. The surface area of exposed skin within the cells was 0.64 cm². Approximately 1.5×1.5 cm sections of split-thickness skin membrane were positioned in the receptor chamber of the diffusion cell. The prepared cells were then placed in the heated manifold and connected to the peristaltic pump providing the receptor fluid. The receptor fluid was phosphate buffered saline (PBS) containing streptomycin (0.1 mg/mL) and penicillin G (100 units/mL). The receptor fluid effluent was dropped into scintillation vials on a fraction collector at a flow rate of $1.5 \text{ mL/h} \pm 0.15 \text{ mL/h}$.

B. STUDY DESIGN AND METHODS

1. Experimental dates

12 October to 29 November 2011

2. Measurement of skin integrity

The method as described by Median and Roper (2008) and modified by Runciman et al. (2009) was used. Tritiated water was applied to the surface of each skin sample and penetration assessed by collecting receptor fluid for 1 h

analysing the sample by LSC. The mean dpm applied for the tritiated water was calculated from the seven mock samples taken at the time of dosing. Absorption was calculated for each skin sample from the receptor fluid sample collected. Any sample exhibiting greater than 0.6% absorption was excluded from subsequent absorption measurements.

3. Experimental procedure

Test Preparation 1 was applied over the *stratum corneum* surface of the exposed skin at 20 mg/cm² with the donor chambers left open to the atmosphere. Test Preparations 2, 3, 4, and 5 were applied over the *stratum corneum* surface of the exposed skin at approximately 10 µL/cm² with the donor chambers left open to the atmosphere. Receptor fluid was collected in hourly fractions from 0 to 8 h then 2 hourly until 24 h post-dose. All receptor fluid samples were mixed with 10 mL scintillation fluid and analysed by LSC.

At 8 h post-dose, the exposure period was terminated by rubbing a commercial hand wash soap into the skin surface and then rinsing the skin with ten 0.5 mL aliquots of a 2% v/v dilution of the hand wash soap. This process was repeated and the skin dried. The soap solution was pooled and duplicate 1 mL aliquots were removed and analysed by LSC. The pipette used to aspirate the soap solution was also analysed by LSC.

At 24 h post-dose, the underside of the skin was rinsed with receptor fluid which was then analysed by LSC. The receptor-rinse represented the absorbed test item, which was in the receptor chamber, but not had not been collected into the 22 to 24 h receptor fluid fraction. The donor and receptor chambers were soaked in deionised water for approximately 30 minutes to extract any test item. Duplicate 1 mL aliquots were removed and analysed by LSC. The skin samples removed from the test equipment were dried with tissue paper swabs; the swabs were then analysed by LSC. The stratum corneum was removed with 20 successive tape strips with each individual strips analysed separately by LSC. The skin under the cell flange (unexposed skin) was cut away from the exposed skin and the samples individually analysed by LSC following solubilisation by exposure to 1 mL Solvable® and heating at approximately 60°C for approximately 1.5 h.

4. Calculations and expression of study results

The following calculations were performed:

Sample amount (µg equiv./cm²) = sample radioactivity (dpm) / (SA (dpm/µg equiv.) x exposure area (cm²))

Sample applied dose (%) = (sample radioactivity (dpm) / applied dose (dpm)) x 100%

II. RESULTS AND DISCUSSION

Test Preparation 1

A total of ten skin samples from five different donors were dosed topically with Test Preparation 1 (215 g/kg). One cell was rejected as it was an outlier for total absorbed dose (mean ± 2SD) and so the following results are provided as mean values of n=9. The mean mass balance was 99.06% of the applied dose at 24 h post dose. At the end of the 8 h exposure period, 98.70% of the applied dose was washed off (52.15%, 46.54%, and 0.01% recovered in the skin wash, tissue swab and pipette tips, respectively). A further 0.15% of the applied dose was removed at 24 h post dose (donor chamber wash and 24 h tissue swabs contained 0.15% and <0.01% of the applied dose, respectively). The material recovered in the donor wash was almost certainly material that had been dislodged from the skin at 8 h post dose during the washing procedure. Therefore, the total dislodgeable dose was 98.85% of the applied dose. The mean total unabsorbed dose was 98.99% of the applied dose. This consisted of the

dislodgeable dose, unexposed skin (0.03%) and the radioactivity associated with the stratum corneum (0.11%). Tape strips 1 and 2 contained 0.04% of the applied dose. These initial tape strips may be considered to be on the stratum corneum surface and potentially sloughed off. Therefore, these initial tape strips are not associated with the stratum corneum. There was a steady decrease in the recovery of radioactivity associated with the stratum corneum. Where any epidermis was removed during tape stripping this tape strip value was added to the epidermis and not the stratum corneum value. Tape strips 3-5, 6-10, 11-15 and 16-20 contained a further 0.03%, 0.02%, 0.01% and 0.01%, respectively. The absorbed dose (0.03%) was the sum of the receptor fluid (0.02%), receptor rinse (<0.01%) and receptor chamber wash (0.01%). Dermal delivery (0.07%) was the sum of the absorbed dose and the exposed skin (0.04%). The absorption was considered 'incomplete' (66.4% of the absorption into the receptor fluid occurred in the first 12 h of the study). The potentially absorbable dose was therefore the sum of the dermal delivery and tape strips 3-20 (0.07%).

Test Preparation 2

A total of ten skin samples from five different donors were dosed topically with Test Preparation 2 (5.1 g/L). One cell was rejected as it was an outlier for total absorbed dose (mean \pm 2SD) and so the following results are provided as mean values of n=9. The mean mass balance was 102.86% of the applied dose at 24 h post dose. At the end of the 8 h exposure period, 101.03% of the applied dose was washed off (47.56%, 53.46%, and 0.01% recovered in the skin wash, tissue swab and pipette tips, respectively). A further 0.29% of the applied dose was removed at 24 h post dose (donor chamber wash and 24 h tissue swabs contained 0.29% and <0.01% of the applied dose, respectively). Therefore, the total dislodgeable dose was 101.32% of the applied dose. The mean total unabsorbed dose was 102.43% of the applied dose. This consisted of the dislodgeable dose, unexposed skin (0.13%) and the radioactivity associated with the stratum corneum (0.98%). Tape strips 1 and 2 contained 0.15% of the applied dose. There was a steady decrease in the recovery of radioactivity associated with the stratum corneum. Tape strips 3-5, 6-10, 11-15 and 16-20 contained a further 0.26%, 0.28%, 0.16% and 0.12%, respectively. The absorbed dose (0.14%) was the sum of the receptor fluid (0.10%), receptor rinse (<0.01%) and receptor chamber wash (0.04%). Dermal delivery (0.43%) was the sum of the absorbed dose and the exposed skin (0.29%). The absorption was considered 'incomplete' (69.2% of the absorption into the receptor fluid occurred in the first 12 h of the study). The potentially absorbable dose was therefore the sum of the dermal delivery and tape strips 3-20 (0.83%).

Test Preparation 3

A total of ten skin samples from five different donors were dosed topically with Test Preparation 3 (0.425 g/L). One cell was rejected as it was an outlier for total absorbed dose (mean \pm 2SD) and so the following results are provided as mean values of n=9. The mean mass balance was 99.98% of the applied dose at 24 h post dose. At the end of the 8 h exposure period, 98.89% of the applied dose was washed off (38.49%, 60.39%, and <0.01% recovered in the skin wash, tissue swab and pipette tips, respectively). A further 0.02% of the applied dose was removed at 24 h post dose (donor chamber wash and 24 h tissue swabs contained 0.02% and <0.01% of the applied dose, respectively). Therefore, the total dislodgeable dose was 98.91% of the applied dose. The mean total unabsorbed dose was 99.74% of the applied dose. This consisted of the dislodgeable dose, unexposed skin (<0.01%) and the radioactivity associated with the stratum corneum (0.83%). Tape strips 1 and 2 contained 0.14% of the applied dose. Tape strips 3-5, 6-10, 11-15 and 16-20 contained a further 0.21%, 0.28%, 0.12% and 0.08%, respectively. The absorbed dose (0.05%) was the sum of the receptor fluid (0.04%), receptor rinse (<0.01%) and

receptor chamber wash (0.01%). Dermal delivery (0.24%) was the sum of the absorbed dose and the exposed skin (0.18%). The absorption was considered ‘incomplete’ (66.7% of the absorption into the receptor fluid occurred in the first 12 h of the study). The potentially absorbable dose was therefore the sum of the dermal delivery and tape strips 3-20 (0.69%).

Test preparation 4

(112 g/L). The following results are provided as mean values (n = 10). The mean mass balance was 101.15% of the applied dose at 24 h post dose. At the end of the 8 h exposure period, 99.99% of the applied dose was washed off (48.80%, 51.18%, and 0.01% recovered in the skin wash, tissue swab and pipette tips, respectively). A further 0.33% of the applied dose was removed at 24 h post dose (donor chamber wash and 24 h tissue swabs contained 0.27% and 0.06% of the applied dose, respectively). Therefore, the total dislodgeable dose was 100.32% of the applied dose. The mean total unabsorbed dose was 100.67% of the applied dose. This consisted of the dislodgeable dose, unexposed skin (0.05%) and the radioactivity associated with the stratum corneum (0.30%). Tape strips 1 and 2 contained 0.18% of the applied dose. There was a steady decrease in the recovery of radioactivity associated with the stratum corneum. Tape strips 3-5, 6-10, 11-15 and 16-20 contained a further 0.04%, 0.04%, 0.02% and 0.02%, respectively. The absorbed dose (0.33%) was the sum of the receptor fluid (0.24%), receptor rinse (<0.01%) and receptor chamber wash (0.09%). Dermal delivery (0.48%) was the sum of the absorbed dose and the exposed skin (0.15%). The absorption was considered ‘complete’ (83.4% of the absorption into the receptor fluid occurred in the first 12 h of the study) and so the potentially absorbable dose was therefore considered equivalent the dermal delivery (i.e. all tape stripped material was excluded).

Test Preparation 5

A total of ten skin samples from five different donors were dosed topically with Test Preparation 5 (11.2 g/L). One of the skin samples failed the barrier integrity assessment and was dosed in error. This cell was rejected and so the following results are provided as mean values of n=9. The mean mass balance was 101.08% of the applied dose at 24 h post dose. At the end of the 8 h exposure period, 100.20% of the applied dose was washed off (53.52%, 46.67%, and 0.01% recovered in the skin wash, tissue swab and pipette tips, respectively). A further 0.26% of the applied dose was removed at 24 h post dose (donor chamber wash and 24 h tissue swabs contained 0.26% and <0.01% of the applied dose, respectively). Therefore, the total dislodgeable dose was 100.47% of the applied dose. The mean total unabsorbed dose was 100.74% of the applied dose. This consisted of the dislodgeable dose, unexposed skin (0.01%) and the radioactivity associated with the *stratum corneum* (0.27%). Tape strips 1 and 2 contained 0.05% of the applied dose. There was a steady decrease in the recovery of radioactivity associated with the *stratum corneum*. Tape strips 3-5, 6-10, 11-15 and 16-20 contained a further 0.05%, 0.08%, 0.05% and 0.03%, respectively. The absorbed dose (0.23%) was the sum of the receptor fluid (0.19%), receptor rinse (<0.01%) and receptor chamber wash (0.04%). The absorption was considered ‘complete’ (87.0% of the absorption into the receptor fluid occurred in the first 12 h of the study). Therefore the potentially absorbable dose was considered equivalent the dermal delivery (i.e. all tape stripped material was excluded).

A summary of the mean results is detailed in Table 6.2.2/01-1 below.

Table 6.2.2/01-1: Summary of mean results

| | Concentrate | Dilution 1 | Dilution 2 | Dilution 3 | Dilution 4 |
|----------------------------------------------|---------------------|---------------------|---------------------|----------------------|----------------------|
| Target concentration | 212.5 g/kg | 5.1 mg/mL | 0.425 mg/mL | 112 mg/mL | 11.2 mg/mL |
| Mean actual applied dose, µg/cm ² | 4647.08 | 50.89 | 4.56 | 1125.14 | 114.79 |
| RECOVERY, % | | | | | |
| <i>Dislodgeable dose</i> | | | | | |
| Skin wash after 8 h | 98.7 ± 5.26 | 101.03 ± 1.47 | 98.89 ± 0.68 | 99.99 ± 1.97 | 100.2 ± 1.48 |
| Donor chamber wash | 0.15 ± 0.21 | 0.26 ± 0.50 | 0.02 ± 0.01 | 0.3 ± 0.28 | 0.26 ± 0.55 |
| <i>Skin associated dose</i> | | | | | |
| Tape strips 1-2 | 0.05 ± 0.05 | 0.15 ± 0.16 | 0.14 ± 0.08 | 0.22 ± 0.37 | 0.05 ± 0.05 |
| Tape strips 3-20 | 0.07 ± 0.05 | 0.83 ± 0.52 | 0.69 ± 0.25 | 0.12 ± 0.11 | 0.22 ± 0.08 |
| Skin preparation | 0.04 ± 0.03 | 0.29 ± 0.29 | 0.18 ± 0.15 | 0.15 ± 0.12 | 0.11 ± 0.05 |
| <i>Absorbed dose</i> | | | | | |
| Receptor fluid | 0.02 ± 0.01 | 0.10 ± 0.09 | 0.04 ± 0.03 | 0.24 ± 0.23 | 0.19 ± 0.19 |
| Receptor chamber wash | 0.04 | 0.06 | 0.02 | 0.14 | 0.11 |
| Total recovery | 99.03 ± 5.18 | 102.7 ± 1.84 | 99.97 ± 0.51 | 101.07 ± 1.97 | 101.07 ± 0.98 |
| Absorbed at t _{0.5} | 56.59 ± 8.23 | 55.26 ± 8.72 | 60.03 ± 5.64 | 46.7 ± 18.03 | 56.41 ± 8.61 |
| Absorption complete? | NO | NO | NO | NO | NO |
| Measured absorption | 0.13 ± 0.09 | 1.26 ± 0.81 | 0.93 ± 0.38 | 0.61 ± 0.50 | 0.55 ± 0.29 |
| Relevant absorption estimate | 0.202 | 1.883 | 1.221 | 0.966 | 0.774 |
| Final estimate (rounded) | 0.2 | 1.9 | 1.2 | 0.97 | 0.77 |

III. CONCLUSION

Following topical application of [14C]-daminozide applied to human skin *in vitro*, the absorbed dose was 0.03%, 0.14%, 0.05%, 0.33% and 0.23% for Test Preparations 1, 2, 3, 4 and 5, respectively. The dermal delivery was 0.07%, 0.43%, 0.24%, 0.48% and 0.34%, respectively. The potentially absorbable dose of [14C]-daminozide was 0.14%, 1.26%, 0.93%, 0.48% and 0.34%, respectively. The majority of the dose was removed by washing the skin;

the total dislodgeable dose was 98.85%, 101.32%, 98.91%, 100.32% and 100.47% of the applied dose, respectively.

| | |
|-----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RMS comments | <p>The results of <i>in vitro</i> dermal absorption study with Dazid Enhance (SG) through human skin were recalculated using EFSA calculator.</p> <p>According to the new Guidance, if the $t_{0.5}$ value is close to 75%, a confidence interval should be estimated to determine reliability of the conclusion that the penetration is essentially complete. The lower limit of the 95% confidence interval should be calculated as $t_{0.5} - ks$, where k is a multiplication factor based on the number of replicates (for $n=9$, $k=0.77$) and s is the standard deviation. The mean relative penetration into the receptor fluid after half time of the sampling period should be calculated from individual replicate data. None of the tested concentrations had complete absorption after 12h, therefore only 1st and 2nd stripped material could be excluded. Details in the Table 6.2.2/01-1.</p> |
| Endpoint / conclusion | <p>Based on results obtained from the <i>in vitro</i> study using human skin, the dermal absorption values were determined to be 0.2% for the concentrate, 1.9% for the highest in-use spray dilution (5.1 g/L) and 1.2% for the lowest in-use spray dilution (0.425 g/L). For the purpose of assessing re-entry worker exposure a further two product dilutions were assessed after being mixed with an artificial sweat, 0.97% for the highest re-entry product dilution (112 g/L) and 0.77% for the lowest re-entry product dilution (11.2 g/L).</p> |

B.6.3 Available Toxicological Data Relating to Co-formulants

Copies of the Safety Data Sheets for the other components of the formulation have been submitted in Document J of the dossier. Acute toxicity, irritation and sensibilisation are addressed with data (see above). All information and toxicological data on non-active substances relating to the composition of Dazide Enhance are confidential and are available in Volume 4 Annex C ‘Confidential information’.

B.6.4 Exposure Data

Dazide Enhance is a water soluble granule (SG) formulation, containing a nominal 850 g/kg of daminozide. The representative uses are as a foliar spray to ornamental flowers and bedding plants. The representative critical GAPs for the purposes of the AIR process are summarised in Table 6.4-1. Application to glasshouse plants is made using hand-held equipment or automated gantry sprayers.

Table B.6.4-1: Summary of critical use pattern (i.e. worst case)

| Crop | Application | | | | Application rate per treatment | | |
|-----------------------|----------------------------------------------------------|-------------------------|-----------------|---------------------------------------|---------------------------------------|-----------------------------------|----------------------|
| | Application technique | Growth stage | Number of appl. | Minimum interval between applications | Maximum individual dose, (kg a.s./ha) | | Water volume, (L/ha) |
| | | | | | (kg product/ha) | (kg a.s./ha) | |
| Ornamentals Protected | Foliar spray using automated gantry or hand-held sprayer | Actively growing plants | 5 | 7 days | 9 | 7.65 daminozide 0.0000026 UDMH | 500-1500 |
| Ornamentals Outdoor | Foliar spray using hand-held sprayer | Actively growing plants | 5 | 7 days | 5 | 4.25 daminozide 0.0000014 UDMH | 500-1500 |

AOEL / Dermal absorption

The AOEL values adopted for the inclusion of daminozide and UDMH (Sanco/3043/99 final, 15 February 2005 from the Review Report) are 0.16 mg/kg bw/day and 0.09 µg/kg bw/day respectively, but according new data new AOEL value for daminozide has been suggested as 0.00875 mg/kg bw/day (see Section B.6.12.3 for the active substance).

Human *in vitro* dermal absorption data have been generated for daminozide/Dazide Enhance since the previous review of daminozide. These data (see B.6.2 above) have been performed with the product formulation and support values of 0.2% for the product concentrate, 1.2 % for a spray concentration of 0.425 g a.s./L and 1.9 % for a spray concentration of 5.1 g/L. A dermal absorption value of 0.97% is used for the worker exposure assessment which is based on a concentration for skin loading appropriate to the predicted levels of worker exposure (1125 µg daminozide/cm²).

For UDMH, values of 10.7% (0.15% solution), 20.1% (1.5% solution) and 24.5% (15% solution) have previously been agreed. Given that the spray concentrations recommended for Dazide Enhance are at a lower concentration of UDMH than the dermal absorption value provides a precautionary value to use for the risk assessment. The 10.7% value for UDMH is assumed for the risk assessment as this is considered the most representative concentration for proposed use, for the undiluted product and the spray dilution (see point B.6.2 above).

Estimations of exposure to Alar have been assessed pursuant to intended uses as shown above in **Table B.6.4-1** and compared to toxicological reference values (Acceptable Operator Exposure Level) taken into account dermal absorption values appropriate for Alar as shown in **Table B.6.4-2** below.

Table B.6.4-2 EU end-points and end-points used in risk assessment for daminozide and UDMH

| End-Point | EU endpoint (Annex I inclusion) | | Endpoint used in risk assessment | |
|--------------------|---------------------------------|-------|----------------------------------|-------|
| | Active Substance | | | |
| | Daminozide | UDMH | Daminozide | UDMH |
| Dermal penetration | | | | |
| Concentrate: | 13% | 10.7% | 0.2% | 10.7% |

| | | | | |
|------------------|----------------------|-------------------------|-------------------------|-------------------------|
| Spray dilutions: | 13% | 10.7% | 1.9% | 10.7% |
| Oral absorption | 35% | 100% | 35% | 100% |
| AOEL | 0.16 mg/kg bw/day | 0.00009 mg/kg bw/day | 0.00875 mg/kg bw/day | 0.00009 mg/kg bw/day |
| AAOEL | not relevant | not relevant | not relevant | not relevant |

B.6.4.1 Operator exposure

Operator exposure was assessed using the following standard approaches:

Operator exposure for daminozide and UDMH was assessed using the following models for outdoor and indoor application:

- German model: Lundehehn, J.-R.; Westphal, D.; Kieczka, H.; Krebs, B.; Locher-Bolz, S; Maasfeld, W.; Pick, E.-D. (1992): Uniform Principles for Safeguarding the Health of Applicators of Plant Protection Products (Uniform Principles for Operator Protection);, Mitteilungen aus der Biologischen Bundesanstalt, Heft 277, Berlin, 1992,
- Revised UK POEM: Estimation of Exposure and Absorption of Pesticides by Spray Operators, Scientific subcommittee on Pesticides and British Agrochemical association Joint Medical Panel Report (UK MAFF), 1986 and the Predictive Operator Exposure Model (POEM) V 7, 1992, 2008 version,
- Dutch greenhouse model for manual up- and downward spraying based on exposure studies in Dutch greenhouses: Golstein Brouwers Y.G.C. van, Marquart J., Hemmen J.J. van, (1996) Assessment of occupational exposure to pesticides in agriculture. Part IV: Protocol for the use of generic exposure data. TNO-report V 96.120. and Snippe R.J., Drooge H.L. van, Schipper H.J., Pater A.J. de, Hemmen J.J. van, (2002). Pesticide exposure assessment for registration purposes. Version 2002. TNO-report V3642
- Southern European Greenhouse model v_2.1 (20101223) with Southern European Greenhouse Model Overview. Members of the European Crop Protection Association. Occupational & Bystander Exposure Expert Group. October 2010 (Revision 9). ECPA, European Crop Protection Association, aisbl 6, Avenue E. Van Nieuwenhuyse, B-1160 Brussels, Belgium.

Regarding ~~the submission time and~~ the current approach, also the risk assessment using the following model has been carried out:

- EFSA AOEM model has been included in the EFSA Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment for Plant Protection Products (EFSA Journal 2014;12(10):3874).
-

Unsymmetrical Dimethyl Hydrazine (UDMH) is an impurity that is permitted to be present at a maximum concentration of 30 mg/kg daminozide. Experimental work has shown that when added to water, a small amount of daminozide hydrolyses to form additional UDMH (Connor J. Hart, 2012). The risk to operators applying prepared spray solutions of daminozide has been considered in the context of these findings.

The results of the exposure calculations for operators are summarized in Table B.6.4-3 below. Details of the calculations are given in Appendix I.

| Table B.6.4-3 Estimated operator exposure to daminozide and UDMH in Dazide Enhance | | | | | |
|--------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------|--------------------------------|----------------------------|-------------------------------------|
| Model data | Level of PPE | Total absorbed dose (mg/kg bw/day) ¹ | | % of AOEL ² | Reference Appendix |
| Hand held application outdoors | | | | | |
| 5 kg Dazide Enhance/ha corresponding to 4.25 kg of daminozide per ha, spray volume 500 L per ha | | | | | |
| UK POEM - 0.8 ha/day - 70 kg operator | M/L: Gloves and RPE (FFP3) Appl: Gloves and Impermeable coveralls | daminozide | 0.05815 | 665 | B.6.4.1-16 |
| | | UDMH | 0.0000056 | 62 | B.6.4.1-17 |
| EFSA AOEM - manual hand held - 4 ha/day - 60 kg operator | M/L and Appl.: Gloves, workwear, RPE (FP2) | daminozide | 0.0022 | 24.78 | B.6.4.1-18 |
| | | UDMH | 0.015959 | 17,732.23 | B.6.4.1-19 |
| EFSA AOEM - manual knapsack - 1 ha/day - 60 kg operator | M/L and Appl.: Gloves, workwear, RPE (FP2) | daminozide | 0.0010 | 11.62 | B.6.4.1-20 |
| | | UDMH | 0.016072 | 17,857.63 | B.6.4.1-21 |
| Hand held application indoor | | | | | |
| 9 kg Dazide Enhance /ha corresponding to 7.65 kg of daminozide per ha, spray volume 500 L per ha | | | | | |
| Dutch Greenhouse Model - 1 ha/day - 70 kg operator | M/L and Appl.: Gloves, Coverall, RPE (FP2) | daminozide | 0.0415 | 600 | B.6.4.1-7 |
| | | UDMH | 0.000051 | 57 | B.6.4.1-8 |
| Southern European Greenhouse Model Low crops - 1 ha/day - 70 kg operator | M/L: Gloves Appl.: Gloves, RPE (FPP2), Coverall | daminozide | 0.0061 | 70.1 | B.6.4.1-9 |
| | | UDMH | 0.000002 | 2.3 | |
| Southern European Greenhouse Model High crops - 1 ha/day - 70 kg operator | M/L: Gloves, RPE (A1P2) Appl.: Gloves, RPE (A1P2), Headgear, Impervious clothing | daminozide | 0.00706 | 80.7 | |
| | | UDMH | 0.000007 | 7.7 | |
| Gantry application indoors | | | | | |
| 9 kg Dazide Enhance /ha corresponding to 7.65 kg of daminozide per ha, spray volume 500 L per ha | | | | | |
| UK POEM mix/loading - 1 ha/day - 70 kg operator | No PPE | daminozide | 0.00516 | 59 | B.6.4.1-10 |
| | | UDMH | 0.000002 | 2.41 | B.6.4.1-11 |
| German Model mix/loading - 1 ha/day - 70 kg operator | No PPE | daminozide | 0.00131 | 15 | B.6.4.1-12 |
| | | UDMH | 0.000001 | 0.8 | B.6.4.1-13 |
| EFSA AOEM mix/loading - 10 ha/day - 60 kg operator | M/L: Gloves, Workwear, RPE (FPP1) | daminozide | 0.00243 0.0014 | 27.78 15.95 | B.6.4.1-23 B.6.4.1-24 |
| | | UDMH | 0.000127 0.00003 | 140.84 33.87 | B.6.4.1-24 B.6.4.1-25 |
| 1) Systemic exposure based on dermal absorption for the respective uses as indicated in Table B.6.4-2. | | | | | |
| 2) Based on a systemic AOEL as indicated in Table B.6.4-2. | | | | | |

Conclusions

Operator exposure and risk evaluations were performed for applications of Dazide Enhance to outdoor ornamentals by means of the UK POEM and EFSA AOEM. Estimates of exposure for use on protected ornamentals were predicted using the Dutch model for manual application in glasshouses and also the ECPA Southern European Greenhouse model. Mixing and loading data taken from the German model, UK POEM and EFSA AOEM were also used to predict levels of exposure for automated gantry application to protected crops. The worst-case in terms of application rates and water volumes were chosen as input parameters in the modelling for the demonstration of uses for the product Dazide Enhance.

Based on these exposure models the assessment shows that levels of exposure to daminozide for spray operators applying Dazide Enhance to ornamentals using automated gantry and hand-held sprayers will be within the AOEL when PPE are worn except outdoor use according UK POEM and indoor use according Dutch model.

The assessment also shows that levels of exposure to UDMH for spray operators applying Dazide Enhance to ornamentals using automated gantry or hand-held sprayers are within the AOEL with the use of PPE except use according EFSA AOEM model.

Overall, it can be concluded that unacceptable health risk for the operator can occur with the intended uses of Dazide Enhance, even where PPE are worn.

B.6.4.1.1 Estimation of operator exposure without personal protective equipment

Regarding the intended use of Alar to ornamentals outdoor and indoor both, following exposure scenarios has been considered:

- Outdoor hand held application
- Indoor hand held application into low and high crop
- Indoor gantry sprayer application

Content of UDMH

UDMH is an impurity of the active substance present up to a maximum of 30 mg/kg technical material. Experimental work has shown that when daminozide is added to water, a small amount of the active substance hydrolyses to form additional UDMH (Connor J. Hart, 2012, see Volume 3 – Annex B.6 (AS)). The risk to operators applying prepared spray solutions of daminozide has been considered in the context of these findings.

The study has taken measurement of the presence of UDMH over a storage period lasting up to 24 hours. A stock solution of 3.75364 g (3750 ppm) daminozide in 1 litre of tap water was prepared and the amount of UDMH presented in the solution was measured at 2, 4, 6 and 24 hours. Results of the study are presented in Table B.6.4.1.1-1 below.

Table B.6.4.1.1-1: Increase in UDMH content measured over 24 hours

| Time interval (hours) | UDMH (mg/L) | Mean UDMH (mg/L) |
|-----------------------|-------------|------------------|
| 0 | 0.035 | 0.043 |
| | 0.051 | |
| 1 | 0.15 | 0.16 |
| | 0.17 | |

| Time interval (hours) | UDMH (mg/L) | Mean UDMH (mg/L) |
|-----------------------|-------------|------------------|
| 2 | 0.35 | 0.36 |
| | 0.37 | |
| 4 | 0.65 | 0.67 |
| | 0.68 | |
| 6 | 1.04 | 1.1 |
| | 1.07 | |
| 24 | 3.7 | 3.7 |
| | 3.72 | |

In terms of risk assessment a typical application may take four hours from the time the product is added to the spray tank to the end of spraying. Allowing for a mechanical breakdown which could delay the application of the prepared spray solution, a longer period is possible. However this scenario would not be representative of a repeat exposure situation. For risk assessment purposes the value determined after four hours is considered to be suitably representative.

Daminozide in Dazide Enhance can be applied at a maximum rate of 7.65 kg a.s./ha. The UDMH impurity is present in the technical material up to a maximum concentration of 30 mg/kg daminozide. Thus 4.25 kg a.s./ha and 7.65 kg a.s./ha Dazide Enhance may contain up to 0.1275g and 0.23 g UDMH respectively.

Using the available data from the spray tank study, i.e. 3.75 g daminozide produced 0.67 mg UDMH over 4 hours, for an application rate of 4.25 kg daminozide/ha the total UDMH applied/ha, taking into account the amount of UDMH from manufacturing (127.5 mg UDMH) and the additional UDMH produced through hydrolysis of daminozide over a 4 hour period (759 mg – calculated from 3.75 g daminozide producing 0.67 mg UDMH over 4 hours) is 887 mg UDMH.

The predicted amount of UDMH in the spray solution is 0.0018 g UDMH per L spray solution (assuming the minimum water volume of 500 L water/ha is applied) for the outdoor use. This parameter is used for the UK POEM assessment which considers the spray solution concentration. The amount of UDMH in the spray tank per kg Daminozide applied is 208.7 mg UDMH (i.e. 887 mg UDMH divided by 4.25 kg a.s./ha.)

For the summary of UDMH content see table B.6.4.1.1-2.

Table B.6.4.1.1-2: Summary of UDMH content after 4h

| Daminozide content (g/ha) | UDMH from manufacturing (g/ha) | UDMH produced through hydrolysis (g/ha) | total amount of UDMH (g/ha) |
|---------------------------|--------------------------------|-----------------------------------------|-----------------------------|
| 4,250 | 0.1275 | 0.759 | 0.887 |
| 7,650 | 0.23 | 1.365 | 1.595 |

Levels of exposure for spray operators are predicted on this basis. The exposure assessment considers both outdoor and protected uses.

The results of the exposure estimations for Daminozide and UDMH taking into account the above mentioned input parameters and assuming that no personal protective equipment (PPE) is worn are presented in Table B.6.4.1.1-3 below. Detailed exposure calculations are provided in the Appendix 1 to this section.

Table B.6.4.1.1-3: Summary of predicted exposures for operators applying Dazide Enhance to protected and outdoor crops without using PPE

| Model data | Level of PPE | Total absorbed dose (mg/kg bw/day) ¹ | | % of AOEL ² | Reference Appendix |
|--------------------------------------------------------------------------------------------------|--------------|-------------------------------------------------|-------------------------------|--------------------------------|--------------------|
| Hand held application outdoors to low crops | | | | | |
| 5 kg Dazide Enhance /ha corresponding to 4.25 kg of daminozide per ha, spray volume 500 L per ha | | | | | |
| UK POEM - 0.8 ha/day - 70 kg operator | No PPE | daminozide | 0.2696 | 3,081 | B.6.4.1-1 |
| | | UDMH | 0.000466 | 518 | B.6.4.1-2 |
| EFSA AOEM - manual hand held - 4 ha/day - 60 kg operator | No PPE | daminozide | 0.0266 | 303.54 | B.6.4.1-3 |
| | | UDMH | 0.019232 | 21,368.88 | B.6.4.1-4 |
| EFSA AOEM - manual knapsack - 1 ha/day - 60 kg operator | No PPE | daminozide | 0.0109 | 124.79 | B.6.4.1-5 |
| | | UDMH | 0.036488 | 40,542.37 | B.6.4.1-6 |
| Hand held application indoor | | | | | |
| 9 kg Dazide Enhance /ha corresponding to 7.65 kg of daminozide per ha, spray volume 500 L per ha | | | | | |
| Dutch Greenhouse Model - 1 ha/day - 70 kg operator | No PPE | daminozide | 0.5246 | 5,995 | B.6.4.1-7 |
| | | UDMH | 0.000510 | 567 | B.6.4.1-8 |
| Southern European Greenhouse Model Low crops - 1 ha/day - 70 kg operator | No PPE | daminozide | 0.06306 | 720.7 | B.6.4.1-9 |
| | | UDMH | 0.00003 | 34.2 | |
| Southern European Greenhouse Model High crops - 1 ha/day - 70 kg operator | No PPE | daminozide | 0.1654 | 1890.2 | |
| | | UDMH | 0.00013 | 140.2 | |
| Gantry application indoors | | | | | |
| 9 kg Dazide Enhance /ha corresponding to 7.65 kg of daminozide per ha, spray volume 500 L per ha | | | | | |
| UK POEM mix/loading - 1 ha/day - 70 kg operator | No PPE | daminozide | 0.00516 | 59 | B.6.4.1-10 |
| | | UDMH | 0.000002 | 2.41 | B.6.4.1-11 |
| German Model mix/loading - 1 ha/day - 70 kg operator | No PPE | daminozide | 0.00131 | 15 | B.6.4.1-12 |
| | | UDMH | 0.000001 | 0.8 | B.6.4.1-13 |
| EFSA AOEM mix/loading - 10 ha/day - 60 kg operator | No PPE | daminozide | 0.00595 0.00432 | 68.05 49.35 | B.6.4.1-14 |
| | | UDMH | 0.017403 0.0001 | 19,336.57 142.49 | B.6.4.1-15 |

¹⁾ Systemic exposure based on dermal absorption for the respective uses as indicated in Table B.6.4-2.

¹) Systemic exposure based on dermal absorption for the respective uses as indicated in Table B.6.4-2.

²⁾ Based on a systemic AOEL as indicated in Table B.6.4-2.

B.6.4.1.2 Estimation of operator exposure using personal protective equipment

Assessment of systemic exposure of unprotected operators indicates that levels of exposure to daminozide from the proposed use of Dazide Enhance are above the AOEL for hand-held application according to UK POEM, NL glasshouse and the Southern European Glasshouse Model (high crop scenario). Exposure assessment for operators wearing personal protective equipment is therefore considered.

The results of the exposure estimations when personal protective equipment (PPE) is worn are presented in Table B.6.4.1.2-1 below. Detailed exposure calculations are provided in the Appendix 1 to this section.

Table B.6.4.1.2-1: Summary of predicted exposures for operators applying Dazide Enhance to protected and outdoor crops using PPE

| Model data | Level of PPE | Total absorbed dose (mg/kg bw/day) ¹ | | % of AOEL ² | Reference Appendix |
|--------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------|-----------|------------------------|--------------------|
| Hand held application outdoors to low crops | | | | | |
| 5 kg Dazide Enhance /ha corresponding to 4.25 kg of daminozide per ha, spray volume 500 L per ha | | | | | |
| UK POEM - 0.8 ha/day - 70 kg operator | M/L: Gloves and RPE (FFP3) Appl: Gloves and Impermeable coveralls | daminozide | 0.05815 | 665 | B.6.4.1-16 |
| | | UDMH | 0.0000056 | 62 | B.6.4.1-17 |
| EFSA AOEM - manual hand held - 4 ha/day - 60 kg operator | M/L and Appl.: Gloves, workwear, RPE (FP2) | daminozide | 0.0022 | 24.78 | B.6.4.1-18 |
| | | UDMH | 0.015959 | 17,732.23 | B.6.4.1-19 |
| EFSA AOEM - manual knapsack - 1 ha/day - 60 kg operator | M/L and Appl.: Gloves, workwear, RPE (FP2) | daminozide | 0.0010 | 11.62 | B.6.4.1-20 |
| | | UDMH | 0.016072 | 17,857.63 | B.6.4.1-21 |
| Hand held application indoor | | | | | |
| 9 kg Dazide Enhance /ha corresponding to 7.65 kg of daminozide per ha, spray volume 500 L per ha | | | | | |
| Dutch Greenhouse Model - 1 ha/day - 70 kg operator | M/L and Appl.: Gloves, Coverall, RPE (FP2) | daminozide | 0.0415 | 600 | B.6.4.1-7 |
| | | UDMH | 0.000051 | 57 | B.6.4.1-8 |
| Southern European Greenhouse Model Low crops - 1 ha/day - 70 kg operator | M/L: Gloves Appl.: Gloves, RPE (FPP2), Coverall | daminozide | 0.0061 | 70.1 | B.6.4.1-9 |
| | | UDMH | 0.000002 | 2.3 | |
| Southern European Greenhouse Model High crops - 1 ha/day - 70 kg operator | M/L: Gloves, RPE (A1P2) Appl.: Gloves, RPE (A1P2), Headgear, Impervious clothing | daminozide | 0.00706 | 80.7 | |
| | | UDMH | 0.000007 | 7.7 | |
| Gantry application indoors | | | | | |
| 9 kg Dazide Enhance /ha corresponding to 7.65 kg of daminozide per ha, spray volume 500 L per ha | | | | | |

| | | | | | |
|--------------------------------------------------------------------------------------------------------|--------------------------------------|------------|------------------------------|---------------------------|-------------------------------------|
| UK POEM mix/loading - 1 ha/day - 70 kg operator | M/L: Gloves, Workwear | daminozide | 0.00392 | 45 | B.6.4.1-21 B.6.4.1-22 |
| | | UDMH | 0.0000001 | 0.16 | B.6.4.1-22 B.6.4.1-23 |
| German Model mix/loading - 1 ha/day - 70 kg operator | M/L: Gloves | daminozide | 0.000879 | 10 | B.6.4.1-12 |
| | | UDMH | 0.000000 | 0.04 | B.6.4.1-13 |
| EFSA AOEM mix/loading - 10 ha/day - 60 kg operator | M/L: Gloves, Workwear, RPE (FFP1) | daminozide | 0.00243 0.0014 | 27.78 15.95 | B.6.4.1-23 B.6.4.1-24 |
| | | UDMH | 0.000127 | 140.84 | B.6.4.1-24 B.6.4.1-25 |
| 1) Systemic exposure based on dermal absorption for the respective uses as indicated in Table B.6.4-2. | | | | | |
| 2) Based on a systemic AOEL as indicated in Table B.6.4-2. | | | | | |

B.6.4.1.3 Measurement of operator exposure

The risk assessments using the German BBA model, UK POEM, NL and EFSA AOEM model indicate that the health-based limit value (AOEL) for daminozide and UDMH will be exceeded under practical conditions of use when outdoor using hand-held sprayers even with appropriate PPE. Studies to provide field data on operator exposure to Dazide Enhance were not carried out.

RMS comments to the operator exposure:

Estimated operator exposure to daminozide and UDMH was recalculated taken into account dermal absorption (DA) and AOEL set proposed during renewal process. As the new proposed AOEL value for daminozide is more critical unacceptable health risk is concluded for outdoor application. For indoor hand held application based on Southern European Greenhouse model there is no unacceptable risk concluded for operator with high level of PPE.

Using Gantry sprayer exposure estimations according to UK POEM, EFSA AOEM model and German model are acceptable. Bystander and Resident exposure

Estimations of bystander and residential exposure have been undertaken for Dazide Enhance using the critical uses (Table B.6.4-1), the German guidance paper¹.

Regarding the current approach, also the risk assessment using the EFSA Guidance² has been carried out for a comparison.

Outdoor application by hand-held sprayers represents a worst case for bystanders and residents. Indoor application has not been conducted as greenhouses are closed areas where there is no assumption of bystander's or resident's occurrence.

Systemic exposure for bystanders and residents for daminozide and UDMH was calculated assuming dermal absorption of 2% and 10.7% for daminozide and UDMH respectively. The estimations of exposure were compared to the AOEL of 0.00875 mg/kg bw/day for daminozide and 0.09 µg/kg bw/day for UDMH.

¹ Guidance for Exposure and Risk Evaluation for Bystanders and Residents exposed to Plant Protection Products during and after Application; S. Martin *et al.*; J. Verbr. Lebensm. 3 (2008): 272 – 281, 1661-5751/08/030272-10 DOI 10.1007/s00003-008-0361-5, ©Birkhäuser Verlag, Basel, 2008

In order to estimate bystander and residential exposure, it was taken into account total UDMH content after 4h.

German model:

It is conservatively assumed that the spray deposit on the foliar surfaces (dislodgeable foliar residues) do not completely decline between the applications. This follows the recommendations given in the German guidance paper in which it is recommended to assume a decay of the dislodgeable foliar residue (DFR) of 50% between successive applications. Consequently, for several potential applications it is recommended that an accumulated application rate of maximum 2 applications should be used (explanation: 100% from the final application plus 50% from the second last application plus 25% from the application before etc. will never result in values > 200%). Therefore, according to German exposure model the worst case for residents is given by a maximum total dose of 8.5 kg a.s./ha.

The vapour pressure for daminozide is 1.27×10^{-5} Pa at 21.6°C and therefore considered as semi-volatile according German guidance. UDMH is a more volatile compound and an assessment is given for this route of exposure based on an 8 hour Time Weighted Average (TWA) value of 8.5×10^{-5} mg/m³ which was measured in a commercial greenhouse over an 8 hour period following an application of Daminozide to Chrysanthemums (see CP B.6.4.3.2). This value therefore provides a precautionary first tier assessment.

EFSA AOEM model:

According to the EFSA Guidance (EFSA Journal 2014;12(10):3874) for plant protection products that do not have significant acute toxicity no bystander risk assessment is required as due to exposure determination by longer duration it is covered by resident risk assessment.

For the assessment by EFSA AOEM model proposed GAP was used with DFR and DT50 values from the DFR study (see B.6.4.3.2)

A summary of the estimated bystander/resident exposure to daminozide and UDMH using the German approach and the EFSA AOEM model is presented in Table B.6.4.2-1, B.6.4.2-2 and B.6.4.2-3, respectively.

Bystander assessment

Table B.6.4.2-1 German model: Summary of bystander exposure during outdoor application of Dazide Enhance

| | Active ingredient | Route of exposure | Estimated bystander exposure | % of AOEL | Reference Appendix |
|--------------------------------------------------------------------------------------------------------------------|-------------------|--------------------------------|------------------------------|-----------|------------------------|
| | | | (mg/kg bw/day) | | |
| German model | | | | | |
| 5 kg Dazide Enhance /ha corresponding to 4.25 kg of daminozide per ha, spray volume 500 L per ha, buffer strip 10m | | | | | |
| adult (60 kg) | daminozide | dermal and inhalation exposure | 0.0063 | 71.92 | B.6.4.2-1 B.6.4.2-2 |
| | UDMH | | 0.000002 | 1.88 | |
| child (16.15 kg) | daminozide | | 0.0129 | 147.52 | |
| | UDMH | | 0.000003 | 3.32 | |

Resident Assessment**Table B.6.4.2-2 German model: Summary of resident exposure during outdoor application of Dazide Enhance**

| | Active ingredient | Route of exposure | Estimated bystander exposure | % of AOEL | Reference Appendix |
|----------------------------------------------------------------------------------------------------------------------|-------------------|---------------------------------------------------------------------------------------------------|------------------------------|-----------|------------------------|
| | | | (mg/kg bw/day) | | |
| German model | | | | | |
| 2x 5 kg Dazide Enhance /ha corresponding to 8.5 kg of daminozide per ha, spray volume 500 L per ha, buffer strip 10m | | | | | |
| adult (60 kg) | daminozide | dermal exposure and inhalation exposure to vapour | 0.00032 | 3.7 | B.6.4.2-3 B.6.4.2-4 |
| | UDMH | | 0.000024 | 26.14 | |
| child (16.15 kg) | daminozide | dermal exposure and inhalation exposure to vapour, oral exposure (hand to mouth, object to mouth) | 0.00069 | 7.86 | |
| | UDMH | | 0.000044 | 48.75 | |

Table B.6.4.2-3 EFSA AOEM model: Summary of residential exposure during outdoor application of Dazide Enhance

| | Active ingredient | Route of exposure | Estimated bystander exposure | % of aAOEL | Reference Appendix |
|----------------------------------------------------------------------------------------------------------------------|-------------------|-------------------|------------------------------|------------|------------------------|
| | | | (mg/kg bw/day) | | |
| EFSA AOEM model | | | | | |
| 2x 5 kg Dazide Enhance /ha corresponding to 8.5 kg of daminozide per ha, spray volume 500 L per ha, buffer strip 10m | | | | | |
| child (10 kg) | daminozide | spray drift | 0.0238 | 271.59 | B.6.4.2-5 B.6.4.2-6 |
| | UDMH | | 0.000027 | 29.53 | |
| | daminozide | vapour | 0.0011 | 12.23 | |
| | UDMH | | 0.001070 | 1188.89 | |
| | daminozide | surface deposits | 0.0021 | 23.48 | |

| | | | | | |
|---------------|------------|--------------------------|-----------|---------|--|
| | UDMH | | 0.000001 | 0.70 | |
| | daminozide | entry into treated crops | 0.0506 | 578.31 | |
| | UDMH | | 0.000000 | 0 | |
| | daminozide | all pathways | 0.0588 | 672.32 | |
| | UDMH | | 0.001088 | 1208.89 | |
| adult (60 kg) | daminozide | spray drift | 0.0127 | 145.42 | |
| | UDMH | | 0.000015 | 16.30 | |
| | daminozide | vapour | 0.0002 | 2.63 | |
| | UDMH | | 0.000230 | 255.56 | |
| | daminozide | surface deposits | 0.0005 | 5.42 | |
| | UDMH | | 0.0000002 | 0.22 | |
| | daminozide | entry into treated crops | 0.0281 | 321.29 | |
| | UDMH | | 0.000000 | 0 | |
| | daminozide | all pathways | 0.0314 | 358.55 | |
| | UDMH | | 0.000240 | 266.39 | |

Conclusion

Estimated outdoor bystander and resident exposure to daminozide and UDMH was recalculated taken into account dermal absorption (DA) and AOEL set proposed during renewal process. As the newly proposed AOEL value for daminozide is more critical unacceptable health risk to daminozide is concluded for bystander – child according to German approach.

According the EFSA AOEM residents exposure estimation is unacceptable for daminozide and UDMH both.

According to the EFSA Guidance (EFSA Journal 2014;12(10):3874) for plant protection products that do not have significant acute toxicity no bystander risk assessment is required as due to exposure determination by longer duration it is covered by resident risk assessment.

As there is bystander and resident unacceptable risk indicated, the representative outdoor use to ornamentals cannot be approved.

Indoor application has not been conducted as greenhouses are closed areas where there is no assumption of bystander's or resident's occurrence.

B.6.4.1 Worker Exposure

Estimations of worker exposure have been undertaken for DAZIDE using the critical uses (Table B.6.4-1). The re-entry scenario considered is for workers handling ornamental plants, including containerised plants and small plants in trays. The worst case is given by the protected crop scenario.

Considering the protected crop scenario the inhalation exposure for worker has to be calculated.

Risk assessment for worker

The worker risk assessment presented has been based according to the EU requirements on the following models:

- German Re-entry Worker model with parameters taken from the EUROPOEM II Worker re-entry report: Hoernicke E. et al. (1998): Details in the instructions for use on the protection of persons carrying out successive work with crops which have been treated with plant protection products. Nachrichtenbl. Deut. Pflanzenschutz. 50, 267-267; in conjunction with: Krevs et al. (2000): Uniform principles for ensuring health protection for workers when re-entering treated crops following the application of plant protection products. Nachrichtenbl. Deut. Pflanzenschutz. 52, 5-9.
- EFSA AOEM model has been included in the EFSA Guidance on the Assessment of Exposure for Operators, Workers, Residents and Bystanders in Risk Assessment for Plant Protection Products (EFSA Journal 2014;12(10):3874).

German model:

It is conservatively assumed that the spray deposit on the foliar surfaces (dislodgeable foliar residues) do not completely decline between the applications. This follows the recommendations given in the German guidance paper in which it is recommended to assume a decay of the dislodgeable foliar residue (DFR) of 50% between successive applications. Consequently, for several potential applications it is recommended that an accumulated application rate of maximum 2 applications should be used (explanation: 100% from the final application plus 50% from the second last application plus 25% from the application before etc. will never result in values > 200%). Therefore, according to German exposure model the worst case for ~~residents~~ workers is given by a maximum total dose of 8.5 kg a.s./ha.

Systemic exposure of worker for daminozide and UDMH was calculated assuming corresponding dermal absorption and was compared to the AOEL (see Table B.6.4-2).

In order to provide worker exposure, it was taken into account total UDMH content after 4h as the worst case for the first tier as the content after longer time of hydrolysis is not needed due to rapid substance degradation.

A summary of the estimated worker exposure to daminozide and UDMH using the German approach and the EFSA AOEM model is presented in Table B.6.4.3-1.

Table B.6.4.3-1 Estimated worker exposure to daminozide and UDMH in Dazide Enhance to ornamental plants

| Model data | Level of PPE | Total absorbed dose (mg/kg bw/day) ¹ | | % of AOEL ² | Reference Appendix |
|-------------------------------------------------------------------------------------------------------------------|----------------|-------------------------------------------------|---------------------------------|-----------------------------|-------------------------|
| Handling ornamentals plants, indoor | | | | | |
| 2 x 9 kg Alar/ha corresponding to 38.25 kg of daminozide per ha | | | | | |
| German model - TC 5000 - working time 8h - 60 kg operator | Gloves and RPE | daminozide | 0.00293 | 294.57 | B.6.4.3-7 B.6.4.3-8 |
| | | UDMH | 0.003381 0.000071 | 3,756.2 79.43 | |
| EFSA AOEM - working time 8h - 60 kg operator | Gloves | daminozide | 0.1248 | 1,426.36 | B.6.4.3-9 B.6.4.3-10 |
| | | UDMH | 0.000086 | 95.86 | |
| ¹⁾ Systemic exposure based on dermal absorption for the respective uses as indicated in Table B.6.4-2. | | | | | |
| ²⁾ Based on a systemic AOEL as indicated in Table B.6.4-2. | | | | | |

Conclusion

In conclusion, there is an unacceptable risk anticipated for persons entering crops where DAZIDE was applied in the manner proposed.

B.6.4.3.1 Estimation of Worker Exposure

The following parameters were used in the re-entry worker assessment:

- Application rate: for a maximum total dose of two treatments is 15.3 kg (2 x 7.65 kg of daminozide/ha and 0.0032 kg (2 x 0.0016 kg of UDMH/ha (for indoor applications)
- Dermal absorption: 0.97% for *Daminozide and 10,7% for UDMH
 *As recommended in current EFSA guidance, in deciding which dermal absorption value to assume for the risk assessment the dose density on the area of exposed skin may be taken into account. The predicted exposures for daminozide for workers handling ornamentals (Appendix 7.2.3.1-1 and 7.2.3.1-2) show, as expected, that a significant portion of the total dermal exposure occurs on the workers hands. The predicted hand exposure is 3672 mg/person. The surface area for adult hands is an uncovered area of 820 cm². Assuming a total surface area for both palms of 820 cm² the resulting skin loading is 4478 µg/cm². This skin loading is closest to the 400 µg daminozide/cm² concentration tested, from which the dermal absorption value of 0.97% was derived (see CP 7.3)
- Body weight: 60 kg

The following parameters from the EFSA Journal 2014;12(10):3874 were used in the assessment:

- DFR: 3 µg a.s./cm² /kg a.s. applied
- TC: 5000 cm²/hr for handling larger ornamental plants assuming arm, body and legs covered. Whilst the TC value for handling smaller plants in trays will be lower than 5000 cm²/hr, use of this TC provides a risk envelope for all worker scenarios. TC 1400 cm²/hr assuming covered body and gloves
- The product is applied into a greenhouse. As pesticide droplets may remain airborne after the treatment when re-entering, levels of inhalation exposure have been predicted using the following inhalation task specific factors:

Cutting 0.1 (mg a.s./hr)/(kg/ha)

Sorting/bundling 0.01(mg a.s./hr)/(kg/ha)

using RPE FP1 25% reduction of inhalation exposure can be assumed

- Working time: A total working time of 8 hours is assumed for handling activities.

A precautionary assessment is given as a Tier 1 assessment. This assumes that the maximum total dose is applied to the crop (7.65 kg daminozide x 2 treatments) and that there is no decline in dislodgeable foliar residues from any of the two treatments at the time of re-entry (minimum interval between treatments is 7 days for protected crops). The use of protective gloves by workers is also considered, which reduce dermal exposure to the hands by 90%³.

The results of the exposure calculations for workers are summarized in Table B.6.4.3.1-1. Full calculations are given in Appendix I.

Table B.6.4.3.1-1 Estimated worker exposure to daminozide and UDMH in Dazide Enhance to ornamental plants

| Ornamental plants | | | | | |
|--------------------------------------------------------------------------------------------------------|----------------|-------------------------------------------------|----------|------------------------|--------------------|
| Model data | Level of PPE | Total absorbed dose (mg/kg bw/day) ¹ | | % of AOEL ² | Reference Appendix |
| Handling ornamentals plants, indoor | | | | | |
| 5x 9 kg Alar/ha corresponding to 38.25 kg of daminozide per ha | | | | | |
| German model - TC 5000 - working time 8h - 60 kg operator | No PPE | daminozide | 0.31722 | 3625.4 | B.6.4.3-1 |
| | | UDMH | 0.000687 | 763.2 | B.6.4.3-2 |
| | Gloves and RPE | daminozide | 0.08821 | 1,008.1 | B.6.4.3-1 |
| | | UDMH | 0.000192 | 213.6 | B.6.4.3-2 |
| EFSA AOEM - working time 8h - 60 kg operator | No PPE | daminozide | 0.6531 | 7,464.3 | B.6.4.3-3 |
| | | UDMH | 0.001289 | 1,432.0 | B.6.4.3-4 |
| | Gloves | daminozide | 0.25631 | 2,929.3 | B.6.4.3-3 |
| | | UDMH | 0.000376 | 417.97 | B.6.4.3-4 |
| 1) Systemic exposure based on dermal absorption for the respective uses as indicated in Table B.6.4-2. | | | | | |
| 2) Based on a systemic AOEL as indicated in Table B.6.4-2. | | | | | |

Conclusion

In conclusion, there is unacceptable risk anticipated for persons entering crops where DAZIDE was applied in the manner proposed even with suitable protective gloves. Further refinement is needed.

³ EFSA (European Food Safety Authority), 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, 55 pp., doi:10.2903/j.efsa.2014.3874

B.6.4.3.2 Measurement of worker exposure (Dislodgeable Foliar Residues)

As the levels of exposure predicted for re-entry workers are above the AOEL for daminozide and UDMH further estimates of exposure are given which consider the use of dislodgeable foliar residues data.

The following report is used to support the assessment:

| | |
|----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Reference: | van der Jagt, K.E, Ravensberg J.C., de Wold J.M. and Links I.H.M., 2002; Dislodgeable foliar residue determination of daminozide, UDMH and NDMA and air monitoring of UDMH, NDMA and formaldehyde following indoor treatment of ornamental plants with Alar® 64 SP |
| Report No.: | V3876 |
| Guideline: | Not stated but the study design broadly follows the US Environmental Protection Agency office of prevention, pesticides and toxic substances (OPTS) Occupational and Residential Exposure Test Guidelines. Foliar Dislodgeable Residue Dissipation Series 875 |
| GLP: | Yes |
| Previous evaluation: | Submitted for the purpose of renewal |

Executive Summary

A study was conducted to quantify the magnitude and decline of dislodgeable foliar residues (DFR) of daminozide, N,N-dimethylhydrazine (UDMH) and N-nitrosodimethylamine (NDMA) following indoor treatment of ornamental plants with a soluble powder formulation of daminozide (Alar® 64 SP) containing 64.7% w/w daminozide. In addition, the magnitude and decline of airborne residues of UDMH, NDMA and formaldehyde were also quantified.

The product was applied to Chrysanthemum plants in a commercial glasshouse in the Netherlands in 2001. Two treatments of daminozide were applied, the second treatment was applied at 4.6 kg a.s/ha with a 6 day interval between treatments.

Dislodgeable foliar residue sampling took place pre and post treatment on the day of application and on days 1, 2, 3, 5, 10 and 14 post-treatment. Stationary air sampling for UDMH, NDMA and formaldehyde took place pre and post treatment on the day of application and on days 1, 2, 3 and 5 post-treatment on the day of application.

The DFR of daminozide on Chrysanthemums declined from 6597 ng/cm² just after the second treatment to 372 ng/cm² 14 days after treatment. The degradation product UDMH also showed a decline in foliar residues, from 1.5 ng/cm² just after the second treatment to 0.2 ng/cm² 14 days later. The highest air concentration of UDMH (191 ng/m³) was recorded 6 to 8 hours post treatment. All other air measurements of UDMH were either below the LOD (45 ng/m³) or between the LOD and the LOQ (107 ng/m³).

| | |
|--------------------------|-----------------------------------------------|
| Test Material: | Alar 64 SP |
| Description: | Soluble Powder (SP) |
| Lot/Batch Number: | SI 7938 |
| Purity: | Not stated. Product contains 64.7% Daminozide |

Stability of test compound: Stable for the duration of the study

Study Design and Methods

A study was conducted to quantify the magnitude and decline of dislodgeable foliar residues (DFR) of daminozide, N,N-dimethylhydrazine (UDMH) and N-nitrosodimethylamine (NDMA) following indoor treatment of ornamental plants with a soluble powder formulation of daminozide (Alar® 64 SP) containing 64.7% w/w daminozide. In addition, the magnitude and decline of airborne residues of UDMH, NDMA and formaldehyde were also quantified. The study, performed in 2001, was conducted in accordance with the requirements of Good Laboratory Practice (GLP).

The product was applied to Chrysanthemum plants in a commercial glasshouse in the Netherlands in 2001. The volume of the greenhouse was 41400 m³. One bed of 1.4 m by 30 m stocked with Chrysanthemum flowers was treated. Two treatments of daminozide were applied, the second treatment was applied at 4.6 kg a.s./ha with a 6 day interval between treatments. Applications were achieved using hand-held sprayers connected to a mobile (200 L) tank.

Dislodgeable foliar residue sampling took place pre and post treatment on the day of application and on days 1, 2, 3, 5, 10 and 14 post-treatment. Stationary air sampling for UDMH, NDMA and formaldehyde took place pre and post treatment on the day of application and on days 1, 2, 3 and 5 post-treatment on the day of application. Leaf samples, taken at 2/3 plant height, were collected from randomly selected plants. None were taken from the borders of the bed. Twelve leaves were picked to give one leaf sample. Leaf surface area was determined using a method based upon a decrease in light intensity with increasing leaf surface area. The average area of 12 leaves was determined to be 550 cm².

Dislodging of DFR from samples was performed within 12 hours of sample collection. Dislodging of leaf samples was achieved using demineralised water containing a dislodging solution (Triton x-100). Samples were shaken for 30 minutes, the dislodging solution was then removed, new solution added and the process repeated. Containers containing the leaves were then rinsed with demineralised water and all extracts combined. Analysis of the DFR extracts was performed using liquid chromatography with tandem mass spectrometry (LC-MS/MS).

Stationary air samples were taken at two locations in the selected bed, at a height of approximately 1 metre which was just above the top of the plants. One sampler was located in the centre of the bed the other at the perimeter. UDMH in air was trapped using two serially connected impingers, each filled with 0.1 M HCl solution. Sampling pumps were operated at a flow rate of 2 L/minute. Four sequential 2 hour samples were collected on the day of application whilst a single 2 hour sample was taken on other days.

For analysis of the UDMH air samples ascorbic acid and sodium hydroxide was added to the 0.1 molar hydrochloric acid taken from the air collection impingers. For analysis of UDMH in DFR solution, the DFR solution was first acidified with fuming hydrochloric acid. Ascorbic acid and sodium hydroxide were then added to the acidified solution. After the addition of 2-nitrobenzaldehyde containers were shaken and kept in a water bath for 2 hours at 30°C. Iso-octane was added to the warm solution and samples were shaken. The iso-octane layer was removed and centrifuged before 3 mL of the solution was concentrated under nitrogen. The volume was adjusted with further iso-octane and ITSD (chlorpyrifos 10 mg/L in iso-octane) added.

Calibration samples were prepared by addition of 1,1-dimethylhydrazine in 0.05 M HCl to either DFR solution or 0.1 molar HCl. Calibration samples were treated identically to the validation and study samples.

Extracts were analysed by GC-NPD on a CP-Sil-19-CB column (25 mL, 0.25 mm i.d., 0.2 µm film).

Results

Temperatures in the greenhouse, where the DFR and air samples were taken ranged from 18.3°C to 24.4°C over the course of the study. Relative humidity ranged from 61.2% to 83.2%. Meteorological conditions in a ‘cutting greenhouse’ where the blank and field control samples for air sampling were taken were similar.

Variability of the analytical method was within acceptable levels. Field recovery samples prepared to determine the potential loss of UDMH during air sampling showed levels of recovery between 77.8% and 94.9%. Therefore no adjustment for field recovery for these samples was required.

The DFR of Daminozide on Chrysanthemums declined from 6597 ng/cm² just after the second treatment to 372 ng/cm² 14 days after treatment. The DFR measured just before the second application was made (360 ng/cm²) showed there was minimal accumulation of DFR from the first application. Using the application rate for the second application (4.6 kg a.s./ha) the DFR of Daminozide measured immediately after the second application was made is 1.434 µg/cm²/kg a.s. applied.

The degradation product UDMH also showed a decline in foliar residues, from 1.5 ng/cm² just after the second treatment to 0.2 ng/cm² 14 days later. The DFR measured just before the second application was made (0.2 ng/cm²) confirmed minimal accumulation of DFR from the first application. The DFR of UDMH measured immediately after the second application was made is 3.3×10^{-4} µg/cm²/kg Daminozide applied.

Table B.6.4.3.2-1: Dislodgeable foliar residues of daminozide and UDMH following application of daminozide to glasshouse Chrysanthemums

| Sampling date | Sample | Leaf surface area (cm ²) | Daminozide DFR (ng/cm ²) | UDMH DFR (ng/cm ²) |
|---------------|--------------------|--------------------------------------|--------------------------------------|--------------------------------|
| Day 0 | Pre-treatment (a) | 574.64 | 360 | 0.2 |
| | Post-treatment (b) | 615.04 | 6597 | 1.5 |
| Day 1 | | 621.06 | 4977 | 1.0 |
| Day 2 | | 642.24 | 3905 | 1.0 |
| Day 3 | | 625.01 | 3411 | 0.9 |
| Day 5 | | 599.22 | 699 | 0.4 |
| Day 10 | | 607.46 | 409 | 0.1 |
| Day 14 | | 616.16 | 372 | 0.2 |

(a) Sample from test bed prior to second application

(b) Sample taken after leaves were dry, approximately 2:40 hours after application

Figure B.6.4.3.2-1: Half-life calculation for daminozide DFR on Chrysanthemums leaves.

DT₅₀ on foliage = 2.37 days

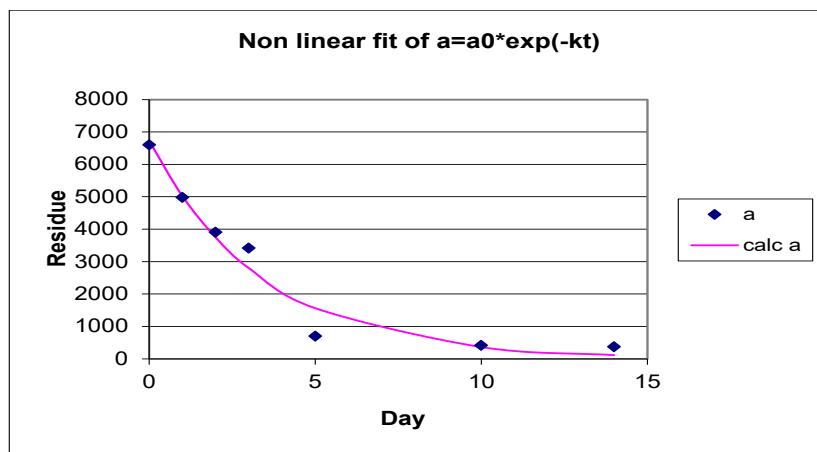
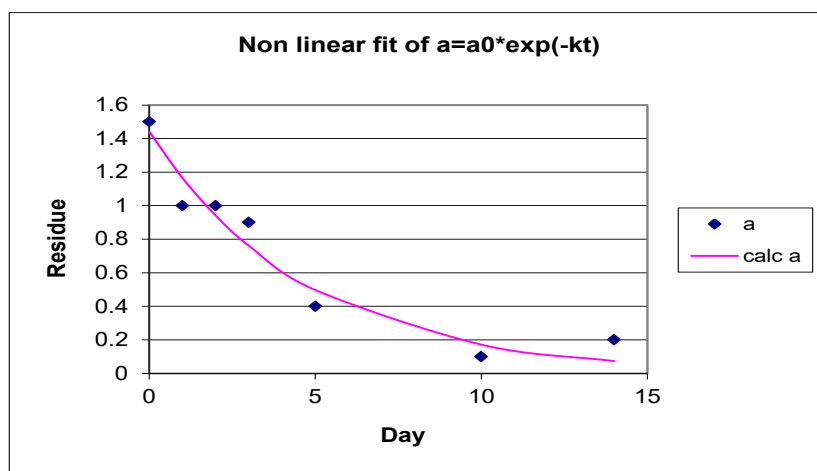


Figure B.6.4.3.2-1: Half-life calculation for UDMH DFR on Chrysanthemums leaves.
 DT_{50} on foliage = 3.25 days



The highest air concentration of UDMH (191 ng/m^3) was recorded 6 to 8 hours post treatment. All other air measurements of UDMH were below the LOD (45 ng/m^3) or between the LOD and the LOQ (107 ng/m^3). For the eight hour period of monitoring on the day of the second application the calculated time weighted average (TWA) value is 85 ng/m^3 .

Table B.6.4.3.2-2: Average air concentrations of UDMH following application of Daminozide to glasshouse Chrysanthemums

| Sampling date | Sample | Calculated air concentration (ng/m3) |
|---------------|----------------------|--------------------------------------|
| Day 0 | Pre-treatment | 45(a) |
| | 0-2 h Post-treatment | 43(a) |
| | 2-4 h Post-treatment | 51(b) |
| | 4-6 h Post-treatment | 54(b) |
| | 6-8 h Post-treatment | 191 |
| Day 1 | | 44(a) |
| Day 2 | | 42(a) |
| Day 3 | | 44(a) |
| Day 5 | | 43(a) |

- (a) <LOD (107 ng/L equals 45 ng/m³ with a sampled volume of 240L)
 (b) <LOQ (256 ng/L equals 107 ng/m³ with a sampled volume of 240L)

Risk Assessment

Exposure is predicted for workers handling ornamentals assuming a maximum individual dose of 7.65 kg daminozide/ha (3.83×10^{-3} kg UDMH/ha), 5 treatments, a 7 day interval between treatments and no pre-harvest interval. Initial DFR after treatment is calculated from the exposure study measurements which are 1.434 µg/cm² and 3.3×10^{-4} µg/cm² for Daminozide and UDMH respectively for each kg of Daminozide which is applied. To allow consideration of the dissipation of daminozide and UDMH DFR between treatments the total DFR is calculated assuming a half-life (DT₅₀) of 2.37 days for daminozide and 3.25 days for UDMH on treated foliage.

| | | | | | | | | | | | | |
|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|--|--|-------------|-----------------------------|------------|------|-------|------|------|---------|
| RMS comments | <p>The study is valid for evaluating. At the study 4.6 kg daminozide./ha was applied onto one bed of 1.4 m by 30 m in a greenhouse . The volume of the greenhouse was 41400 m3. Rapid degradation of the parent active substance daminozide and metabolite UDMH both has been demonstrated. DT50 values have been set based on DFR decrease in time. Initial DFR after 2nd application can be used instead of default value for the risk assessment refinement.</p> <p>The highest average air concentration of UDMH was measured 6-8h after application. Considering application conditions, suggested TWA value can be used for calculation refinement of outdoor uses only.</p> | | | | | | | | | | | |
| Endpoint / conclusion | <p>For the purpose of exposure assessments of DAZIDE followed values can be used:</p> <table><tr><td></td><td>DT50 [days]</td><td>DFR [µg/cm2/kg daminozide]</td></tr><tr><td>daminozide</td><td>2.37</td><td>1.434</td></tr><tr><td>UDMH</td><td>3.25</td><td>0.00033</td></tr></table> | | | | DT50 [days] | DFR [µg/cm2/kg daminozide] | daminozide | 2.37 | 1.434 | UDMH | 3.25 | 0.00033 |
| | DT50 [days] | DFR [µg/cm2/kg daminozide] | | | | | | | | | | |
| daminozide | 2.37 | 1.434 | | | | | | | | | | |
| UDMH | 3.25 | 0.00033 | | | | | | | | | | |

Considered short DT50 value for both substances, for refinement instead of number of applications Multiple Application Factor (MAF) can be used (EFSA Journal 2014;12(10):3874). According the critical GAP 5 applications with 7 days interval between applications, estimated number of applications is 1.15 for daminozide and 1.3 for UDMH.

The predicted exposures are summarised below at Table B.6.4.3.2-3. Full calculations are given in Appendix I.

Table B.6.4.3.2-3 Estimated worker exposure to daminozide and UDMH in Dazide Enhance to ornamental plants

| Model data | Level of PPE | Total absorbed dose (mg/kg bw/day) ¹ | | % of AOEL ² | Reference Appendix |
|-----------------------------------------------------------------------------------------------|----------------|-------------------------------------------------|-----------------------------------------|------------------------------|--------------------|
| Handling ornamentals plants, indoor | | | | | |
| 5x 9 kg Alar/ha corresponding to 5x 7.65 kg of daminozide per ha and 5x1.595 g of UDMH per ha | | | | | |
| German model - TC 5000 - working time 8h - 60 kg operator | No PPE | daminozide | 0.09331 | 1,066.4 | B.6.4.3-7 |
| | | UDMH | 0.0132 0.00026 | 14,993.5 286.5 | B.6.4.3-8 |
| | Gloves and RPE | daminozide | 0.00293 | 294.57 | B.6.4.3-7 |
| | | UDMH | 0.00338 + 0.00007 1 | 3,756.2 79.43 | B.6.4.3-8 |
| EFSA AOEM - working time 8h - 60 kg operator | No PPE | daminozide | 0.18345 | 2,096.6 | B.6.4.3-9 |
| | | UDMH | 0.00025 3 | 281.62 | B.6.4.3-10 |
| | Gloves | daminozide | 0.1248 | 1,426.36 | B.6.4.3-9 |
| | | UDMH | 0.00008 6 | 95.86 | B.6.4.3-10 |

¹⁾ Systemic exposure based on dermal absorption for the respective uses as indicated in Table B.

²⁾ Based on a systemic AOEL as indicated in Table B.

The risk assessment performed has been undertaken for protected crops as this scenario has a higher maximum individual dose and maximum total dose than the outdoor uses. As DFR dissipation data generated for a protected crop are expected to be a worst case for outdoor crops the half-life values used for the dissipation of daminozide and UDMH DFR in the risk assessment are expected to be precautionary values for ornamental crops grown outdoors. The worker exposure assessment for the use of DAZIDE on protected crops therefore provides a suitable risk envelope for use on outdoor grown ornamentals.

Conclusion

In conclusion, there is unacceptable risk anticipated for persons entering crops where DAZIDE was applied in the manner proposed

RMS comments and conclusion:

Estimated indoor worker exposure to daminozide and UDMH was recalculated taken into account dermal absorption (DA) and AOEL set proposed during renewal process. As the newly proposed AOEL value for daminozide is more critical unacceptable health risk to daminozide is concluded for worker according to German and EFSA approach both.

As a further refinement a re-entry interval could be set, but as there is no harmonised approach the refinement was not carried out and could be done on national level.

B.6.5 Summary of operator, bystander/resident and worker exposure

The operator, bystander/resident and worker exposure and risk assessment are summarized in Volume 1, level 2.

Comments by the RMS:

Based on evaluation given by calculation method safe use of product Dazide cannot be guaranteed.

B.6.6 References relied on**Toxicological studies on the Plant Protection Product (Annex IIIA, Point 7)****New studies**

| Data point | Author(s) | Year | Title Company Report No. Source (where different from company) GLP or GEP status Published or not | Vertebrate study Y/N | Data protection claimed Y/N | Justification if data protection is claimed | Owner |
|---------------|-----------------------------------------------------------------------------|-------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|-----------------------------|---------------------------------------------|---------------------------|
| CP 7.1.1/01 | ████████ | 2003a | Dazide 85 WG: Acute Oral Toxicity Study in the Female Rat (Acute Toxic Class) ████████. Report No. 2242/004 GLP Unpublished | Y | Y | New data for AIR3 renewal | Fine Agrochemical Limited |
| CP 7.1.2/01 | ████████ | 2003b | Dazide 85 WG: Acute Dermal Toxicity Study in the Rat ████████. Report No. 2242/005 GLP Unpublished | Y | Y | New data for AIR3 renewal | Fine Agrochemical Limited |
| CP 7.1.4/01 | ████████ | 2002a | Dazide WSG (New Formulation) Skin Irritation to the Rabbit ████████. Report No. FNA 106/022932 GLP Unpublished | Y | Y | New data for AIR3 renewal | Fine Agrochemical Limited |
| CP 7.1.5/01 | ████████ | 2002b | Dazide WSG (New Formulation) Eye Irritation to the Rabbit ████████. Report No. FNA 107/023169 GLP Unpublished | Y | Y | New data for AIR3 renewal | Fine Agrochemical Limited |
| CP 7.1.6/01 | ████████ | 2003c | Dazide 85 WSG: Local Lymph Node Assay in the Mouse (Individual Method) ████████ Report No. 2242/006 GLP Unpublished | Y | Y | New data for AIR3 renewal | Fine Agrochemical Limited |
| CP 7.2.3.2/01 | van der Jagt, K.E., Ravensberg, J.C., de Wold, J.M., Links, I.H.M. | 2002 | Dislodgeable foliar residue determination of daminozide, UDMH and NDMA and air monitoring of UDMH, NDMA and formaldehyde following indoor treatment of ornamental plants with Alar® 64 SP TNO Nutrition and Research. Report No. V3876 | N | Y | New data for AIR3 renewal | |

| | | | | | | | |
|-----------|----------------|------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---|---|---------------------------|---------------------------------|
| | | | GLP Unpublished | | | | |
| CP 7.3/01 | Blackstock, C. | 2012 | Daminozide: The <i>In Vitro</i> Percutaneous Absorption of Radiolabelled Daminozide in the Water Soluble Granule (SG) Concentrate, Two In-Use Spray Dilutions and Two Test Preparations Representing Re-Entry Scenarios Through Human Skin Charles River, UK. Report No. 32807 GLP Unpublished | N | Y | New data for AIR3 renewal | Fine Agrochemical Limited |

APPENDIX 1

Daminozide

OPERATOR, BYSTANDER/RESIDENT AND WORKER EXPOSURE ASSESSMENT

Appendix B.6.4.1-1: Hand held application outdoors to low crops, UK POEM: daminozide – no PPE
THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM) WITH GERMAN MODEL MIX/LOAD DATA (75th PERCENTILE)

| | | | |
|--------------------------------|-----------------------------------------------------------------------------|------------------------------|-------------|
| Application method | Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target | | |
| Product | Alar | Active substance | daminozide |
| Formulation type | WG or SG | a.s. concentration | 850 mg/g |
| Dermal absorption from product | 0,2 % | Dermal absorption from spray | 1,9 % |
| PPE during mix/loading | None | PPE during application | None |
| Dose | 5 kg product/ha | Work rate/day | 0,8 ha |
| Application volume | 500 l/ha | Duration of spraying | 6 h |
| AOEL _{sys} | 0,00875 mg/kg bw/day | Total exposure (result): | 3081 % AOEL |

DERMAL EXPOSURE DURING MIXING AND LOADING

| | |
|----------------------------|------------------|
| Hand contamination/kg a.s. | 171,4 mg/kg a.s. |
| Hand contamination/day | 582,76 mg/day |
| Protective clothing | None |
| Transmission to skin | 100 % |
| Dermal exposure to a.s. | 582,76 mg/day |

INHALATION EXPOSURE DURING MIXING AND LOADING

| | |
|-----------------------------|-------------------|
| Inhalation exposure/kg a.s. | 0,0628 mg/kg a.s. |
| Inhalation exposure/day | 0,21352 mg/day |
| RPE | None |
| Transmission through RPE | 100 % |
| Inhalation exposure to a.s. | 0,21352 mg/day |

DERMAL EXPOSURE DURING SPRAY APPLICATION

| | | | |
|------------------------------------|-----------------------------------------------------------------------------|-----------|-----------|
| Application technique | Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target | | |
| Application volume | 500 spray/ha | | |
| Volume of surface contamination | 50 ml/h | | |
| Distribution | Hands | Trunk | Legs |
| | 25 % | 25 % | 50 % |
| Clothing | None | Permeable | Permeable |
| Penetration | 100 % | 20 % | 18 % |
| Dermal exposure | 10 | 2,5 | 4,5 ml/h |
| Duration of exposure | 6 h | | |
| Total dermal exposure to spray | 102 ml/day | | |
| Concentration of a.s. in spray sol | 8,5 mg/ml | | |
| Dermal exposure to a.s. | 867 mg/day | | |

INHALATION EXPOSURE DURING SPRAYING

| | |
|--------------------------------|-------------|
| Inhalation exposure to spray | 0,02 ml/h |
| Duration of exposure | 6 h |
| Concentration of a.s. in spray | 8,5 mg/ml |
| Inhalation exposure to a.s. | 1,02 mg/day |
| Percent absorbed | 100 % |
| Absorbed dose | 1,02 mg/day |

ABSORBED DOSE

| | | |
|------------------------------|----------------|---------------|
| | Mix/load | Application |
| Dermal exposure to a.s. | 582,76 mg/day | 867 mg/day |
| Percent absorbed | 0,2 % | 1,9 % |
| Absorbed dose (dermal route) | 1,16552 mg/day | 16,473 mg/day |
| Inhalation exposure to a.s. | 0,21352 mg/day | 1,02 mg/day |
| Absorbed dose | 1,37904 mg/day | 17,493 mg/day |

PREDICTED EXPOSURE

| | |
|----------------------|--------------------------|
| Total absorbed dose | 18,87204 mg/day |
| Operator body weight | 70 kg |
| Operator exposure | 0,269600571 mg/kg bw/day |

Appendix B.6.4.1-2: Hand held application outdoors to low crops, UK POEM: UDMH – no PPE
THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM) WITH GERMAN MODEL MIX/LOAD DATA (75th PERCENTILE)

| | | | |
|--------------------------------|-----------------------------------------------------------------------------|------------------------------|------------|
| Application method | Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target | | |
| Product | Alar | Active substance | UDMH |
| Formulation type | WG or SG | a.s. concentration | 0,177 mg/g |
| Dermal absorption from product | 10,7 % | Dermal absorption from spray | 10,7 % |
| PPE during mix/loading | None | PPE during application | None |
| Dose | 5 kg product/ha | Work rate/day | 0,8 ha |
| Application volume | 500 l/ha | Duration of spraying | 6 h |
| AOEL _{sys.} | 0,00009 mg/kg bw/day | Total exposure (result): | 518 % AOEL |

DERMAL EXPOSURE DURING MIXING AND LOADING

| | |
|----------------------------|-------------------|
| Hand contamination/kg a.s. | 171,4 mg/kg a.s. |
| Hand contamination/day | 0,12162544 mg/day |
| Protective clothing | None |
| Transmission to skin | 100 % |
| Dermal exposure to a.s. | 0,12162544 mg/day |

INHALATION EXPOSURE DURING MIXING AND LOADING

| | |
|-----------------------------|--------------------|
| Inhalation exposure/kg a.s. | 0,0628 mg/kg a.s. |
| Inhalation exposure/day | 4,45629E-05 mg/day |
| RPE | None |
| Transmission through RPE | 100 % |
| Inhalation exposure to a.s. | 4,45629E-05 mg/day |

DERMAL EXPOSURE DURING SPRAY APPLICATION

| | | | |
|---------------------------------------|-----------------------------------------------------------------------------|-----------|-----------|
| Application technique | Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target | | |
| Application volume | 500 spray/ha | | |
| Volume of surface contamination | 50 ml/h | | |
| Distribution | Hands | Trunk | Legs |
| | 25% | 25% | 50% |
| Clothing | None | Permeable | Permeable |
| Penetration | 100% | 20% | 18% |
| Dermal exposure | 10 | 2,5 | 4,5 ml/h |
| Duration of exposure | 6 h | | |
| Total dermal exposure to spray | 102 ml/day | | |
| Concentration of a.s. in spray soluti | 0,001774 mg/ml | | |
| Dermal exposure to a.s. | 0,180948 mg/day | | |

INHALATION EXPOSURE DURING SPRAYING

| | |
|--------------------------------|-------------------|
| Inhalation exposure to spray | 0,02 ml/h |
| Duration of exposure | 6 h |
| Concentration of a.s. in spray | 0,001774 mg/ml |
| Inhalation exposure to a.s. | 0,00021288 mg/day |
| Percent absorbed | 100 % |
| Absorbed dose | 0,00021288 mg/day |

ABSORBED DOSE

| | Mix/load | Application |
|------------------------------|--------------------|--------------------|
| Dermal exposure to a.s. | 0,12162544 mg/day | 0,180948 mg/day |
| Percent absorbed | 10,7 % | 10,7 % |
| Absorbed dose (dermal route) | 0,013013922 mg/day | 0,019361436 mg/day |
| Inhalation exposure to a.s. | 4,45629E-05 mg/day | 0,00021288 mg/day |
| Absorbed dose | 0,013058485 mg/day | 0,019574316 mg/day |

PREDICTED EXPOSURE

| | |
|----------------------|--------------------------|
| Total absorbed dose | 0,032632801 mg/day |
| Operator body weight | 70 kg |
| Operator exposure | 0,000466183 mg/kg bw/day |

Appendix B.6.4.1-3: Hand held application outdoors to low crops, EFSA AOEM (manual hand-held): daminozide – no PPE
Exposure assessment

| | | | | | |
|-----------------------|------------------------------------------------------------|---------------------------------------------------|-----------------------------------|-------------------------------|-----------------------------------------------------------------------|
| Substance | Daminozide | Formulation = Wettable granules, soluble granules | Application rate-4,25 kg a.s. /ha | Spray dilution = 8,5 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Hand held | | | Buffer = 5 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 0,4 | Dermal for in use dilution = 2 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00875 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |

| Operator Model | | Mixing, loading and application AOEM | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|------------|-------------------|
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,0587 | % of RVNAS | 671,13% |
| | Acute systemic exposure mg/kg bw/day | 0,1149 | % of RVAAS | |
| Mixing and Loading | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Soluble bags = No |
| Application | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Closed cabin = No |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0266 | % of RVNAS | 303,54% |
| | Acute systemic exposure mg/kg bw/day | 0,0520 | % of RVAAS | |

Appendix B.6.4.1-4: Hand held application outdoors to low crops, EFSA AOEM (manual hand-held): UDMH – no PPE

Exposure assessment

| | | | | | |
|-----------------------|--------------------------------------------------------------|---------------------------------------------------|----------------------------------------|------------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,000887 kg a.s. /ha | Spray dilution = 0,001774 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Downward spraying / Manual-Hand held | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 10,7 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm2 per kg a.s./ha | | DT50 | 30 days | |

| Operator Model | | Mixing, loading and application AOEM | | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|------------|-------------------|--|
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,1619 | % of RVNAS | 179864,20% | |
| | Acute systemic exposure mg/kg bw/day | 0,2619 | % of RVAAS | | |
| Mixing and Loading | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Soluble bags = No | |
| Application | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Closed cabin = No | |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0192 | % of RVNAS | 21368,88% | |
| | Acute systemic exposure mg/kg bw/day | 0,1237 | % of RVAAS | | |

Appendix B.6.4.1-5: Hand held application outdoors to low crops, EFSA AOEM (manual knapsack): daminozide – no PPE

Exposure assessment

| | | | | | |
|-----------------------|-----------------------------------------------------------|---------------------------------------------------|-----------------------------------|-------------------------------|-----------------------------------------------------------------------|
| Substance | Daminozide | Formulation = Wettable granules, soluble granules | Application rate-4,25 kg a.s. /ha | Spray dilution = 8,5 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Knapsack | | | Buffer = 5 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 0,4 | Dermal for in use dilution = 2 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00875 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |

| Operator Model | | Mixing, loading and application AOEM | | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|------------|-------------------|--|
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,0364 | % of RVNAS | 416,19% | |
| | Acute systemic exposure mg/kg bw/day | 0,0835 | % of RVAAS | | |
| Mixing and Loading | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Soluble bags = No | |
| Application | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Closed cabin = No | |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0109 | % of RVNAS | 124,79% | |
| | Acute systemic exposure mg/kg bw/day | 0,0232 | % of RVAAS | | |

Appendix B.6.4.1-6: Hand held application outdoors to low crops, EFSA AOEM (manual knapsack): UDMH – no PPE

Exposure assessment

| | | | | | |
|-----------------------|-------------------------------------------------------------|---------------------------------------------------|----------------------------------------|------------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,000887 kg a.s. /ha | Spray dilution = 0,001774 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Downward spraying / Manual-Knapsack | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 10,7 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |

| | | | | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|------------|-------------------|--|
| Operator Model | | Mixing, loading and application AOEM | | | |
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,1805 | % of RVNAS | 200533,13% | |
| | Acute systemic exposure mg/kg bw/day | 0,3033 | % of RVAAS | | |
| Mixing and Loading | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Soluble bags = No | |
| Application | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Closed cabin = No | |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0365 | % of RVNAS | 40542,37% | |
| | Acute systemic exposure mg/kg bw/day | 0,1659 | % of RVAAS | | |

Appendix B.6.4.1-7: Hand held indoor application, Dutch Greenhouse model: daminozide

| OPERATOR EXPOSURE | | DUTCH GREENHOUSE MODEL | |
|---------------------------------------|-----------------|------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| form | Alar | Application including mixing and loading | |
| a.s. | daminozide | | |
| Parameter | Value | Unit | References, comments |
| MANUAL SPRAYING in greenhouses | | | |
| AR Application rate | 7,65 | kg a.s./ha | summary of intended uses |
| A Area treated | 1 | ha/ day | Dutch model |
| Inhalation Exposure | | | |
| SV Surrogate Exposure Value | 1 | mg a.s./ kg a.s. | without PPE For dusting see note* (Dutch model) |
| Inhalation Exposure (without PPE) | 7,65 | mg a.s./ day | IE = SV x AR x A |
| Inhalation Exposure (with PPE) | | | |
| PPE-factor | 10 | | with PPE Non-powered mask filtertype 2 (most conservative): 10; more advanced RPE: see note** (Dutch model) |
| Inhalation Exposure (with PPE) | 0,765 | mg a.s./ day | IE(PPE) = (1/PPE factor) x IE |
| Dermal Exposure | | | |
| SV Surrogate Exposure Value | 200 | mg a.s./ kg a.s. | without PPE For dusting see note* (Dutch model) |
| Dermal Exposure | 1530 | mg a.s./ day | DE = SV x AR x A |
| Dermal Exposure (with PPE) | | | |
| PPE-factor | 10 | | with PPE Gloves + overall: 10 (Dutch model) |
| Dermal Exposure (with PPE) | 153 | mg a.s./ day | DE(PPE) = (1/PPE-factor) x DE |
| Internal exposure | | | |
| IA Inhalation Absorption | 100 | % | |
| DA Dermal Absorption | 1,9 | % | |
| AOEL | 0,6125 | mg a.s./ day | based on 70 kg bw |
| | | | |
| | Without PPE | With PPE | |
| Internal exposure | [mg a.s. / day] | [mg a.s. / day] | |
| Inhalation | 7,6500 | 0,7650 | IE(Int) = IE x (IA/100) |
| Dermal | 29,0700 | 2,9070 | DE(Int) = DE x (DA/100) |
| Total | 36,7200 | 3,6720 | sum |
| | | | |
| % AOEL | | | |
| Inhalation | 1249 | 125 | %AOEL = 100 x IE(Int) / AOEL |
| Dermal | 4746 | 475 | %AOEL = 100 x DE(Int) / AOEL |
| Total | 5995 | 600 | sum |

Appendix B.6.4.1-8: Hand held indoor application, Dutch Greenhouse model: UDMH

| OPERATOR EXPOSURE | | | DUTCH GREENHOUSE MODEL | |
|-----------------------------------|--------------------------|------------------|------------------------------------------|----------------------------------------------------------------------------------------------------|
| form | Alar | | Application including mixing and loading | |
| a.s. | daminozide | | | |
| Parameter | | Value | Unit | References, comments |
| MANUAL SPRAYING in greenhouses | | | | |
| AR | Application rate | 0,001595 | kg a.s./ha | summary of intended uses |
| A | Area treated | 1 | ha/ day | Dutch model |
| Inhalation Exposure | | | without PPE | |
| SV | Surrogate Exposure Value | 1 | mg a.s./ kg a.s. | For dusting see note* (Dutch model) |
| Inhalation Exposure (without PPE) | | 0,001595 | mg a.s./ day | IE = SV x AR x A |
| Inhalation Exposure (with PPE) | | | with PPE | |
| | PPE-factor | 10 | | Non-powered mask filtertype 2 (most conservative): 10; more advanced RPE: see note** (Dutch model) |
| Inhalation Exposure (with PPE) | | 0,0001595 | mg a.s./ day | IE(PPE) = (1/PPE factor) x IE |
| Dermal Exposure | | | without PPE | |
| SV | Surrogate Exposure Value | 200 | mg a.s./ kg a.s. | For dusting see note* (Dutch model) |
| Dermal Exposure | | 0,319 | mg a.s./ day | DE = SV x AR x A |
| Dermal Exposure (with PPE) | | | with PPE | |
| | PPE-factor | 10 | | Gloves + coverall: 10 (Dutch model) |
| Dermal Exposure (with PPE) | | 0,0319 | mg a.s./ day | DE(PPE) = (1/PPE-factor) x DE |
| Internal exposure | | | | |
| IA | Inhalation Absorption | 100 | % | |
| DA | Dermal Absorption | 10,7 | % | |
| | AOEL | 0,0063 | mg a.s./ day | based on 70 kg bw |
| | | Without PPE | With PPE | |
| | Internal exposure | [mg a.s. / day] | [mg a.s. / day] | |
| | Inhalation | 0,0016 | 0,0002 | IE(int) = IE x (IA/100) |
| | Dermal | 0,0341 | 0,0034 | DE(int) = DE x (DA/100) |
| | Total | 0,0357 | 0,0036 | sum |
| | % AOEL | | | |
| | Inhalation | 25 | 3 | %AOEL = 100 x IE(int) / AOEL |
| | Dermal | 542 | 54 | %AOEL = 100 x DE(int) / AOEL |
| | Total | 567 | 57 | sum |

Appendix B.6.4.1-9: Hand held indoor application, Southern European Greenhouse Model

| Data entry screen & summary calculation sheet | | | GREENHOUSE MODEL v_2.1 | |
|---------------------------------------------------------------------------|------------|----------------------------------|------------------------|-------------|
| Product: | Alar | 75th percentile | | |
| Formulation: | WG | | | |
| Body weight [kg]: | 70 | | | |
| Active substance(s): | daminozide | UDMH | Na 8-ND | Substance 4 |
| Concentration [g/l or kg]: | 850 | 0 | 0 | 0 |
| Inhalation absorption [%] | 100 | 100 | 100 | 0 |
| Dermal absorption [%] | | | | |
| Concentrate: | 0,2 | 10,7 | 4,23 | 0,0 |
| Dilution: | 1,9 | 10,7 | 25,19 | 0,0 |
| AOEL [mg/kg bw/day] | 0,0088 | 0,0001 | 0,0007 | 0,0 |
| Scenario 1: Low crop, standard | | | | |
| Application rate [l or kg product/ha]: | 9,0 | | | |
| Dose [kg a.s./ha]: | 7,65 | 0,0016 | 0,0009 | 0,0 |
| Work rate [ha/day]: | 1,00 | | | |
| PPE during application: | | | | |
| PPE during mix/loading: | | Respiration: | Mask FFP2 | |
| Respiration: | None | Hands: | Gloves | |
| Hands: | Gloves | Head: | None | |
| Body: Overall | | | | |
| Scenario 2: High crop, standard | | | | |
| Application rate [l or kg product/ha]: | 9,0 | | | |
| Dose [kg a.s./ha]: | 7,65 | 0,0016 | 0,0009 | 0,0 |
| Work rate [ha/day]: | 1,00 | | | |
| PPE during application: | | | | |
| PPE during mix/loading: | | Respiration: | Mask A1P2 | |
| Respiration: | Mask A1P2 | Hands: | Gloves | |
| Hands: | Gloves | Head: | Headgear | |
| Body: Impervious clothing | | | | |
| Summary | | | | |
| Predicted systemic exposure as a percentage of the AOEL: Greenhouse Model | | | | |
| 75th percentile | | | | |
| Active substance | Protection | Systemic exposure [mg/kg bw/day] | AOEL [mg/kg bw/day] | % of AOEL |
| Low crop, standard | | | | |
| daminozide | None | 0,06306 | 0,0088 | 720,7 |
| | With | 0,006134 | | 70,1 |
| UDMH | None | 0,00003 | 0,0001 | 34,2 |
| | With | 0,000002 | | 2,3 |
| High crop, standard | | | | |
| daminozide | None | 0,1654 | 0,0088 | 1890,2 |
| | With | 0,007058 | | 80,7 |
| UDMH | None | 0,00013 | 0,0001 | 140,2 |
| | With | 0,000007 | | 7,7 |

Appendix B.6.4.1-10: Gantry indoor application, UK POEM M/L: daminozide – no PPE
THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM) WITH GERMAN MODEL MIX/LOAD DATA (75th PERCENTILE)

| | | | |
|--------------------------------|---------------------------------------------------------|------------------------------|------------|
| Application method | Tractor-mounted/trailed boom sprayer: hydraulic nozzles | | |
| Product | Alar | Active substance | daminozide |
| Formulation type | WG or SG | a.s. concentration | 850 mg/g |
| Dermal absorption from product | 0,2 % | Dermal absorption from spray | 0 % |
| PPE during mix/loading | None | PPE during application | None |
| Dose | 9 kg product/ha | Work rate/day | 1 ha |
| Application volume | 500 l/ha | Duration of spraying | 6 h |
| AOEL _{syst.} | 0,00875 mg/kg bw/day | Total exposure (result): | 59 % AOEL |

DERMAL EXPOSURE DURING MIXING AND LOADING

| | |
|----------------------------|-----------------|
| Hand contamination/kg a.s. | 5,72 mg/kg a.s. |
| Hand contamination/day | 43,758 mg/day |
| Protective clothing | None |
| Transmission to skin | 100 % |
| Dermal exposure to a.s. | 43,758 mg/day |

INHALATION EXPOSURE DURING MIXING AND LOADING

| | |
|-----------------------------|-------------------|
| Inhalation exposure/kg a.s. | 0,0358 mg/kg a.s. |
| Inhalation exposure/day | 0,27387 mg/day |
| RPE | None |
| Transmission through RPE | 100 % |
| Inhalation exposure to a.s. | 0,27387 mg/day |

DERMAL EXPOSURE DURING SPRAY APPLICATION

| | | | |
|---------------------------------------|---------------------------------------------------------|-----------|------------|
| Application technique | Tractor-mounted/trailed boom sprayer: hydraulic nozzles | | |
| Application volume | 500 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 | | |
| Concentration of a.s. in spray soluti | 15,3 mg/ml | | |
| Dermal exposure to a.s. | 635,715 mg/day | | |

INHALATION EXPOSURE DURING SPRAYING

| | |
|--------------------------------|--------------|
| Inhalation exposure to spray | 0,01 ml/h |
| Duration of exposure | 6 h |
| Concentration of a.s. in spray | 15,3 mg/ml |
| Inhalation exposure to a.s. | 0,918 mg/day |
| Percent absorbed | 100 % |
| Absorbed dose | 0,918 mg/day |

ABSORBED DOSE

| | | | |
|------------------------------|-----------------|-------------|--------|
| | Mix/load | Application | |
| Dermal exposure to a.s. | 43,758 mg/day | | mg/day |
| Percent absorbed | 0,2 % | | % |
| Absorbed dose (dermal route) | 0,087516 mg/day | | mg/day |
| Inhalation exposure to a.s. | 0,27387 mg/day | | mg/day |
| Absorbed dose | 0,361386 mg/day | | mg/day |

PREDICTED EXPOSURE

| | |
|----------------------|--------------------------|
| Total absorbed dose | 0,361386 mg/day |
| Operator body weight | 70 kg |
| Operator exposure | 0,005162657 mg/kg bw/day |

Appendix B.6.4.1-11: Gantry indoor application, UK POEM M/L: UDMH – no PPE.
THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM) WITH GERMAN MODEL MIX/LOAD DATA (75th PERCENTILE)

| | | | |
|--------------------------------|---------------------------------------------------------|------------------------------|-------------|
| Application method | Tractor-mounted/trailed boom sprayer: hydraulic nozzles | | |
| Product | Alar | Active substance | UDMH |
| Formulation type | WG or SG | a.s. concentration | 0,026 mg/g |
| Dermal absorption from product | 10,7 % | Dermal absorption from spray | 0 % |
| PPE during mix/loading | None | PPE during application | None |
| Dose | 9 kg product/ha | Work rate/day | 1 ha |
| Application volume | 500 l/ha | Duration of spraying | 6 h |
| AOEL _{sys.} | 0,00009 mg/kg bw/day | Total exposure (result): | 2,41 % AOEL |

DERMAL EXPOSURE DURING MIXING AND LOADING

| | |
|----------------------------|-------------------|
| Hand contamination/kg a.s. | 5,72 mg/kg a.s. |
| Hand contamination/day | 0,00133848 mg/day |
| Protective clothing | None |
| Transmission to skin | 100 % |
| Dermal exposure to a.s. | 0,00133848 mg/day |

INHALATION EXPOSURE DURING MIXING AND LOADING

| | |
|-----------------------------|-------------------|
| Inhalation exposure/kg a.s. | 0,0358 mg/kg a.s. |
| Inhalation exposure/day | 8,3772E-06 mg/day |
| RPE | None |
| Transmission through RPE | 100 % |
| Inhalation exposure to a.s. | 8,3772E-06 mg/day |

DERMAL EXPOSURE DURING SPRAY APPLICATION

| | | | |
|-----------------------------------------|---------------------------------------------------------|-----------|------------|
| Application technique | Tractor-mounted/trailed boom sprayer: hydraulic nozzles | | |
| Application volume | 500 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 | ml/day | | |
| Concentration of a.s. in spray solution | mg/ml | | |
| Dermal exposure to a.s. | mg/day | | |

INHALATION EXPOSURE DURING SPRAYING

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

ABSORBED DOSE

| | | | |
|------------------------------|--------------------|-------------|--------|
| | Mix/load | Application | |
| Dermal exposure to a.s. | 0,00133848 mg/day | | mg/day |
| Percent absorbed | 10,7 % | | % |
| Absorbed dose (dermal route) | 0,000143217 mg/day | | mg/day |
| Inhalation exposure to a.s. | 8,3772E-06 mg/day | | mg/day |
| Absorbed dose | 0,000151595 mg/day | | mg/day |

PREDICTED EXPOSURE

| | |
|----------------------|--------------------------|
| Total absorbed dose | 0,000151595 mg/day |
| Operator body weight | 70 kg |
| Operator exposure | 2,16564E-06 mg/kg bw/day |

Appendix B.6.4.1-12: Gantry indoor application, German model M/L: daminozide

| Estimation of operator exposure (acc. to the German model) | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|----------------------------|-------------------|
| Active substance (a.s.) | Daminozide | | |
| Product | Alar | | |
| Intended use(s) | ornamentals | | |
| Field Close, Tractor Mounted (PS1M) | | | |
| Type of preparation | | | |
| Application rate (AR) | 7,65 | kg a.s./ha | |
| Treated area per day (A) | 1 | ha/d | |
| Systemic AOEL | 0,00875 | mg/kg bw/d | |
| Dermal absorption (DA) | 0,2 | % for mixing/loading (m/l) | |
| | | % for application (appl.) | |
| Inhalation absorption (IA) | 100 | % | |
| Body weight (BW) | 70 | kg | |
| Personal protective equipment: | BVL code | Reduction factor | to lower: |
| Particle filtering half mask (m/l) ¹⁾ | ST1102 | 0,08 | I _M |
| Half mask with combined filter (m/l) | ST2102 | 0,02 | I _M |
| Particle filtering half mask (appl.) ¹⁾ | ST1203 | 0,08 | I _A |
| | | 0,8 | D _{A(C)} |
| Half mask with combined filter (appl.) ¹⁾ | ST2202 | 0,02 | I _A |
| | | 0,8 | D _{A(C)} |
| Protective gloves (m/l) ²⁾ | SS110 | 0,01 | D _{M(H)} |
| Protective gloves (appl.) ²⁾ | SS120 | 0,01 | D _{A(H)} |
| Protective garment + sturdy footwear (appl.) ²⁾ | SS2202 | 0,05 | D _{A(B)} |
| Broad-brimmed headgear (appl.) ²⁾ | SS420 | 0,5 | D _{A(C)} |
| Hood and visor (appl.) ²⁾ | SS520 | 0,05 | D _{A(C)} |
| ¹⁾ DIN EN 149 (2001), ²⁾ BVL (2006) Guidelines for requirements concerning personal protective equipment in plant protection | | | |
| Estimated inhalation exposure: | Personal protective equipment (PPE) | | Factor |
| I _M | no PPE | | 1 |
| I _A | no PPE | | 1 |
| Estimated dermal exposure: | Personal protective equipment (PPE) | | Factor |
| D _{M(H)} | SS110 | | 0,01 |
| D _{A(H)} | no PPE | | 1 |
| D _{A(C)} | no PPE | | 1 |
| D _{A(B)} | no PPE | | 1 |

Estimation of operator exposure: German model

Input parameters considered for the estimation of operator exposure:

| | | | |
|-----------------------------|--------------------|------------------------------------|-------------------------------------|
| Formulation type: | Water soluble or | Application technique: | Field Crops, Tractor Mounted (FCTM) |
| Application rate (AR): | 7,65 kg | | |
| Area treated per day (A): | 1 ha | Dermal hands m/l ($D_{M(H)}$): | 2 mg/person/kg |
| Dermal absorption (DA): | 0,2 % (concentr.) | Dermal hands appl. ($D_{A(H)}$): | 0,38 mg/person/kg |
| | % (dilution) | Dermal body appl. ($D_{A(B)}$): | 1,6 mg/person/kg |
| Inhalation absorption (IA): | 100 % | Dermal head appl. ($D_{A(C)}$): | 0,06 mg/person/kg |
| Body weight (BW): | 70 kg/person | Inhalation m/l (I_M): | 0,008 mg/person/kg |
| AOEL | 0,00875 mg/kg bw/d | Inhalation appl. (I_A): | 0,001 mg/person/kg |

| Operator exposure towards Daminozide | | | |
|-----------------------------------------------------------------------------------------------------|---------------------|-----------------------------------------------------------------------------------------------------|---------------------|
| Without PPE | | With PPE | |
| Operators: Systemic dermal exposure after application in ornamentals | | | |
| Dermal exposure during mixing/loading | | | |
| Hands | | Hands | |
| $SDE_{OAM(H)} = (D_{M(H)} \times AR \times A \times DA) / BW$ | | $SDE_{OAM(H)} = (D_{M(H)} \times AR \times A \times PPE^{-1} \times DA) / BW$ | |
| $(2 \times 7,65 \times 1 \times 0,2\%) / 70$ | | $(2 \times 7,65 \times 1 \times 0,01 \times 0,2\%) / 70$ | |
| External dermal exposure | 15,3 mg/person | External dermal exposure | 0,153 mg/person |
| External dermal exposure | 0,218571 mg/kg bw/d | External dermal exposure | 0,002186 mg/kg bw/d |
| Systemic dermal exposure | 0,000437 mg/kg bw/d | Systemic dermal exposure | 0,000004 mg/kg bw/d |
| Dermal exposure during application | | | |
| Hands | | Hands | |
| $SDE_{OAH(H)} = (D_{A(H)} \times AR \times A \times DA) / BW$ | | $SDE_{OAH(H)} = (D_{A(H)} \times AR \times A \times PPE^{-1} \times DA) / BW$ | |
| $(0,38 \times 7,65 \times 1 \times 0\%) / 70$ | | $(0,38 \times 7,65 \times 1 \times 1 \times 0\%) / 70$ | |
| External dermal exposure | mg/person | External dermal exposure | mg/person |
| External dermal exposure | mg/kg bw/d | External dermal exposure | mg/kg bw/d |
| Systemic dermal exposure | mg/kg bw/d | Systemic dermal exposure | mg/kg bw/d |
| Body | | Body | |
| $SDE_{OAB(B)} = (D_{A(B)} \times AR \times A \times DA) / BW$ | | $SDE_{OAB(B)} = (D_{A(B)} \times AR \times A \times PPE^{-1} \times DA) / BW$ | |
| $(1,6 \times 7,65 \times 1 \times 0\%) / 70$ | | $(1,6 \times 7,65 \times 1 \times 1 \times 0\%) / 70$ | |
| External dermal exposure | mg/person | External dermal exposure | mg/person |
| External dermal exposure | mg/kg bw/d | External dermal exposure | mg/kg bw/d |
| Systemic dermal exposure | mg/kg bw/d | Systemic dermal exposure | mg/kg bw/d |
| Head | | Head | |
| $SDE_{OAC(C)} = (D_{A(C)} \times AR \times A \times DA) / BW$ | | $SDE_{OAC(C)} = (D_{A(C)} \times AR \times A \times PPE^{-1} \times DA) / BW$ | |
| $(0,06 \times 7,65 \times 1 \times 0\%) / 70$ | | $(0,06 \times 7,65 \times 1 \times 1 \times 0\%) / 70$ | |
| External dermal exposure | mg/person | External dermal exposure | mg/person |
| External dermal exposure | mg/kg bw/d | External dermal exposure | mg/kg bw/d |
| Systemic dermal exposure | mg/kg bw/d | Systemic dermal exposure | mg/kg bw/d |
| Total systemic dermal exposure: $SDE_O = SDE_{OAM(H)} + SDE_{OAH(H)} + SDE_{OAB(B)} + SDE_{OAC(C)}$ | | Total systemic dermal exposure: $SDE_O = SDE_{OAM(H)} + SDE_{OAH(H)} + SDE_{OAB(B)} + SDE_{OAC(C)}$ | |
| Total external dermal exposure | 15,3 mg/person | Total external dermal exposure | 0,153 mg/person |
| Total external dermal exposure | 0,218571 mg/kg bw/d | Total external dermal exposure | 0,002186 mg/kg bw/d |
| Total systemic dermal exposure | 0,000437 mg/kg bw/d | Total systemic dermal exposure | 4,37E-06 mg/kg bw/d |

| Operators: Systemic inhalation exposure after application in ornamentals | | | | | |
|--------------------------------------------------------------------------------------------------------------------------------------|-----------------|-------------------|--------------------------------------------------------------------|-----------------|-------------------|
| Inhalation exposure during mixing/loading | | | | | |
| $SIE_{OM} = (I_M \times AR \times A \times IA) / BW$ | | | $SIE_{OM} = (I_M \times AR \times A \times PPE^4) \times IA) / BW$ | | |
| $(0,008 \times 7,65 \times 1 \times 100\%) / 70$ | | | $(0,008 \times 7,65 \times 1 \times 1 \times 100\%) / 70$ | | |
| External inhalation exposure | 0,0612 | mg/person | External inhalation exposure | 0,0612 | mg/person |
| External inhalation exposure | 0,000874 | mg/kg bw/d | External inhalation exposure | 0,000874 | mg/kg bw/d |
| Systemic inhalation | 0,000874 | mg/kg bw/d | Systemic inhalation | 0,000874 | mg/kg bw/d |
| Inhalation exposure during application | | | | | |
| $SIE_{OA} = (I_A \times AR \times A \times IA) / BW$ | | | $SIE_{OA} = (I_A \times AR \times A \times PPE^4) \times IA) / BW$ | | |
| $(0,001 \times 7,65 \times 1 \times 100\%) / 70$ | | | $(0,001 \times 7,65 \times 1 \times 1 \times 100\%) / 70$ | | |
| External inhalation exposure | | mg/person | External inhalation exposure | | mg/person |
| External inhalation exposure | | mg/kg bw/d | External inhalation exposure | | mg/kg bw/d |
| Systemic inhalation | | mg/kg bw/d | Systemic inhalation | | mg/kg bw/d |
| Total systemic inhalation exposure: $SIE_O = SIE_{OM} +$ | | | Total systemic inhalation exposure: $SIE_O = SIE_{OM} +$ | | |
| Total external inhalation exposure | 0,061200 | mg/person | Total external inhalation exposure | 0,061200 | mg/person |
| Total external inhalation exposure | 0,000874 | mg/kg bw/d | Total external inhalation exposure | 0,000874 | mg/kg bw/d |
| Total systemic inhalation exposure | 0,000874 | mg/kg bw/d | Total systemic inhalation exposure | 0,000874 | mg/kg bw/d |
| Total systemic exposure: $SE_O = SDE_O + SIE_O$ | | | Total systemic exposure: $SE_O = SDE_O + SIE_O$ | | |
| Total systemic exposure | 0,09180 | mg/person | Total systemic exposure | 0,06151 | mg/person |
| Total systemic exposure | 0,001311 | mg/kg bw/d | Total systemic exposure | 0,000879 | mg/kg bw/d |
| % of AOEL | 15,0 | % | % of AOEL | 10,0 | % |
| ¹⁾ reduction factor for gloves is 0.01 (professional applications) and 0.5 (home/allotment garden applications), resp. | | | | | |
| ²⁾ reduction factor for protective garment is 0.05 (prof. appl.) and 0.5 (workwear, home/allotment garden appl.), resp. | | | | | |
| ³⁾ reduction factor for broad brimmed headgear and hood and visor is 0.5 and 0.05, respectively (professional appl.) | | | | | |
| ⁴⁾ reduction factor for RPE is 0.08 (particle filter) and 0.02 (combined vapour and particle filter), resp. (prof. appl.) | | | | | |

Appendix B.6.4.1-13: Gantry indoor application, German model M/L: UDMH

| Estimation of operator exposure (acc. to the German model) | | | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------|----------------------------|-------------------|-------------------------------------|
| Active substance (a.s.) | UDMH -M/L | | | |
| Product | Alar | | | |
| Intended use(s) | ornamentals | | | |
| Type of preparation | Field Crops, Tractor Mounted (FCTM) ▼ | | | |
| | Water soluble or dispersible granules (WG) ▼ | | | |
| Application rate (AR) | 0,00023 | kg a.s./ha | | |
| Treated area per day (A) | 1 | ha/d | | |
| Systemic AOEL | 0,00009 | mg/kg bw/d | | |
| Dermal absorption (DA) | 10,7 | % for mixing/loading (m/l) | | |
| | | % for application (appl.) | | |
| Inhalation absorption (IA) | 100 | % | | |
| Body weight (BW) | 70 | kg | | |
| Personal protective equipment: | BVL code | Reduction factor | to lower: | |
| Particle filtering half mask (m/l) ¹⁾ | ST1102 | 0,08 | I _M | <input type="checkbox"/> |
| Half mask with combined filter (m/l) | ST2102 | 0,02 | I _M | <input type="checkbox"/> |
| Particle filtering half mask (appl.) ¹⁾ | ST1203 | 0,08 | I _A | <input type="checkbox"/> |
| | | 0,8 | D _{A(C)} | |
| Half mask with combined filter (appl.) ¹⁾ | ST2202 | 0,02 | I _A | <input type="checkbox"/> |
| | | 0,8 | D _{A(C)} | |
| Protective gloves (m/l) ²⁾ | SS110 | 0,01 | D _{M(H)} | <input checked="" type="checkbox"/> |
| Protective gloves (appl.) ²⁾ | SS120 | 0,01 | D _{A(H)} | <input type="checkbox"/> |
| Protective garment + sturdy footwear (appl.) ²⁾ | SS2202 | 0,05 | D _{A(B)} | <input type="checkbox"/> |
| Broad-brimmed headgear (appl.) ²⁾ | SS420 | 0,5 | D _{A(C)} | <input type="checkbox"/> |
| Hood and visor (appl.) ²⁾ | SS520 | 0,05 | D _{A(C)} | <input type="checkbox"/> |
| ¹⁾ DIN EN 149 (2001), ²⁾ BVL (2006) Guidelines for requirements concerning personal protective equipment in plant protection | | | | |
| Estimated inhalation exposure: | Personal protective equipment (PPE) | | Factor | |
| I _M | no PPE | | 1 | |
| I _A | no PPE | | 1 | |
| Estimated dermal exposure: | Personal protective equipment (PPE) | | Factor | |
| D _{M(H)} | SS110 | | 0,01 | |
| D _{A(H)} | no PPE | | 1 | |
| D _{A(C)} | no PPE | | 1 | |
| D _{A(B)} | no PPE | | 1 | |

Estimation of operator exposure: German model

Input parameters considered for the estimation of operator exposure:

| | | | |
|-----------------------------|--------------------|------------------------------------|-------------------------------------|
| Formulation type: | Water soluble or | Application technique: | Field Crops, Tractor Mounted (FCTM) |
| Application rate (AR): | 0,00023 kg | | |
| Area treated per day (A): | 1 ha | Dermal hands m/l ($D_{M(H)}$): | 2 mg/person/kg |
| Dermal absorption (DA): | 10,7 % (concentr.) | Dermal hands appl. ($D_{A(H)}$): | 0,38 mg/person/kg |
| | % (dilution) | Dermal body appl. ($D_{A(B)}$): | 1,6 mg/person/kg |
| Inhalation absorption (IA): | 100 % | Dermal head appl. ($D_{A(C)}$): | 0,06 mg/person/kg |
| Body weight (BW): | 70 kg/person | Inhalation m/l (I_M): | 0,008 mg/person/kg |
| AOEL | 0,00009 mg/kg bw/d | Inhalation appl. (I_A): | 0,001 mg/person/kg |

Operator exposure towards UDMH -M/L

| Without PPE | | | | With PPE | | | |
|-----------------------------------------------------------------------------------------------------|----------|------------|--|-----------------------------------------------------------------------------------------------------|----------|------------|--|
| Operators: Systemic dermal exposure after application in ornamentals | | | | | | | |
| Dermal exposure during mixing/loading | | | | | | | |
| Hands | | | | Hands | | | |
| $SDE_{O(M/H)} = (D_{M(H)} \times AR \times A \times DA) / BW$ | | | | $SDE_{O(M/H)} = (D_{M(H)} \times AR \times A \times PPE^{-1} \times DA) / BW$ | | | |
| $(2 \times 0,00023 \times 1 \times 10,7\%) / 70$ | | | | $(2 \times 0,00023 \times 1 \times 0,01 \times 10,7\%) / 70$ | | | |
| External dermal exposure | 0,00046 | mg/person | | External dermal exposure | 4,6E-06 | mg/person | |
| External dermal exposure | 6,57E-06 | mg/kg bw/d | | External dermal exposure | 6,57E-08 | mg/kg bw/d | |
| Systemic dermal exposure | 0,000001 | mg/kg bw/d | | Systemic dermal exposure | 0,000000 | mg/kg bw/d | |
| Dermal exposure during application | | | | | | | |
| Hands | | | | Hands | | | |
| $SDE_{O(A/H)} = (D_{A(H)} \times AR \times A \times DA) / BW$ | | | | $SDE_{O(A/H)} = (D_{A(H)} \times AR \times A \times PPE^{-1} \times DA) / BW$ | | | |
| $(0,38 \times 0,00023 \times 1 \times 0\%) / 70$ | | | | $(0,38 \times 0,00023 \times 1 \times 1 \times 0\%) / 70$ | | | |
| External dermal exposure | | mg/person | | External dermal exposure | | mg/person | |
| External dermal exposure | | mg/kg bw/d | | External dermal exposure | | mg/kg bw/d | |
| Systemic dermal exposure | | mg/kg bw/d | | Systemic dermal exposure | | mg/kg bw/d | |
| Body | | | | Body | | | |
| $SDE_{O(A/B)} = (D_{A(B)} \times AR \times A \times DA) / BW$ | | | | $SDE_{O(A/B)} = (D_{A(B)} \times AR \times A \times PPE^{-1} \times DA) / BW$ | | | |
| $(1,6 \times 0,00023 \times 1 \times 0\%) / 70$ | | | | $(1,6 \times 0,00023 \times 1 \times 1 \times 0\%) / 70$ | | | |
| External dermal exposure | | mg/person | | External dermal exposure | | mg/person | |
| External dermal exposure | | mg/kg bw/d | | External dermal exposure | | mg/kg bw/d | |
| Systemic dermal exposure | | mg/kg bw/d | | Systemic dermal exposure | | mg/kg bw/d | |
| Head | | | | Head | | | |
| $SDE_{O(A/C)} = (D_{A(C)} \times AR \times A \times DA) / BW$ | | | | $SDE_{O(A/C)} = (D_{A(C)} \times AR \times A \times PPE^{-1} \times DA) / BW$ | | | |
| $(0,06 \times 0,00023 \times 1 \times 0\%) / 70$ | | | | $(0,06 \times 0,00023 \times 1 \times 1 \times 0\%) / 70$ | | | |
| External dermal exposure | | mg/person | | External dermal exposure | | mg/person | |
| External dermal exposure | | mg/kg bw/d | | External dermal exposure | | mg/kg bw/d | |
| Systemic dermal exposure | | mg/kg bw/d | | Systemic dermal exposure | | mg/kg bw/d | |
| Total systemic dermal exposure: $SDE_O = SDE_{O(M/H)} + SDE_{O(A/H)} + SDE_{O(A/B)} + SDE_{O(A/C)}$ | | | | Total systemic dermal exposure: $SDE_O = SDE_{O(M/H)} + SDE_{O(A/H)} + SDE_{O(A/B)} + SDE_{O(A/C)}$ | | | |
| Total external dermal exposure | 0,00046 | mg/person | | Total external dermal exposure | 4,6E-06 | mg/person | |
| Total external dermal exposure | 6,57E-06 | mg/kg bw/d | | Total external dermal exposure | 6,57E-08 | mg/kg bw/d | |
| Total systemic dermal exposure | 7,03E-07 | mg/kg bw/d | | Total systemic dermal exposure | 7,03E-09 | mg/kg bw/d | |

| Operators: Systemic inhalation exposure after application in ornamentals | | | | | |
|--------------------------------------------------------------------------|----------|------------|----------------------------------------------------------------------|----------|------------|
| Inhalation exposure during mixing/loading | | | | | |
| $SIE_{OM} = (I_M \times AR \times A \times IA) / BW$ | | | $SIE_{OM} = (I_M \times AR \times A \times PPE^{-4} \times IA) / BW$ | | |
| $(0,008 \times 0,00023 \times 1 \times 100\%) / 70$ | | | $(0,008 \times 0,00023 \times 1 \times 1 \times 100\%) / 70$ | | |
| External inhalation exposure | 1,84E-06 | mg/person | External inhalation exposure | 1,84E-06 | mg/person |
| External inhalation exposure | 2,63E-08 | mg/kg bw/d | External inhalation exposure | 2,63E-08 | mg/kg bw/d |
| Systemic inhalation | 0,000000 | mg/kg bw/d | Systemic inhalation | 0,000000 | mg/kg bw/d |
| Inhalation exposure during application | | | | | |
| $SIE_{OA} = (I_A \times AR \times A \times IA) / BW$ | | | $SIE_{OA} = (I_A \times AR \times A \times PPE^{-4} \times IA) / BW$ | | |
| $(0,001 \times 0,00023 \times 1 \times 100\%) / 70$ | | | $(0,001 \times 0,00023 \times 1 \times 1 \times 100\%) / 70$ | | |
| External inhalation exposure | | mg/person | External inhalation exposure | | mg/person |
| External inhalation exposure | | mg/kg bw/d | External inhalation exposure | | mg/kg bw/d |
| Systemic inhalation | | mg/kg bw/d | Systemic inhalation | | mg/kg bw/d |
| Total systemic inhalation exposure: $SIE_O = SIE_{OM} +$ | | | Total systemic inhalation exposure: $SIE_O = SIE_{OM} +$ | | |
| Total external inhalation exposure | 0,000002 | mg/person | Total external inhalation exposure | 0,000002 | mg/person |
| Total external inhalation exposure | 0,000000 | mg/kg bw/d | Total external inhalation exposure | 0,000000 | mg/kg bw/d |
| Total systemic inhalation exposure | 0,000000 | mg/kg bw/d | Total systemic inhalation exposure | 0,000000 | mg/kg bw/d |
| Total systemic exposure: $SE_O = SDE_O + SIE_O$ | | | Total systemic exposure: $SE_O = SDE_O + SIE_O$ | | |
| Total systemic exposure | 0,000005 | mg/person | Total systemic exposure | 0,000000 | mg/person |
| Total systemic exposure | 0,000001 | mg/kg bw/d | Total systemic exposure | 0,000000 | mg/kg bw/d |
| % of AOEL | 0,8 | % | % of AOEL | 0,04 | % |

Appendix B.6.4.1-14: Gantry indoor application, EFSA AOEM model M/L: daminozide – no PPE

| | | |
|--------------------------------------|-------------------------------------|------------------------|
| Application rate of active substance | 7,65 kg a.s./ha | <i>i_AppRate</i> |
| Assumed area treated | 1 ha/day | <i>d_AreaTreated</i> |
| Amount of active substance applied | 7,65 kg a.s./day | <i>i_AmountAS</i> |
| Dermal absorption of the product | 0,20 % | <i>i_AbsorpProduct</i> |
| Dermal absorption of in-use dilution | 0,00 % | <i>i_Absorinuse</i> |
| Formulation type | Wettable granules, soluble granules | |
| Indoor or Outdoor application | Outdoor | |
| Application method | Downward spraying | |
| Application equipment | Manual-Knapsack | |
| Season | not relevant | |

| Mixing and loading | Exposure values | µg exposure/day mixed and loaded | | Reference | Comment |
|--------------------|---------------------------------------------------------------------|-----------------------------------------|--------------------------|---------------------------|-------------------------------------|
| | | 75 th centile | 95 th centile | | |
| | Hands | 48425 | 129958 | AOEM | |
| | Body | 4095 | 14214 | AOEM | |
| | Head | 26 | 56 | AOEM | |
| | Protected hands (gloves) | 92 | 836 | AOEM | |
| | Protected body (workwear or protective garment and sturdy footwear) | 128 | 525 | AOEM | |
| | Protected head (hood and face shield) | 26 | 56 | AOEM | |
| | Inhalation | 128 | 133 | AOEM | |
| | Protective Equipment | Select for inclusion | | Penetration factor | Inhalation Protection factor |
| | Gloves | No | | | |
| | Clothing | Work wear - arms, body and legs covered | | Incl. in AOEM model | |
| | Head and respiratory PPE | None | | 1 | 1 |
| | Water soluble bag | No | | 1 | |

| Application | Exposure values | µg exposure/day applied | | Reference | Comment |
|-------------|---------------------------------------------------------------------|-----------------------------------------|--------------------------|--------------------------------------|-------------------------------------|
| | | 75 th centile | 95 th centile | | |
| | Hands | 7874 | 21486 | AOEM | |
| | Body | 453227 | 698736 | AOEM | |
| | Head | 61 | 434 | AOEM | |
| | Protected hands (gloves) | 26 | 112 | AOEM | |
| | Protected body (workwear or protective garment and sturdy footwear) | 45405 | 319413 | AOEM | |
| | Inhalation | 133 | 133 | AOEM | |
| | Protective Equipment | Select for inclusion | | Penetration factor | Inhalation Protection factor |
| | Gloves | No | | | |
| | Clothing | Work wear - arms, body and legs covered | | Incl. in AOEM model | |
| | Head and respiratory PPE | None | | 1 | 1 |
| | Closed cab | No | | vehicle mounted upward spraying only | |

1. Total

| | Without RPE/PPE | With RPE/PPE | |
|------------------------------------------------------------------------------------------------|-----------------|----------------|--|
| Longer term | | | |
| Total systemic exposure from mixing, loading and application (mg a.s./day) | 0,3651906 | 0,3572550 | |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0,0060865 | 0,0059543 | |
| % of RVNAS | 69,56 % | 68,05 % | |
| Acute | | | |
| Total systemic exposure from mixing, loading and application (mg a.s./day) | 0,5536560 | 0,5262792 | |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0,0092276 | 0,0087713 | |
| % of RVAAS | #DĚLENÍ NULOU! | #DĚLENÍ NULOU! | |

| | | | | | |
|----------------------------------------------------------------------------|---------------------------------------------------------------------|-----------------------------------------|--------------------------|--------------------------------------|---------------------------------------------------------|
| Application rate of active substance | 7,65 kg a.s./ha | | | i_AppRate | |
| Assumed area treated | 10 ha/day | | | d_AreaTreated | |
| Amount of active substance applied | 76,5 kg a.s./day | | | i_AmountAS | |
| Dermal absorption of the product | 0,20 % | | | i_AbsorpProduct | |
| Dermal absorption of in-use dilution | 0,00 % | | | i_AbsorInuse | |
| Formulation type | Wettable granules, soluble granules | | | | |
| Indoor or Outdoor application | Outdoor | | | | |
| Application method | Downward spraying | | | | |
| Application equipment | Vehicle-mounted | | | | |
| Season | not relevant | | | | |
| OutdoorWettable granules, soluble granulesDownward sprayingVehicle-mounted | | | | | |
| Mixing and loading | Exposure values | µg exposure/day mixed and loaded | | Reference | Comment |
| | | 75 th centile | 95 th centile | | |
| | Hands | 36956 | 183121 | AOEM | |
| | Body | 26048 | 56660 | AOEM | |
| | Head | 497 | 6849 | AOEM | |
| | Protected hands (gloves) | 278 | 2407 | AOEM | |
| | Protected body (workwear or protective garment and sturdy footwear) | 869 | 4760 | AOEM | |
| | Protected head (hood and face shield) | 8 | 388 | AOEM | |
| | Inhalation | 136 | 288 | AOEM | |
| | Protective Equipment | Select for inclusion | | Penetration factor | Inhalation Protection factor |
| | Gloves | No | | | |
| | Clothing | Work wear - arms, body and legs covered | | Incl. in AOEM model | |
| | Head and respiratory PPE | None | | 1 | 1 |
| | Water soluble bag | No | | 1 | |
| Application | Exposure values | µg exposure/day applied | | Reference | Comment |
| | | 75 th centile | 95 th centile | | |
| | Hands | 123955 | 89835 | AOEM | This scenario assumes that small area equipment is used |
| | Body | 170070 | 215502 | AOEM | |
| | Head | 1018 | 11953 | AOEM | |
| | Protected hands (gloves) | 229 | 35 | AOEM | |
| | Protected body (workwear or protective garment and sturdy footwear) | 2127 | 2513 | AOEM | |
| | Inhalation | 47 | 490 | AOEM | |
| | Protective Equipment | Select for inclusion | | Penetration factor | Inhalation Protection factor |
| | Gloves | No | | | |
| | Clothing | Work wear - arms, body and legs covered | | Incl. in AOEM model | |
| | Head and respiratory PPE | None | | 1 | 1 |
| | Closed cab | No | | vehicle mounted upward spraying only | |
| | | | | | |

1. Total

| | Without RPE/PPE | With RPE/PPE | |
|------------------------------------------------------------------------------------------------|-----------------|----------------|--|
| Longer term | | | |
| Total systemic exposure from mixing, loading and application (mg a.s./day) | 0,3094561 | 0,2590984 | |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0,0051576 | 0,0043183 | |
| % of RVNAS | 58,94 % | 49,35 % | |
| Acute | | | |
| Total systemic exposure from mixing, loading and application (mg a.s./day) | 1,2710533 | 1,1672518 | |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0,0211842 | 0,0194542 | |
| % of RVAAS | #DĚLENÍ NULOU! | #DĚLENÍ NULOU! | |

Appendix B.6.4.1-15: Gantry indoor application, EFSA AOEM model M/L: UDMH – no PPE

Exposure assessment

| | | | | | |
|-----------------------|-----------------------------------------------------------|---------------------------------------------------|---------------------------------------|-----------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,00023 kg a.s. /ha | Spray dilution = 0,00046 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Knapsack | | | Buffer = 5 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 0 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm2 per kg a.s./ha | | DT50 | 30 days | |

| Operator Model | | Mixing, loading and application AOEM | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|------------|-------------------|
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,0188 | % of RVNAS | 20879,58% |
| | Acute systemic exposure mg/kg bw/day | 0,0509 | % of RVAAS | |
| Mixing and Loading | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Soluble bags = No |
| Application | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Closed cabin = No |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0174 | % of RVNAS | 19337,99% |
| | Acute systemic exposure mg/kg bw/day | 0,0461 | % of RVAAS | |

| | | | | | |
|-----------------------|-------------------------------------------------------------|---------------------------------------------------|---------------------------------------|-----------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,00023 kg a.s. /ha | Spray dilution = 0,00046 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Downward spraying / Vehicle-mounted | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 0 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm2 per kg a.s./ha | | DT50 | 30 days | |

| Operator Model | | Mixing, loading and application AOEM | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|------------|-------------------|
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,0002 | % of RVNAS | 176,53% |
| | Acute systemic exposure mg/kg bw/day | 0,0088 | % of RVAAS | |
| Mixing and Loading | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Soluble bags = No |
| Application | Gloves = No | Clothing = Work wear - arms, body and legs covered | RPE = None | Closed cabin = No |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0001 | % of RVNAS | 142,49% |
| | Acute systemic exposure mg/kg bw/day | 0,0039 | % of RVAAS | |

Appendix B.6.4.1-16: Hand held application outdoors to low crops, UK POEM: daminozide – with PPE
THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM) WITH GERMAN MODEL MIX/LOAD DATA (75th PERCENTILE)

| | | | |
|--------------------------------|-----------------------------------------------------------------------------|------------------------------|---------------------------------|
| Application method | Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target | | |
| Product | Alar | Active substance | daminozide |
| Formulation type | WG or SG | a.s. concentration | 850 mg/g |
| Dermal absorption from product | 0,2 % | Dermal absorption from spray | 1,9 % |
| PPE during mix/loading | Gloves and RPE (FFP3) | PPE during application | Gloves and impermeable coverall |
| Dose | 5 kg product/ha | Work rate/day | 0,8 ha |
| Application volume | 500 l/ha | Duration of spraying | 6 h |
| AOEL _{system} | 0,00875 mg/kg bw/day | Total exposure (result): | 665 % AOEL |

DERMAL EXPOSURE DURING MIXING AND LOADING

| | |
|----------------------------|------------------|
| Hand contamination/kg a.s. | 171,4 mg/kg a.s. |
| Hand contamination/day | 582,76 mg/day |
| Protective clothing | Gloves |
| Transmission to skin | 1 % |
| Dermal exposure to a.s. | 5,8276 mg/day |

INHALATION EXPOSURE DURING MIXING AND LOADING

| | |
|-----------------------------|-------------------|
| Inhalation exposure/kg a.s. | 0,0628 mg/kg a.s. |
| Inhalation exposure/day | 0,21352 mg/day |
| RPE | RPE (FFP3) |
| Transmission through RPE | 5 % |
| Inhalation exposure to a.s. | 0,010676 mg/day |

DERMAL EXPOSURE DURING SPRAY APPLICATION

| | | | |
|------------------------------------|-----------------------------------------------------------------------------|-------------|-------------|
| Application technique | Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target | | |
| Application volume | 500 spray/ha | | |
| Volume of surface contamination | 50 ml/h | | |
| Distribution | Hands | Trunk | Legs |
| | 25 % | 25 % | 50 % |
| Clothing | Gloves | Impermeable | Impermeable |
| Penetration | 10 % | 5 % | 5 % |
| Dermal exposure | 1,25 | 0,625 | 1,25 ml/h |
| Duration of exposure | 6 h | | |
| Total dermal exposure to spray | 18,75 ml/day | | |
| Concentration of a.s. in spray sol | 8,5 mg/ml | | |
| Dermal exposure to a.s. | 159,375 mg/day | | |

INHALATION EXPOSURE DURING SPRAYING

| | |
|--------------------------------|-------------|
| Inhalation exposure to spray | 0,02 ml/h |
| Duration of exposure | 6 h |
| Concentration of a.s. in spray | 8,5 mg/ml |
| Inhalation exposure to a.s. | 1,02 mg/day |
| Percent absorbed | 100 % |
| Absorbed dose | 1,02 mg/day |

ABSORBED DOSE

| | | | |
|------------------------------|------------------|-----------------|--|
| | Mix/load | Application | |
| Dermal exposure to a.s. | 5,8276 mg/day | 159,375 mg/day | |
| Percent absorbed | 0,2 % | 1,9 % | |
| Absorbed dose (dermal route) | 0,0116552 mg/day | 3,028125 mg/day | |
| Inhalation exposure to a.s. | 0,010676 mg/day | 1,02 mg/day | |
| Absorbed dose | 0,0223312 mg/day | 4,048125 mg/day | |

PREDICTED EXPOSURE

| | |
|----------------------|--------------------------|
| Total absorbed dose | 4,0704562 mg/day |
| Operator body weight | 70 kg |
| Operator exposure | 0,058149374 mg/kg bw/day |

Appendix B.6.4.1-17: Hand held application outdoors to low crops, UK POEM: UDMH – with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM) WITH GERMAN MODEL MIX/LOAD DATA (75th PERCENTILE)

| | | | |
|--------------------------------|-----------------------------------------------------------------------------|------------------------------|---------------------------------|
| Application method | Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target | | |
| Product | Alar | Active substance | UDMH |
| Formulation type | WG or SG | a.s. concentration | 0,177 mg/g |
| Dermal absorption from product | 10,7 % | Dermal absorption from spray | 10,7 % |
| PPE during mix/loading | Gloves and RPE (FFP3) | PPE during application | Gloves and impermeable coverall |
| Dose | 5 kg product/ha | Work rate/day | 0,8 ha |
| Application volume | 500 l/ha | Duration of spraying | 6 h |
| AOEL _{sys.} | 0,00009 mg/kg bw/day | Total exposure (result): | 62 % AOEL |

DERMAL EXPOSURE DURING MIXING AND LOADING

| | |
|----------------------------|--------------------|
| Hand contamination/kg a.s. | 171,4 mg/kg a.s. |
| Hand contamination/day | 0,12162544 mg/day |
| Protective clothing | Gloves |
| Transmission to skin | 1 % |
| Dermal exposure to a.s. | 0,001216254 mg/day |

INHALATION EXPOSURE DURING MIXING AND LOADING

| | |
|-----------------------------|--------------------|
| Inhalation exposure/kg a.s. | 0,0628 mg/kg a.s. |
| Inhalation exposure/day | 4,45629E-05 mg/day |
| RPE | RPE (FFP3) |
| Transmission through RPE | 5 % |
| Inhalation exposure to a.s. | 2,22814E-06 mg/day |

DERMAL EXPOSURE DURING SPRAY APPLICATION

| | | | |
|-----------------------------------------|-----------------------------------------------------------------------------|-------------|-------------|
| Application technique | Hand-held sprayer (15 l tank): hydraulic nozzles. Outdoor, low level target | | |
| Application volume | 500 spray/ha | | |
| Volume of surface contamination | 50 ml/h | | |
| Distribution | Hands | Trunk | Legs |
| | 25% | 25% | 50% |
| Clothing | Gloves | Impermeable | Impermeable |
| Penetration | 10% | 5% | 5% |
| Dermal exposure | 1,25 | 0,625 | 1,25 ml/h |
| Duration of exposure | 6 h | | |
| Total dermal exposure to spray | 18,75 ml/day | | |
| Concentration of a.s. in spray solution | 0,001774 mg/ml | | |
| Dermal exposure to a.s. | 0,0332625 mg/day | | |

INHALATION EXPOSURE DURING SPRAYING

| | |
|--------------------------------|-------------------|
| Inhalation exposure to spray | 0,02 ml/h |
| Duration of exposure | 6 h |
| Concentration of a.s. in spray | 0,001774 mg/ml |
| Inhalation exposure to a.s. | 0,00021288 mg/day |
| Percent absorbed | 100 % |
| Absorbed dose | 0,00021288 mg/day |

ABSORBED DOSE

| | Mix/load | Application |
|------------------------------|--------------------|--------------------|
| Dermal exposure to a.s. | 0,001216254 mg/day | 0,0332625 mg/day |
| Percent absorbed | 10,7 % | 10,7 % |
| Absorbed dose (dermal route) | 0,000130139 mg/day | 0,003559088 mg/day |
| Inhalation exposure to a.s. | 2,22814E-06 mg/day | 0,00021288 mg/day |
| Absorbed dose | 0,000132367 mg/day | 0,003771968 mg/day |

PREDICTED EXPOSURE

| | |
|----------------------|--------------------------|
| Total absorbed dose | 0,003904335 mg/day |
| Operator body weight | 70 kg |
| Operator exposure | 5,57762E-05 mg/kg bw/day |

Appendix B.6.4.1-18: Hand held application outdoors to low crops, EFSA AOEM (manual hand-held): daminozide – with PPE
Exposure assessment

| | | | | | |
|-----------------------|------------------------------------------------------------|---------------------------------------------------|-----------------------------------|-------------------------------|-----------------------------------------------------------------------|
| Substance | Daminozide | Formulation = Wettable granules, soluble granules | Application rate-4,25 kg a.s. /ha | Spray dilution = 8,5 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Hand held | | | Buffer = 5 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 0,4 | Dermal for in use dilution = 2 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00875 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |

| Operator Model | | Mixing, loading and application AOEM | | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|---------------------------|-------------------|--|
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,0587 | % of RVNAS | 671,13% | |
| | Acute systemic exposure mg/kg bw/day | 0,1149 | % of RVAAS | | |
| Mixing and Loading | Gloves = Yes | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Soluble bags = No | |
| Application | Gloves = Yes | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Closed cabin = No | |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0022 | % of RVNAS | 24,78% | |
| | Acute systemic exposure mg/kg bw/day | 0,0042 | % of RVAAS | | |

Appendix B.6.4.1-19: Hand held application outdoors to low crops, EFSA AOEM (manual hand-held): UDMH – with PPE
Exposure assessment

| | | | | | |
|-----------------------|--------------------------------------------------------------|---------------------------------------------------|----------------------------------------|------------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,000887 kg a.s. /ha | Spray dilution = 0,001774 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Downward spraying / Manual-Hand held | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 10,7 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm2 per kg a.s./ha | | DT50 | 30 days | |

| | | | | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|---------------------------|-------------------|--|
| Operator Model | | Mixing, loading and application AOEM | | | |
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,1619 | % of RVNAS | 179864,20% | |
| | Acute systemic exposure mg/kg bw/day | 0,2619 | % of RVAAS | | |
| Mixing and Loading | Gloves = Yes | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Soluble bags = No | |
| Application | Gloves = Yes | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Closed cabin = No | |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0160 | % of RVNAS | 17732,23% | |
| | Acute systemic exposure mg/kg bw/day | 0,1123 | % of RVAAS | | |

Appendix B.6.4.1-20: Hand held application outdoors to low crops, EFSA AOEM (manual knapsack): daminozide – with PPE
Exposure assessment

| | | | | | |
|-----------------------|-----------------------------------------------------------|---------------------------------------------------|-----------------------------------|-------------------------------|-----------------------------------------------------------------------|
| Substance | Daminozide | Formulation = Wettable granules, soluble granules | Application rate-4,25 kg a.s. /ha | Spray dilution = 8,5 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Knapsack | | | Buffer = 5 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 0,4 | Dermal for in use dilution = 2 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00875 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |

| Operator Model | | Mixing, loading and application AOEM | | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|---------------------------|-------------------|--|
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,0364 | % of RVNAS | 416,19% | |
| | Acute systemic exposure mg/kg bw/day | 0,0835 | % of RVAAS | | |
| Mixing and Loading | Gloves = Yes | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Soluble bags = No | |
| Application | Gloves = Yes | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Closed cabin = No | |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0010 | % of RVNAS | 11,62% | |
| | Acute systemic exposure mg/kg bw/day | 0,0021 | % of RVAAS | | |

Appendix B.6.4.1-21: Hand held application outdoors to low crops, EFSA AOEM (manual knapsack): UDMH – with PPE

Exposure assessment

| | | | | | |
|-----------------------|-------------------------------------------------------------|---------------------------------------------------|----------------------------------------|------------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,000887 kg a.s. /ha | Spray dilution = 0,001774 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Downward spraying / Manual-Knapsack | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 10,7 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |

| Operator Model | | Mixing, loading and application AOEM | | | |
|----------------------------------------|--------------------------------------------|----------------------------------------------------|---------------------------|-------------------|--|
| Potential exposure | Longer term systemic exposure mg/kg bw/day | 0,1805 | % of RVNAS | 200533,13% | |
| | Acute systemic exposure mg/kg bw/day | 0,3033 | % of RVAAS | | |
| Mixing and Loading | Gloves = Yes | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Soluble bags = No | |
| Application | Gloves = Yes | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Closed cabin = No | |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | 0,0161 | % of RVNAS | 17857,63% | |
| | Acute systemic exposure mg/kg bw/day | 0,1124 | % of RVAAS | | |

Appendix B.6.4.1-22: Gantry indoor application, UK POEM M/L: daminozide – with PPE

| THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM) WITH GERMAN MODEL MIX/LOAD DATA (75th PERCENTILE) | | | |
|----------------------------------------------------------------------------------------------------|---------------------------------------------------------|------------------------------|------------|
| Application method | Tractor-mounted/trailed boom sprayer: hydraulic nozzles | | |
| Product | Alar | Active substance | daminozide |
| Formulation type | WG or SG | a.s. concentration | 850 mg/g |
| Dermal absorption from product | 0,2 % | Dermal absorption from spray | 0 % |
| PPE during mix/loading | Gloves | PPE during application | None |
| Dose | 9 kg product/ha | Work rate/day | 1 ha |
| Application volume | 500 l/ha | Duration of spraying | 6 h |
| AOEL _{sys.} | 0,00875 mg/kg bw/day | Total exposure (result): | 45 % AOEL |
| DERMAL EXPOSURE DURING MIXING AND LOADING | | | |
| Hand contamination/kg a.s. | 5,72 mg/kg a.s. | | |
| Hand contamination/day | 43,758 mg/day | | |
| Protective clothing | Gloves | | |
| Transmission to skin | 1 % | | |
| Dermal exposure to a.s. | 0,43758 mg/day | | |
| INHALATION EXPOSURE DURING MIXING AND LOADING | | | |
| Inhalation exposure/kg a.s. | 0,0358 mg/kg a.s. | | |
| Inhalation exposure/day | 0,27387 mg/day | | |
| RPE | None | | |
| Transmission through RPE | 100 % | | |
| Inhalation exposure to a.s. | 0,27387 mg/day | | |
| DERMAL EXPOSURE DURING SPRAY APPLICATION | | | |
| Application technique | Tractor-mounted/trailed boom sprayer: hydraulic nozzles | | |
| Application volume | 500 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 | | |
| Concentration of a.s. in spray solution | 15,3 mg/ml | | |
| Dermal exposure to a.s. | 635,715 mg/day | | |
| INHALATION EXPOSURE DURING SPRAYING | | | |
| Inhalation exposure to spray | 0,01 ml/h | | |
| Duration of exposure | 6 h | | |
| Concentration of a.s. in spray | 15,3 mg/ml | | |
| Inhalation exposure to a.s. | 0,918 mg/day | | |
| Percent absorbed | 100 % | | |
| Absorbed dose | 0,918 mg/day | | |
| ABSORBED DOSE | | | |
| | Mix/load | Application | |
| Dermal exposure to a.s. | 0,43758 mg/day | | mg/day |
| Percent absorbed | 0,2 % | | % |
| Absorbed dose (dermal route) | 0,00087516 mg/day | | mg/day |
| Inhalation exposure to a.s. | 0,27387 mg/day | | mg/day |
| Absorbed dose | 0,27474516 mg/day | | mg/day |
| PREDICTED EXPOSURE | | | |
| Total absorbed dose | 0,27474516 mg/day | | |
| Operator body weight | 70 kg | | |
| Operator exposure | 0,003924931 mg/kg bw/day | | |

Appendix B.6.4.1-23: Gantry indoor application, UK POEM M/L: UDMH – with PPE

THE UK PREDICTIVE OPERATOR EXPOSURE MODEL (POEM) WITH GERMAN MODEL MIX/LOAD DATA (75th PERCENTILE)

| | | | |
|--------------------------------|---------------------------------------------------------|------------------------------|-------------|
| Application method | Tractor-mounted/trailed boom sprayer: hydraulic nozzles | | |
| Product | Alar | Active substance | UDMH |
| Formulation type | WG or SG | a.s. concentration | 0,026 mg/g |
| Dermal absorption from product | 10,7 % | Dermal absorption from spray | 0 % |
| PPE during mix/loading | Gloves | PPE during application | None |
| Dose | 9 kg product/ha | Work rate/day | 1 ha |
| Application volume | 500 l/ha | Duration of spraying | 6 h |
| AOEL _{syst.} | 0,00009 mg/kg bw/day | Total exposure (result): | 0,16 % AOEL |

DERMAL EXPOSURE DURING MIXING AND LOADING

| | |
|----------------------------|--------------------|
| Hand contamination/kg a.s. | 5,72 mg/kg a.s. |
| Hand contamination/day | 0,00133848 mg/day |
| Protective clothing | Gloves |
| Transmission to skin | 1 % |
| Dermal exposure to a.s. | 1,33848E-05 mg/day |

INHALATION EXPOSURE DURING MIXING AND LOADING

| | |
|-----------------------------|-------------------|
| Inhalation exposure/kg a.s. | 0,0358 mg/kg a.s. |
| Inhalation exposure/day | 8,3772E-06 mg/day |
| RPE | None |
| Transmission through RPE | 100 % |
| Inhalation exposure to a.s. | 8,3772E-06 mg/day |

DERMAL EXPOSURE DURING SPRAY APPLICATION

| | | | |
|-----------------------------------------|---------------------------------------------------------|-----------|------------|
| Application technique | Tractor-mounted/trailed boom sprayer: hydraulic nozzles | | |
| Application volume | 500 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 | ml/day | | |
| Concentration of a.s. in spray solution | mg/ml | | |
| Dermal exposure to a.s. | mg/day | | |

INHALATION EXPOSURE DURING SPRAYING

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

ABSORBED DOSE

| | | |
|------------------------------|--------------------|-------------|
| | Mix/load | Application |
| Dermal exposure to a.s. | 1,33848E-05 mg/day | mg/day |
| Percent absorbed | 10,7 % | % |
| Absorbed dose (dermal route) | 1,43217E-06 mg/day | mg/day |
| Inhalation exposure to a.s. | 8,3772E-06 mg/day | mg/day |
| Absorbed dose | 9,80937E-06 mg/day | mg/day |

PREDICTED EXPOSURE

| | |
|----------------------|--------------------------|
| Total absorbed dose | 9,80937E-06 mg/day |
| Operator body weight | 70 kg |
| Operator exposure | 1,40134E-07 mg/kg bw/day |

Appendix B.6.4.1-24: Gantry indoor application, EFSA AOEM model M/L: daminozide – with PPE

| | | |
|--------------------------------------|-------------------------------------|------------------------|
| Application rate of active substance | 7,65 kg a.s./ha | <i>i_AppRate</i> |
| Assumed area treated | 1 ha/day | <i>d_AreaTreated</i> |
| Amount of active substance applied | 7,65 kg a.s./day | <i>i_AmountAS</i> |
| Dermal absorption of the product | 0,20 % | <i>i_AbsorpProduct</i> |
| Dermal absorption of in-use dilution | 0,00 % | <i>i_AbsorInuse</i> |
| Formulation type | Wettable granules, soluble granules | |
| Indoor or Outdoor application | Outdoor | |
| Application method | Downward spraying | |
| Application equipment | Manual-Knapsack | |
| Season | not relevant | |

| Mixing and loading | Exposure values | µg exposure/day mixed and loaded | | Reference | Comment |
|--------------------|---------------------------------------------------------------------|-----------------------------------------|--------------------------|---------------------|------------------------------|
| | | 75 th centile | 95 th centile | | |
| | Hands | 48425 | 129958 | AOEM | |
| | Body | 4095 | 14214 | AOEM | |
| | Head | 26 | 56 | AOEM | |
| | Protected hands (gloves) | 92 | 836 | AOEM | |
| | Protected body (workwear or protective garment and sturdy footwear) | 128 | 525 | AOEM | |
| | Protected head (hood and face shield) | 26 | 56 | AOEM | |
| | Inhalation | 128 | 133 | AOEM | |
| | Protective Equipment | Select for inclusion | | Penetration factor | Inhalation Protection factor |
| | Gloves | Yes | | Incl. in AOEM model | |
| | Clothing | Work wear - arms, body and legs covered | | Incl. in AOEM model | |
| | Head and respiratory PPE | FP2, P2 and similar | | 0,8 | 0,1 |
| | Water soluble bag | No | | 1 | |

| Application | Exposure values | µg exposure/day applied | | Reference | Comment |
|-------------|---------------------------------------------------------------------|-----------------------------------------|--------------------------|--------------------------------------|------------------------------|
| | | 75 th centile | 95 th centile | | |
| | Hands | 7874 | 21486 | AOEM | |
| | Body | 453227 | 698736 | AOEM | |
| | Head | 61 | 134 | AOEM | |
| | Protected hands (gloves) | 26 | 111 | AOEM | |
| | Protected body (workwear or protective garment and sturdy footwear) | 45405 | 319413 | AOEM | |
| | Inhalation | 133 | 133 | AOEM | |
| | Protective Equipment | Select for inclusion | | Penetration factor | Inhalation Protection factor |
| | Gloves | No | | | |
| | Clothing | Work wear - arms, body and legs covered | | Incl. in AOEM model | |
| | Head and respiratory PPE | None | | 1 | 1 |
| | Closed cab | No | | vehicle mounted upward spraying only | |

| | | | |
|------------------------------------------------------------------------------------------------|-----------------|----------------|--|
| 1. Total | | | |
| | Without RPE/PPE | With RPE/PPE | |
| Longer term | | | |
| Total systemic exposure from mixing, loading and application (mg a.s./day) | 0,3651906 | 0,1458294 | |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0,0060865 | 0,0024305 | |
| % of RVNAS | 69,56 % | 27,78 % | |
| Acute | | | |
| Total systemic exposure from mixing, loading and application (mg a.s./day) | 0,5536560 | 0,1486732 | |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0,0092276 | 0,0024779 | |
| % of RVAAS | #DĚLENÍ NULOU! | #DĚLENÍ NULOU! | |

| | | | | | |
|----------------------------------------------------------------------------|---------------------------------------------------------------------|-----------------------------------------|--------------------------|--------------------------------------|---------------------------------------------------------|
| Application rate of active substance | 7,65 kg a.s./ha | i_AppRate | | | |
| Assumed area treated | 10 ha/day | d_AreaTreated | | | |
| Amount of active substance applied | 76,5 kg a.s./day | i_AmountAS | | | |
| Dermal absorption of the product | 0,20 % | i_AbsorpProduct | | | |
| Dermal absorption of in-use dilution | 0,00 % | i_AbsorInuse | | | |
| Formulation type | Wettable granules, soluble granules | | | | |
| Indoor or Outdoor application | Outdoor | | | | |
| Application method | Downward spraying | | | | |
| Application equipment | Vehicle-mounted | | | | |
| Season | not relevant | | | | |
| OutdoorWettable granules, soluble granulesDownward sprayingVehicle-mounted | | | | | |
| Mixing and loading | Exposure values | µg exposure/day mixed and loaded | | Reference | Comment |
| | | 75 th centile | 95 th centile | | |
| | Hands | 36956 | 183121 | AOEM | |
| | Body | 26048 | 56660 | AOEM | |
| | Head | 497 | 6849 | AOEM | |
| | Protected hands (gloves) | 278 | 2407 | AOEM | |
| | Protected body (workwear or protective garment and sturdy footwear) | 869 | 4760 | AOEM | |
| | Protected head (hood and face shield) | 8 | 388 | AOEM | |
| | Inhalation | 136 | 288 | AOEM | |
| | Protective Equipment | Select for inclusion | | Penetration factor | Inhalation Protection factor |
| | Gloves | Yes | | Incl. in AOEM model | 0,25 |
| | Clothing | Work wear - arms, body and legs covered | | Incl. in AOEM model | |
| | Head and respiratory PPE | FP1, P1 and similar | | 0,8 | |
| | Water soluble bag | No | | 1 | |
| Application | Exposure values | µg exposure/day applied | | Reference | Comment |
| | | 75 th centile | 95 th centile | | |
| | Hands | 123955 | 89835 | AOEM | This scenario assumes that small area equipment is used |
| | Body | 170070 | 215502 | AOEM | |
| | Head | 1018 | 11953 | AOEM | |
| | Protected hands (gloves) | 229 | 35 | AOEM | |
| | Protected body (workwear or protective garment and sturdy footwear) | 2127 | 2513 | AOEM | |
| | Inhalation | 47 | 490 | AOEM | |
| | Protective Equipment | Select for inclusion | | Penetration factor | Inhalation Protection factor |
| | Gloves | No | | | |
| | Clothing | Work wear - arms, body and legs covered | | Incl. in AOEM model | |
| | Head and respiratory PPE | None | | 1 | 1 |
| | Closed cab | No | | vehicle mounted upward spraying only | |
| | | | | | |

1. Total

| | Without RPE/PPE | With RPE/PPE | |
|------------------------------------------------------------------------------------------------|-----------------|----------------|--|
| Longer term | | | |
| Total systemic exposure from mixing, loading and application (mg a.s./day) | 0,3094561 | 0,0837262 | |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0,0051576 | 0,0013954 | |
| % of RVNAS | 58,94 % | 15,95 % | |
| Acute | | | |
| Total systemic exposure from mixing, loading and application (mg a.s./day) | 1,2710533 | 0,5872544 | |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0,0211842 | 0,0097876 | |
| % of RVAAS | #DĚLENÍ_NULOU! | #DĚLENÍ_NULOU! | |

Appendix B.6.4.1-25: Gantry indoor application, EFSA AOEM model M/L: UDMH – with PPE
Exposure assessment

| | | | | | |
|-----------------------|-----------------------------------------------------------|---------------------------------------------------|---------------------------------------|-----------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,00023 kg a.s. /ha | Spray dilution = 0,00046 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Knapsack | | | Buffer = 5 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 0 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |

| | | | | | |
|------------------------------------------------------------|--------------------------------------------|--|----------------------------------------------------|---------------------------|-------------------|
| Operator Model Mixing, loading and application AOEM | | | | | |
| Potential exposure | Longer term systemic exposure mg/kg bw/day | | 0,0188 | % of RVNAS | 20879,58% |
| | Acute systemic exposure mg/kg bw/day | | 0,0509 | % of RVAAS | |
| Mixing and Loading | Gloves = Yes | | Clothing = Work wear - arms, body and legs covered | RPE = FP2, P2 and similar | Soluble bags = No |
| Application | Gloves = No | | Clothing = Work wear - arms, body and legs covered | RPE = None | Closed cabin = No |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | | 0,0001 | % of RVNAS | 140,84% |
| | Acute systemic exposure mg/kg bw/day | | 0,0006 | % of RVAAS | |

| | | | | | |
|-----------------------|-------------------------------------------------------------|---------------------------------------------------|---------------------------------------|-----------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,00023 kg a.s. /ha | Spray dilution = 0,00046 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Downward spraying / Vehicle-mounted | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 0 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |

| | | | | | |
|------------------------------------------------------------|--------------------------------------------|--|----------------------------------------------------|---------------------------|-------------------|
| Operator Model Mixing, loading and application AOEM | | | | | |
| Potential exposure | Longer term systemic exposure mg/kg bw/day | | 0,0002 | % of RVNAS | 176,53% |
| | Acute systemic exposure mg/kg bw/day | | 0,0088 | % of RVAAS | |
| Mixing and Loading | Gloves = Yes | | Clothing = Work wear - arms, body and legs covered | RPE = FP1, P1 and similar | Soluble bags = No |
| Application | Gloves = No | | Clothing = Work wear - arms, body and legs covered | RPE = None | Closed cabin = No |
| Exposure (including PPE options above) | Longer term systemic exposure mg/kg bw/day | | 0,0000 | % of RVNAS | 33,87% |
| | Acute systemic exposure mg/kg bw/day | | 0,0010 | % of RVAAS | |

Estimation of resident exposure after application in High crops, hand held (HCHH)

Input parameters considered for the estimation of resident exposure:

| | | | |
|------------------------------|----------------------------|-------------------------------------------------|------------------------------------|
| Intended use(s): | | Drift (D): | 0,24 % (HCHH, 10 m) |
| Application rate (AR): | 4,25 kg a.s./ha | Transfer coefficient (TC): | 7300 cm ² /h (adults) |
| | | | 2600 cm ² /h (children) |
| Number of applications (NA): | 2 | Turf Transferable Residues (TTR): | 5 % |
| Body weight (BW): | 60 kg/person (adults) | Exposure Duration | 2 h |
| | 16,15 kg/person (children) | Airborne Concentration of | 0,001 mg/m ³ |
| Dermal absorption (DA): | 1,90 % ("worst case") | Inhalation Rate (IR): | 16,57 m ³ /d (adults), |
| Inhalation absorption (IA): | 100 % | | 8,31 m ³ /d (children) |
| Oral absorption (OA) | 35 % | Saliva Extraction Factor (SE): | 50 % |
| AOEL | 0,00875 mg/kg bw/d | Surface Area of Hands (SA): | 20 cm ² |
| | | Frequency of Hand to Mouth (Freq): | 20 events/h |
| | | Dislodgeable foliar residues (DFR): | 20 % |
| | | Ingestion Rate for Mouthing of Grass/Dav (IgR): | 25 cm ² /d |

Resident exposure towards daminoride

| Adults | | | Children | | |
|---------------------------------------------------------------------------------------------|-----------|------------|--------------------------------------------------------------------------------------------------------|-----------|------------|
| Residents: Dermal exposure after application in (via deposits caused by spray drift) | | | | | |
| $SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$ | | | $SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$ | | |
| $(0,0425 \times 2 \times 0,24\% \times 5\% \times 7300 \times 2 \times 1,9\%) / 60$ | | | $(0,0425 \times 2 \times 0,24\% \times 5\% \times 2600 \times 2 \times 1,9\%) / 16,15$ | | |
| External exposure | 0,14892 | mg/person | External exposure | 0,05304 | mg/person |
| External exposure | 0,002482 | mg/kg bw/d | External exposure | 0,0032842 | mg/kg bw/d |
| Absorbed dose: | 0,0000472 | mg/kg bw/d | Absorbed dose: | 0,0000624 | mg/kg bw/d |
| Residents: Inhalation exposure to vapour | | | | | |
| $SIE_R = (AC_V \times IR \times IA) / BW$ | | | $SIE_R = (AC_V \times IR \times IA) / BW$ | | |
| $(0,001 \times 16.57 \times 100\%) / 60$ | | | $(0,001 \times 8.31 \times 100\%) / 16.15$ | | |
| External exposure | 0,01657 | mg/person | External exposure | 0,00831 | mg/person |
| External exposure | 0,0002762 | mg/kg bw/d | External exposure | 0,0005146 | mg/kg bw/d |
| Absorbed dose: | 0,0002762 | mg/kg bw/d | Absorbed dose: | 0,0005146 | mg/kg bw/d |
| | | | Residents: Oral exposure (hand-to-mouth transfer) | | |
| | | | $SOE_H = (AR \times NA \times D \times TTR \times SE \times SA \times Freq \times H \times OA) / BW$ | | |
| | | | $(0,0425 \times 2 \times 0,24\% \times 5\% \times 50\% \times 20 \times 20 \times 2 \times 35\%) / 60$ | | |
| | | | External exposure | 0,00408 | mg/person |
| | | | External exposure | 0,0002526 | mg/kg bw/d |
| | | | Absorbed dose | 0,0000884 | mg/kg bw/d |
| | | | Residents: Oral exposure (object-to-mouth transfer) | | |
| | | | $SOE_O = (AR \times NA \times D \times DFR \times IgR \times OA) / BW$ | | |
| | | | $(0,0425 \times 2 \times 0,24\% \times 20\% \times 25 \times 35\%) / 16,15$ | | |
| | | | External exposure | 0,00102 | mg/person |
| | | | External exposure | 6,316E-05 | mg/kg bw/d |
| | | | Absorbed dose | 0,0000221 | mg/kg bw/d |
| Total systemic exposure: $SE_R = SDE_R + SIE_R$ | | | Total systemic exposure: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$ | | |
| Total systemic exposure (absorbed dose) | 0,0193995 | mg/person | Total systemic exposure (absorbed dose) | 0,0111028 | mg/person |
| Total systemic exposure (absorbed) | 0,0003233 | mg/kg bw/d | Total systemic exposure (absorbed) | 0,0006875 | mg/kg bw/d |
| % of AOEL: | 3.70 | % | % of AOEL: | 7.86 | % |

Appendix B.6.4.2-2: Bystander estimation, German model: UDMH

Estimation of bystander exposure during/after application in High crops, hand held (HCHH)

Input parameters considered for the estimation of bystander exposure:

| | | | | |
|-----------------------------|----------------------------|--------------------------------------------------|---------|----------------------------------------------|
| Intended use(s): | | Drift (D): | 0,29 | % (HCHH, 10 m) |
| Application rate (AR): | 0,000887 kg a.s./ha | Exposed Body Surface Area (BSA): | 1 | m ² (adults) |
| | | | 0,21 | m ² (children) |
| Body weight (BW): | 60 kg/person (adults) | Specific Inhalation Exposure (I* _A): | 0,3 | mg/kg a.s. (6 hours, adults) |
| | 16,15 kg/person (children) | | 0,17241 | mg/kg a.s. (6 hours, children) |
| Dermal absorption (DA): | 10,70 % ('worst case') | Area Treated (A): | 20 | ha/d (based on High crops, hand held (HCHH)) |
| Inhalation absorption (IA): | 100 % | Exposure duration (T): | 5 | min |
| AOEL: | 0,00009 mg/kg bw/d | | | |

| Bystander exposure towards UDMH | | | | | |
|----------------------------------------------------------------------|------------|------------|-------------------------------------------------------------------------|------------|------------|
| Adults | | | Children | | |
| Bystander: Dermal exposure after application in (via spray drift) | | | | | |
| $SDE_B = (AR \times D \times BSA \times DA) / BW$ | | | $SDE_B = (AR \times D \times BSA \times DA) / BW$ | | |
| $(0,0887 \times 0,29\% \times 1 \times 10,7\%) / 60$ | | | $(0,0887 \times 0,29\% \times 0,21 \times 10,7\%) / 16,15$ | | |
| External exposure | 0,00025723 | mg/person | External exposure | 5,4018E-05 | mg/person |
| External exposure | 4,2872E-06 | mg/kg bw/d | External exposure | 3,3448E-06 | mg/kg bw/d |
| Absorbed dose: | 0,0000005 | mg/kg bw/d | Absorbed dose: | 0,0000004 | mg/kg bw/d |
| Bystander: Inhalation exposure after application in | | | | | |
| $SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$ | | | $SIE_B = (I^*_A \times AR \times A \times T \times IA) / BW$ | | |
| $(0,300 / 360 \times 0,000887 \times 20 \times 5 \times 100\%) / 60$ | | | $(0,172 / 360 \times 0,000887 \times 20 \times 5 \times 100\%) / 16,15$ | | |
| External exposure | 7,3917E-05 | mg/person | External exposure | 4,2481E-05 | mg/person |
| External exposure | 1,2319E-06 | mg/kg bw/d | External exposure | 2,6304E-06 | mg/kg bw/d |
| Absorbed dose: | 0,0000012 | mg/kg bw/d | Absorbed dose: | 0,0000026 | mg/kg bw/d |
| Total systemic exposure: $SE_B = SDE_B + SIE_B$ | | | Total systemic exposure: $SE_B = SDE_B + SIE_B$ | | |
| Total systemic exposure (absorbed dose) | 0,00010144 | mg/person | Total systemic exposure (absorbed dose) | 4,8261E-05 | mg/person |
| Total systemic exposure (absorbed dose) | 0,0000017 | mg/kg bw/d | Total systemic exposure (absorbed dose) | 0,0000030 | mg/kg bw/d |
| % of AOEL: | 1.88 | % | % of AOEL: | 3.32 | % |

Appendix B.6.4.2-3: Resident estimation, German model: daminozide

Appendix B.6.4.2-4: Resident estimation, German model: UDMH
Estimation of resident exposure after application in High crops, hand held (HCHH)

Input parameters considered for the estimation of resident exposure:

| | | | | |
|------------------------------|----------------------------|-------------------------------------------------|----------|-------------------------------|
| Intended use(s): | | Drift (D): | 0,24 | % (HCHH, 10 m) |
| Application rate (AR): | 0,000887 kg a.s./ha | Transfer coefficient (TC): | 7300 | cm ² /h (adults) |
| | | | 2600 | cm ² /h (children) |
| Number of applications (NA): | 2 | Turf Transferable Residues (TTR): | 5 | % |
| Body weight (BW): | 60 kg/person (adults) | Exposure Duration (H): | 2 | h |
| | 16,15 kg/person (children) | Airborne Concentration of Vapour (ACV): | 0,000085 | mg/m ³ |
| Dermal absorption (DA): | 10,70 % ('worst case') | Inhalation Rate (IR): | 16,57 | m ³ /d (adults), |
| Inhalation absorption (IA): | 100 % | | 8,31 | m ³ /d (children) |
| Oral absorption (OA) | 100 % | Saliva Extraction Factor (SE): | 50 | % |
| AOEL | 0,00009 mg/kg bw/d | Surface Area of Hands (SA): | 20 | cm ² |
| | | Frequency of Hand to Mouth (Freq): | 20 | events/h |
| | | Dislodgeable foliar residues (DFR): | 20 | % |
| | | Ingestion Rate for Mouthing of Grass/Day (IgR): | 25 | cm ² /d |

Resident exposure towards UDMH

| Adults | | | Children | | |
|-----------------------------------------------------------------------------------------|------------|------------|---------------------------------------------------------------------------------------------------|------------|------------|
| Residents: Dermal exposure after application in (via deposits caused by spray drift) | | | | | |
| $SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$ | | | $SDE_R = (AR \times NA \times D \times TTR \times TC \times H \times DA) / BW$ | | |
| $(0,0000887 \times 2 \times 0,24\% \times 5\% \times 7300 \times 2 \times 10,7\%) / 60$ | | | $(0,0000887 \times 2 \times 0,24\% \times 5\% \times 2600 \times 2 \times 10,7\%) / 16,15$ | | |
| External exposure | 3,108E-05 | mg/person | External exposure | 1,107E-05 | mg/person |
| External exposure | 5,1801E-07 | mg/kg bw/d | External exposure | 6,8543E-07 | mg/kg bw/d |
| Absorbed dose: | 0,0000001 | mg/kg bw/d | Absorbed dose: | 0,0000001 | mg/kg bw/d |
| Residents: Inhalation exposure to vapour | | | | | |
| $SIE_R = (AC_V \times IR \times IA) / BW$ | | | $SIE_R = (AC_V \times IR \times IA) / BW$ | | |
| $(0,000085 \times 16,57 \times 100\%) / 60$ | | | $(0,000085 \times 8,31 \times 100\%) / 16,15$ | | |
| External exposure | 0,00140845 | mg/person | External exposure | 0,00070635 | mg/person |
| External exposure | 2,3474E-05 | mg/kg bw/d | External exposure | 4,3737E-05 | mg/kg bw/d |
| Absorbed dose: | 0,0000235 | mg/kg bw/d | Absorbed dose: | 0,0000437 | mg/kg bw/d |
| | | | Residents: Oral exposure (hand-to-mouth transfer) | | |
| | | | $SOE_H = (AR \times NA \times D \times TTR \times SE \times SA \times Freq \times H \times OA) /$ | | |
| | | | $(0,0000887 \times 2 \times 0,24\% \times 5\% \times 50\% \times 20 \times 2 \times 100\%) /$ | | |
| | | | External exposure | 8,5152E-07 | mg/person |
| | | | External exposure | 5,2726E-08 | mg/kg bw/d |
| | | | Absorbed dose | 0,0000001 | mg/kg bw/d |
| | | | Residents: Oral exposure (object-to-mouth transfer) | | |
| | | | $SOE_O = (AR \times NA \times D \times DFR \times IgR \times OA) / BW$ | | |
| | | | $(0,0000887 \times 2 \times 0,24\% \times 20\% \times 25 \times 100\%) / 16,15$ | | |
| | | | External exposure | 2,1288E-07 | mg/person |
| External exposure | 1,3181E-08 | mg/kg bw/d | | | |
| Absorbed dose | 0,0000000 | mg/kg bw/d | | | |
| Total systemic exposure: $SE_R = SDE_R + SIE_R$ | | | Total systemic exposure: $SE_R = SDE_R + SIE_R + SOE_H + SOE_O$ | | |
| Total systemic exposure (absorbed dose) | 0,00141178 | mg/person | Total systemic exposure (absorbed dose) | 0,0007086 | mg/person |
| Total systemic exposure (absorbed dose) | 0,0000235 | mg/kg bw/d | Total systemic exposure (absorbed dose) | 0,0000439 | mg/kg bw/d |
| % of AOEL: | 26,14 | % | % of AOEL: | 48,75 | % |

Appendix B.6.4.2-5: Resident estimation, EFSA AOEM model: daminozide

| | | | | | |
|-----------------------|-----------------------------------------------------------|---------------------------------------------------|-----------------------------------|-------------------------------|----------------------------------------------------------------------------------------------|
| Substance | Daminozide | Formulation = Wettable granules, soluble granules | Application rate-4,25 kg a.s. /ha | Spray dilution = 8,5 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of <5*10 ⁻³ Pa |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Knapsack | | | Buffer = 10 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 0,2 | Dermal for in use dilution = 1,9 | Oral = 35 | Inhalation = 100 | |
| RVNAS | 0,00875 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm ² per kg a.s./ha | | DT50 | 30 days | |
| Resident - child | Spray drift (75th percentile) mg/kg bw/day | | 0,0238 | % of RVNAS | 271,59 % |
| | Vapour (75th percentile) mg/kg bw/day | | 0,0011 | % of RVNAS | 12,23 % |
| | Surface deposits (75th percentile) mg/kg bw/day | | 0,0021 | % of RVNAS | 23,48 % |
| | Entry into treated crops (75th percentile) mg/kg bw/day | | 0,0506 | % of RVNAS | 578,31 % |
| | All pathways (mean) mg/kg bw/day | | 0,0588 | % of RVNAS | 672,32 % |
| Resident - adult | Spray drift (75th percentile) mg/kg bw/day | | 0,0127 | % of RVNAS | 145,42 % |
| | Vapour (75th percentile) mg/kg bw/day | | 0,0002 | % of RVNAS | 2,63 % |
| | Surface deposits (75th percentile) mg/kg bw/day | | 0,0005 | % of RVNAS | 5,42 % |
| | Entry into treated crops (75th percentile) mg/kg bw/day | | 0,0281 | % of RVNAS | 321,29 % |
| | All pathways (mean) mg/kg bw/day | | 0,0314 | % of RVNAS | 358,55 % |

Appendix B.6.4.2-6: Resident estimation, EFSA AOEM model: UDMH
Exposure assessment

| | | | | | |
|-------------------------|------------------------------------------------------------|---------------------------------------------------|----------------------------------------|------------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate- 0,000887 kg a.s. /ha | Spray dilution = 0,001774 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Hand held | | | Buffer = 10 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 10,7 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 0,00033 µg a.s./cm2 per kg a.s./ha | | DT50 | 3,25 days | |
| Resident - child | Spray drift (75th percentile) mg/kg bw/day | | 0,0000 | % of RVNAS | 29,53% |
| | Vapour (75th percentile) mg/kg bw/day | | 0,0011 | % of RVNAS | 1188,89% |
| | Surface deposits (75th percentile) mg/kg bw/day | | 0,0000 | % of RVNAS | 0,70% |
| | Entry into treated crops (75th percentile) mg/kg bw/day | | 0,0000 | % of RVNAS | 0,00% |
| | All pathways (mean) mg/kg bw/day | | 0,0011 | % of RVNAS | 1208,89% |
| Resident - adult | Spray drift (75th percentile) mg/kg bw/day | | 0,0000 | % of RVNAS | 16,30% |
| | Vapour (75th percentile) mg/kg bw/day | | 0,0002 | % of RVNAS | 255,56% |
| | Surface deposits (75th percentile) mg/kg bw/day | | 0,0000 | % of RVNAS | 0,22% |
| | Entry into treated crops (75th percentile) mg/kg bw/day | | 0,0000 | % of RVNAS | 0,00% |
| | All pathways (mean) mg/kg bw/day | | 0,0002 | % of RVNAS | 266,39% |

Appendix B.6.4.3-1: Worker estimation, German model: daminozide

| Estimation of post-application exposure of workers (re-entry exposure) | | | |
|------------------------------------------------------------------------|--------------------|-----------------------------------|----|
| Active substance (a.s.) | Daminozide | | |
| Product | Dazide | | |
| Intended use(s) | ornamentals_indoor | | |
| Application rate (AR) | 7,65 | kg a.s./ha | 1) |
| Number of applications (NA) | 2 | | |
| Dislodgeable foliar residues (DFR) | 3 | µg/cm ² /kg a.s. | 2) |
| Transfer coefficient (TC) | 5000 | cm ² /person/h | 3) |
| Work rate per day (WR) | 8 | h/d | 4) |
| Penetration through clothing (P) | 0,28 | (28 %) | 5) |
| Systemic AOEL | 0,00875 | mg/kg bw/d | |
| Dermal absorption DA) | 0,97 | % (worst case, e.g. for dilution) | |
| Body weight (BW) | 60 | kg | |

1) consideration of more than two applications will not be necessary if degradation on foliage of at least 50 % can be assumed between 2 applications (otherwise use multiple application factor)

2) default of 1 µg a.s./cm² per kg a.s./ha acc. to Krebs et al. (2000)

3) TC 30000 cm²/person/hour ("worst case", hand harvesting, both sides of leaves) acc. to Krebs et al. (2000), acc. EUROPEM II (2002): 2500 (vegetables), 3000 (strawberries), 4500 (fruits from trees), 5000 (ornamentals) acc. US EPA Policy # 3.1 (2000): 1500 (cereals, e.g. crop inspection), 10000 (grapes)

4) 8 h/day for professional applications if re-entry tasks are intended, 2 h/day for professional applications if re-entry tasks are not intended (e.g. irrigation, maintenance) or for applications in the home and allotment garden area

5) 5 % of dermal exposure corresponding to protective clothing incl. gloves for professionals, 50 % reduction of dermal exposure corresponding to long sleeved shirt, long trousers and gloves for applications in the home and allotment garden area

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

| | | | | | |
|------------------------------|--------------------|-------------------------------------|----------------------------|----------------|--------------|
| Intended use(s): | ornamentals_indoor | Dislodgeable foliar residues (DFR): | 3 | µg/cm²/kg a.s. | |
| Application rate (AR): | 7,65 | kg a.s./ha | Transfer coefficient (TC): | 5000 | cm²/person/h |
| Number of applications (NA): | 2 | | Work rate per day (WR): | 8 | h/d |
| Body weight (BW): | 60 | kg/person | PPE | 28 | % |
| Dermal absorption (DA): | 0,97 | % ("worst case") | | | |
| AOEL | 0.00875 | mg/kg bw/d | | | |

Worker exposure towards Daminozide

| Without PPE ¹⁾ | | | With PPE ²⁾ | | |
|-------------------------------------------------------------------------------------|----------|------------|-----------------------------------------------------------|----------|------------|
| Worker (re-entry): Systemic dermal exposure after application in ornamentals indoor | | | | | |
| SDE _W = (DFR x TC x WR x AR x NA x DA) / BW | | | SDE _W = (DFR x TC x WR x AR x NA x PPE x DA) / | | |
| (3 x 5000 x 8 x 7,65 x 2 x 0,97%) / 60 | | | (3 x 5000 x 8 x 7,65 x 2 x 28% x 0,97%) / 60 | | |
| External dermal exposure | 1836,00 | mg/person | External dermal exposure | 514,08 | mg/person |
| External dermal exposure | 30,60 | mg/kg bw/d | External dermal exposure | 8,57 | mg/kg bw/d |
| Total systemic exposure | 17,81 | mg/person | Total systemic exposure | 4,99 | mg/person |
| Total systemic exposure | 0,296820 | mg/kg bw/d | Total systemic exposure | 0,083110 | mg/kg bw/d |
| % of AOEL | 3392,2 | % | % of AOEL | 949,8 | % |
| Inhalation exposure | | | | | |
| Without RPE | | | With RPE | | |
| TSF: 0.1 cutting; <u>0.01 sorting and bundling</u> | | | RPE FP1 25% | | |
| PIE = (AR x MAF x TSF x WR) / BW | | | PIE = (AR x MAF x TSF x WR x PPE) / BW | | |
| 0,0204 | | | 0,0051 | | |
| | | | | | |
| Total systemic exposure | 0,31722 | mg/kg bw/d | 0,088210 | | |
| % of AOEL | 3625,4 | % | 1008,109714 % | | |

Appendix B.6.4.3-2: Worker estimation, German model: UDMH

| Estimation of post-application exposure of workers (re-entry exposure) | | | |
|------------------------------------------------------------------------|--------------------|-----------------------------------|----|
| Active substance (a.s.) | UDMH | | |
| Product | Alar | | |
| Intended use(s) | ornamentals_indoor | | |
| Application rate (AR) | 0,001595 | kg a.s./ha | 1) |
| Number of applications (NA) | 2 | | |
| Dislodgeable foliar residues (DFR) | 3 | µg/cm ² /kg a.s. | 2) |
| Transfer coefficient (TC) | 5000 | cm ² /person/h | 3) |
| Work rate per day (WR) | 8 | h/d | 4) |
| Penetration through clothing (P) | 0,28 | (28 %) | 5) |
| Systemic AOEL | 0,00009 | mg/kg bw/d | |
| Dermal absorption (DA) | 10,7 | % (worst case, e.g. for dilution) | |
| Body weight (BW) | 60 | kg | |

1) consideration of more than two applications will not be necessary if degradation on foliage of at least 50 % can be assumed between 2 applications (otherwise use multiple application factor)

2) default of 1 µg a.s./cm² per kg a.s./ha acc. to Krebs et al. (2000)

3) TC 30000 cm²/person/hour ("worst case", hand harvesting, both sides of leaves) acc. to Krebs et al. (2000), acc. EUROPEM II (2002): 2500 (vegetables), 3000 (strawberries), 4500 (fruits from trees), 5000 (ornamentals) acc. US EPA Policy # 3.1 (2000): 1500 (cereals, e.g. crop inspection), 10000 (grapes)

4) 8 h/day for professional applications if re-entry tasks are intended, 2 h/day for professional applications if re-entry tasks are not intended (e.g. irrigation, maintenance) or for applications in the home and allotment garden area

5) 5 % of dermal exposure corresponding to protective clothing incl. gloves for professionals, 50 % reduction of dermal exposure corresponding to long sleeved shirt, long trousers and gloves for applications in the home and allotment garden area

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

| | | | | | |
|------------------------------|--------------------|------------------|-------------------------------------|------|-----------------------------|
| Intended use(s): | ornamentals_indoor | | Dislodgeable foliar residues (DFR): | 3 | µg/cm ² /kg a.s. |
| Application rate (AR): | 0,0016 | kg a.s./ha | Transfer coefficient (TC): | 5000 | cm ² /person/h |
| Number of applications (NA): | 2 | | Work rate per day (WR): | 8 | h/d |
| Body weight (BW): | 60 | kg/person | PPE | 28 | % |
| Dermal absorption (DA): | 10,7 | % ("worst case") | | | |
| AOEL | 0.00009 | mg/kg bw/d | | | |

Worker exposure towards UDMH

| Without PPE ¹⁾ | | With PPE ²⁾ | |
|-------------------------------------------------------------------------------------|---------------------|-----------------------------------------------------------|---------------------|
| Worker (re-entry): Systemic dermal exposure after application in ornamentals indoor | | | |
| SDE _W = (DFR x TC x WR x AR x NA x DA) / BW | | SDE _W = (DFR x TC x WR x AR x NA x PPE x DA) / | |
| (3 x 5000 x 8 x 0,001595 x 2 x 10,7%) / 60 | | (3 x 5000 x 8 x 0,001595 x 2 x 28% x 10,7%) / 60 | |
| External dermal exposure | 0,38 mg/person | External dermal exposure | 0,11 mg/person |
| External dermal exposure | 0,01 mg/kg bw/d | External dermal exposure | 0,00 mg/kg bw/d |
| Total systemic exposure | 0,04 mg/person | Total systemic exposure | 0,01 mg/person |
| Total systemic exposure | 0,000683 mg/kg bw/d | Total systemic exposure | 0,000191 mg/kg bw/d |
| % of AOEL | 758,5 % | % of AOEL | 212,4 % |

Inhalation exposure

| Without RPE | | With RPE | |
|----------------------------------------------------|----------|----------------------------------------|------------|
| TSF: 0.1 cutting; <u>0.01 sorting and bundling</u> | | RPE FP1 25% | |
| PIE = (AR x MAF x TSF x WR) / BW | | PIE = (AR x MAF x TSF x WR x PPE) / BW | |
| 4,25333E-06 | | 1,06333E-06 | mg/kg bw/d |
| Total systemic exposure | 0,00069 | 0,000192 | mg/kg bw/d |
| % of AOEL | 763.24 % | 213.5645926 % | |

Appendix B.6.4.3-3: Worker estimation, EFSA AOEM model: daminozide

| | | | | | |
|-----------------------------------------------|------------------------------------------------------------|---------------------------------------------------|-----------------------------------|--------------------------------|-----------------------------------------------------------------------|
| Substance | Daminozide | Formulation = Wettable granules, soluble granules | Application rate-7,65 kg a.s. /ha | Spray dilution = 15,3 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Indoor / Spray application / Manual-Knapsack | | | Buffer = 5 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 0,97 | Dermal for in use dilution = 0 | Oral = 35 | Inhalation = 100 | |
| RVNAS | 0,00875 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm2 per kg a.s./ha | | DT50 | 30 days | |
| Worker - Cutting, sorting, bundling, carrying | Potential exposure mg/kg bw/day | | 1,6451 | % of RVNAS | 18801,67 % |
| | Working clothing mg/kg bw/day | | 0,6531 | % of RVNAS | 7464,27 % |
| | Working clothing and gloves mg/kg bw/day | | 0,2563 | % of RVNAS | 2929,31 % |

Appendix B.6.4.3-4: Worker estimation, EFSA AOEM model: UDMH**Exposure assessment**

| | | | | | |
|-----------------------------------------------|------------------------------------------------------------|---------------------------------------------------|---------------------------------------|-----------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH | Formulation = Wettable granules, soluble granules | Application rate-0,001595 kg a.s. /ha | Spray dilution = 0,00319 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Indoor / Spray application / Manual-Knapsack | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 10,7 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm2 per kg a.s./ha | | DT50 | 30 days | |
| Worker - Cutting, sorting, bundling, carrying | Potential exposure mg/kg bw/day | | 0,0036 | % of RVNAS | 3967,08% |
| | Working clothing mg/kg bw/day | | 0,0013 | % of RVNAS | 1432,00% |
| | Working clothing and gloves mg/kg bw/day | | 0,0004 | % of RVNAS | 417,97% |

Appendix B.6.4.3.1-5: Estimate of total dislodgeable foliar residue for daminozide assuming an application rate of 7.65 kg a.s./ha for a single application, five treatments, a 7 day interval between treatments and a half-life of 2.37 days for daminozide on treated foliage

$$N_t = N_o \times (0.5)^{\text{number of half-lives}}$$

N_t = amount remaining after specified number of half-lives

N_o = original amount

Number of half-lives = elapsed time ÷ half-life

| | |
|-------------------------------|------|
| Application rate (kg a.s./ha) | 7.65 |
| Interval between applications | 7 |
| Exclusion period | 0 |

Application 1

| Nt | No | Time | Half life | No of half-lives | |
|--------|----|-------|-----------|------------------|--------|
| | | 10.97 | 28 | 2.37 | 11.814 |
| 0.0030 | | | | | |

Application 2

| Application 2 | | Time | Half life | No of half-lives | |
|---------------|----|-------|-----------|------------------|-------|
| N_t | No | 10.97 | 21 | 2.37 | 8.861 |
| 0.0236 | | | | | |

Application 3

| Nt | No | Time | Half life | No of half-lives | |
|--------|----|-------|-----------|------------------|-------|
| | | 10.97 | 14 | 2.37 | 5.907 |
| 0.1828 | | | | | |

Application 4

| Application 4 | | | | |
|---------------|-------|------|-----------|------------------|
| N_t | No | Time | Half life | No of half-lives |
| | 10.97 | 7 | 2.37 | 2.954 |
| 1.4162 | | | | |

Application 5

| N_t | No | Time | Half life | No of half-lives |
|---------|-------|------|-----------|------------------|
| | 10.97 | 0 | 2.37 | 0 |
| 10.9711 | | | | |

Total N_t = 12.60

Appendix B.6.4.3.1-6: Estimate of dislodgeable foliar residue for UDMH assuming an application rate of 3.83×10^{-3} kg UDMH/ha for a single application, five applications, a 7 day interval between treatments and a half-life of 3.25 days for UDMH on treated foliage

$$N_t = N_o \times (0.5)^{\text{number of half-lives}}$$

N_t = amount remaining after specified number of half-lives

N_o = original amount

Number of half-lives = elapsed time ÷ half-life

| | |
|------------------------------------------|----------|
| Application rate daminozide (kg a.s./ha) | 7.65 |
| Application rate UDMH (kg/ha) | 3.83E-03 |
| Interval between applications | 7 |
| Exclusion period | 0 |

Application 1

| Nt | No | Time | Half life | No of half-lives | |
|-------|----|---------|-----------|------------------|-------|
| 6E-06 | | 2.5E-03 | 28 | 3.25 | 8.615 |

Application 2

| Nt | No | Time | Half life | No of half-lives | |
|-------|----|---------|-----------|------------------|-------|
| 3E-05 | | 2.5E-03 | 21 | 3.25 | 6.462 |

Application 3

| Nt | No | Time | Half life | No of half-lives | |
|-------|----|---------|-----------|------------------|-------|
| 1E-04 | | 2.5E-03 | 14 | 3.25 | 4.308 |

Application 4

| Nt | No | Time | Half life | No of half-lives | |
|-------|----|---------|-----------|------------------|-------|
| 6E-04 | | 2.5E-03 | 7 | 3.25 | 2.154 |

Application 5

| Nt | No | Time | Half life | No of half-lives | |
|-------|----|---------|-----------|------------------|-----|
| 2E-03 | | 2.5E-03 | 0 | 3.25 | 0.0 |

Total $N_t = 3.2 \times 10^{-3}$

Appendix B.6.4.3-7: Worker estimation, German model: daminozide, incorporating DFR data

| Estimation of post-application exposure of workers (re-entry exposure) | | | |
|------------------------------------------------------------------------|--------------------|-----------------------------------|----|
| Active substance (a.s.) | Daminozide | | |
| Product | Dazide | | |
| Intended use(s) | ornamentals_indoor | | |
| Application rate (AR) | 7,65 | kg a.s./ha | 1) |
| Number of applications (NA) | 1,15 | | |
| Dislodgeable foliar residues (DFR) | 1,434 | µg/cm ² /kg a.s. | 2) |
| Transfer coefficient (TC) | 5000 | cm ² /person/h | 3) |
| Work rate per day (WR) | 8 | h/d | 4) |
| Penetration through clothing (P) | 0,28 | (28 %) | 5) |
| Systemic AOEL | 0,00875 | mg/kg bw/d | |
| Dermal absorption DA) | 0,97 | % (worst case, e.g. for dilution) | |
| Body weight (BW) | 60 | kg | |

1) consideration of more than two applications will not be necessary if degradation on foliage of at least 50 % can be assumed between 2 applications (otherwise use multiple application factor)

2) default of 1 µg a.s./cm² per kg a.s./ha acc. to Krebs et al. (2000)

3) TC 30000 cm²/person/hour ("worst case", hand harvesting, both sides of leaves) acc. to Krebs et al. (2000), acc. EUROPEM II (2002): 2500 (vegetables), 3000 (strawberries), 4500 (fruits from trees), 5000 (ornamentals) acc. US EPA Policy # 3.1 (2000): 1500 (cereals, e.g. crop inspection), 10000 (grapes)

4) 8 h/day for professional applications if re-entry tasks are intended, 2 h/day for professional applications if re-entry tasks are not intended (e.g. irrigation, maintenance) or for applications in the home and allotment garden area

5) 5 % of dermal exposure corresponding to protective clothing incl. gloves for professionals, 50 % reduction of dermal exposure corresponding to long sleeved shirt, long trousers and gloves for applications in the home and allotment garden area

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

| | | | | | |
|------------------------------|--------------------|------------------|-------------------------------------|-------|----------------|
| Intended use(s): | ornamentals_indoor | | Dislodgeable foliar residues (DFR): | 1,434 | µg/cm²/kg a.s. |
| Application rate (AR): | 7,65 | kg a.s./ha | Transfer coefficient (TC): | 5000 | cm²/person/h |
| Number of applications (NA): | 1,15 | | Work rate per day (WR): | 8 | h/d |
| Body weight (BW): | 60 | kg/person | PPE | 28 | % |
| Dermal absorption (DA): | 0,97 | % ("worst case") | | | |
| AOEL | 0.00875 | mg/kg bw/d | | | |

Worker exposure towards Daminozide

| Without PPE ¹⁾ | | With PPE ²⁾ | |
|--------------------------------------------------------------------------------------------|---------------------|-----------------------------------------------------------|---------------------|
| Worker (re-entry): Systemic dermal exposure after application in ornamentals indoor | | | |
| SDE _W = (DFR x TC x WR x AR x NA x DA) / BW | | SDE _W = (DFR x TC x WR x AR x NA x PPE x DA) / | |
| (1,434 x 5000 x 8 x 7,65 x 1,15 x 0,97%) / 60 | | (1,434 x 5000 x 8 x 7,65 x 1,15 x 28% x 0,97%) / 60 | |
| External dermal exposure | 504,62 mg/person | External dermal exposure | 141,29 mg/person |
| External dermal exposure | 8,41 mg/kg bw/d | External dermal exposure | 2,35 mg/kg bw/d |
| Total systemic exposure | 4,89 mg/person | Total systemic exposure | 1,37 mg/person |
| Total systemic exposure | 0,081581 mg/kg bw/d | Total systemic exposure | 0,022843 mg/kg bw/d |
| % of AOEL | 932,4 % | % of AOEL | 261,1 % |
| Inhalation exposure | | | |
| Without RPE | | With RPE | |
| TSF: 0.1 cutting; <u>0.01 sorting and bundling</u> | | RPE FP1 25% | |
| PIE = (AR x MAF x TSF x WR) / BW | | PIE = (AR x MAF x TSF x WR x PPE) / BW | |
| 0,01173 | mg/kg bw/d | 0,0029325 | mg/kg bw/d |
| Total systemic exposure | 0,09331 mg/kg bw/d | 0,025775 | mg/kg bw/d |
| % of AOEL | 1066,4 % | 294,5734121 % | |

Appendix B.6.4.3-8: Worker estimation, German model: UDMH, incorporating DFR data

| Estimation of post-application exposure of workers (re-entry exposure) | | | |
|------------------------------------------------------------------------|--------------------|-----------------------------------|----|
| Active substance (a.s.) | UDMH | | |
| Product | Alar | | |
| Intended use(s) | ornamentals_indoor | | |
| Application rate (AR) | 7,65 | kg a.s./ha | 1) |
| Number of applications (NA) | 1,3 | | |
| Dislodgeable foliar residues (DFR) | 0,00033 | µg/cm ² /kg a.s. | 2) |
| Transfer coefficient (TC) | 5000 | cm ² /person/h | 3) |
| Work rate per day (WR) | 8 | h/d | 4) |
| Penetration through clothing (P) | 0,28 | (28 %) | 5) |
| Systemic AOEL | 0,00009 | mg/kg bw/d | |
| Dermal absorption (DA) | 10,7 | % (worst case, e.g. for dilution) | |
| Body weight (BW) | 60 | kg | |

1) consideration of more than two applications will not be necessary if degradation on foliage of at least 50 % can be assumed between 2 applications (otherwise use multiple application factor)

2) default of 1 µg a.s./cm² per kg a.s./ha acc. to Krebs et al. (2000)

3) TC 30000 cm²/person/hour ("worst case", hand harvesting, both sides of leaves) acc. to Krebs et al. (2000), acc. EU/POEM II (2002): 2500 (vegetables), 3000 (strawberries), 4500 (fruits from trees), 5000 (ornamentals) acc. US EPA Policy # 3.1 (2000): 1500 (cereals, e.g. crop inspection), 10000 (grapes)

4) 8 h/day for professional applications if re-entry tasks are intended, 2 h/day for professional applications if re-entry tasks are not intended (e.g. irrigation, maintenance) or for applications in the home and allotment garden area

5) 5 % of dermal exposure corresponding to protective clothing incl. gloves for professionals, 50 % reduction of dermal exposure corresponding to long sleeved shirt, long trousers and gloves for applications in the home and allotment garden area

| Estimation of worker (re-entry) exposure | | | |
|--------------------------------------------------------------------|-----------------------|-------------------------------------|-------------------------------------|
| Input parameters considered for the estimation of worker exposure: | | | |
| Intended use(s): | ornamentals_indoor | Dislodgeable foliar residues (DFR): | 0,00033 µg/cm ² /kg a.s. |
| Application rate (AR): | 7,65 kg a.s./ha | Transfer coefficient (TC): | 5000 cm ² /person/h |
| Number of applications (NA): | 1,3 | Work rate per day (WR): | 8 h/d |
| Body weight (BW): | 60 kg/person | PPE | 28 % |
| Dermal absorption (DA): | 10,7 % ("worst case") | | |
| AOEL | 0,00009 mg/kg bw/d | | |

| Worker exposure towards UDMH | | | |
|-------------------------------------------------------------------------------------|---------------------|-----------------------------------------------------------|---------------------|
| Without PPE ¹⁾ | | With PPE ²⁾ | |
| Worker (re-entry): Systemic dermal exposure after application in ornamentals_indoor | | | |
| SDE _W = (DFR x TC x WR x AR x NA x DA) / BW | | SDE _W = (DFR x TC x WR x AR x NA x PPE x DA) / | |
| (0,00033 x 5000 x 8 x 7,65 x 1,3 x 10,7%) / 60 | | (0,00033 x 5000 x 8 x 7,65 x 1,3 x 28% x 10,7%) / 60 | |
| External dermal exposure | 0,13 mg/person | External dermal exposure | 0,04 mg/person |
| External dermal exposure | 0,00 mg/kg bw/d | External dermal exposure | 0,00 mg/kg bw/d |
| Total systemic exposure | 0,01 mg/person | Total systemic exposure | 0,00 mg/person |
| Total systemic exposure | 0,000234 mg/kg bw/d | Total systemic exposure | 0,000066 mg/kg bw/d |
| % of AOEL | 260,1 % | % of AOEL | 72,8 % |
| Inhalation exposure | | | |
| Without RPE | | With RPE | |
| TSF: 0.1 cutting; 0.01 sorting and bundling | | RPE FP1 25% | |
| PIE = (AR x MAF x TSF x WR) / BW | | PIE = (AR x MAF x TSF x WR x PPE) / BW | |
| 0,01326 mg/kg bw/d | | 0,003315 mg/kg bw/d | |
| Total systemic exposure | 0,01349 mg/kg bw/d | Total systemic exposure | 0,003381 mg/kg bw/d |
| % of AOEL | 14993 % | % of AOEL | 3756,166093 % |

| Estimation of post-application exposure of workers (re-entry exposure) | | | | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|-----------------------------------|--|----|
| Active substance (a.s.) | UDMH | | | |
| Product | Alar | | | |
| Intended use(s) | ornamentals_indoor | | | |
| Application rate (AR) | 7,65 | kg a.s./ha | | |
| Number of applications (NA) | 1,3 | | | 1) |
| Dislodgeable foliar residues (DFR) | 0,00033 | µg/cm ² /kg a.s. | | 2) |
| Transfer coefficient (TC) | 5000 | cm ² /person/h | | 3) |
| Work rate per day (WR) | 8 | h/d | | 4) |
| Penetration through clothing (P) | 0,28 | (28 %) | | 5) |
| Systemic AOEL | 0,00009 | mg/kg bw/d | | |
| Dermal absorption DA) | 10,7 | % (worst case, e.g. for dilution) | | |
| Body weight (BW) | 60 | kg | | |
| <p>1) consideration of more than two applications will not be necessary if degradation on foliage of at least 50 % can be assumed between 2 applications (otherwise use multiple application factor)</p> <p>2) default of 1 µg a.s./cm² per kg a.s./ha acc. to Krebs et al. (2000)</p> <p>3) TC 30000 cm²/person/hour ('worst case', hand harvesting, both sides of leaves) acc. to Krebs et al. (2000), acc. EUROPEM II (2002): 2500 (vegetables), 3000 (straw berries), 4500 (fruits from trees), 5000 (ornamentals) acc. US EPA Policy # 3.1 (2000): 1500 (cereals, e.g. crop inspection), 10000 (grapes)</p> <p>4) 8 h/day for professional applications if re-entry tasks are intended, 2 h/day for professional applications if re-entry tasks are not intended (e.g. irrigation, maintenance) or for applications in the home and allotment garden area</p> <p>5) 5 % of dermal exposure corresponding to protective clothing incl. gloves for professionals, 50 % reduction of dermal exposure corresponding to long sleeved shirt, long trousers and gloves for applications in the home and allotment garden area</p> | | | | |

Estimation of worker (re-entry) exposure

Input parameters considered for the estimation of worker exposure:

| | | | | |
|------------------------------|-----------------------|-------------------------------------|---------|-----------------------------|
| Intended use(s): | ornamentals_indoor | Dislodgeable foliar residues (DFR): | 0,00033 | µg/cm ² /kg a.s. |
| Application rate (AR): | 7,65 kg a.s./ha | Transfer coefficient (TC): | 5000 | cm ² /person/h |
| Number of applications (NA): | 1,3 | Work rate per day (WR): | 8 | h/d |
| Body weight (BW): | 60 kg/person | PPE | 28 | % |
| Dermal absorption (DA): | 10,7 % ('worst case') | Application rate of UDMH | 0,00137 | kg a.s./ha |
| AOEL | 0,00009 mg/kg bw/d | | | |

| Worker exposure towards UDMH | | | | | |
|-------------------------------------------------------------------------------------|----------|------------|--------------------------------------------------------------|----------|------------|
| Without PPE ¹⁾ | | | With PPE ²⁾ | | |
| Worker (re-entry): Systemic dermal exposure after application in ornamentals_indoor | | | | | |
| SDE _w = (DFR x TC x WR x AR x NA x DA) / BW | | | SDE _w = (DFR x TC x WR x AR x NA x PPE x DA) / BW | | |
| (0,00033 x 5000 x 8 x 7,65 x 1,3 x 10,7%) / 60 | | | (0,00033 x 5000 x 8 x 7,65 x 1,3 x 28% x 10,7%) / 60 | | |
| External dermal exposure | 0,13 | mg/person | External dermal exposure | 0,04 | mg/person |
| External dermal exposure | 0,00 | mg/kg bw/d | External dermal exposure | 0,00 | mg/kg bw/d |
| Total systemic exposure | 0,01 | mg/person | Total systemic exposure | 0,00 | mg/person |
| Total systemic exposure | 0,000234 | mg/kg bw/d | Total systemic exposure | 0,000066 | mg/kg bw/d |
| % of AOEL | 260,1 | % | % of AOEL | 72,8 | % |
| Inhalation exposure | | | | | |
| Without RPE | | | With RPE | | |
| TSF: 0.1 cutting ; 0.01 sorting and bundling | | | RPE FP1 25% | | |
| PIE = (AR _{UDMH} x MAF x TSF x WR) / BW | | | PIE = (AR _{UDMH} x MAF x TSF x WR x PPE) / BW | | |
| 2,37467E-05 | | mg/kg bw/d | 5,93667E-06 | | mg/kg bw/d |
| Total systemic exposure | 0,00026 | mg/kg bw/d | 0,000071 | | mg/kg bw/d |
| % of AOEL | 286,502 | % | 79,4290563 | | % |

Appendix B.6.4.3-9: Worker estimation, EFSA AOEM model: daminozide, incorporating DFR data

| | | | | | |
|-----------------------------------------------|------------------------------------------------------------|---------------------------------------------------|-----------------------------------|--------------------------------|-----------------------------------------------------------------------|
| Substance | Daminozide | Formulation = Wettable granules, soluble granules | Application rate-7,65 kg a.s. /ha | Spray dilution = 15,3 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Indoor / Spray application / Manual-Knapsack | | | Buffer = 5 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 0,97 | Dermal for in use dilution = 0 | Oral = 35 | Inhalation = 100 | |
| RVNAS | 0,00875 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 3 µg a.s./cm2 per kg a.s./ha | | DT50 | 30 days | |
| Worker - Cutting, sorting, bundling, carrying | Potential exposure mg/kg bw/day | | 1,6451 | % of RVNAS | 18801,67 % |
| | Working clothing mg/kg bw/day | | 0,6531 | % of RVNAS | 7464,27 % |
| | Working clothing and gloves mg/kg bw/day | | 0,2563 | % of RVNAS | 2929,31 % |

Appendix B.6.4.3-10: Worker estimation, EFSA AOEM model: UDMH, incorporating DFR data, dermal + inhal. absorption**Exposure assessment**

| | | | | | |
|-----------------------------------------------|------------------------------------------------------------|---------------------------------------------------|-----------------------------------|--------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH - dermal absorption as daminozide proportion | Formulation = Wettable granules, soluble granules | Application rate-7,65 kg a.s. /ha | Spray dilution = 15,3 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Outdoor / Upward spraying / Manual-Hand held | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 10,7 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 0,00033 µg a.s./cm2 per kg a.s./ha | | DT50 | 3,25 days | |
| Worker - Cutting, sorting, bundling, carrying | Potential exposure mg/kg bw/day | | 0,0007 | % of RVNAS | 722,22% |
| | Working clothing mg/kg bw/day | | 0,0002 | % of RVNAS | 257,94% |
| | Working clothing and gloves mg/kg bw/day | | 0,0001 | % of RVNAS | 72,22% |

Exposure assessment

| | | | | | |
|-----------------------------------------------|------------------------------------------------------------|---------------------------------------------------|---------------------------------------|-----------------------------------|-----------------------------------------------------------------------|
| Substance | UDMH - inhalation absorption | Formulation = Wettable granules, soluble granules | Application rate-0,001595 kg a.s. /ha | Spray dilution = 0,00319 g a.s./l | Vapour pressure = low volatile substances having a vapour pressure of |
| Scenario | Ornamentals / Indoor / Spray application / Manual-Knapsack | | | Buffer = 2-3 | Number applications = 5, Application interval = 7 days |
| Percentage Absorption | Dermal for product = 10,7 | Dermal for in use dilution = 10,7 | Oral = 100 | Inhalation = 100 | |
| RVNAS | 0,00009 mg/kg bw/day | | RVAAS | mg/kg bw/day | |
| DFR | 0,00033 µg a.s./cm2 per kg a.s./ha | | DT50 | 3,25 days | |
| Worker - Cutting, sorting, bundling, carrying | Potential exposure mg/kg bw/day | | 0,0000 | % of RVNAS | 23,78% |
| | Working clothing mg/kg bw/day | | 0,0000 | % of RVNAS | 23,68% |
| | Working clothing and gloves mg/kg bw/day | | 0,0000 | % of RVNAS | 23,64% |

Total exposure to UDMH: 72.22+23.64 = 95,86 % AOEL