Summary of the toxicological studies for Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)

Data Requirement(s)

Document MCP
Section 7: Toxicological studies

According to the Guidance Document SANCO/10181/2013 for applicants on preparing dossiers for the approval of a chemical active substance

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on behalf of
Bayer AG
Crop Science Division
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### Version history

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<thead>
<tr>
<th>Date</th>
<th>Data points containing amendments or additions(^1) and brief description</th>
<th>Document identifier and version number</th>
</tr>
</thead>
<tbody>
<tr>
<td>[yyyy-mm-dd]</td>
<td></td>
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</tbody>
</table>

\(^1\) It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4, ‘How to revise an Assessment Report’.
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TOXICOLOGICAL STUDIES ON THE PLANT PROTECTION PRODUCT

Fluopicolide (AE C638206) was included in Annex I to Council Directive 91/414/EEC in 2010 (Commission Directive 2010/15/EU, Entry into Force on June 1, 2010). The expiration of approval of fluopicolide is May 31, 2023 (Commission Implementing Regulation (EU) 2017/1527). The Supplementary Dossier contains only data which were not submitted at the time of the Annex I inclusion of fluopicolide under Council Directive 91/414/EEC and which were therefore not evaluated during the first EU review. All data which were already submitted by Bayer AG (former Bayer CropScience) for the Annex I inclusion under Council Directive 91/414/EEC are contained in the Draft Assessment Report (DAR) and its Addenda, and are included in the Baseline Dossier provided by Bayer AG.

The formulation Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L), abbreviation FLC+PCH SC 687.5, is a suspension concentrate formulation (SC) containing 62.5 g/L of fluopicolide. This formulation is registered throughout Europe under trade names such as Infinito and Volare. FLC+PCH SC 687.5 was already a representative formulation of Bayer AG for the Annex I inclusion of fluopicolide under Council Directive 91/414/EEC.

Fluopicolide (AE C638206) is a fungicidal active substance developed by Bayer. It is the only active substance in Europe representing a class of chemistry (pyridinylmethyl-benzamides) with a unique mode of action via delocalization of a spectrin-like protein in the Oomycetes fungi.

Fluopicolide has a long track record of safe use in a large number of targeted crops within horticulture, e.g. cucumbers, lettuce and on arable crops (e.g. potato).

Fluopicolide is active against a wide range of Oomycete fungi, the causal agents of devastating plant diseases of economic importance in EU-27 such as potato late blight (Phytophthora infestans) or downy mildew diseases in a broad range of crops.

It provides effective, long lasting protection at low application rate against Oomycetes diseases at different stage of development of the fungi, giving flexibility of use to the farmer.

Fluopicolide can be formulated with other active ingredients in different types of formulations to optimise and complete its activity.

The development of resistances of Oomycetes against existing, well-established fungicide groups represent a threat for European farmers by increasing the complexity of their plant protection programs leading to severe economic impacts. With Fluopicolide, farmers in EU-27 have access to a modern tool for their integrated crop protection programs, contributing to effective and sustainable management of resistance development and preserving high level of protection against Oomycete diseases.

By reducing the Oomycete damages, applications of Fluopicolide + Propamocarb SC 687.5 on target crops contribute to the achievement of optimum yield and quality, thus securing sufficient supply of high-quality potatoes and horticultural produces for European consumer destinations and markets abroad, being it fresh or for the processing industry.
CP 7.1  
**Acute toxicity**

Flupicilide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) is not acutely toxic via the oral route (LD$_{50} > 2000$ mg/kg bw), the dermal route (LD$_{50} > 4000$ mg/kg bw) or the inhalation route (LC$_{50} > 3195$ mg/m$^3$) and was not irritating to the skin or eyes. Flupicilide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) was not sensitising to the skin in a modified Beuhler test; however, a mouse LLNA revealed a skin sensitising potential. Based on the doses administered it was possible to exclude category 1A for skin sensitisation. Overall, therefore, Flupicilide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) should be classified with skin sensitisation category 1B (H317).

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Species (sex)</th>
<th>Results</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute oral toxicity</td>
<td>Rat (M &amp; F)</td>
<td>LD$_{50} &gt; 2000$ mg/kg bw</td>
<td>M220853-02-1</td>
</tr>
<tr>
<td>Acute dermal toxicity</td>
<td>Rat (M &amp; F)</td>
<td>LD$_{50} &gt; 4000$ mg/kg bw/d</td>
<td>M220850-02-1</td>
</tr>
<tr>
<td>Acute inhalation toxicity</td>
<td>Rat (M &amp; F)</td>
<td>LC$_{50} &gt; 3195$ mg/m$^3$</td>
<td>M220835-02-1</td>
</tr>
<tr>
<td>Acute skin irritation</td>
<td>Rabbit (M)</td>
<td>Not irritating</td>
<td>M224063-01-4</td>
</tr>
<tr>
<td>Acute eye irritation</td>
<td>Rabbit (M)</td>
<td>Not irritating</td>
<td>M224063-01-2</td>
</tr>
<tr>
<td>Skin sensitisation (modified Beuhler)</td>
<td>Guinea pig (M &amp; F)</td>
<td>Non-sensitising</td>
<td>M227614-01-1</td>
</tr>
<tr>
<td>Skin sensitisation (LLNA)</td>
<td>Mice (F)</td>
<td>Skin sensitiser category 1B</td>
<td>M223765-01-1</td>
</tr>
</tbody>
</table>

CP 7.1.1  
**Oral toxicity**

All studies for this endpoint were presented and evaluated during the EU process for the Annex I inclusion of flupicilide under Council Directive 91/414/EEC. Please refer to the DAR and the Baseline Dossier of Flupicilide. One acute oral toxicity study is available for FLC+PCH SC 687.5, a short summary of which is presented below.

<table>
<thead>
<tr>
<th>Data Point:</th>
<th>KCP7.1.1/01</th>
</tr>
</thead>
<tbody>
<tr>
<td>Report Author:</td>
<td></td>
</tr>
<tr>
<td>Report Year:</td>
<td>2004</td>
</tr>
<tr>
<td>Report Title:</td>
<td>AE B06752-0 SC61 A1-EXP11120A - Study for acute oral toxicity in rats</td>
</tr>
<tr>
<td>Report No:</td>
<td>CO2530</td>
</tr>
<tr>
<td>Document No:</td>
<td>M220853-02-1</td>
</tr>
<tr>
<td>Deviations from current test guideline:</td>
<td>6 animals (3 males and 3 females) were dosed concurrently rather than sequentially.</td>
</tr>
<tr>
<td>Previous evaluation:</td>
<td>Yes, evaluated and accepted DAR 2005 for Propamocarb RAR June 2017</td>
</tr>
<tr>
<td>GLP/Officially recognised testing facilities:</td>
<td>Yes, conducted under GLP/Officially recognised testing facilities</td>
</tr>
</tbody>
</table>

**Executive Summary:**

Three male and three female fasted rats were administered a single oral gavage dose of Flupicilide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L), in demineralized water at a dose level of 2000 mg/kg bw. The animals were observed daily for mortality and clinical signs (several times on the day of dosing) and body weights were measured weekly. Animals were sacrificed following a 14-day observation period and were subject to a gross necropsy.
There were no deaths; in 3/3 females, reduced motility was observed from 10 minutes to three hours following dosing. There were no clinical signs observed in males. Body weight development was considered normal for rats of this age and strain and there were no unusual findings on necropsy.

The acute oral LD$_{50}$ of Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) in rats was therefore greater than 2000 mg/kg bw. No classification for acute oral toxicity is warranted.

I. Materials and Methods

A. Materials

1. Test material

   Test substance: Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)
   Purity: Fluopicolide 62.5 g/L, Propamocarb 625 g/L
   Batch no.: OP220159

2. Vehicle and/or positive control

   Vehicle: Demineralized water

3. Test animals

   Species: Rat
   Strain: HsdCpb:WU
   Age: 8-9 weeks
   Weight at start: 195 – 196 g (males), 162 – 164g (females)
   Source: Acclimation period: 5 days
   Identification: Cage cards and individual markings
   Diet: PROVIMI KLIBA 3883.0.15, Switzerland
   Water: Available ad libitum
   Housing: Polycarbonate cages
   Temperature: 22 ± 2˚ C
   Humidity: Approx. 55 ± 5%
   Air changes: Approx. 10 times/hour
   Photoperiod: 12-hours

B. Study design

1. In-life dates: 6 November 2002 to 22 November 2002

2. Animal assignment and treatment

   No. of animals (group size): 3/sex
   Dose(s): 2000 mg/kg bw
   Exposure: Once via gavage
   Post-exposure observation period: 14 days

Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) was administered to fasted male and female rats (3/sex) at a dose of 2000 mg/kg bw and a volume of 10 ml/kg bw. Food was reintroduced two hours following dosing. The day of dose administration was designated day 1 of the test.
C. Methods

1. Observations
Animals were examined for clinical signs and mortality several times on the day of treatment and at least once daily thereafter. Body weights were recorded prior to dosing, once weekly and on sacrifice or death.

2. Necropsy
Animals were anesthetized by diethyl ether and sacrificed at the end of the observation period. All animals were subject to a gross necropsy.

II. Results and Discussion

A. Results

1. Dose-response table (LD₅₀)
The results of the study for acute oral toxicity in the fasted rat are summarized in Table 7.1.1.1 below.

<table>
<thead>
<tr>
<th>Dose (mg/kg bw)</th>
<th>Toxicological result*</th>
<th>Duration of signs</th>
<th>Time of death (14 days)</th>
<th>LD₅₀ (mg/kg bw) (44 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male rats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>0/0/3</td>
<td></td>
<td></td>
<td>&gt;2000</td>
</tr>
<tr>
<td>Female rats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>0/3/3</td>
<td>10 mins to 3 hours</td>
<td></td>
<td>&gt;2000</td>
</tr>
</tbody>
</table>

* Number of animals which died / number of animals with signs / total number of animals

The LD₅₀ was therefore 2000 mg/kg bw.

2. Clinical signs
There were no mortalities and no clinical signs were observed in males. In females, reduced motility was observed from 10 minutes following dosing and had resolved by 3 hours post-dose.

3. Body weights
There were no effects on body weight or body weight development in males or females.

4. Necropsy findings
No unusual gross pathology findings were noted in the animals sacrificed at the end of the observation period.

III. Conclusion

The acute oral LD₅₀ of Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) in rats was greater than 2000 mg/kg bw. Classification for acute oral toxicity in accordance with regulation (EC) No. 1272/2008 is therefore not required.

Assessment and conclusion by applicant:
The study is valid and acceptable to determine the acute oral toxicity of Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L).

Under the conditions of this study, Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) is of low acute oral toxicity (LD₅₀ > 2000 mg/kg bw), and classification for acute oral toxicity is not required.

**CP 7.1.2 Dermal toxicity**

All studies for this endpoint were presented and evaluated during the EU process for the Annex I inclusion of fluopicolide under Council Directive 91/414/EEC. Please refer to the DAR and the Baseline Dossier of fluopicolide. One acute dermal toxicity study is available for FLC+PCH SC 687.5, a short overall summary of which is provided below.

**Data Point:** KCP 7.1.2/01
**Report Author:**
**Report Year:** 2004
**Report Title:** AE B066752 SC61 EXP11120A - Study for acute dermal toxicity in rats
**Report No:** C036532
**Document No:** M-22088402-1


**Deviations from current test guideline:** none

**Previous evaluation:** Yes, evaluated and accepted DAR 2005 for Propamocarb RAR June 2017

**GLP/Officially recognised testing facilities:** Yes, conducted under GLP/Officially recognised testing facilities

**Acceptability/Reliability:** Yes

**Executive Summary**

Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) was applied to the shorn back and flanks of 5/sex fasted rats and occluded with a gauze dressing. Following a 24-hour exposure period, the dressing was removed, and the area washed with soap and water. An observation period of 14 days followed. Animals were observed daily for mortality and clinical signs (several times on the day of treatment). Body weights were recorded prior to dosing and once weekly thereafter. All animals were subject to full gross necropsy.

There were no deaths or clinical signs of systemic toxicity. Local irritation, comprising partial reddening and encrusting of the treatment area was observed in one female from day 5 to day 11 post-application. There was no effect on body weight in males; however, one female showed a small transient reduction in body weight on days 5–7 of the study only. There were no unusual gross necropsy findings in any animal.

The acute dermal LD₅₀ of Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) in rats was greater than 4000 mg/kg bw. Classification for acute dermal toxicity in accordance with regulation (EC) No 1272/2008 is therefore not required.

**A. Materials**

1. **Test material**
Test substance: Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)
Purity: Fluopicolide 62.5 g/L, Propamocarb 625 g/L
Batch no.: OP220159

2. Vehicle and/or positive control

Vehicle: None

3. Test animals

Species: Rat
Strain: HsdCpb:WU
Age: 9 weeks (males) & 12 weeks (females)
Weight at start: 227-239g (males) & 206-221g (females)
Source: Acclimation period: 5 days
Identification: Cage cards and individual markings
Diet: PROVIMI KLIBA 3883.0.15, Switzerland
Water: Available ad libitum
Housing: Housed individually in polycarbonate cages
Temperature: 22˚ ± 2˚ C
Humidity: Approx. 55 ± 5%
Air changes: Approx. 10 times/hour
Photoperiod: 12 hours

B. Study design

1. In-life dates: November 13, 2002 to November 27, 2002

2. Animal assignment and treatment:
   No. of animals (group size): 5/sex
   Dose(s): 4000 mg/kg bw
   Exposure: 24 hours, dermal
   Post exposure observation period: 14 days

   The test substance was applied to a gauze strip and attached to the shorn back and flanks of the rats (covering an area of 18 cm²). The test item was left in place for 24 hours, after which the area was washed with soap and water.

C. Methods

1. Observations

   The animals were examined for mortality and clinical signs several times on the day of dosing and then daily thereafter for the remainder of the observation period. Body weights were recorded prior to dosing and then weekly thereafter. Animals were also weighed upon death or sacrifice.

2. Necropsy

   Animals were sacrificed by diethyl ether inhalation following the 14-day observation period. All animals (including intercurrent deaths) were subject to a full gross necropsy examination.
II. Results and Discussion

A. Results

1. Dose-response table (LD₅₀)

<table>
<thead>
<tr>
<th>Dose (mg/kg bw)</th>
<th>Toxicological result*</th>
<th>Duration of signs</th>
<th>Time of death</th>
<th>LD₅₀ (mg/kg bw) (14 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Male rats</td>
</tr>
<tr>
<td>4000</td>
<td>0/0/5</td>
<td>-</td>
<td>4000</td>
<td></td>
</tr>
<tr>
<td>Female rats</td>
<td></td>
<td></td>
<td></td>
<td>Female rats</td>
</tr>
<tr>
<td>4000</td>
<td>0/1/5</td>
<td>5 days to 11 days</td>
<td>4000</td>
<td></td>
</tr>
</tbody>
</table>

* Number of animals which died /number of animals with signs / total number of animals

The LD₅₀ was therefore > 4000 mg/kg bw

2. Clinical signs

There were no deaths or clinical signs of systemic toxicity. Local signs of toxicity (partly reddened and encrusted treatment area) were observed in one female from day 5 until day 11 of treatment.

3. Body weights

A slight, transient decrease in body weight was observed on day 8 of the study. The body weight development of males was not affected.

4. Necropsy findings

No unusual gross pathology findings were noted in the animals sacrificed at the end of the observation period.

III. Conclusion

The acute dermal LD₅₀ of Fluopicolide + Propamocarb hydrochloride SC 687.5 (62.5+625 g/L) in rats was greater than 4000 mg/kg bw. Classification for acute dermal toxicity in accordance with regulation (EC) No. 1272/2008 is therefore not required.

Assessment and conclusion by applicant:
The study is valid and acceptable to determine the acute dermal toxicity of FLC+PCH SC 687.5. Under the conditions of this study, FLC+PCH SC 687.5 is of low acute dermal toxicity (LD₅₀ > 4000 mg/kg bw), and classification for acute dermal toxicity is not required.

CP 7.1.3 Inhalation toxicity

All studies for this endpoint were presented and evaluated during the EU process for the Annex I inclusion of fluopicolide under Council Directive 91/414/EEC. Please refer to the DAR and the Baseline Dossier of fluopicolide. One acute inhalation study is available for FLC+PCH SC 687.5, a short overall summary of which is provided below.
### Executive Summary:

The acute inhalation toxicity of Fluopicolide + Propamocarb hydrochloride SC 687.5 was investigated by exposing groups of five male and five female rats to an aerosol atmosphere of the test substance for a 4-hour continuous nose-only exposure. The target concentration was the limit concentration of 5000 mg/m³; however, the maximum technically obtainable concentration was 3195 mg/m³. The mass median aerodynamic diameters (MMAD) was in the recommended range of 1.5 to 4 µm with a geometric standard deviation (GSD) of 1.5 to 3 (2.96±2.43 µm).

Animals were then subjected to a 14-day observation period in which they were examined for mortality and clinical signs several times on the day of exposure and daily thereafter. Body weights were recorded prior to exposure on day 3 and 7 and then weekly for the duration of the study. At the end of the observation period, the animals were sacrificed, and a full gross necropsy was performed (with a particular emphasis on the respiratory tract).

There were no deaths or clinical signs of toxicity and body weights were not affected by treatment (a slight decrease in body weight gain in females during the observation was considered to be incidental and not related to treatment with Fluopicolide + Propamocarb hydrochloride SC 687.5). There were no unusual findings on gross necropsy.

The 4-hour acute inhalation LC₅₀ of Fluopicolide + Propamocarb hydrochloride SC 687.5 in rats was >3195 mg/m³ (the maximum attainable concentration); therefore, classification for acute inhalation toxicity is not required.

### A. Materials

1. **Test material**

   - **Test substance:** Fluopicolide + Propamocarb hydrochloride SC 687.5 (62.5+625 g/L)
   - **Purity:** Fluopicolide 62.5 g/L, Propamocarb 625 g/L
   - **Batch no.:** OP220159

2. **Vehicle and/or positive control**

   - **Vehicle:** None
3. Test animals

Species: Rat
Strain: HsdCpb:WU
Age: Approximately 2 months
Weight at start: Weight range was within ± 10% of the mean
Source: 
Acclimation period: 5 days
Identification: Cage cards and individual markings
Diet: PROVIMI KLBA 3883.0.15, Switzerland
Water: Available ad libitum
Housing: Housed individually in conventional Makrolo type III cages
Temperature: 22˚ ± 2˚ C
Humidity: Approx. 40-60%
Air changes: Approx. 10 times/hour
Photoperiod: 12-hours

B. Study design

1. In-life dates: November 20, 2002 to December 04, 2002

2. Animal assignment and treatment

No. of animals (group size) 5/sex
Dose(s) 0 (control) and 5000 mg/kg bw (target concentration)
Exposure 4 hours, nose-only
Post exposure observation period 14 days

The acute inhalation toxicity of FLC+PCH SC 687.5 was investigated by exposing groups of five male and five female rats to an aerosol atmosphere of the test substance for a 4-hour continuous nose-only exposure. The target concentration was the limit concentration 5000 mg/m³; however, the maximum technically obtainable concentration was 3195 mg/m³. Animals were then subject a 14-day observation period, following which the animals were sacrificed and a full gross necropsy was performed.

Table 7.1.3-1: Concentrations of the test substance

<table>
<thead>
<tr>
<th>Mean concentration (mg/m³)</th>
<th>Nominal concentration (mg/m³)</th>
<th>MMAD ± GSD (µm)</th>
<th>Resp. fraction (% &lt; 3 µm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3195</td>
<td>1493</td>
<td>2.96 ±2.43</td>
<td>50.8</td>
</tr>
</tbody>
</table>

The mass median aerodynamic diameters (MMAD) was in the recommended range of 1 to 4 µm with a geometric standard deviation (GSD) of 1.5 to 3 (2.96±2.43 μm).

C. Methods

1. Observations

The animals were examined for mortality and clinical signs several times on the day of exposure and at least once daily thereafter. Body weights were recorded prior to exposure, on days 3 and 7 and then on a weekly basis.

2. Necropsy
All rats were subject to a gross necropsy; the respiratory tract was examined in detail.

II. Results and Discussion

A. Results

The results of the acute inhalation toxicity study with FLC+PCH SC 687.5 are summarised in the table below.

1. Dose-response table (LD_{50})

<table>
<thead>
<tr>
<th>Target concentration (mg/m³)</th>
<th>Toxicological result*</th>
<th>Duration of signs</th>
<th>Time of death</th>
<th>LD_{50} mg/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male rats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0/0/5</td>
<td>-</td>
<td></td>
<td>&gt;5000</td>
</tr>
<tr>
<td>5000</td>
<td>0/0/5</td>
<td>-</td>
<td></td>
<td>&gt;5000</td>
</tr>
<tr>
<td>Female rats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0/0/5</td>
<td>-</td>
<td></td>
<td>&gt;5000</td>
</tr>
<tr>
<td>5000</td>
<td>0/0/5</td>
<td>-</td>
<td></td>
<td>&gt;5000</td>
</tr>
</tbody>
</table>

* Number of animals which died / number of animals with signs / total number of animals

The LD_{50} was therefore > 3195 mg/m³.

2. Clinical signs

There was no deaths or clinical signs of toxicity and no animals experienced any abnormal reflexes in a battery of reflex measurements performed on day one following exposure.

3. Body weights

There were no effects on body weights in the treated animals in comparison with controls. A slight decrease in body weight gain in treated females during the observation period, was considered to be incidental and not an effect of treatment with FLC+PCH SC 687.5.

4. Necropsy findings

There were no unusual gross necropsy findings in animals sacrificed at the end of the observation period.

III. Conclusion

The 4-hour acute inhalation LC_{50} of FLC+PCH SC 687.5 in rats was 3195 mg/m³ (the maximum attainable concentration); therefore, classification for acute inhalation toxicity is not required.

Assessment and conclusion by applicants

The study is valid and acceptable to determine the acute inhalation toxicity of FLC+PCH SC 687.5. Under the conditions of this study, FLC+PCH SC 687.5 is of low acute inhalation toxicity (LC_{50} > 3195 mg/m³), and classification for acute inhalation toxicity is not required.

CP 7.1.4 Skin irritation

All studies for this endpoint were presented and evaluated during the EU process for the Annex I inclusion of fluopicolide under Council Directive 91/414/EEC. Please refer to the DAR and the Baseline
Dossier of fluopicolide. One skin irritation study is available for FLC+PCH SC 687.5, a short overall summary of which is provided below.

<table>
<thead>
<tr>
<th>Data Point:</th>
<th>KCP 7.1.4/01</th>
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<tr>
<td>Report Author:</td>
<td></td>
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<tr>
<td>Report Year:</td>
<td>2003</td>
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<tr>
<td>Report Title:</td>
<td>AE B066752 04 SC61 A1 (EXP11120A) - Acute dermal irritation in rabbits</td>
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<tr>
<td>Report No:</td>
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<td>M-224065-01-1</td>
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<tr>
<td>Deviations from</td>
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<td>test guideline:</td>
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</tr>
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<td>GLP/Officially</td>
<td>Yes, conducted under GLP/Officially recognised testing facilities</td>
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<td>recognised testing</td>
<td></td>
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<td>facilities:</td>
<td></td>
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<td>Acceptability/Reliability:</td>
<td>Yes</td>
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Executive Summary:

The potential of FLC+PCH SC 687.5 to irritate the skin was investigated in three male New Zealand White rabbits. Approximately 24 hours prior to treatment, both flanks of each animal were shorn with electric clippers and the skin examined; animals with healthy intact skin were selected for the study. The undiluted test item (0.5mL) was applied to the right flank of three animals, via application onto a gauze pad, and held in situ with a semi-occlusive dressing for four hours. The untreated skin served as a control. After the 4-hour exposure period, the dressings were removed, and the area wiped with a moistened cotton pad.

The treated skin was examined approximately 1-, 24-, 48- and 72-hours following removal of the dressing. Local dermal irritation was evaluated for each animal and assigned a numerical value.

The mean scores over 24, 48 and 72 hours for each animal were 0.3, 0.3 and 0.3 for erythema and 0.0, 0.0 and 0.0 for oedema. The slight erythema observed, had recovered by day 2 of the observation period in all animals.

Therefore, FLC+PCH SC 687.5 is not irritating to the skin of rabbits following a 4-hour exposure period and no classification for dermal irritation is thus required.

I. Materials and Methods

A. Materials

1. Test material

   Test substance: Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)
   Purity: Fluopicolide 62.5 g/L, Propamocarb 625 g/L
   Batch No.: OP220159

2. Vehicle and/or positive control

   Vehicle: None
3. Test animals

Species: Rabbit
Strain: New Zealand White
Age: 2-4 months old
Weight at start: 2.6±0.3 kg
Source: 
Acclimation period: At least 5 days
Identification: Metal ear tag
Diet: 110 pelleted diet, UAR, Villemoisson, France
Water: Provided ad libitum
Housing: Individually in polystyrene cages
Temperature: 18 ± 3°C
Humidity: 30 to 70%
Air changes: Approximately 12 cycles
Photoperiod: 12 hours light/12 hours dark

B. Study design

1. In-life dates: Not stated

2. Animal assignment and treatment

   No. of animals (group size): 3 males
   Dose(s): 0.5 mL
   Exposure: 4 hours, semi-occlusive
   Post exposure observation period: 4 days

   Approximately 24-hours prior to treatment, both flanks of each animal were shorn with electric clippers and the skin examined; animals with healthy intact skin were selected for the study. The undiluted test item (0.5mL) was applied to the right flank of 3 animals, via application onto a gauze pad, and held in situ with a semi-occlusive dressing for 4 hours. The untreated skin served as a control. After the 4-hour exposure period, the dressings were removed, and the area wiped with a moistened cotton pad.

C. Methods

1. Observations

   The treated skin was examined approximately 1, 24, 48- and 72-hours following removal of the dressing. Local dermal irritation was evaluated for each animal using the following numerical scale:

   **Erythema and Eschar Formation**

   - No erythema: 0
   - Very slight erythema (barely perceptible): 1
   - Well-defined erythema: 2
   - Moderate to severe erythema: 3
   - Severe erythema (redness) to slight eschar formation (injuries in depth) preventing

   **Consequence:**
Oedema formation

No oedema                           0
Very slight oedema (barely perceptible) 1
Slight oedema (edges of area well-defined by definite raising) 2
Moderate oedema (edges raised approximately 1 mm) 3
Severe oedema (raised more than 1 mm and extending beyond the area of exposure) 4

II. Results and Discussion

1. Dermal reactions

The observed dermal reactions for each animal, and the mean scores for 24, 48 and 72 hours for each animal are provided in the table below:

Table 7.1.4-1: Dermal irritation scores

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Erythema</th>
<th>Oedema</th>
<th>1 h</th>
<th>24 h</th>
<th>48 h</th>
<th>Mean scores (24-72 h)</th>
<th>Reversible (day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>287</td>
<td></td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0.3</td>
<td>2</td>
</tr>
<tr>
<td>288</td>
<td></td>
<td></td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0.3</td>
<td>2</td>
</tr>
<tr>
<td>289</td>
<td></td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.0</td>
<td>2</td>
</tr>
</tbody>
</table>

The mean scores over 24, 48 and 72 hours for each animal were 0.3, 0.3 and 0.3 for erythema and 0.0, 0.0 and 0.0 for oedema. The slight erythema observed had recovered by day 2 of the observation period in all animals.

III. Conclusion

Under the conditions of this study, FLC+PCH SC 687.5 is not irritating to the skin of rabbits following a 4-hour exposure; therefore, no classification for dermal irritation is required.

Assessment and conclusion by applicant:

The study is valid and acceptable to determine the dermal irritation potential of FLC+PCH SC 687.5. Under the conditions of this study, FLC+PCH SC 687.5 is not irritating to the skin of the rabbit, and classification for dermal irritation is not required.

CP 7.1.5 Eye irritation

All studies for this endpoint were presented and evaluated during the EU process for the Annex I inclusion of fluopicolide under Council Directive 91/414/EEC. Please refer to the DAR and the Baseline Dossier of fluopicolide. One eye irritation study is available for FLC+PCH SC 687.5, a short overall summary of which is provided below.
Executive Summary:
The eye irritating potential of FLC+PCH SC 687.5 was investigated in three male New Zealand White rabbits only animals without irritation, ocular defects or pre-existing injury were used). A single dose (0.1 mL) of the undiluted test item was installed into the conjunctival sac of the left eye of each animal. No irrigation of the eyes was performed. The untreated (right) eye served as the control.

The eyes were examined 1-, 24-, 48- and 72-hours following administration of the test item. Conjunctival reactions, iritis and corneal opacity were evaluated daily for each animal; the detection of the presence or absence of corneal opacity was aided with fluorescein. The ocular reactions were assigned a numerical score.

The mean scores for each animal over 24, 48 and 72 hours were 1.0, 0.7 and 1.0 for conjunctivae chemosis, 0.3, 0.3 and 0.3 for conjunctivae redness, 0.0, 0.0 and 0.0 for iritis and 0.3, 0.0 and 0.0 for corneal opacity.

Very slight chemosis (grade 1 or 2) and very slight redness (grade 1) were observed in all animals from day 1 and had fully reversed by day 2. Similarly, a very slight corneal opacity (grade 1) observed in 2/3 animals on day 2 had fully reversed by day 3. Other findings comprised a clear discharge and alopecia around the eyes in 2/3 animals on day 1 only.

Under the conditions of this study, FLC+PCH SC 687.5 is not irritating to the eyes of rabbits; therefore, no classification for acute eye irritation is required.

I. Materials and Methods

A. Materials

1. Test material

Test substance: Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)
Purity: Fluopicolide 62.5 g/L, Propamocarb 625 g/L
Batch no.: OP220159

2. Vehicle and/or positive control

Vehicle: None
3. Test animals

Species: Rabbit
Strain: New Zealand White
Age: 2-4 months old
Weight at start: 2.9 ± 0.3 kg
Source: 
Acclimation period: At least 5 days
Identification: Metal ear tag
Diet: 110 pelleted diet, UAR, Villemoisson, France
Water: Provided ad libitum
Housing: Individually in polystyrene cages
Temperature: 18 ± 3°C
Humidity: 30 to 70%
Air changes: Approximately 12 cycles
Photoperiod: 12 hours light/12 hours dark

B. Study design

1. In-life dates: Not stated

2. Animal assignment and treatment

No. of animals (group size): 3 males
Dose(s): 0.1 mL
Exposure: Single instillation in conjunctival sac
Irrigation: No
Post exposure observation period: 4 days

Approximately 24 hours prior to treatment, the eyes of each animal were examined. Only animals without irritation, ocular defects or pre-existing injury were selected. A single dose of 0.1 mL of the test item was instilled into the conjunctival sac of the left eye of each animal. The lower and upper eyelids were held together for approximately one second to ensure the test item was retained in the eye and the eyes were not rinsed following administration of the test item. The untreated (right) eye served as the control.

C. Methods

1. Observations

The eyes were examined 1-, 24-, 48- and 72-hours following administration of the test item. Conjunctival reactions, iritis and corneal opacity were evaluated daily for each animal; the presence or absence of corneal opacity was aided with a UV lamp following the addition of one or two drops of 0.5% sodium fluorescein to the eye (performed on day 1 and day 2 in animal 287 and 288 and on day 1 in animal number 289). The ocular reactions were assigned a score in accordance with the following numerical scale:
Conjunctival lesions and discharge

Chemosis (lids and/or nictitating membranes):
- No swelling: 0
- Any swelling above normal (includes nictitating membranes): 1
- Obvious swelling with partial eversion of lids: 2
- Swelling with lids half closed: 3
- Swelling with lids more than half closed: 4

Redness (refers to palpebral and bulbar conjunctivae, corna and iris):
- Blood vessels normal: 0
- A number of blood vessels definitely hyperemic (injected): 1
- Diffuse, crimson colour, individual vessels not easily discernible: 2
- Diffuse, beefy red: 3

Discharge:
- Absence of discharge: 0
- Slight discharge: 1
- Discharge with moistening of lids and hairs adjacent to lids: 2
- Discharge with moistening of lids and hairs on wide area around eyes: 3

Iris lesions

Normal
- Markedly deepened rugae, congestion, swelling, moderate circumcorneal hyperemia, or injection (any combination), iris still reacting to light: 1
- No reaction to light: 2

Corneal lesions

Degree of opacity:
- No ulceration or opacity: 0
- Scattered or diffuse areas of opacity, details of iris clearly visible: 1
- Easily discernible translucent area, details of iris slightly obscured: 2
- Nacreous areas, no details of iris visible, size of pupil barely discernible: 3
- Opaque cornea, iris not discernible through the opacity: 4

Area of opacity:
- One quarter (or less) but not zero: 1
- Greater than one quarter but less than a half: 2
- Greater than one half but less than three quarters: 3
- Greater than three quarters up to whole area: 4

II. Results and Discussion

1. Ocular reactions

The observed ocular reactions for each animal, and the mean scores for 24, 48 and 72 hours for each animal are provided in the table below:
Table 7.1.5-1: Ocular irritation scores

<table>
<thead>
<tr>
<th>Animal No.</th>
<th>Region of eye</th>
<th>Description</th>
<th>Scores after treatment *</th>
<th>Mean scores (24-72 h)</th>
<th>Reversible (day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1 h</td>
<td>24 h</td>
<td>48 h</td>
</tr>
<tr>
<td>287</td>
<td>Conjunctiva</td>
<td>Chemosis</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Redness</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discharge</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Iris</td>
<td>Lesions</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Cornea</td>
<td>Opacity intensity</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opacity area</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>288</td>
<td>Conjunctiva</td>
<td>Chemosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Redness</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discharge</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Iris</td>
<td>Lesions</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td></td>
<td>Cornea</td>
<td>Opacity intensity</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opacity area</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>289</td>
<td>Conjunctiva</td>
<td>Chemosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td></td>
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<td>Discharge</td>
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<tr>
<td></td>
<td>Iris</td>
<td>Lesions</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Cornea</td>
<td>Opacity intensity</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opacity area</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

The mean scores for each animal over 24, 48 and 72 hours were 1.0, 0.7 and 1.0 for conjunctivae chemosis, 0.3, 0.3 and 0.3 for conjunctivae redness, 0.0, 0.0 and 0.0 for iritis and 0.3, 0.0 and 0.0 for corneal opacity.

Very slight chemosis (grade 1 or 2) and very slight redness (grade 3) were observed in all animals from day 1 and had fully reversed by day 2. Similarly, very slight corneal opacity (grade 1) observed in 2/3 animals on day 2 had fully reversed by day 3. Other findings comprised a clear discharge and alopecia around the eyes in 2/3 animals on day 1 only.

**III. Conclusion**

Under the conditions of this study, FLC+PCH SC 687.5 is not irritating to the eyes of rabbits; therefore, no classification for acute eye irritation is required.

**Assessment and conclusion by applicant:**

The study is valid and acceptable to determine the eye irritating potential of FLC+PCH SC 687.5. Under the conditions of this study, FLC+PCH SC 687.5 is not irritating to the eyes of the rabbit, and classification for acute eye irritation is therefore not required.

**CP 7.1.6 Skin sensitization**

All studies for this endpoint were presented and evaluated during the EU process for the Annex I inclusion of fluopicolide under Council Directive 91/414/EEC. Please refer to the DAR and the Baseline
Dossier of fluopicolide. Two skin sensitisation studies are available for FLC+PCH SC 687.5 (a modified Beuhler test in guinea pigs and a mouse LLNA). A short overall summary of these studies is provided below.

**Data Point:** KCP 7.1.6/01
**Report Author:** 
**Report Year:** 2003
**Report Title:** AE B066752 04 SC61 A1 (EXP11120A) - Skin sensitization test in guinea pigs (Modified Buehler test: 9 applications)
**Report No:** C038042
**Document No:** M-224078-01-1
**Guideline(s) followed in study:** EC Directive No. 96/54/EEC, B.6 (1996); OECD 406 (1992)
**Deviations from current test guideline:** none
**Previous evaluation:** yes, evaluated and accepted DAR 2005 for Propamocarb RAR June 2017
**GLP/Officially recognised testing facilities:** Yes, conducted under GLP/Officially recognised testing facilities
**Acceptability/Reliability:** Yes

**Executive Summary:**
A preliminary test was conducted in which the test item was applied at concentrations of 100% and 50% (w/w) to the shaved flanks of 2 male and 2 female Hartley guinea pigs (4 applications).

The highest concentration selected for the induction phase of the main study should cause weak/moderate skin reactions, whilst the highest concentration for the challenge phase should cause no irritant effect; therefore, as no dermal effects were noted with 50% (w/w) and only mild irritation effects were noted with undiluted test substance, the undiluted test substance (100%) was selected for the main study.

For the main study, concentrations of 100% were applied to the animals of the treated group on days 1 and 3; this was reduced to 50% for days 5, 8, 10, 12, 15, 17 and 19 owing to the severity of skin reactions observed. Animals of the control group received purified water under the same experimental conditions.

On day 29, a challenge application of 100% was applied to the clipped posterior right flank, whilst vehicle only was applied to the posterior left flank of the same animal. As equivocal reactions were noted, a second challenge was performed after an interval of 14-days (day 44) in which 50% (w/w) was applied to the left flank and vehicle to the right flank.

There were no deaths or clinical signs of toxicity and body weight development was normal.

Following the first challenge application, discrete erythema (grade 1) was observed at the 24-hour reading in 6/10 and 9/20 of the control and treated groups respectively, persisting until the 48-hour reading in 3/10 and 6/10 animals, respectively. Following the second challenge application, no dermal reactions were noted. Therefore, it is considered that the dermal reactions following the first challenge were secondary to irritation and not elicitation.

Under the conditions of this modified Beuhler test, FLC+PCH SC 687.5 is not a skin sensitisier, therefore no classification for skin sensitisation is warranted.
A. Materials

1. Test material

Test substance: Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)
Purity: Fluopicolide 62.5 g/L, Propamocarb 625 g/L
Batch no.: OP220159

2. Vehicle and/or positive control

Vehicle: Purified water

3. Test animals

Species: Guinea pigs
Strain: Hartley Crl: (HA) BR
Age: 1 to 2 months old
Weight at start: 453 ± 30 g (males) and 432 ± 32 g (females)
Source: Acclimation period: At least 5 days
Identification: Individual ear tattoo
Diet: 106 pelleted diet, SAFE, Villemoisson, France
Water: Provided ad libitum
Housing: Housed individually in polycarbonate cages with stainless steel lids
Temperature: 22 ± 2˚C
Humidity: 30 to 70%
Air changes: Approximately 12 hours
Photoperiod: 12 hours light/12 hours dark

B. Study design

1. In-life dates: November 18, 2002 to January 3, 2003

2. Animal assignment and treatment

<table>
<thead>
<tr>
<th>No. of animals (group size)</th>
<th>Test substance group: 15 and 15 female guinea pigs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle control group: 5 male and 5 female guinea pigs</td>
<td></td>
</tr>
<tr>
<td>Range finding</td>
<td>Yes (preliminary study with 2 male and 2 female guinea pigs)</td>
</tr>
<tr>
<td>Exposure (Concentration(s), no. of applications)</td>
<td>Induction phase: 100% on days 1 &amp; 3 and 50% (w/w) on days 5, 8, 10, 12, 15, 17 and 19</td>
</tr>
<tr>
<td>Challenge 1: 100% on day 29</td>
<td></td>
</tr>
<tr>
<td>Challenge 2: 50% (w/w) on day 44</td>
<td></td>
</tr>
<tr>
<td>Reliability check</td>
<td>Regularly assessed with Mercaptobenzothiazole</td>
</tr>
</tbody>
</table>

For the preliminary and main tests, the application sites of each animal were clipped and shaved the day before application of the induction phase and challenge phase and again before the 48-hour reading of the challenge phase. Appropriate concentrations of the test substance were loaded on to a filter paper (approximately 8cm²) which was applied to the shaved skin of the flank and held in place with an occlusive dressing for 6 hours.

For the preliminary induction phase, concentrations of 100% and 50% were applied (one concentration per flank). The treatment was repeated to obtain a total of 4 applications (with an interval of 2 or 3 days between applications). Cutaneous reactions were evaluated approximately 24 hours after each treatment. A challenge was performed at 100% and 50% using the same method and skin examined for reactions.
24- and 48-hours following dressing removal. The highest concentration selected for the induction phase of the main study should cause weak/moderate skin reactions, whilst the highest concentration for the challenge phase should cause no irritant effect.

For the main study, concentrations of 100% were applied to the animals of the treated group on days 1 and 3; this was reduced to 50% for days 5, 8, 10, 12, 15, 17 and 19 owing to the severity of skin reactions observed. Animals of the control group received purified water under the same experimental conditions.

On day 29 a challenge application of 100% was applied to the clipped posterior right flank, whilst vehicle only was applied to the posterior left flank of the same animal. As equivocal reactions were noted, a second challenge was performed after an interval of 14-days.

On day 44, a second challenge of 50% (w/w) was applied to the left flank and vehicle to the right flank. No residual test item was noted on removal of the dressing for the induction or challenge phases.

C. Methods

1. Observations

Animals were observed at least once daily for mortality and clinical signs. Animals were weighed on the day of group allocation, and on days 1, 31 and 46 of the study.

2. Dermal observations

Twenty-four hours after each application of the induction phase, before the second challenge and 24 and 48 hours after removal of the dressing in each challenge application, both flanks of the treated and control animals were examined and any dermal reactions were evaluated according to the following numerical scale:

| No visible change | 0 |
| Discrete or patchy erythema | 1 |
| Moderate and confluent erythema | 2 |
| Intense erythema | 3 |

In addition, any observed oedema or other lesions were recorded. Any reactions in the treated group (score ≥ 1) persisting for at least 48-hours and/or appearing after 24-hours are considered positive reactions. If a positive reaction is observed in the control animals, only reactions in the treated animals with a greater intensity and/or duration of those in the control animals are considered positive.

II. Results and Discussion

A. Results

1. Clinical signs

There were no mortalities or clinical signs of toxicity and the body weight development of the treated animals was comparable to that of the controls.

2. Dermal reactions

In the preliminary study, No, irritation was noted at scoring (induction phase) with 50% (w/w) test item. A scoring of 1 was noted on day 2 in the female animal and on day 9 in the male animal with the undiluted test item. No dermal reactions were noted during the preliminary challenge phase with either...
concentration. Therefore 100% was selected as the concentration for the induction and challenge phases of the main study.

In the main study, dermal reactions were noted during the induction phase, following application of the undiluted test item on days 1 and 3. Therefore, the concentration was reduced to 50% (w/w).

The scoring of the dermal reactions during the challenge phase of the main study are summarised in the table below.

Table 7.1.6-1: Scoring of dermal reaction during the challenge phase of the main study

<table>
<thead>
<tr>
<th></th>
<th>24 hours</th>
<th>48 hours</th>
<th>Total number of animals affected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male LF</td>
<td>Female LF</td>
<td>Male RF</td>
</tr>
<tr>
<td>Control</td>
<td>0/5</td>
<td>5/5</td>
<td>0/5</td>
</tr>
<tr>
<td>Treated</td>
<td>0/10</td>
<td>6/10</td>
<td>3/10</td>
</tr>
</tbody>
</table>

*Number of animals with positive dermal response (scores of 1-3) /number of animals in dose group, LF = Left flank (vehicle), RF = right flank (test item)

Following the first challenge application, discrete erythema (grade 1) was observed at the 24-hour reading in 6/10 and 9/20 of the control and treated groups, respectively, persisting until the 48-hour reading in 3/10 and 6/10 animals, respectively. As the challenge results were equivocal, a second challenge application was administered (following an interval of 14 days).

Following the second challenge application, no dermal reactions were noted. Therefore, it is considered that the dermal reactions following the first challenge were secondary to irritation and not elicitation.

**III. Conclusion**

Under the conditions of this modified Buehler test, FLC+PCH SC 687.5 is not a skin sensitiser, therefore no classification for skin sensitisation is warranted on the basis of this study.

**Assessment and conclusion by applicant:**

The study is valid and acceptable to determine the skin sensitising potential of FLC+PCH SC 687.5. Under the conditions of this study, FLC+PCH SC 687.5 is not a skin sensitiser, and classification for skin sensitisation is therefore not required on the basis of this study.
**Fluopicolide + Propamocarb-hydrochloride SC 687.5**

**Executive Summary:**

The skin sensitising potential of FLC+PCH SC 687.5 was investigated in a mouse local lymph node assay (LLNA). Groups of 4 female CBA mice were topically administered control item or test substance at concentrations of 10, 25, 50 or 100 %; 1% aqueous Pluronic acid provided the vehicle/vehicle control whilst p-Benzoquinone 0.1% in 50:50 test-substance: vehicle provided the positive control. The test substance or control was applied to the dorsal surface of each ear, daily on days 0, 1 and 2 of the study. The test site was examined for dermal reactions and animals were examined daily for mortality and clinical signs; body weights were recorded at the start of the study and at sacrifice. Following injection with \(^3\)H methyl thymidine, the nodes of each group of mice were removed and pooled and prepared for the determination of proliferation indices. A proliferation index of ≥3 is considered a positive response.

There were no deaths or clinical signs of toxicity and the animals gained the expected amount of weight. No local dermal irritation was seen at the application site. Simulation index values were 0.96, 0.66, 1.6 and 6.3 at concentrations of 10, 25, 50 and 100 % respectively. As the simulation index at 100% was >3 FLC+PCH SC 687.5 is considered a mild sensitiser. The solvent and positive controls gave the expected results thus confirming the validity of the assay.

As the EC3 value was >2 and the lower concentrations showed no positive proliferative response, FLC+PCH SC 687.5 should be classified for skin sensitisation category 1B (H317).

**A. Materials**

1. **Test material**

   Test substance: Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)
   Purity: Fluopicolide 62.5 g/L, Propamocarb 625 g/L
   Batch no.: OP220829

2. **Vehicle and/or positive control**

   Vehicle: Pluronic acid
   Positive control: p-Benzoquinone
3. Test animals

Species: Mice  
Strain: CBA/J  
Sex: Female  
Age: At least 8 weeks old  
Weight at start: Not stated  
Source:  
Acclimation period: At least 5 days  
Identification: Cage card  
Diet: Certified rodent pellet diet AO4C-10, SAFE, France  
Water: Provide ad libitum  
Housing: Individually housed in suspended, stainless steel, wire mesh cages  
Temperature: 20˚C to 24˚C  
Humidity: 40% to 70%  
Air changes: 10 to 15 changes per hour  
Photoperiod: 12 hours light/12 hours dark

B. Study design

1. In-life dates: October 20, 2004 to October 26, 2004

2. Animal assignment and treatment

No. of animals (group size) 4 female/group  
Range finding No  
Exposure (concentration(s), no. of applications) 0 (vehicle control), 10, 25, 50 & 100% and 0.1% p-Benzoquinone in a 50:50 test substance: vehicle mixture

Each mouse was topically dosed on the dorsal surface of each ear, once daily on days 0, 1 and 2 with 25µl of the test substance using an Eppendorf pipette; the applied dose remained on the ear reflecting realistic exposure to the test substance.

C. Methods

1. Observations

The animals were examined daily for mortality and clinical signs of toxicity. Body weights were recorded at the start of the test and at sacrifice.

2. Dermal observations

The site of application was examined for signs of local irritation.

3. Proliferation assay

On day 5 of the study, the tail vein of each mouse was injected with 250 µl of sodium chloride (0.9%) containing 20 µCi of 3H thymidine; the mice were retained in a plastic cage for 5 hours. The nodes form each group of 4 mice were pooled in a tube of physiological saline and disaggregated with a plastic piston to obtain a connective-tissue-free cell suspension.

Cell suspensions were washed with 10 mL of 0.9% physiological saline, centrifuged for 20 minutes at 1800 rpm. The resulting pellets were resuspended in 4 L of 5% trichloroacetic acid (TCA) and stored
overnight at approximately +4˚V. following a final centrifugation, the pellets were resuspended in 1 mL of saline. Mixed and placed in an ultrasonic bath for 25 minutes. The dispersed cell suspensions were then added to 10 mL of scintillation fluid and assayed in a beta counter. Results were expressed as disintegrations per minute (DPM) per animal. Stimulation indices (SI) were calculated according to the formula SI = DPM of treated group/DPM of control group.

4. Evaluation criteria
A test substance is regarded as a skin sensitiser if one concentration of the test substance results in an increase of $^3$H-TdR incorporation of 3-fold or greater (i.e. an SI of 3) when compared with control values. A dose response should be excluded, and no skin irritation should be seen. The concentration causing the 3-fold increase is known as the EC3.

III. Results and Discussion

A. Results

1. Clinical signs
There were no deaths or clinical signs of toxicity. Animals of the treated and control groups gained the expected amount of weight during the study.

2. Dermal reactions
No cutaneous reactions were observed at the treatment site in either the treated, negative control or positive control groups.

3. Proliferation assay

<table>
<thead>
<tr>
<th>Group No.</th>
<th>Concentration</th>
<th>Mean DPM</th>
<th>Simulation index</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>792</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10%</td>
<td>764</td>
<td>0.96</td>
</tr>
<tr>
<td>3</td>
<td>25%</td>
<td>524</td>
<td>0.66</td>
</tr>
<tr>
<td>4</td>
<td>50%</td>
<td>1261</td>
<td>1.6</td>
</tr>
<tr>
<td>5</td>
<td>100%</td>
<td>4961</td>
<td>6.3</td>
</tr>
<tr>
<td>6</td>
<td>Positive control</td>
<td>58</td>
<td>4.4</td>
</tr>
</tbody>
</table>

*1% Aqueous Pluronic acid **0.1% p-Benzoquinone in 50% test substance & 50% vehicle

A positive lymphoproliferative response was noted for 100% FLC+PCH SC 687.5 which gave an SI>3 (6.3). The positive and negative controls gave the expected results, thus confirming the validity of the assay. According to the guidance on the application of the CLP criteria, it is possible to sub categorise a substance into either 1A or 1B based on the EC3 value. As the EC value was >2%, and no positive proliferative responses were seen at the lower doses, FLC+PCH SC 687.5 should be classified as H317 subcategory 1B for skin sensitisation.

III. Conclusion
A positive proliferative was seen at a concentration of 100% test substance. Therefore, classification for skin sensitisation 1B (H317) is warranted for FLC+PCH SC 687.5 based on this mouse LLNA.
### Assessment and conclusion by applicant:

The study is valid and acceptable to determine the skin sensitising potential of FLC+PCH SC 687.5. Under the conditions of this study, FLC+PCH SC 687.5 is a mild skin sensitisier, and classification for skin sensitisation category 1B (H317) is appropriate.

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**CP 7.1.7 Supplementary studies on the plant protection product**

No such studies are necessary since there are no concerns arising, e.g., from potential synergistic or additive effects exerted by the active substance(s) or other components in FLC+PCH SC 687.5 that would require further investigations.

**CP 7.1.8 Supplementary studies for combinations of plant protection products**

No such studies are necessary since FLC+PCH SC 687.5 is not intended for use in combination with other plant protection products.
CP 7.2 Data on exposure

Evaluations of the exposure of operators, bystanders, residents and re-entry workers to fluopicolide when used in the FLC+PCH SC 687.5 formulation are provided in the following sections.

For operators, exposure estimates predict acceptable risks for all the intended use of FLC+PCH SC 687.5, with no PPE required for outdoor uses on potatoes or lettuce only normal workwear (with arms, legs, torso covered). For glasshouse use acceptable exposure on cucumbers requires gloves and coveralls to be worn. Exposure estimates for residents predict acceptable risks for all intended uses of FLC+PCH SC 687.5. Since no AAOEL has been set for either active, the exposure estimate for residents also covers bystanders; therefore, exposure estimates for bystanders are also considered acceptable for all intended uses. Regarding worker exposure, exposure estimates predict acceptable risks for workers for all intended uses of FLC+PCH SC 687.5, provided normal workwear covering arms, body and legs are worn for outdoor uses on potatoes or lettuce. For glasshouse use acceptable exposure on cucumbers requires workwear covering arms, body and legs and protective gloves to be worn. As the product is a mixture of two active substances, a combined exposure assessment is required. Only long-term combined exposure needs to be considered as neither active is acutely toxic. Exposure estimates predict acceptable risk for operators, residents, and workers for all intended uses of FLC+PCH SC 687.5 from combined long-term exposure to fluopicolide and propamocarb. Propamocarb and fluopicolide are not acutely toxic therefore a combined acute exposure risk assessment is not needed.

FLC+PCH SC 687.5 is a fungicide for the control of some acute phytopathogens especially in potato plants, but also in vegetables (indoors and outdoors). It combines fluopicolide (FLC), a fungicide with a novel mode of action and propamocarb-hydrochloride (PCH), a well-known antifungal compound. It is a suspension concentrate (SC) formulation containing 62.5 g/L fluopicolide (FLC) and 625 g/L propamocarb-hydrochloride (PCH) for the control of foliar, stem and tuber blight. It is applied by spraying, up to 4 applications per crop with a minimum spraying interval of 7 days between repeat applications.

Uses supported in this renewal are field crops of potatoes and lettuces and indoor crops of cucumbers. Details of supported uses are presented in Appendix 1 at the end of this document and summarised in the table below.

Table 7.2.01: Summary of critical uses patterns (i.e. worst case) of FLC+PCH SC 687.5

<table>
<thead>
<tr>
<th>Crop</th>
<th>Application max rate of formulation (L/ha)</th>
<th>Application rate (kg/ha per application)</th>
<th>Spray dilution water (L/ha)</th>
<th>Application equipment</th>
<th>Number of applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Field Crops</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potato</td>
<td>1.6</td>
<td>0.1</td>
<td>1</td>
<td>100-1000</td>
<td>Field Crop Sprayer</td>
</tr>
<tr>
<td>Lettuce</td>
<td>0.1</td>
<td>1</td>
<td>200-1000</td>
<td>Handheld Sprayer</td>
<td>1-2</td>
</tr>
</tbody>
</table>

Potatoes treated with a tractor boom (Field Crop Sprayer). AOEM model used.
This scenario also covers potatoes treated with 1-3 applications and 1-2 applications per crop.

Lettuce treated with a manual hand-held and knapsack sprayer. AOEM model used.
This scenario also covers lettuces treated with only 1 application per crop.
Fluopicolide + Propamocarb-hydrochloride SC 687.5

Greenhouse Crop

| Cucumber (high tech glasshouse) | 1.6 | 0.1 | 1 | 1000-1250 | Handheld Sprayer | 14 |

Cucumbers treated with manual sprayer, and worker re-entry after roof-fogger. Up to 3 applications per crop.

The Dutch greenhouse model used for operators and AOEM model used for workers.

Estimations of potential operator exposure have been undertaken for fluopicolide and propamocarb-hydrochloride using the list of intended uses (Appendix 2 of this document) and the following predictive models:

Field crops: The current EFSA modelling tool on the assessment of exposure of operators, workers, residents, and bystanders, was used to estimate the respective exposures from the application of FLC+PCH SC 687.5 on potatoes and lettuces. The AOEM calculator released on 30 March 2015 supports the EFSA guidance document¹ that was last updated on 31 April 2016.

Glasshouse crops: The Dutch greenhouse model has been used².

Dermal absorption and AOEL values

The estimations of human dermal penetration of fluopicolide and propamocarb which are the active substances in the mixed formulation FLC+PCH SC 687.5 were obtained from two in vitro dermal absorption studies using human skin conducted by 2003; M-222382-01-1, and 2015; M-516805-01-1 respectively. The proposed values including the AOEL values are summarised below. The vapour pressures of both actives are below 5x10⁻³ Pa.

Table: 7.2-02: Proposed values for EU endpoints used on the non-dietary human risk assessment.

<table>
<thead>
<tr>
<th>Endpoints used in risk assessment</th>
<th>Fluopicolide</th>
<th>Propamocarb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermal penetration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concentrate % (g/L of active)</td>
<td>0.26% (62.5 g/L)</td>
<td>2% (625 g/L)</td>
</tr>
<tr>
<td>Spray dilution % (g/L of active)</td>
<td>13%* (0.4 g/L outdoor use)</td>
<td>8.6%** (1 g/L outdoor use)</td>
</tr>
<tr>
<td></td>
<td>16%* (0.08 g/L indoor use)</td>
<td>8.6%** (0.8 g/L indoor use)</td>
</tr>
<tr>
<td>Reference</td>
<td>Study M-222382-01 in vitro human</td>
<td>Study M-516805-01-1 in vitro human</td>
</tr>
<tr>
<td>Reference values</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AOEL (mg/kg body weight/day)</td>
<td>0.07</td>
<td>0.29</td>
</tr>
<tr>
<td></td>
<td>(based on 90 day rat study NOAEL of 7.4 mg/kg bw/day)</td>
<td>(EFSA Scientific Report (2006) 78, 1-80)</td>
</tr>
</tbody>
</table>


**Summary of estimates**

Exposure assessments pertinent to the assessment of non-dietary exposure are summarized below.

<table>
<thead>
<tr>
<th>Crop</th>
<th>Model</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potatoes (Field)</td>
<td>AOEM</td>
<td>Can be used safely with vehicle mounted sprayers provided normal workwear is worn (arms, legs, torso covered).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acceptable risk to bystanders and residents.</td>
</tr>
<tr>
<td>Lettuce (Field)</td>
<td>AOEM</td>
<td>Can be used safely with manual hand-held sprayers and manual knapsack sprayers provided normal workwear is worn (arms, legs, torso covered).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acceptable risk to bystanders and residents.</td>
</tr>
<tr>
<td>Cucumber (glasshouse)</td>
<td>Dutch Greenhouse</td>
<td>Can be used safely with hand-held sprayers provided workers wear gloves and protective coveralls.</td>
</tr>
<tr>
<td></td>
<td>(operators)</td>
<td>Can be used safely for worker re-entry following roof fogging provided normal workwear (arms, legs, torso covered) and gloves are worn.</td>
</tr>
<tr>
<td></td>
<td>AOEM (workers)</td>
<td>Acceptable risk to bystanders and residents.</td>
</tr>
</tbody>
</table>

**Overall conclusion**

Exposure estimates predict acceptable risks for all the intended use of FLC+PCH SC 687.5 as long as normal workwear (arms, legs, torso covered) is worn for all uses and in addition protective gloves should be used by operators and workers in glasshouses.
**CP 7.2.1 Operator exposure**

**CP 7.2.1.1 Estimation of operator exposure**

**Potatoes**

**Table 7.2.1-01: Input parameters considered for the estimation of operator exposure for potatoes**

<table>
<thead>
<tr>
<th>AOEM EFSA calculator</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product name and code</strong></td>
<td>FLC+PCH SC 687.5</td>
<td></td>
</tr>
<tr>
<td><strong>Formulation type</strong></td>
<td>SC soluble or suspension concentrate</td>
<td></td>
</tr>
<tr>
<td><strong>Category</strong></td>
<td>Fungicide</td>
<td></td>
</tr>
<tr>
<td><strong>Crop type</strong></td>
<td>Potatoes</td>
<td></td>
</tr>
<tr>
<td><strong>Indoor/outdoor</strong></td>
<td>Outdoor</td>
<td></td>
</tr>
<tr>
<td><strong>Application method</strong></td>
<td>Downward spraying</td>
<td></td>
</tr>
<tr>
<td><strong>Application equipment</strong></td>
<td>Vehicle-mounted</td>
<td></td>
</tr>
<tr>
<td><strong>Minimum water volume</strong></td>
<td>100 L/ha</td>
<td></td>
</tr>
<tr>
<td><strong>DT50</strong></td>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td><strong>DFR</strong></td>
<td>3 μg/cm²</td>
<td></td>
</tr>
<tr>
<td><strong>Buffer strip</strong></td>
<td>2-3 metres</td>
<td></td>
</tr>
<tr>
<td><strong>Number of applications</strong></td>
<td>1-4</td>
<td></td>
</tr>
<tr>
<td><strong>Interval between multiple applications</strong></td>
<td>7 days</td>
<td></td>
</tr>
<tr>
<td><strong>Assumed area treated</strong></td>
<td>10 ha/day</td>
<td></td>
</tr>
<tr>
<td><strong>Active substance(s) (incl. content)</strong></td>
<td>Fluopicolide (FLC) 62.5 g/L, Propamocarb (PCH) 625 g/L</td>
<td></td>
</tr>
<tr>
<td><strong>Maximum application rate of active substance</strong></td>
<td>0.1 kg/ha</td>
<td>1 kg/ha</td>
</tr>
<tr>
<td><strong>AOEL systemic</strong></td>
<td>0.07 mg/kg bw/day</td>
<td>0.29 mg/kg bw/day</td>
</tr>
<tr>
<td><strong>AAOEL</strong></td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Inhalation absorption</strong></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Oral absorption</strong></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Dermal absorption</strong></td>
<td>Concentrate: 0.26%, Dilution: 13%</td>
<td>Concentrate: 2%, Dilution: 8.6%</td>
</tr>
</tbody>
</table>

The scenario of a tractor mounted sprayer in low crops was assessed and the default settings of the EFSA calculator were used with no refinements. The following sections show the summary results from the calculator. An attached appendix 2 depicts the related full output pages from the calculator.
### Table 7.2.1-02: Estimated operator exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on potatoes

<table>
<thead>
<tr>
<th>Model data</th>
<th>Level of PPE</th>
<th>Fluopicolide</th>
<th>Propamocarb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total absorbed dose (mg/kg bw/day)</td>
<td>% of AOEL</td>
</tr>
<tr>
<td>Potato Field Crop Application, vehicle-mounted sprayer</td>
<td>no PPE; work wear - arms, body and legs covered during mixing/loading and during application</td>
<td>0.0026</td>
<td>3.65</td>
</tr>
<tr>
<td>AOEM 75th percentile 75th percentile</td>
<td>longer term</td>
<td>systemic exposure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>no PPE; work wear - arms, body and legs covered during mixing/loading and during application</td>
<td>0.0197</td>
<td>NA</td>
</tr>
</tbody>
</table>

* This scenario also applies to the following:

3 applications a crop, 7 days between applications
2 applications a crop, 7 days between applications

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### Lettuce

Table 7.2.1-03: Input parameters considered for the estimation of operator exposure for lettuce

<table>
<thead>
<tr>
<th>AOEM EFSA calculator</th>
<th>FLC+PCH SC 687.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product name and code</td>
<td>FLC+PCH SC 687.5</td>
</tr>
<tr>
<td>Formulation type</td>
<td>SC soluble or suspension concentrate</td>
</tr>
<tr>
<td>Category</td>
<td>Fungicide</td>
</tr>
<tr>
<td>Crop type</td>
<td>Lettuce</td>
</tr>
<tr>
<td>Indoor/outdoor</td>
<td>Outdoor</td>
</tr>
<tr>
<td>Application method</td>
<td>Downward spraying</td>
</tr>
<tr>
<td>Application equipment</td>
<td>Manual Knapsack and Manual Hand-held</td>
</tr>
<tr>
<td>Minimum water volume</td>
<td>1000 L/ha</td>
</tr>
<tr>
<td>DT50</td>
<td>30 days</td>
</tr>
<tr>
<td>DFR</td>
<td>3 μg/cm2</td>
</tr>
<tr>
<td>Buffer strip</td>
<td>2-3 metres</td>
</tr>
<tr>
<td>Number of applications</td>
<td>1-2</td>
</tr>
</tbody>
</table>
The scenario of a manual-knapsack sprayer and manual hand-held sprayer in low crops (lettuces) was assessed and the defaults settings of the EFSA calculator was used with no refinements. The following sections show the summary results from the calculator. An attached appendix 2 depicts the related full output pages from the calculator.

**Table 7.2.1-04: Estimated operator exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on lettuce**

<table>
<thead>
<tr>
<th>Lettuce Field Crop Application</th>
<th>Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and 1.0 kg/ha PCH)</th>
<th>Body weight 60 kg</th>
<th>2 applications a crop, 7 days between applications</th>
<th>2 applications a crop, 7 days between applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual-knapsack sprayer 1 ha/day</td>
<td>Total absorbed dose (mg/kg bw/day)</td>
<td>Total absorbed dose (mg/kg bw/day)</td>
<td>% of AOEL</td>
<td>% of AOEL</td>
</tr>
<tr>
<td><strong>Model data</strong></td>
<td><strong>Level of PPE</strong></td>
<td><strong>Fluopicolide</strong></td>
<td><strong>Propamocarb</strong></td>
<td><strong>Fluopicolide</strong></td>
</tr>
<tr>
<td>Concentrate: 2%</td>
<td>Dilution: 8.6%</td>
<td>0.26%</td>
<td>13%</td>
<td>2%</td>
</tr>
<tr>
<td><strong>For more information please refer to section 7.3</strong></td>
<td>13%</td>
<td>0.26%</td>
<td>10%</td>
<td>13%</td>
</tr>
</tbody>
</table>
### Table 7.2.1-05: Input parameters considered for the estimation of operator exposure for cucumbers grown under glass

<table>
<thead>
<tr>
<th>Dutch Glasshouse Model</th>
<th>Product name and code</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLC+PCH SC 687.5</td>
<td></td>
</tr>
</tbody>
</table>

### Cucumber
The Dutch Glasshouse Model has been used to estimate exposure to operators applying the product to cucumbers in glasshouses. The following assumptions are made:

**Manual hand-held 4 ha/day**

<table>
<thead>
<tr>
<th>AOEM 75th percentile longer term systemic exposure</th>
<th>Potential exposure (no clothing)</th>
<th>0.197</th>
<th>281.74</th>
<th>0.1339</th>
<th>46.17</th>
</tr>
</thead>
<tbody>
<tr>
<td>no PPE: work wear - arms, body and legs covered during mixing/loading and during application.</td>
<td>0.0239</td>
<td>34.18</td>
<td>0.0190</td>
<td>6.56</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AOEM 75th percentile acute systemic exposure</th>
<th>Potential exposure (no clothing)</th>
<th>0.308</th>
<th>N/A</th>
<th>0.2123</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>no PPE: work wear - arms, body and legs covered during mixing/loading and during application.</td>
<td>0.02470</td>
<td>N/A</td>
<td>0.0053</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Manual hand-held 4 ha/day</th>
<th>AOEM 75th percentile longer term systemic exposure</th>
<th>Potential exposure (no clothing)</th>
<th>0.1966</th>
<th>280.84</th>
<th>0.3548</th>
<th>122.34</th>
</tr>
</thead>
<tbody>
<tr>
<td>no PPE: work wear - arms, body and legs covered during mixing/loading and during application.</td>
<td>0.0232</td>
<td>33.21</td>
<td>0.0460</td>
<td>15.87</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AOEM 75th percentile acute systemic exposure</th>
<th>Potential exposure (no clothing)</th>
<th>N/A</th>
<th>0.5955</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>no PPE: work wear - arms, body and legs covered during mixing/loading and during application.</td>
<td>N/A</td>
<td>0.2755</td>
<td>N/A</td>
<td></td>
</tr>
</tbody>
</table>

The Dutch Glasshouse Model has been used to estimate exposure to operators applying the product to cucumbers in glasshouses. The following assumptions are made:
Fluopicolide + Propamocarb-hydrochloride SC 687.5

<table>
<thead>
<tr>
<th>Formulation type</th>
<th>SC soluble or suspension concentrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category</td>
<td>Fungicide</td>
</tr>
<tr>
<td>Crop type</td>
<td>Cucumber</td>
</tr>
<tr>
<td>Indoor/outdoor</td>
<td>Indoor</td>
</tr>
<tr>
<td>Application method</td>
<td>Spraying</td>
</tr>
<tr>
<td>Application equipment</td>
<td>Manual sprayer</td>
</tr>
<tr>
<td>Minimum water volume</td>
<td>1000 L/ha</td>
</tr>
<tr>
<td>Number of applications</td>
<td>1-3</td>
</tr>
<tr>
<td>Interval between multiple applications</td>
<td>7 days</td>
</tr>
<tr>
<td>Assumed area treated</td>
<td>1 ha/day</td>
</tr>
<tr>
<td>Active substance(s) (incl. content)</td>
<td>Fluopicolide (FLC) 62.5 g/L</td>
</tr>
<tr>
<td>Maximum application rate of active substance</td>
<td>0.1 kg/ha</td>
</tr>
<tr>
<td>AOEL systemic</td>
<td>0.07 mg/kg bw/day</td>
</tr>
<tr>
<td>Inhalation absorption</td>
<td>100%</td>
</tr>
<tr>
<td>Oral absorption</td>
<td>100%</td>
</tr>
<tr>
<td>Dermal absorption</td>
<td>Concentrate: 0.26%</td>
</tr>
</tbody>
</table>

The following sections show the summary results from the Dutch Glasshouse model calculator. An attached appendix 2 depicts the related full output pages from the calculator.

**Table 7.2.1-06: Estimated operator exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on cucumbers**

<table>
<thead>
<tr>
<th>Model data</th>
<th>Fluopicolide</th>
<th>Propamocarb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total absorbed dose (mg/kg bw/day)</td>
<td>% of AOEL</td>
</tr>
<tr>
<td>Cucumber glasshouse application, manual-knapsack sprayer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and 1.0 kg/ha PCH)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight 60 kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 applications a crop, 7 days between applications*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Fluopicolide + Propamocarb-hydrochloride SC 687.5

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>78.6</th>
<th>0.30</th>
<th>104.6*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gloves and coveralls</td>
<td>0.007</td>
<td>10</td>
<td>0.0453</td>
<td>15.6</td>
</tr>
</tbody>
</table>

* This scenario also applies to the following:
  2 applications a crop, 7 days between applications
  1 application a crop

Overall conclusion on operator exposure

Exposure estimates predict acceptable risks for all the intended use of FLC+PCH SC 687.5, with no PPE required for outdoor uses on potatoes or lettuce only normal workwear (with arms, legs, torso covered). For glasshouse use acceptable exposure on cucumbers requires gloves and coveralls to be worn.

CP 7.2.1.2 Measurement of operator exposure
Not required as assessments demonstrated safe use using the accepted models.

CP 7.2.2 Bystander and resident exposure

CP 7.2.2.1 Estimation of bystander and resident exposure

The following definitions and assumptions for bystanders and residents may be applied.

Bystanders and residents are not involved in application or handling plant protection products or the professional handling of treated crops. The question arises whether it is necessary to distinguish between bystanders and residents in terms of the potential for exposure and health risks. However, because the circumstances of this exposure could differ with respect to amount, frequency, and duration, this seems to be reasonable.

Bystanders may inadvertently be present within or directly adjacent to an area for a short period of time, typically a matter of minutes, where application of a plant protection product is in progress or has recently taken place. They may be exposed to plant protection products mainly via the dermal route from spray drift and by inhalation of drifting spray droplets. Handheld application is considered to be worse case compared to field crop sprayer.

Residents may live or work in areas of the application of plant protection products (e.g. standing, working, or sitting in a garden in the vicinity of the application). They may be exposed to plant protection products mainly via the dermal route from spray drift deposits and by inhalation of vapour drift (depending on the vapour pressure of the active substance). For infants and toddlers, exposure might also occur orally (e.g. through hand-to-mouth transfer and/or object-to-mouth transfer).
**Bystander exposure**

Propamocarb: No AAOEL has been set for propamocarb as it does not present an acute toxicity hazard. For plant protection products with no potential acute systemic toxicity the long-term risk assessment for bystander may be considered to be covered by the risk assessment for residents.

For fluopicolide: No AAOEL is proposed for this renewal as it does not present acute toxicity hazard. For plant protection products with no potential acute systemic toxicity the long-term risk assessment for bystander may be considered to be covered by the risk assessment for residents.

Therefore, no bystander exposure assessment is required for FLC+PCH SC 687.5 as bystanders are considered to be covered by the risk assessment for residents.

**Resident exposure**

The assessment of potential resident exposure has been conducted using the EFSA AOEM model.

**Potatoes**

Table 7.2.2-01: Input parameters considered for the estimation of resident exposure for potatoes

<table>
<thead>
<tr>
<th>AOEM ENSA calculator</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Product name and code</td>
<td>FLC+PCH SC 687.5</td>
</tr>
<tr>
<td>Formulation type</td>
<td>SC soluble or suspension concentrate</td>
</tr>
<tr>
<td>Category</td>
<td>Fungicide</td>
</tr>
<tr>
<td>Crop type</td>
<td>Potatoes</td>
</tr>
<tr>
<td>Indoor/outdoor</td>
<td>Outdoor</td>
</tr>
<tr>
<td>Application method</td>
<td>Downward spraying</td>
</tr>
<tr>
<td>Application equipment</td>
<td>Vehicle</td>
</tr>
<tr>
<td>Minimum water volume</td>
<td>100 L/ha</td>
</tr>
<tr>
<td>DT50</td>
<td>30 days</td>
</tr>
<tr>
<td>DFR</td>
<td>3 μg/cm2</td>
</tr>
<tr>
<td>Buffer strip</td>
<td>2-3 metres</td>
</tr>
<tr>
<td>Number of applications</td>
<td>1-4</td>
</tr>
<tr>
<td>Interval between multiple applications</td>
<td>7 days</td>
</tr>
<tr>
<td>Assumed area treated</td>
<td>50 ha/day</td>
</tr>
<tr>
<td>Active substance(s) (incl. content)</td>
<td>Fluopicolide (FLC) 62.5 g/L</td>
</tr>
<tr>
<td>Maximum application rate of active substance</td>
<td>0.1 kg/ha</td>
</tr>
<tr>
<td>AOEL systemic</td>
<td>0.07 mg/kg bw/day</td>
</tr>
<tr>
<td>AAOEL</td>
<td>none</td>
</tr>
<tr>
<td>Inhalation absorption</td>
<td>100%</td>
</tr>
<tr>
<td>Oral absorption</td>
<td>100%</td>
</tr>
<tr>
<td>Dermal absorption</td>
<td>Concentrate: 0.26% Dilution: 13%</td>
</tr>
</tbody>
</table>
For more information please refer to section 7.3

The scenario of a tractor mounted sprayer in low crops was assessed and the defaults settings of the EFSA calculator was used with no refinements. The following sections show the summary results from the calculator. An attached appendix 2 depicts the related full output pages from the calculator.

Table 7.2.2-02: Estimated resident exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on potatoes

<table>
<thead>
<tr>
<th>Model data</th>
<th>Exposure route</th>
<th>Fluopicolide</th>
<th></th>
<th></th>
<th>Propamocarb</th>
<th>% of AOEL</th>
<th>% of AOEL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total absorbed dose (mg/kg bw/day)</td>
<td>% of AOEL</td>
<td>Total absorbed dose (mg/kg bw/day)</td>
<td>% of AOEL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potato Field Crop Application, vehicle-mounted sprayer</td>
<td></td>
<td>0.0035</td>
<td>5.01</td>
<td>0.0233</td>
<td>8.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and 1.0 kg/ha PCH)</td>
<td>Body weight 60 kg</td>
<td>3 applications a crop, 7 days between applications</td>
<td>4 applications a crop, 7 days between applications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spray drift</td>
<td>0.0008</td>
<td>1.20</td>
<td>0.0055</td>
<td>1.91</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vapour</td>
<td>0.0002</td>
<td>0.33</td>
<td>0.0002</td>
<td>0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surface deposits</td>
<td>0.0003</td>
<td>0.40</td>
<td>0.0019</td>
<td>0.64</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Entry into treated crops</td>
<td>0.0039</td>
<td>5.55</td>
<td>0.0257</td>
<td>8.87</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All pathways (mean)</td>
<td>0.0092</td>
<td>13.17</td>
<td>0.0557</td>
<td>19.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potato Field Crop Application, vehicle-mounted sprayer</td>
<td></td>
<td>0.0007</td>
<td>1.23</td>
<td>0.0066</td>
<td>2.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and 1.0 kg/ha PCH)</td>
<td>Body weight 60 kg</td>
<td>3 applications a crop, 7 days between applications</td>
<td>2 applications a crop, 7 days between applications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Spray drift</td>
<td>0.0011</td>
<td>4.53</td>
<td>0.0041</td>
<td>0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vapour</td>
<td>0.0009</td>
<td>1.25</td>
<td>0.0066</td>
<td>2.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surface deposits</td>
<td>0.0009</td>
<td>1.25</td>
<td>0.0066</td>
<td>2.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Entry into treated crops</td>
<td>0.0070</td>
<td>10.00</td>
<td>0.0463</td>
<td>15.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>All pathways (mean)</td>
<td>0.0092</td>
<td>13.17</td>
<td>0.0557</td>
<td>19.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>* This scenario is worst case so also applies to the following application rates:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 applications a crop, 7 days between applications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 applications a crop, 7 days between applications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Lettuce

Table 7.2.2-03: Input parameters considered for the estimation of resident exposure for lettuce

<table>
<thead>
<tr>
<th>AOEM EFSA calculator</th>
<th>Product name and code</th>
<th>Formulation type</th>
<th>Category</th>
<th>Crop type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FLC+PCH SC 687.5</td>
<td>SC soluble or suspension concentrate</td>
<td>Fungicide</td>
<td>Lettuce</td>
</tr>
<tr>
<td>Indoor/outdoor</td>
<td>Outdoor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application method</td>
<td>Downward spraying</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application equipment</td>
<td>Manual-Knapsack and Manual Hand-held</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum water volume</td>
<td>200 L/ha</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DT50</td>
<td>30 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DFR</td>
<td>3 μg/cm²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buffer strip</td>
<td>2-3 metres</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of applications</td>
<td>1-2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interval between multiple applications</td>
<td>7 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assumed area treated</td>
<td>1 ha/day for manual-knapsack, 4 ha/day for manual hand-held</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active substance(s) (incl. content)</td>
<td>Fluopicolide (FLC) 62.5 g/L  Propamocarb (PCH) 25 g/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum application rate of active substance</td>
<td>0.1 kg/ha  1 kg/ha</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AOEL systemic</td>
<td>0.07 mg/kg bw/day 0.29 mg/kg bw/day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalation absorption</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral absorption</td>
<td>100%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal absorption</td>
<td>Concentrate: 0.26% Dilution: 13%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Concentrate: 2% Dilution: 8.6%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The scenario of a manual knapsack sprayer, and manual hand-held sprayer in low crops (lettuces) was assessed and the defaults settings of the EFSA calculator was used with no refinements. The following sections show the summary results from the calculator. An attached appendix 2 depicts the related full output pages from the calculator.
Table 7.2.2-04: Estimated resident exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on lettuces

<table>
<thead>
<tr>
<th>Model data</th>
<th>Exposure route</th>
<th>Fluopicolide</th>
<th>Propamocarb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total absorbed dose</td>
<td>% of AOEL</td>
<td>Total absorbed dose</td>
</tr>
<tr>
<td></td>
<td>(mg/kg bw/day)</td>
<td></td>
<td>(mg/kg bw/day)</td>
</tr>
</tbody>
</table>

**Lettuce Field Crop Application - manual-knapsack sprayer**

Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and 1.4 kg/ha PCH)

2 applications a crop, 7 days between applications (this scenario is worst case so also covers 1 application a crop)

AOEM 75th percentile systemic exposure
1-3-year-old child

<table>
<thead>
<tr>
<th></th>
<th>Spray drift</th>
<th>0.0011</th>
<th>2.51</th>
<th>0.011</th>
<th>4.01</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vapour</td>
<td>0.0005</td>
<td>0.12</td>
<td>0.035</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>Surface deposits</td>
<td>0.0008</td>
<td>0.23</td>
<td>0.003</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Entry into treated crops</td>
<td>0.0041</td>
<td>0.72</td>
<td>0.009</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
<td>All pathways (mean)</td>
<td>0.0056</td>
<td>8.06</td>
<td>0.031</td>
<td>10.94</td>
</tr>
</tbody>
</table>

AOEM 75th percentile systemic exposure
Adult

<table>
<thead>
<tr>
<th></th>
<th>Spray drift</th>
<th>0.0004</th>
<th>0.60</th>
<th>0.0028</th>
<th>0.96</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vapour</td>
<td>0.0002</td>
<td>0.33</td>
<td>0.0002</td>
<td>0.08</td>
</tr>
<tr>
<td></td>
<td>Surface deposits</td>
<td>0.0002</td>
<td>0.25</td>
<td>0.0011</td>
<td>0.37</td>
</tr>
<tr>
<td></td>
<td>Entry into treated crops</td>
<td>0.0023</td>
<td>3.22</td>
<td>0.0149</td>
<td>5.15</td>
</tr>
<tr>
<td></td>
<td>All pathways (mean)</td>
<td>0.0025</td>
<td>3.35</td>
<td>0.0142</td>
<td>4.91</td>
</tr>
</tbody>
</table>

Cucumber

Resident exposure to cucumbers grown in glasshouses will not occur so no exposure estimate is necessary.

**Overall conclusion on resident exposure**

Exposure estimates predict acceptable risks for residents for all intended uses of FLC+PCH SC 687.5.

**CP 7.2.22 Measurement of bystander and resident exposure**

Since the exposure estimate carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under practical conditions of use, a study to provide a measure of bystander and resident exposure was not necessary and was therefore not carried out.
CP 7.2.3 Worker exposure

CP 7.2.3.1 Estimation of worker exposure

The worker re-entry exposure has been calculated for fluopicolide following application of FLC+PCH SC 687.5 formulation for the representative use(s) on potatoes (field), lettuce (field) and cucumbers (indoor). The estimation(s) is/are provided in the following sections.

FLC+PCH SC687.5 is a fungicide that is applied to various crops. Work activities are tasks like pruning/thinning or harvesting which are done by workers usually throughout the growing season. For some crops (potato) harvesting is fully automatized. For lettuce and cucumber harvesting may be manual or semi-manual operation. Re-entry exposure is therefore evaluated and compared with the AOEL of fluopicolide (FLC) and propamocarb-hydrochloride (PCH). Predicted exposures are calculated from a cumulative foliar deposit based on a maximum number of applications made at the maximum dose and 8 hours contact with foliage per day. Systemic exposure values are calculated using worst case dermal absorption values.

Potatoes
The AOEM EFSA calculator has been used to estimate exposure to workers for crop inspection and irrigation activities. The following assumptions were made:
### Table 7.2.3-01: Input parameters considered for the estimation of worker exposure for potatoes

<table>
<thead>
<tr>
<th><strong>AOEM EFSA calculator</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product name and code</strong></td>
<td><strong>FLC+PCH SC 687.5</strong></td>
</tr>
<tr>
<td><strong>Formulation type</strong></td>
<td>SC soluble or suspension concentrate</td>
</tr>
<tr>
<td><strong>Category</strong></td>
<td>Fungicide</td>
</tr>
<tr>
<td><strong>Crop type</strong></td>
<td>Potatoes</td>
</tr>
<tr>
<td><strong>Indoor/outdoor</strong></td>
<td>Outdoor</td>
</tr>
<tr>
<td><strong>DT50</strong></td>
<td>30 days</td>
</tr>
<tr>
<td><strong>DFR</strong></td>
<td>3 μg/cm²</td>
</tr>
<tr>
<td><strong>Buffer strip</strong></td>
<td>2-3 metres</td>
</tr>
<tr>
<td><strong>Number of applications</strong></td>
<td>1-4</td>
</tr>
<tr>
<td><strong>Interval between multiple applications</strong></td>
<td>7 days</td>
</tr>
<tr>
<td><strong>Work rate per day</strong></td>
<td>2 hours/day</td>
</tr>
<tr>
<td><strong>Active substance(s) (incl. content)</strong></td>
<td></td>
</tr>
<tr>
<td>Fluopicolide (FLC)</td>
<td>62.5 g/L</td>
</tr>
<tr>
<td>Propamocarb (PCH)</td>
<td>625 g/L</td>
</tr>
<tr>
<td><strong>Maximum application rate of active substance</strong></td>
<td></td>
</tr>
<tr>
<td>Fluopicolide (FLC)</td>
<td>0.1 kg/ha</td>
</tr>
<tr>
<td>Propamocarb (PCH)</td>
<td>1 kg/ha</td>
</tr>
<tr>
<td><strong>AOEL systemic</strong></td>
<td>0.07 mg/kg bw/day</td>
</tr>
<tr>
<td>AAOEL</td>
<td>none</td>
</tr>
<tr>
<td><strong>Inhalation absorption</strong></td>
<td>100%</td>
</tr>
<tr>
<td><strong>Oral absorption</strong></td>
<td>100%</td>
</tr>
<tr>
<td><strong>Dermal absorption</strong></td>
<td></td>
</tr>
<tr>
<td>Fluopicolide (FLC)</td>
<td>13% (worst case)</td>
</tr>
<tr>
<td>Propamocarb (PCH)</td>
<td>8.6% (worst case)</td>
</tr>
</tbody>
</table>

The scenario of inspection and irrigation in low crops was assessed and the defaults settings of the EFSA calculator were used with no refinements. The following sections show the summary results from the calculator. An attached appendix 2 depicts the related full output pages from the calculator.
Document MCP – Section 7: Toxicological studies
Fluopicolide + Propamocarb-hydrochloride SC 687.5

Table 7.2.3-02: Estimated worker exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on potatoes

<table>
<thead>
<tr>
<th>Model data</th>
<th>Level of PPE</th>
<th>Fluopicolide</th>
<th>Propamocarb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total absorbed dose (mg/kg bw/day)</td>
<td>% of AOEL</td>
<td>Total absorbed dose (mg/kg bw/day)</td>
</tr>
<tr>
<td>Potato Field Crop Application, worker inspection, irrigation 2 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and 1.0 kg/ha PCH)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight 60 kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 applications a crop, 7 days between applications*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### AOEM longer term systemic exposure

- **Potential exposure (no clothing)**
  - Fluopicolide: 0.0518 mg/kg bw/day, 74.05% of AOEL
  - Propamocarb: 0.03429 mg/kg bw/day, 118.25% of AOEL

- **Workwear covering arms, body, and legs**
  - Fluopicolide: 0.0058 mg/kg bw/day, 8.29% of AOEL
  - Propamocarb: 0.0384 mg/kg bw/day, 13.24% of AOEL

* This scenario is worst case so also applies to the following application rates:
  3 applications a crop, 7 days between applications
  2 applications a crop, 7 days between applications

Lettuce

The AOEM EFSA calculator has been used to estimate exposure to workers for reaching and picking. The following assumptions were made:
Table 7.2.3-03: Input parameters considered for the estimation of worker exposure for lettuces

<table>
<thead>
<tr>
<th>AOEM EFSA calculator</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Product name and code</td>
<td>FLC+PCH SC 687.5</td>
<td></td>
</tr>
<tr>
<td>Formulation type</td>
<td>SC soluble or suspension concentrate</td>
<td></td>
</tr>
<tr>
<td>Category</td>
<td>Fungicide</td>
<td></td>
</tr>
<tr>
<td>Crop type</td>
<td>Lettuces</td>
<td></td>
</tr>
<tr>
<td>Indoor/outdoor</td>
<td>Outdoor</td>
<td></td>
</tr>
<tr>
<td>DT50</td>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td>DFR</td>
<td>3 μg/cm²</td>
<td></td>
</tr>
<tr>
<td>Buffer strip</td>
<td>2-3 metres</td>
<td></td>
</tr>
<tr>
<td>Number of applications</td>
<td>1-2</td>
<td></td>
</tr>
<tr>
<td>Interval between multiple applications</td>
<td>7 days</td>
<td></td>
</tr>
<tr>
<td>Work rate per day</td>
<td>8 hours/day</td>
<td></td>
</tr>
<tr>
<td>Active substance(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(incl. content)</td>
<td>Fluopicolide (FLC) 62.5 g/L</td>
<td>Propamocarb (PCH) 625 g/L</td>
</tr>
<tr>
<td>Maximum application rate of active substance</td>
<td>0.1 kg/ha</td>
<td>1 kg/ha</td>
</tr>
<tr>
<td>AOEL systemic</td>
<td>0.07 mg/kg bw/day</td>
<td>0.29 mg/kg bw/day</td>
</tr>
<tr>
<td>AAOEL</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>Inhalation absorption</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Oral absorption</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Dermal absorption</td>
<td>Dilation: 13% (worst case)</td>
<td>Dilation: 8.6% (worst case)</td>
</tr>
</tbody>
</table>

The scenario of workers reaching and picking in low crops was assessed and the defaults settings of the EFSA calculator were used with no refinements. The following sections show the summary results from the calculator. An attached appendix 2 depicts the related full output pages from the calculator.
### Table 7.2.3-04: Estimated worker exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on lettuces

<table>
<thead>
<tr>
<th>Model data</th>
<th>Level of PPE</th>
<th>Fluopicolide</th>
<th>Propamocarb</th>
<th>Total absorbed dose (mg/kg bw/day)</th>
<th>% of AOEL</th>
<th>Total absorbed dose (mg/kg bw/day)</th>
<th>% of AOEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lettuce Field Crop Application, worker reaching and picking 8 hours</td>
<td></td>
<td></td>
<td></td>
<td>% of AOEL</td>
<td></td>
<td>% of AOEL</td>
<td></td>
</tr>
<tr>
<td>Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and 1.0 kg/ha PCH)</td>
<td>Body weight 60 kg</td>
<td></td>
<td></td>
<td>% of AOEL</td>
<td></td>
<td>% of AOEL</td>
<td></td>
</tr>
<tr>
<td>2 applications a crop, 7 days between applications*</td>
<td></td>
<td></td>
<td></td>
<td>% of AOEL</td>
<td></td>
<td>% of AOEL</td>
<td></td>
</tr>
</tbody>
</table>

| Potential exposure (no clothing) | 0.0558 | 79.74 | 0.3692 | 127.33 |
| Workwear covering arms, body, and legs | 0.0241 | 34.39 | 0.1592 | 54.88 |
| Workwear covering arms, body and legs and protective gloves | 0.0056 | 7.90 | 0.0369 | 12.73 |

* This scenario is worst case so also applies to the following application rates:
1 application a crop

**Cucumbers**

The AOEM EFSA calculator has been used to estimate exposure to workers where the product is applied to cucumbers in glasshouses assuming the roof-fogger as the worst-case for indoor application method. The following assumptions are made.
### Table 7.2.3-05: Input parameters considered for the estimation of operator exposure for cucumbers grown under glass

<table>
<thead>
<tr>
<th>AOEM EFSA calculator</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Product name and code</strong></td>
<td>FLC+PCH SC 687.5</td>
</tr>
<tr>
<td><strong>Formulation type</strong></td>
<td>SC soluble or suspension concentrate</td>
</tr>
<tr>
<td><strong>Category</strong></td>
<td>Fungicide</td>
</tr>
<tr>
<td><strong>Crop type</strong></td>
<td>Cucumber</td>
</tr>
<tr>
<td><strong>Indoor/outdoor</strong></td>
<td>Indoor</td>
</tr>
<tr>
<td><strong>DT50</strong></td>
<td>30 days</td>
</tr>
<tr>
<td><strong>DFR</strong></td>
<td>3 μg/cm²</td>
</tr>
<tr>
<td><strong>Number of applications</strong></td>
<td>1-3</td>
</tr>
<tr>
<td><strong>Interval between multiple applications</strong></td>
<td>7 days</td>
</tr>
<tr>
<td><strong>Work rate per day</strong></td>
<td>8 hours/day</td>
</tr>
<tr>
<td><strong>Active substance(s) (incl. content)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fluopicolide (FLC) 62.5 g/L</td>
</tr>
<tr>
<td></td>
<td>Propamocarb (PCH) 125 g/L</td>
</tr>
<tr>
<td><strong>Maximum application rate of active substance</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.1 kg/ha</td>
</tr>
<tr>
<td></td>
<td>1 kg/ha</td>
</tr>
<tr>
<td><strong>AOEL systemic</strong></td>
<td>0.07 mg/kg bw/day</td>
</tr>
<tr>
<td></td>
<td>0.29 mg/kg bw/day</td>
</tr>
<tr>
<td><strong>AAOEL</strong></td>
<td>none</td>
</tr>
<tr>
<td></td>
<td>none</td>
</tr>
<tr>
<td><strong>Inhalation absorption</strong></td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
</tr>
<tr>
<td><strong>Oral absorption</strong></td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>100%</td>
</tr>
<tr>
<td><strong>Dermal absorption</strong></td>
<td>Concentrate: 0.26% Dilution: 16%</td>
</tr>
<tr>
<td></td>
<td>Concentrate: 2% Dilution: 8.6%</td>
</tr>
</tbody>
</table>

The scenario of reaching and picking fruiting vegetables in glasshouse crops was assessed and the defaults settings of the EFSA calculator was used with no refinements. The following sections show the summary results from the calculator. An attached appendix 2 depicts the related full output pages from the calculator.
Table 7.2.3-06: Estimated worker exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on lettuces

<table>
<thead>
<tr>
<th>Model data</th>
<th>Level of PPE</th>
<th>Fluopicolide</th>
<th>Propamocarb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Total absorbed dose (mg/kg bw/day)</td>
<td>% of AOEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cucumber Glasshouse Application - Roof fogger, worker reaching and picking 8 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and 1.0 kg/ha PCH)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight 60 kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 applications a crop, 7 days between applications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potential exposure (no clothing)</td>
<td></td>
<td>0.976</td>
<td>139.37</td>
</tr>
<tr>
<td>Workwear covering arms, body, and legs</td>
<td></td>
<td>0.0432</td>
<td>61.70</td>
</tr>
<tr>
<td>Workwear covering arms, body, and legs and protective gloves</td>
<td>0.0116</td>
<td>16.51</td>
<td>0.1156</td>
</tr>
</tbody>
</table>

Overall conclusion on worker exposure

Exposure estimates predict acceptable risks for workers for all intended uses of FLC+PCH SC 687.5, provided normal workwear covering arms, body and legs are worn for outdoor uses on potatoes or lettuce. For glasshouse use acceptable exposure on cucumbers requires workwear covering arms, body and legs and protective gloves to be worn.

CP 7.2.3.2 Measurement of worker exposure

Not considered to be necessary, as a safe use was predicted in the previous section.

The following study has been conducted to determine the dislodgeable foliar reside of fluopicolide and propamocarb on cucumbers. The study may be used to refine the default DFR.
### Executive Summary:

The GLP study is valid and acceptable to determine the dislodgeable foliar residue (DFR) of fluopicolide and propamocarb on cucumber leaves from a glasshouse study conducted in Italy. Under the conditions of this study, the mean (geometric) DFR on cucumber leaves was 1.1 μg/cm² per kg a.s./ha for fluopicolide and 0.2 μg/cm² per kg a.s./ha for propamocarb. The DFR from this study may be used to refine the default DFR value in exposure assessments if a higher tier assessment is required.

### I. Material and Methods

#### A. Materials

1. **Test material**
   - **Test substance:** Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)
   - **Purity:** Fluopicolide 62.5 g/L, Propamocarb 625 g/L
   - **Batch no.:** EV5000993

#### B. Study design

The study consisted of one field trial in a glasshouse in Italy.

1. **Trial dates, location, crop and plot size**

<table>
<thead>
<tr>
<th>Location</th>
<th>I-00050 Palidoro-Fiumicino, Italy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of trial</td>
<td>Indoor, glasshouse</td>
</tr>
<tr>
<td>Crop</td>
<td>Cucumber, Marketmore</td>
</tr>
<tr>
<td>Date of planting</td>
<td>12-09-2012</td>
</tr>
<tr>
<td>Date of harvest</td>
<td>01-10 to 30-11 2012</td>
</tr>
<tr>
<td>Number of plants per ha</td>
<td>11110</td>
</tr>
<tr>
<td>Soil</td>
<td>Sand</td>
</tr>
</tbody>
</table>
2. Application conditions

<table>
<thead>
<tr>
<th>Application type</th>
<th>Spraying</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nozzle type</td>
<td>Albuz AVI ISO 11003, size 110 03</td>
</tr>
<tr>
<td>Pressure</td>
<td>5.0 bar</td>
</tr>
<tr>
<td>Date of application</td>
<td>05-10-2012, 15-10-2012 and 25-10-2012 (3 applications with 10-day interval between spraying)</td>
</tr>
<tr>
<td>Water</td>
<td>750 L/ha</td>
</tr>
<tr>
<td>Crop height</td>
<td>0.45, 0.8, and 1.2 meters at 1&lt;sup&gt;st&lt;/sup&gt;, 2&lt;sup&gt;nd&lt;/sup&gt;, and 3&lt;sup&gt;rd&lt;/sup&gt; application respectively</td>
</tr>
<tr>
<td>Application rate</td>
<td>0.125 kg/ha fluopicolide, 1.25 kg/ha propamocarb</td>
</tr>
<tr>
<td>Concentration of active substance (%) in spray dilution</td>
<td>0.0167% fluopicolide, 0.167% propamocarb</td>
</tr>
<tr>
<td>Growth stage [BBCH]</td>
<td>61, 63, 71 at 1&lt;sup&gt;st&lt;/sup&gt;, 2&lt;sup&gt;nd&lt;/sup&gt;, and 3&lt;sup&gt;rd&lt;/sup&gt; applications respectively</td>
</tr>
<tr>
<td>Air temperature °C</td>
<td>30, 25, 30 at 1&lt;sup&gt;st&lt;/sup&gt;, 2&lt;sup&gt;nd&lt;/sup&gt;, and 3&lt;sup&gt;rd&lt;/sup&gt; applications respectively</td>
</tr>
<tr>
<td>Relative humidity [%]</td>
<td>36, 43, 43 at 1&lt;sup&gt;st&lt;/sup&gt;, 2&lt;sup&gt;nd&lt;/sup&gt;, and 3&lt;sup&gt;rd&lt;/sup&gt; applications respectively</td>
</tr>
</tbody>
</table>

3. Leaf sample collections

Leaf punches were collected using a leaf punch sampler. Each sample consisted of 40 disks of 2.523 cm diameter and a disk area of 5cm². A sample was collected from each of the three sub-plots to provide three replicates of each sampling date. Leaf punches were taken from upper, middle and lower portions of the foliage and interior and exterior positions. Control punch samples were taken prior to the first product application. After the first treatment samples were first taken on the day of application after the spray had dried.

4. Dislodgeable residue collection

Dislodging was performed not later than 4 hours after sample collection. Samples were dislodged by adding 100 mL of a 0.01% aqueous solution of Aerosol OT (a docusate sodium salt surfactant) to the jars containing the leaf punch samples. These were placed on a shaker for 10 minutes. The solution was decanted, and the process repeated by adding a fresh sample of dislodging solution to the leaf samples. Each final dislodged sample consisted of 200 mL of dislodging solution.

5. Control and field recovery samples

Unspiked untreated control samples were collected using the same method as for the treated leaf samples.

Spiked samples were used to demonstrate stability of the samples during the study and the ability of the analytical method to recover an analyte. For spiked samples, fluopicolide and propamocarb were applied in the field and leaf samples collected prior to the first spray application. Spikes were 0.01, 0.1 and 1.0 μg/cm² of test substance (corresponding to 20, 200 and 2000 μg/L respectively). Dislodgeable residue was collected from the leaves in the same manner as described for treated crop.
control samples of dislodged residue solution were also spiked. Three replicate samples were collected for each spike.

6. Analytical method
The method was by Stuke, S. and Diehl, P. (2013), method number 01353.
Acetonitrile and an internal standard solution were added to samples, the samples were filtered and analyzed by HPLC-MS/MS. The limit of quantification (LoQ) was set to 20 μg/L.

II. Results and Discussion
No residues above the LoQ were found in the control samples. Spiked leaf wash sample recoveries showed acceptability of the analytical method. For fluopicolide mean recovery was 93% at the LOQ of 0.01 μg/cm². For propamocarb mean recovery was 98% at the LOQ of 0.01 μg/cm².
Mean recovery of spiked field samples were 92% and 83% for fluopicolide and propamocarb respectively which is within acceptability criteria (of 70 to 110%). Relative standard deviation was 11.5% for fluopicolide and 12.8% for propamocarb samples with is within acceptable levels (of ≤ 20%).
The residues from field samples are shown in the table below. To convert to DFR a correction for the application rate the values of the DFR are expressed in μg/cm² per kg a.s./ha.

<table>
<thead>
<tr>
<th>DA1.T</th>
<th>DA2.T</th>
<th>DA3.T</th>
<th>Fluopicolide μg/cm²</th>
<th>DFR Fluopicolide μg/cm² per kg a.s./ha</th>
<th>Propamocarb μg/cm²</th>
<th>DFR Propamocarb μg/cm² per kg a.s./ha</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td>0.373</td>
<td>2.844</td>
<td>0.150</td>
<td>2.52</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>0.262</td>
<td>2.096</td>
<td>0.130</td>
<td>1.096</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>0.260</td>
<td>1.844</td>
<td>0.277</td>
<td>0.2216</td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td>0.084</td>
<td>0.652</td>
<td>0.075</td>
<td>0.06</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td>0.018</td>
<td>0.144</td>
<td>0.018</td>
<td>0.0144</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
<td></td>
<td>0.289</td>
<td>1.312</td>
<td>1.825</td>
<td>1.46</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
<td></td>
<td>0.283</td>
<td>1.704</td>
<td>0.562</td>
<td>0.4496</td>
</tr>
<tr>
<td>13</td>
<td>3</td>
<td></td>
<td>0.184</td>
<td>1.472</td>
<td>0.180</td>
<td>0.144</td>
</tr>
<tr>
<td>17</td>
<td>7</td>
<td></td>
<td>0.099</td>
<td>0.672</td>
<td>0.061</td>
<td>0.0488</td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td></td>
<td>0.038</td>
<td>0.304</td>
<td>0.020</td>
<td>0.016</td>
</tr>
<tr>
<td>20</td>
<td>10</td>
<td>0</td>
<td>0.228</td>
<td>1.824</td>
<td>1.312</td>
<td>1.0496</td>
</tr>
<tr>
<td>21</td>
<td>11</td>
<td>1</td>
<td>0.183</td>
<td>1.464</td>
<td>0.410</td>
<td>0.328</td>
</tr>
<tr>
<td>23</td>
<td>13</td>
<td>3</td>
<td>0.142</td>
<td>1.128</td>
<td>0.188</td>
<td>0.1504</td>
</tr>
<tr>
<td>27</td>
<td>17</td>
<td>7</td>
<td>0.019</td>
<td>0.952</td>
<td>0.212</td>
<td>0.1696</td>
</tr>
<tr>
<td>34</td>
<td>24</td>
<td>14</td>
<td>0.079</td>
<td>0.632</td>
<td>0.060</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Geometric Mean: 0.134, 1.072, 0.239, 0.191

DA(1.1)T = Days after (first) treatment.
DA(2.1)T = Days after (second) treatment.
DA(3.1)T = Days after (third) treatment; LOQ = 0.01 μg/cm².
Application rate was 0.125 kg/ha fluopicolide and 1.25 kg/ha propamocarb.

The mean DFR was 1.1 μg/cm² per kg a.s./ha for fluopicolide and 0.2 μg/cm² per kg a.s./ha for propamocarb. This value may be used to refine worker exposure assessments if a higher-tier exposure assessment is required.
III. Conclusion

Under the conditions of this study, the mean DFR for fluopicolide was 1.1 μg/cm² per kg a.s./ha and the mean DFR for propamocarb was 0.2 μg/cm² per kg a.s./ha. This value may be used to refine worker exposure assessments if a higher tier exposure assessment is required.

Assessment and conclusion by applicant:

The GLP study is valid and acceptable to determine the dislodgeable foliar residue (DFR) of fluopicolide and propamocarb on cucumber leaves. Under the conditions of this study, the mean DFR for fluopicolide was 1.1 μg/cm² per kg a.s./ha and the mean DFR for propamocarb was 0.2 μg/cm² per kg a.s./ha. This value may be used to refine worker exposure assessments if a higher tier exposure assessment is required.

Combined exposure

The product is a mixture of two active substances. Therefore, a combined exposure assessment is provided. Only a long-term combined exposure assessment is required as propamocarb and fluopicolide are not acutely toxic. At the first tier, combined exposure is calculated as the sum of the component exposures without regard to the mode of action or mechanism/target of toxicity. Initially, the individual Hazard Quotients (HQ) are calculated for all active substances in the PPP by assessing the exposure according to appropriate models and dividing the individual exposure levels by the respective systemic AOEL/RVNAS. This is equivalent to the predicted exposure as % of systemic AOEL/RVNAS to decimal. The Hazard Index (HI) is the sum of the individual HQs.

Table 7.2.3-08: Long-term risk assessment from combined exposure to fluopicolide and propamocarb on potatoes

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Active Substance</th>
<th>Estimated exposure / AOEL (RVNAS) (HQ)³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crop: Potatoes (Field)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application rate: 4 kg/ha fluopicolide / 1 kg/ha propamocarb applied by vehicle-mounted sprayer</td>
<td>Fluopicolide</td>
<td>0.0365</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Propamocarb</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cumulative risk Operators (HI)²</td>
</tr>
<tr>
<td>Operators, normal workwear,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For details please refer to 7.2.1. Only the worst-case scenario is presented</td>
<td>Fluopicolide</td>
<td>0.0562</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Propamocarb</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cumulative risk Resident-Adult (HI)²</td>
</tr>
<tr>
<td>Resident – Adult</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For details please refer to 7.2.2. Only the worst-case scenario is presented</td>
<td>Fluopicolide</td>
<td>0.1317</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Propamocarb</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cumulative risk Resident-Child (HI)²</td>
</tr>
<tr>
<td>Resident – Child</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For details please refer to 7.2.2. Only the worst-case scenario is presented</td>
<td>Fluopicolide</td>
<td>0.0829</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Propamocarb</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cumulative risk Workers (HI)²</td>
</tr>
</tbody>
</table>

Workers, with Workwear

For details please refer to 7.2.3. Only the worst-case scenario is presented
The higher exposure value either from the 75th percentile of each of the four pathways (spray drift, vapour, surface deposits, entry into treated crops) or the sum of the mean exposure values is taken into consideration.

HI = Hazard Index
HQ = Hazard Quotient

For potato uses the Hazard Index is < 1. Therefore, the combined exposure to all active substances in FLC+PCH SC 687.5 is not expected to present a risk for operators, workers, bystanders, and residents. No further refinement of the assessment is required.

Table 7.2.3-09: Long-term risk assessment from combined exposure to fluopicolide and propamocarb on lettuces

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Active Substance</th>
<th>Estimated exposure / AOEL (RVNAS) (HQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crop: Lettuces (Field)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application rate: 0.1 kg/ha fluopicolide / 1 kg/ha propamocarb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Applied by manual hand-held sprayer</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Operators, normal workwear</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For details please refer to 7.2.1. Only the worst-case scenario is presented</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluopicolide</td>
<td>0.3321</td>
<td></td>
</tr>
<tr>
<td>Propamocarb</td>
<td>0.1587</td>
<td></td>
</tr>
<tr>
<td><strong>Cumulative risk Operators (HI)</strong></td>
<td>0.4908</td>
<td></td>
</tr>
<tr>
<td><strong>Resident – Adult</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For details please refer to 7.2.2. Only the worst case scenario is presented</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluopicolide</td>
<td>0.0335</td>
<td></td>
</tr>
<tr>
<td>Propamocarb</td>
<td>0.0491</td>
<td></td>
</tr>
<tr>
<td><strong>Cumulative risk Resident-Adult (HI)</strong></td>
<td>0.0826</td>
<td></td>
</tr>
<tr>
<td><strong>Resident – Child</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For details please refer to 7.2.2. Only the worst-case scenario is presented</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluopicolide</td>
<td>0.0806</td>
<td></td>
</tr>
<tr>
<td>Propamocarb</td>
<td>0.1094</td>
<td></td>
</tr>
<tr>
<td><strong>Cumulative risk Resident-Child (HI)</strong></td>
<td>0.1900</td>
<td></td>
</tr>
<tr>
<td><strong>Workers, with Workwear</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For details please refer to 7.2.3. Only the worst case scenario is presented</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluopicolide</td>
<td>0.3437</td>
<td></td>
</tr>
<tr>
<td>Propamocarb</td>
<td>0.5488</td>
<td></td>
</tr>
<tr>
<td><strong>Cumulative risk Workers (HI)</strong></td>
<td>0.8925</td>
<td></td>
</tr>
</tbody>
</table>

For lettuce uses, the Hazard Index is < 1. Therefore, the combined exposure to all active substances in FLC+PCH SC 687.5 is not expected to present a risk for operators, workers, bystanders, and residents. No further refinement of the assessment is required.
Table 7.2.3-10: Long-term risk assessment from combined exposure to fluopicolide and propamocarb on cucumbers

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Active Substance</th>
<th>Estimated exposure / AOEL (RVNAS) (HQ)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crop: Cucumbers (Indoor)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Application rate</strong>: 0.1 kg/ha fluopicolide / 1 kg/ha propamocarb</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Applied by manual-knapsack sprayer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operators, with gloves and coveralls during mixing and loading and application.</td>
<td>Fluopicolide</td>
<td>0.02</td>
</tr>
<tr>
<td>For details please refer to 7.2.1. Only the worst-case scenario is presented</td>
<td>Propamocarb</td>
<td>0.156</td>
</tr>
<tr>
<td><strong>Cumulative risk Operators (HI)</strong></td>
<td></td>
<td>0.256</td>
</tr>
<tr>
<td>Resident – Adult¹</td>
<td>Fluopicolide</td>
<td>N/A</td>
</tr>
<tr>
<td>For details please refer to 7.2.2. Only the worst-case scenario is presented</td>
<td>Propamocarb</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Cumulative risk Resident-Adult (HI)</strong></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Resident – Child¹</td>
<td>Fluopicolide</td>
<td>N/A</td>
</tr>
<tr>
<td>For details please refer to 7.2.2. Only the worst-case scenario is presented</td>
<td>Propamocarb</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Cumulative risk Resident-Child (HI)</strong></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>Workers, with workwear and protective gloves</td>
<td>Fluopicolide</td>
<td>0.1651</td>
</tr>
<tr>
<td>For details please refer to 7.2.3. Only the worst-case scenario is presented</td>
<td>Propamocarb</td>
<td>0.2461</td>
</tr>
<tr>
<td><strong>Cumulative risk Worker (HI)</strong></td>
<td></td>
<td>0.4112</td>
</tr>
</tbody>
</table>

¹ The higher exposure value either from the 75th percentile of each of the four pathways (spray drift, vapour, surface deposits, entry into treated crops) or the sum of the mean exposure values is taken into consideration

2 HI = Hazard Index
3 HQ = Hazard Quotient

For lettuce uses the Hazard Index is < 1. Therefore, the combined exposure to all active substances in FLC+PCH SC 687.5 is not expected to present a risk for operators, workers, bystanders, and residents. No further refinement of the assessment is required.

**Overall conclusion on combined exposure**

Exposure estimates predict acceptable risk for operators, residents, and workers for all intended uses of FLC+PCH SC 687.5 from combined long-term exposure to fluopicolide and propamocarb. Propamocarb and fluopicolide are not acutely toxic therefore a combined acute exposure risk assessment is not needed.
**CP 7.3**

**Dermal adsorption**

**Fluopicolide**

A summary of the dermal absorption rates for fluopicolide in the fluopicolide + propamocarb hydrochloride SC 687.5 (62.5+625 g/L) (also named FLC+PCH SC 687.5) formulation is presented in the following table.

**Table 7.3-1: Dermal absorption rates for fluopicolide in FLC+PCH SC 687.5**

<table>
<thead>
<tr>
<th>Concentrate</th>
<th>Value (% of dose applied)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluopicolide</td>
<td>0.26%</td>
</tr>
</tbody>
</table>

**Dilution (dilution factor)**

<table>
<thead>
<tr>
<th>Dilution</th>
<th>Value (% @ 0.25 g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1%</td>
<td></td>
</tr>
</tbody>
</table>

**Justification for proposed values – Fluopicolide**

The proposed dermal absorption rates for fluopicolide are based on an *in vitro* human skin dermal absorption study using the FLC+PCH SC 687.5 formulation. The study results are summarized in the following table. A summary of the study considering the human skin absorption is described in detail below. The absorption through rat skin is not described in this summary because it will not be used for non-dietary human exposure assessment.

**Table 7.3-2: Summary of the results of submitted dermal absorption studies for Fluopicolide**

<table>
<thead>
<tr>
<th>Test</th>
<th>Concentrate</th>
<th>Spray dilution (dilution factor)</th>
<th>Formulation in study</th>
<th>Justification provided on representativity of study formulation for current product</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>In vitro (rat/human)</td>
<td>Human: 0.26%</td>
<td>Human: 5.1% (1 in 250)</td>
<td>FLC+PCH SC 687.5</td>
<td>Not required</td>
<td>M-222382-01-1 2003.</td>
</tr>
</tbody>
</table>

**Data Point:** KCP 7.3/01

**Report Author:**

**Report Year:** 2003

**Report Title:** (14C)-EXP 120A: Comparative in vitro dermal penetration study using human and rat skin

**Report No:** C03721

**Document No:** M-222382-01-1

**Guideline(s) followed in study:** EU Directive 91/414/EEC Annex III, Section 7.3; OECD 417, 428 (draft) (2002)

**Deviations from current test guideline:**

**Previous Evaluation:** yes, evaluated and accepted DAR (2005)

**GLP/Officially recognised testing facilities:** Yes, conducted under GLP/Officially recognised testing facilities

**Acceptability/Reliability:** Yes
Material and methods:

**Rat:**
- Species, strain: Rat, Sprague-Dawley CD
- Source: Charles River (UK) Ltd, Margate, Kent, UK.
- Sex: Male
- Number: 6
- Anatomical site: Dorsal

Skin Preparation:
Each rat (identified by tail mark) was killed by cervical dislocation or overdose of carbon dioxide. After sacrifice, the rat was shaved with electric clippers and the skin removed. Connective tissue, blood and any residual fat were removed from the dermis using absorbent tissue. The resulting full thickness skin membrane was then wiped briefly with 70% ethanol/water to remove residual fat and blood, wiped dry and rehydrated with distilled water ready for dermatoming. A mini dermatome was used to cut slices of skin which contained epidermis and some dermis.

**Human skin:**
- Source: International Institute for the Advancement of Medicine, USA
- Number and sex: 2 donors, female
- Anatomical region: Back
- Thickness: approximately 300 µm

**Test Material:**
- Non-radiolabelled:
  - Batch: PAN02/02
  - Purity = 99.3% w/w.
- Radiolabelled:
  - Phenyl-U-14C-fluopicolide
  - Batch: SEL/1200
  - Specific activity: 5.50 MBq/mg
  - Radiopurity of the formulation: 99.8%

**Formulation:**
The formulation used in this experiment was the Fluopicolide + propamocarb hydrochloride 687.5 formulation (EXP11120A, specification N°10200011064) containing fluopicolide at a concentration of 62.5 g/L. It was used at two nominal concentrations of fluopicolide: neat, 62.5 g/L and 0.25 g/L. The same formulations were used concurrently in the in vivo dermal study BAG/369.

**Test system:**
The Scott-Dick flow-through diffusion cell (Lockley, Roper, Howes and Williams, 1997) was constructed from stainless steel and permitted the contents of the receptor chamber to be continuously stirred. The skin membranes were maintained at approximately 32°C using a water-heated manifold. The flowrate of 1.5 mL/hr allowed approximately 6 receptor chamber content changes per hour. The receptor fluid used was physiological saline, supplemented 5% w/v with bovine serum albumin, adjusted to pH 7.4. Skin samples were cut from the dermatomed slice and placed onto the receptor chamber of the flow-through diffusion cell. The donor chamber was then fixed in place providing an exposure area of 0.64 cm² skin and the assembled diffusion cell inserted in-line in the flow-through set-up. The receptor chamber was warmed by a constant circulation of warm water which maintained the receptor fluid at 32 ± 2°C (close to the normal skin temperature). The receptor fluid was pumped through the receptor chamber at a rate of 1.5 mL/hr and stirred continuously whilst in the receptor chamber by means of a magnetic bar.
Skin integrity:

The integrity of the selected skin samples was estimated by measuring the penetration of tritiated water ($^3$H$_2$O) through each membrane prior to application of [14C]-fluopicolide. An aliquot (250 µL, occluded) was applied to the surface of the skin membrane and the lower chamber perfused with distilled water at a flow rate of approximately 1.5 mL/hr and eluant collected at 30-minute intervals. After 5 hours, residual $^3$H$_2$O on the surface of the membrane was removed, the surface washed with distilled water, and residual $^3$H$_2$O removed by priming the upper chamber with distilled water and perfusing the lower chamber with distilled water overnight.

Tritiated water was used as an indicator for the skin membranes, as a number of the samples fulfilled the exclusion criterion of having a permeability coefficient of less than 3.0 x 10$^{-3}$ cm/hr. On examination of the fluopicolide absorption data from skin membranes with Kp values greater than 3.0 x 10$^{-3}$ cm/hr, it was considered that if the total absorption and absorption profiles were similar to those of membranes with Kp values of less than 3.0 x 10$^{-3}$ cm/hr, in the same group, the data from these cells would be acceptable.

Two human cells (cells 4 and 7) from the high dose, Group 1 and one cell (cell 7) from the human low dose group, Group 3 as the Kp values were greater than 3.0 x 10$^{-3}$ cm/hr.

Cells 12 and 13 from the rat high dose group (group 2) were excluded because of poor recoveries of radioactivity.

Treatment:

Prior to dosing, the flow-rate was checked (approximately 1.5 mL/hr) by weighing the receptor fluid passed over a measured period of time and adjusted accordingly. Samples of receptor fluid were taken and analysed for background radioactivity (residual tritiated water). All cells used had acceptably low radioactivity levels (< 50 dpm) in the receptor fluid prior to dosing.

The dose preparation was applied to the skin membrane with a calibrated positive displacement pipette at the rate of approximately 10 µL/cm$^2$ exposed skin area (6.4 µL dose, un-occluded). The actual amount of [14C]-fluopicolide applied was determined using quality control (QC) checks taken before, during and after dosing each dose group.

Sampling:

The receptor fluid passing through the receptor chamber was collected into plastic scintillation vials held in a fraction collector. The fraction collector was moved on after dose application for each group was complete. Samples were then collected hourly for the duration of the experiment (24 hours).

At 8 hours after application, the skin was swabbed with 1% v/v Tween 80 in aqueous sodium chloride solution (0.9 g/L) until no further radioactivity was removed (confirmed with a Geiger-Müller mini-monitor).

At the end of the study, the skin membranes were tape stripped using 3M Scotch “Magic” tape. The initial two tape strips (1 and 2) were collected separately into glass vials and represented residual surface (non-absorbed) dose. Subsequent tape strips containing the stratum corneum were pooled in batches of three and analysed separately (6 to 12 strips for human skin). The remaining skin was retained separately.
The receptor fluid remaining in the cell and outlet tubing at the end of the experiment was retained and analysed for mass balance purposes only. The diffusion cell components were also retained, washed and the washings analysed for mass balance purposes.

Radioassay:
The amounts of radioactivity in the various samples were determined by liquid scintillation counting (LSC).

Findings:
Fluopicolide was demonstrated to be sufficiently soluble in the receptor fluid to avoid any risk of back diffusion.

Measurements of the homogeneity of the three concentrations of formulation applied indicated that this was acceptable.

The study results are presented in the following table.

Table 7.3-3: Distribution of radioactivity at 24 hours after dose application of [14C]-fluopicolide in a SC 687.5 formulation at the rate of 62.5 g/L to human skin samples (All cells).

<table>
<thead>
<tr>
<th>Dose Level: 62.5 g/L</th>
<th>Distribution of radioactivity (% dose applied)</th>
<th>Group Human HD</th>
<th>K N°% 1.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor N°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cell N°</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin wash 8h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total swabs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total SC 1+SC 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Donor chamber</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL NON ABSORBED</td>
<td>100.02</td>
<td>82.87</td>
<td>94.60</td>
</tr>
<tr>
<td>Total skin</td>
<td>0.037</td>
<td>0.016</td>
<td>1.823</td>
</tr>
<tr>
<td>SC3-5</td>
<td>0.076</td>
<td>0.098</td>
<td>0.109</td>
</tr>
<tr>
<td>SC6-8</td>
<td>n.d.</td>
<td>n.d.</td>
<td>0.015</td>
</tr>
<tr>
<td>SC9-11</td>
<td>0.016</td>
<td>n.d.</td>
<td>0.088</td>
</tr>
<tr>
<td>SC12-15</td>
<td>0.048</td>
<td>n.d.</td>
<td>n.d.</td>
</tr>
<tr>
<td>TOTAL SC 3+</td>
<td>0.085</td>
<td>0.098</td>
<td>0.255</td>
</tr>
<tr>
<td>TOTAL DOSE SITE</td>
<td>0.191</td>
<td>0.108</td>
<td>0.264</td>
</tr>
<tr>
<td>Receptor fluid (0-24h)</td>
<td>0.006</td>
<td>0.015</td>
<td>0.007</td>
</tr>
<tr>
<td>%Ratio receptor 24h</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Residual receptor fluid</td>
<td>n.d.</td>
<td>n.d.</td>
<td>0.000</td>
</tr>
<tr>
<td>TOTAL DIRECT</td>
<td>0.006</td>
<td>0.015</td>
<td>0.007</td>
</tr>
</tbody>
</table>
Document MCP – Section 7: Toxicological studies
Flupicolid + Propamocarb-hydrochloride SC 687.5

<table>
<thead>
<tr>
<th>Dose Level: 62.5 g/L</th>
<th>Distribution of radioactivity (% dose applied)</th>
<th>Group Human HD N=5 K N° = 1.2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>POTENTIAL (dose site+ receptor)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.20 0.12 0.27 0.15 0.18 0.06</td>
<td></td>
</tr>
<tr>
<td></td>
<td>POTENTIAL (skin+ receptor)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.01 0.03 0.02 0.03 0.02 0.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TOTAL RECOVERY 100.02 82.99 94.77 95.67 91.26 92.8 6.4</td>
<td></td>
</tr>
</tbody>
</table>

Evaluation according to EFSA Guidance

- Absorption >75% within half of study duration?
  - No.
- Recovery <95%?
  - Correction needed

Total % Potentially Absorbable adjusted according to EFSA (2017)

- Mean (% dose site + % receptor) + (SD*1.2) = 0.25%

* Normalisation was applied to all values as no specific sample type appeared to be responsible for the lower than 95% recovery from any of the “absorbed” fractions. Most probably due to losses during the skin swabbing procedures or an over-estimate of the amount applied.

SD: standard deviation
n.d.: below limit of detection; n.s.: no sample; n.a: not applicable.

In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

The mean recovery of the cells is below 95% therefore the data were normalized for all cells except cell 1.

Table 7.3-4: Distribution of radioactivity at 24 hours after dose application of [14C]-flupicolid in a SC 687.5 formulation at the rates of 62.5 g/L to human skin samples (All cells), Normalized

<table>
<thead>
<tr>
<th>Dose Level: 62.5 g/L</th>
<th>Distribution of radioactivity (% dose applied)</th>
<th>Group Human HD N=5 K N° = 1.2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Donor N° H1 H1 H2 H2</td>
<td></td>
</tr>
<tr>
<td>N°</td>
<td>Female Female Female Female</td>
<td></td>
</tr>
<tr>
<td>Cell N°</td>
<td>1 5 6</td>
<td></td>
</tr>
<tr>
<td>Skin wash 8h</td>
<td>99.95 99.47 97.41 99.63 98.58</td>
<td>99.01 1.03</td>
</tr>
<tr>
<td>Total swabs</td>
<td>99.96 99.47 97.41 99.63 98.58</td>
<td>99.01 1.03</td>
</tr>
<tr>
<td>Total SC 1 + SC 2</td>
<td>907 0.39 2.30 0.22 1.26</td>
<td>0.85 0.94</td>
</tr>
<tr>
<td>TOTAL NON ABSORBED</td>
<td>100.02 99.86 99.72 99.85 99.84</td>
<td>99.86 0.11</td>
</tr>
<tr>
<td>Total Skin</td>
<td>0.006 0.012 0.009 0.013 0.013</td>
<td>0.01 0.00</td>
</tr>
<tr>
<td>SC 3x</td>
<td>0.076 0.118 0.114 0.090 0.093</td>
<td>0.10 0.02</td>
</tr>
<tr>
<td>6-8</td>
<td>n.d. n.d. 0.062 n.d. 0.039</td>
<td>0.02 0.03</td>
</tr>
<tr>
<td>9-11</td>
<td>0.061 n.d. 0.093 0.038 n.d.</td>
<td>0.04 0.04</td>
</tr>
<tr>
<td>12-15</td>
<td>0.048 n.d. n.d. n.d. n.d.</td>
<td>0.01 0.02</td>
</tr>
</tbody>
</table>
Fluopicolide + Propamocarb hydrochloride SC 687.5

Dose Level: 62.5 g/L

<table>
<thead>
<tr>
<th>Group Human HD</th>
<th>Distribution of radioactivity (% dose applied)</th>
<th>N= 5</th>
<th>K N° = 1.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL DOSE SITE</td>
<td>0.185 0.118 0.269 0.128 0.133</td>
<td>0.17</td>
<td>0.06</td>
</tr>
<tr>
<td>Receptor fluid (0 - 24h)</td>
<td>0.006 0.018 0.007 0.017 0.019</td>
<td>0.04</td>
<td>0.01</td>
</tr>
<tr>
<td>%Ratio receptor 12h/24h</td>
<td>n.a. n.a. n.a. n.a. n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Residual receptor fluid</td>
<td>n.d. n.d. 0.000 n.d. n.d.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>TOTAL DIRECT</td>
<td>0.01 0.02 0.01 0.02 0.02</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>POTENTIAL (dose site+ receptor)</td>
<td>0.197 0.148 0.286 0.157 0.165</td>
<td>0.19</td>
<td>0.09</td>
</tr>
<tr>
<td>POTENTIAL (skin+ receptor)</td>
<td>0.01 0.03 0.02 0.03 0.03</td>
<td>0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>TOTAL RECOVERY</td>
<td>100.02 100.00 100.00 100.00 100.00 100.00 100.00</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Evaluation according to EFSA Guidance

- Absorption >75% within half of study duration?
  - No. (include SC values)
- Recovery <95%?
  - Not applicable – data normalised

Total % Potentially Absorbable adjusted according to EFSA (2017): Mean (%dose site +%receptor) + (SD*1.2) = 0.26%

SD: standard deviation
n.d.: below limit of detection; n.s.: no sample; n.a: not applicable.
In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

Table 7.3-5: Distribution of radioactivity at 24 hours after dose application of [14C]-fluopicolide in a SC 687.5 formulation at the rates of 0.25 g/L to human skin samples (Reported cells).

<table>
<thead>
<tr>
<th>Dose Level: 0.25 g/L</th>
<th>Distribution of radioactivity (% dose applied)</th>
<th>Group Human HD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Donor N°</td>
<td>N= 6</td>
</tr>
<tr>
<td>H1</td>
<td>Cell N°</td>
<td>Female</td>
</tr>
<tr>
<td>Skin wash 8h</td>
<td>0.74</td>
<td>80.91</td>
</tr>
<tr>
<td>Total swabs</td>
<td>0.74</td>
<td>80.91</td>
</tr>
<tr>
<td>Total SC 1 + SC 2</td>
<td>1.33</td>
<td>4.96</td>
</tr>
<tr>
<td>Donor chamber</td>
<td>0.966</td>
<td>1.847</td>
</tr>
<tr>
<td>TOTAL NON-ABSORBED</td>
<td>83.03</td>
<td>87.72</td>
</tr>
<tr>
<td>Total skin</td>
<td>0.22</td>
<td>0.40</td>
</tr>
</tbody>
</table>
**Document MCP – Section 7: Toxicological studies**

**Fluopicolide + Propamocarb-hydrochloride SC 687.5**

### Table 7.3-6: Distribution of radioactivity at 24 hours after dose application of [14C]-fluopicolide in a SC 687.5 formulation at the rates of 0.25 g/L to human skin samples (All cells), Normalized

<table>
<thead>
<tr>
<th>Dose Level: 0.25 g/L</th>
<th>Distribution of radioactivity (% dose applied)</th>
<th>Group Human HD N° 6 K N° = 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N° 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>K N° = 1</td>
</tr>
<tr>
<td>SC3-5</td>
<td>1.151</td>
<td>0.985</td>
</tr>
<tr>
<td></td>
<td>0.843</td>
<td>1.734</td>
</tr>
<tr>
<td></td>
<td>2.395</td>
<td>0.904</td>
</tr>
<tr>
<td></td>
<td>1.36</td>
<td>0.61</td>
</tr>
<tr>
<td>SC6-8</td>
<td>0.259</td>
<td>0.230</td>
</tr>
<tr>
<td></td>
<td>0.235</td>
<td>0.413</td>
</tr>
<tr>
<td></td>
<td>1.003</td>
<td>0.695</td>
</tr>
<tr>
<td>SC9-11</td>
<td>0.155</td>
<td>0.266</td>
</tr>
<tr>
<td></td>
<td>0.332</td>
<td>0.135</td>
</tr>
<tr>
<td></td>
<td>0.288</td>
<td>0.349</td>
</tr>
<tr>
<td></td>
<td>0.25</td>
<td>0.09</td>
</tr>
<tr>
<td>SC12-15</td>
<td>n.s.</td>
<td>0.117</td>
</tr>
<tr>
<td></td>
<td>n.d.</td>
<td>n.s.</td>
</tr>
<tr>
<td></td>
<td>n.s.</td>
<td>0.142</td>
</tr>
<tr>
<td></td>
<td>0.142</td>
<td>0.07</td>
</tr>
<tr>
<td>TOTAL SC 3+</td>
<td>1.57</td>
<td>1.60</td>
</tr>
<tr>
<td></td>
<td>1.418</td>
<td>2.28</td>
</tr>
<tr>
<td></td>
<td>3.83</td>
<td>2.06</td>
</tr>
<tr>
<td></td>
<td>3.00</td>
<td>1.00</td>
</tr>
<tr>
<td>TOTAL DOSE SITE</td>
<td>1.78</td>
<td>2.00</td>
</tr>
<tr>
<td></td>
<td>2.00</td>
<td>2.75</td>
</tr>
<tr>
<td></td>
<td>4.48</td>
<td>2.38</td>
</tr>
<tr>
<td></td>
<td>2.56</td>
<td>1.00</td>
</tr>
<tr>
<td>Receptor fluid (0 - 24h)</td>
<td>0.621</td>
<td>0.899</td>
</tr>
<tr>
<td></td>
<td>1.818</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>1.160</td>
<td>0.010</td>
</tr>
<tr>
<td>%Ratio receptor 12h/24h</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Residual receptor fluid</td>
<td>0.009</td>
<td>0.021</td>
</tr>
<tr>
<td></td>
<td>0.039</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>0.006</td>
<td>0.02</td>
</tr>
<tr>
<td>Receptor chamber</td>
<td>n.d.</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>0.18</td>
<td>0.06</td>
</tr>
<tr>
<td>TOTAL DIRECT</td>
<td>0.63</td>
<td>1.12</td>
</tr>
<tr>
<td></td>
<td>0.916</td>
<td>0.946</td>
</tr>
<tr>
<td></td>
<td>0.62</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td>0.47</td>
<td>1.19</td>
</tr>
<tr>
<td>POTENTIAL (dose site+ receptor)</td>
<td>2.41</td>
<td>3.02</td>
</tr>
<tr>
<td></td>
<td>3.86</td>
<td>5.87</td>
</tr>
<tr>
<td></td>
<td>5.87</td>
<td>2.00</td>
</tr>
<tr>
<td>POTENTIAL (skin+ receptor)</td>
<td>1.52</td>
<td>1.45</td>
</tr>
<tr>
<td></td>
<td>1.39</td>
<td>0.91</td>
</tr>
<tr>
<td></td>
<td>1.52</td>
<td>0.91</td>
</tr>
<tr>
<td>TOTAL RECOVERY</td>
<td>94.56</td>
<td>90.83</td>
</tr>
<tr>
<td></td>
<td>104.00</td>
<td>96.93</td>
</tr>
<tr>
<td></td>
<td>93.97</td>
<td>95.54</td>
</tr>
<tr>
<td></td>
<td>94.45</td>
<td>6.2</td>
</tr>
</tbody>
</table>

**Evaluation according to EFSA Guidance**

- **Absorption >75% within half of study duration?**
  - No.
- **Recovery <95%?**
  - Correction needed
- **Normalisation**
  - Applied to all values as no specific sample type appeared to be responsible for the lower than 95% recovery from any of the “absorbed” fractions. Most probably due to losses during the skin swabbing procedures or an over-estimate of the amount applied.

**Note:**
- The mean recovery of cells is below 95% therefore the data were normalized for all cells except cell 3.
- The mean recovery of cells is below 95% therefore the data were normalized for all cells except cell 3.
- The mean recovery of cells is below 95% therefore the data were normalized for all cells except cell 3.

**Fluopicolide + Propamocarb-hydrochloride SC 687.5**

<table>
<thead>
<tr>
<th>Dose Level: 0.25 g/L</th>
<th>Distribution of radioactivity (% dose applied)</th>
<th>Group Human HD N° 6 K N° = 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N° 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>K N° = 1</td>
</tr>
<tr>
<td>Donor N°</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>H1</td>
<td>H2</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>Cell N°</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Skin wash 8h</td>
<td>94.16</td>
<td>89.08</td>
</tr>
<tr>
<td></td>
<td>93.37</td>
<td>89.67</td>
</tr>
<tr>
<td></td>
<td>87.87</td>
<td>94.40</td>
</tr>
<tr>
<td></td>
<td>91.48</td>
<td>2.94</td>
</tr>
<tr>
<td>Total swabs</td>
<td>94.40</td>
<td>89.08</td>
</tr>
<tr>
<td></td>
<td>93.37</td>
<td>89.67</td>
</tr>
<tr>
<td></td>
<td>87.87</td>
<td>94.40</td>
</tr>
<tr>
<td></td>
<td>91.48</td>
<td>2.94</td>
</tr>
<tr>
<td>Total SC 1 + SC 2</td>
<td>1.55</td>
<td>5.46</td>
</tr>
<tr>
<td></td>
<td>4.15</td>
<td>5.27</td>
</tr>
<tr>
<td></td>
<td>5.12</td>
<td>1.93</td>
</tr>
<tr>
<td></td>
<td>3.91</td>
<td>1.75</td>
</tr>
<tr>
<td>Donor chamber</td>
<td>1.13</td>
<td>2.03</td>
</tr>
<tr>
<td></td>
<td>2.59</td>
<td>1.27</td>
</tr>
<tr>
<td></td>
<td>0.79</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>1.39</td>
<td>0.78</td>
</tr>
<tr>
<td>TOTAL NON-ABSORBED</td>
<td>97.17</td>
<td>96.57</td>
</tr>
<tr>
<td></td>
<td>100.11</td>
<td>96.22</td>
</tr>
<tr>
<td></td>
<td>93.79</td>
<td>96.86</td>
</tr>
<tr>
<td></td>
<td>96.79</td>
<td>2.03</td>
</tr>
</tbody>
</table>

---

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### Distribution of radioactivity (% dose applied)

<table>
<thead>
<tr>
<th>Group Human HD</th>
<th>N = 6</th>
<th>K N° = 1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total skin</strong></td>
<td>0.25</td>
<td>0.44</td>
</tr>
<tr>
<td>SC3-5</td>
<td>1.35</td>
<td>1.08</td>
</tr>
<tr>
<td>SC6-8</td>
<td>0.30</td>
<td>0.25</td>
</tr>
<tr>
<td>SC9-11</td>
<td>0.18</td>
<td>0.29</td>
</tr>
<tr>
<td>SC12-15</td>
<td>n.s.</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>TOTAL SC 3+</strong></td>
<td>1.83</td>
<td>1.76</td>
</tr>
<tr>
<td><strong>Receptor fluid</strong></td>
<td>2.08</td>
<td>2.20</td>
</tr>
<tr>
<td>(0 - 24h)</td>
<td>0.727</td>
<td>0.990</td>
</tr>
<tr>
<td><strong>% Ratio receptor</strong></td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>12h/24h</td>
<td>0.01</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Residual receptor fluid</strong></td>
<td>0.01</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>TOTAL DIRECT</strong></td>
<td>0.74</td>
<td>1.28</td>
</tr>
<tr>
<td><strong>POTENTIAL (dose site + receptor)</strong></td>
<td>2.82</td>
<td>3.43</td>
</tr>
<tr>
<td><strong>POTENTIAL (skin + receptor)</strong></td>
<td>n.d.</td>
<td>0.99</td>
</tr>
<tr>
<td><strong>TOTAL RECOVERY</strong></td>
<td>100.00</td>
<td>100.00</td>
</tr>
</tbody>
</table>

### Evaluation according to EFSA Guidance

- Absorption >75% within half of study duration? No (include SC values)
- Recovery <95%? No (data normalisation correction needed)

**Total % Potentially Absorbable adjusted according to EFSA (2017)**

Mean (% dose site + % receptor) + (SD*1) = 5.1%

- : tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.
- SD: standard deviation
- n.d.: below limit of detection; n.s.: no sample; n.a: not applicable

In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

### Conclusion:

The dermal penetration through human dermatomed skin of $[^{14}C]$-fluopicolide in the fluopicolide SC 687.5 formulation was investigated at two nominal concentrations corresponding to the neat product (62.5 g/L) and a representative spray dilution of 0.25 g/L.

**Concentrate (62.5 g/L):**

The mean percentage of fluopicolide in the FLC+PCH SC 687.5 formulation that was considered to be potentially absorbable for the neat formulation applying the EFSA guidance (2017) to the study data was 0.26%.

**Low Dose level (Spray dilution at 0.25 g/L)**
The mean percentage of fluopicolide in the FLC+PCH SC 687.5 formulation that was considered to be potentially absorbable for the neat formulation applying the EFSA guidance (2017) to the study data was 5.1%.

Therefore, the following dermal absorption values can be proposed for use in the non-dietary risk assessments for fluopicolide in the FLC+PCH SC 687.5 formulation:

<table>
<thead>
<tr>
<th></th>
<th>Human Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentrate (62.5 g/L)</td>
<td>0.26%</td>
</tr>
<tr>
<td>Low dose (0.25 g/L)</td>
<td>5.1%</td>
</tr>
</tbody>
</table>

Assessment and conclusion by applicant:
An acceptable study yielding valid conclusions.

Propamocarb

A summary of the dermal absorption rates for propamocarb in the fluopicolide + propamocarb-HCl SC 687.5 (FLC+PCH SC 687.5) formulation is presented in the following table:
### Table 7.3-7: Dermal absorption rates for propamocarb in FLC+PCH SC 687.5

<table>
<thead>
<tr>
<th>Propamocarb</th>
<th>Value (% of dose applied)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentrate</td>
<td>2.0%</td>
</tr>
<tr>
<td>Dilution (dilution factor)</td>
<td>2.9% @ 5 g/L</td>
</tr>
<tr>
<td></td>
<td>8.6% @ 0.3 g/L</td>
</tr>
</tbody>
</table>

### Justification for proposed values – Propamocarb

The proposed dermal absorption rates for propamocarb are based on an *in vitro* human skin dermal absorption study using the FLC+PCH SC 687.5 formulation. The study results are summarized in the following table. A full summary of the study is described in detail below.

### Table 7.3-8: Summary of the results of submitted dermal absorption studies for Propamocarb

<table>
<thead>
<tr>
<th>Test</th>
<th>Concentrate</th>
<th>Spray dilution (dilution factor)</th>
<th>Formulation in study</th>
<th>Justification provided or representativity of study formulation, for current product</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>In vitro</td>
<td>2.0%</td>
<td>2.9% (1 in 125)</td>
<td>FLC+PCH SC 687.5</td>
<td>Not required</td>
<td>2015; M-510805-01-1</td>
</tr>
<tr>
<td>(Human)</td>
<td></td>
<td>8.6% (1 in 2083)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

This study is an *in vivo* dermal absorption study in rats. This study is no longer relevant as an *in vitro* study through human skin is available, which provides the best estimate of dermal absorption. Therefore, this study has not been considered further for this renewal.
<table>
<thead>
<tr>
<th>Data Point:</th>
<th>KCP 7.3/04</th>
</tr>
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<tbody>
<tr>
<td>Report Author:</td>
<td>[Redacted]</td>
</tr>
<tr>
<td>Report Year:</td>
<td>2015</td>
</tr>
<tr>
<td>Report Title:</td>
<td>Fluopicolide + Propamocarb - hydrochloride SC 687.5 - In vitro dermal absorption study using human skin</td>
</tr>
<tr>
<td>Report No:</td>
<td>SA 14050</td>
</tr>
<tr>
<td>Document No:</td>
<td>M-516805-01-1</td>
</tr>
<tr>
<td>Guideline(s) followed in study:</td>
<td>OECD 428 (2004); OECD Assessment No 28, (2004); EFSA Panel on Plant Protection Products and their Residues (PPR), : Guidance on Dermal Absorption (2012)</td>
</tr>
<tr>
<td>Deviations from current test guideline:</td>
<td>None</td>
</tr>
<tr>
<td>Previous evaluation:</td>
<td>No, not previously submitted</td>
</tr>
<tr>
<td>GLP/Officially recognised testing facilities:</td>
<td>Yes, conducted under GLP/Officially recognised testing facilities</td>
</tr>
<tr>
<td>Acceptability/Reliability:</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Material and methods:**

**Human skin:**
- Source: Biopredic, Rennes & Xenometrics, Hegenheim, France.
- Number and sex: minimum of 4 donors per dose level, female.
- Anatomical Region: Abdomen.
- Thickness: 365 to 491 µm.

**Test Material:**

- Non-radiolabelled: Batch: EK1C000430.
  - Purity = 70.4% (w/w).
- Radiolabelled: [1-14C]-propamocarb
  - Batch: KML 9864.
  - Specific activity: 3.75 MBq/mg.
  - Radiopurity of the formulation >98.5%.

**Formulation:**
- The formulation used in this experiment was the fluopicolide + propamocarb HCl SC 687.5 formulation (specification N° 102000013376) containing fluopicolide (62.5 g/L) and propamocarb (625 g/L). It was used at three nominal concentrations of propamocarb: neat, 625 g/L with 2 spray dilutions of 62.5 g/L and 6.25 g/L.

**Test system:**
- A flow-through diffusion cell system (Franz’s cell modified, Gallas, France) was used to study the absorption of the test substance (exposure area of 1 cm² skin). A diffusion cell consisted of a donor chamber and a receptor chamber between which the skin was positioned. The receptor fluid was Eagle's medium supplemented with 5% bovine serum albumin and gentamycin (50 mg/L) at a pH of 7.4. The receptor chamber was warmed by a constant circulation of warm water which maintained the receptor fluid at 32 ± 2°C (close to the normal skin temperature). The receptor fluid was pumped through the receptor chamber at a rate of 1.5 mL/h and stirred continuously whilst in the receptor chamber by means of a magnetic bar.

**Skin integrity:**
- Before dose application, the integrity of the skin samples was assessed by measuring the trans-epidermal water loss (TEWL) from the stratum corneum. An evaporimeter probe (Tewameter TM300° System, Courage & Khazaka) was placed securely on the top of the donor chamber and the amount of water diffusing through the skin was measured. Skin samples with a TEWL of
greater than 15 g/hm² were considered potentially damaged and were not used. These samples were replaced by new skin fragments which were also tested for integrity before use in the study.

**Treatment:**

The dose preparation was applied to the split-thickness skin sample with a pipette at the rate of approximately 10 μL/cm² exposed skin. The dose preparations were assayed for radioactivity content (by LSC) by using dose checks (surrogate dose) taken before, during and after the dosing process.

**Sampling:**

The receptor fluid passing through the receptor chamber was collected in glass vials held in a fraction collector. The fraction collector was started after dose application. Samples were then collected hourly for the duration of the experiment (24 hours). At 8 hours post-application, the skin was swabbed with freshly prepared 1% v/v Tween 80 in PBS (phosphate buffer saline) using precision wipes (Kimtech Sciences from Kimberly-Clark professional), in order to remove and retain the non-absorbed dose until no radioactivity was detected with a Geiger-Müller monitor. At the end of the study (24 hours after application), the treated skin and the skin adjacent to the treatment site (surrounding swabs) were swabbed. Each skin sample was tape-stripped to remove the stratum corneum. This involved the application of Monaderm adhesive tape (Monaderm, Monaco) for 5 seconds before the tape was carefully removed against the direction of hair growth. This procedure was continued until a ‘shiny’ appearance of the epidermis was evident, which indicated that the stratum corneum had been removed. The tape strips were collected into scintillation vials for analysis. The skin surrounding the application site (surrounding skin) was separated from the treated skin. Both surrounding skin and tape-stripped treated skin were retained for analysis.

**Radioassay:**

The amounts of radioactivity in the various samples were determined by liquid scintillation counting (LSC). Samples were counted for 10 minutes or for 2 σ counts in an appropriate scintillation cocktail using a Packard 1900 Tri-Carb with on-line computing facilities. Quenching effects were determined using an external standard and spectral quench parameter (tSIE) method. Efficiency correlation curves were prepared for each scintillation cocktail and were regularly checked by the use of [14C]-n-hexadecane standards. The scintillation counter was recalibrated when a deviation of greater than 2% was observed when counting quality control standards. The limit of detection was taken to be twice the background values for blank samples in appropriate scintillation cocktails.

**Findings:**

Propamocarb was demonstrated to be sufficiently soluble in the receptor fluid to avoid any risk of back diffusion.

Measurements of the homogeneity of the three concentrations of formulation applied indicated that it was acceptable.

The study results are presented in the following Table.
Table 7.3-9: Distribution of radioactivity at 24 hours after dose application of \[^{14}C\]-propamocarb in a SC 687.5 formulation at the rates of 625 g/L to human skin samples (All cells).

<table>
<thead>
<tr>
<th>Donor No.</th>
<th>X2014/1-6</th>
<th>X2014/3-7</th>
<th>X2014/1-1</th>
<th>X2014/1-20</th>
<th>608-01-044-1III-1</th>
<th>Group Human HD</th>
<th>MEAN</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>MEAN</td>
<td>SD</td>
</tr>
<tr>
<td>Cell No.</td>
<td>H01</td>
<td>H02</td>
<td>H03</td>
<td>H04</td>
<td>H05, H06</td>
<td>MEAN</td>
<td>97.39</td>
<td>0.32</td>
</tr>
<tr>
<td>Skin wash 8h</td>
<td>78.47</td>
<td>93.40</td>
<td>96.26</td>
<td>93.70</td>
<td>78.71</td>
<td>96.25</td>
<td>95.30</td>
<td>0.11</td>
</tr>
<tr>
<td>Skin wash 24h</td>
<td>0.0041</td>
<td>0.0055</td>
<td>0.0015</td>
<td>0.0056</td>
<td>0.0014</td>
<td>0.0010</td>
<td>0.0014</td>
<td>0.0011</td>
</tr>
<tr>
<td>Surrounding swabs 24h</td>
<td>0.0041</td>
<td>0.0055</td>
<td>0.0015</td>
<td>0.0056</td>
<td>0.0014</td>
<td>0.0010</td>
<td>0.0014</td>
<td>0.0011</td>
</tr>
<tr>
<td>Total swabs</td>
<td>78.48</td>
<td>93.45</td>
<td>96.27</td>
<td>93.82</td>
<td>78.71</td>
<td>96.25</td>
<td>95.30</td>
<td>0.11</td>
</tr>
<tr>
<td>SC 1</td>
<td>0.0023</td>
<td>0.0016</td>
<td>0.0016</td>
<td>0.0016</td>
<td>0.0014</td>
<td>0.0012</td>
<td>0.0013</td>
<td>0.0011</td>
</tr>
<tr>
<td>SC 2</td>
<td>0.0013</td>
<td>0.0002</td>
<td>0.0003</td>
<td>0.0021</td>
<td>0.0000</td>
<td>0.0002</td>
<td>0.0003</td>
<td>0.0004</td>
</tr>
<tr>
<td>Total SC 1 + SC 2</td>
<td>0.0036</td>
<td>0.0019</td>
<td>0.0019</td>
<td>0.0037</td>
<td>0.0014</td>
<td>0.0015</td>
<td>0.0016</td>
<td>0.0013</td>
</tr>
<tr>
<td>Donor chamber</td>
<td>n.d.</td>
<td>n.d.</td>
<td>0.0180</td>
<td>0.0217</td>
<td>1.3156</td>
<td>0.0278</td>
<td>0.31</td>
<td>0.56</td>
</tr>
<tr>
<td>TOTAL NON-ABSORBED</td>
<td>78.48</td>
<td>93.52</td>
<td>96.39</td>
<td>94.62</td>
<td>95.47</td>
<td>96.48</td>
<td>95.33</td>
<td>0.07</td>
</tr>
<tr>
<td>Skin</td>
<td>0.0027</td>
<td>0.0014</td>
<td>0.0007</td>
<td>0.0031</td>
<td>0.0010</td>
<td>0.0013</td>
<td>0.0015</td>
<td>0.0025</td>
</tr>
<tr>
<td>Surrounding skin</td>
<td>0.0041</td>
<td>0.0019</td>
<td>0.0019</td>
<td>0.0037</td>
<td>0.0014</td>
<td>0.0015</td>
<td>0.0016</td>
<td>0.0013</td>
</tr>
<tr>
<td>Total skin</td>
<td>0.0039</td>
<td>0.0014</td>
<td>0.0007</td>
<td>0.0031</td>
<td>0.0010</td>
<td>0.0013</td>
<td>0.0015</td>
<td>0.0025</td>
</tr>
<tr>
<td>SC3</td>
<td>0.0096</td>
<td>0.0088</td>
<td>0.0024</td>
<td>0.1856</td>
<td>0.1666</td>
<td>0.0040</td>
<td>0.05</td>
<td>0.07</td>
</tr>
<tr>
<td>SC4</td>
<td>0.0015</td>
<td>0.0050</td>
<td>0.0111</td>
<td>0.0156</td>
<td>0.1278</td>
<td>0.0515</td>
<td>0.03</td>
<td>0.05</td>
</tr>
<tr>
<td>SC5</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>SC6</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>SC7</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>SC8</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>TOTAL SC8</td>
<td>0.0106</td>
<td>0.0083</td>
<td>0.0032</td>
<td>0.2310</td>
<td>0.2881</td>
<td>0.0839</td>
<td>0.10</td>
<td>0.10</td>
</tr>
<tr>
<td>TOTAL DOSE SITE</td>
<td>0.0118</td>
<td>0.0095</td>
<td>0.0037</td>
<td>0.2315</td>
<td>0.2872</td>
<td>1.4845</td>
<td>0.4945</td>
<td>0.42</td>
</tr>
<tr>
<td>Receptor fluid (0 - 12h)</td>
<td>0.0270</td>
<td>0.0653</td>
<td>0.0313</td>
<td>0.0375</td>
<td>0.0552</td>
<td>0.0445</td>
<td>0.043</td>
<td>0.014</td>
</tr>
<tr>
<td>Receptor fluid (0 - 24h)</td>
<td>0.0053</td>
<td>0.0290</td>
<td>0.0549</td>
<td>0.0692</td>
<td>0.1967</td>
<td>0.1105</td>
<td>0.120</td>
<td>0.082</td>
</tr>
<tr>
<td>%Ratio receptor 12h/24h</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Residual SC Fluid</td>
<td>0.0025</td>
<td>0.0501</td>
<td>0.0104</td>
<td>0.0441</td>
<td>0.4323</td>
<td>0.0974</td>
<td>0.18</td>
<td>0.23</td>
</tr>
<tr>
<td>Receptor chamber</td>
<td>0.0560</td>
<td>0.0010</td>
<td>0.0000</td>
<td>0.1809</td>
<td>0.2455</td>
<td>0.1434</td>
<td>0.12</td>
<td>0.10</td>
</tr>
<tr>
<td>TOTAL DIRECT</td>
<td>0.2150</td>
<td>0.7548</td>
<td>0.0644</td>
<td>0.2942</td>
<td>0.8745</td>
<td>0.3513</td>
<td>0.43</td>
<td>0.32</td>
</tr>
<tr>
<td>POTENTIAL (dose site+receptor)</td>
<td>0.2275</td>
<td>0.9636</td>
<td>0.0759</td>
<td>0.5814</td>
<td>2.3590</td>
<td>0.8458</td>
<td>0.84</td>
<td>0.82</td>
</tr>
<tr>
<td>POTENTIAL (skin+receptor)</td>
<td>0.2275</td>
<td>0.9636</td>
<td>0.0759</td>
<td>0.5814</td>
<td>2.3590</td>
<td>0.8458</td>
<td>0.84</td>
<td>0.82</td>
</tr>
<tr>
<td>TOTAL RECOVERY</td>
<td>0.871</td>
<td>94.48</td>
<td>96.37</td>
<td>94.61</td>
<td>97.83</td>
<td>97.32</td>
<td>93.2</td>
<td>7.2</td>
</tr>
</tbody>
</table>

Evaluation according to EFSA Guidance

- Absorption >75% within half of study duration?
- Recovery <95%?

<table>
<thead>
<tr>
<th>No.</th>
<th>(include SC values except SC1 &amp;2)</th>
<th>Yes (due to H01) correction needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total % Potentially Absorbable adjusted according to EFSA (2017)</td>
<td>Provided in the next table</td>
<td></td>
</tr>
</tbody>
</table>
t: tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.
SD: standard deviation
n.d.: below limit of detection; n.s.: no sample; n.a: not applicable.
In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

The cell H01 showed very low recovery outside of the acceptable range indicated in the OECD 428 guideline and is therefore considered to be an outlier and was excluded in the study report, therefore the updated results are presented in the table below.

### Table 7.3-10: Distribution of radioactivity at 24 hours after dose application of [14C]-propamocarb in a SC 687.5 formulation at the rates of 625 g/L to human skin samples (Reported cells).

<table>
<thead>
<tr>
<th>Group Human HD</th>
<th>N= 5</th>
<th>K N° = 1.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>Cell N°</td>
<td>H02</td>
<td>H03</td>
</tr>
<tr>
<td>Skin wash 8h</td>
<td>93.40</td>
<td>96.26</td>
</tr>
<tr>
<td>Skin wash 24h</td>
<td>0.0441</td>
<td>0.0035</td>
</tr>
<tr>
<td>Surrounding swabs 24 h</td>
<td>0.0055</td>
<td>0.0026</td>
</tr>
<tr>
<td>Total swabs</td>
<td>93.49</td>
<td>90.26</td>
</tr>
<tr>
<td>SC 1</td>
<td>0.0166</td>
<td>0.0424</td>
</tr>
<tr>
<td>SC 2</td>
<td>0.0092</td>
<td>0.0063</td>
</tr>
<tr>
<td>Total SC 1 + SC 2</td>
<td>0.0258</td>
<td>0.0479</td>
</tr>
<tr>
<td>Donor chamber</td>
<td>0.0441</td>
<td>0.0237</td>
</tr>
<tr>
<td>TOTAL NON-ABSORBED</td>
<td>93.52</td>
<td>90.29</td>
</tr>
<tr>
<td>Skin</td>
<td>0.1214</td>
<td>0.0049</td>
</tr>
<tr>
<td>Surrounding skin</td>
<td>0.0191</td>
<td>0.0034</td>
</tr>
<tr>
<td>Total skin</td>
<td>0.1405</td>
<td>0.0083</td>
</tr>
<tr>
<td>SC3</td>
<td>0.0068</td>
<td>0.0027</td>
</tr>
<tr>
<td>SC4</td>
<td>0.0059</td>
<td>0.0015</td>
</tr>
<tr>
<td>SC5</td>
<td>0.0093</td>
<td>n.s.</td>
</tr>
<tr>
<td>SC6</td>
<td>0.0032</td>
<td>n.s.</td>
</tr>
<tr>
<td>SC7</td>
<td>0.0069</td>
<td>n.s.</td>
</tr>
<tr>
<td>SC8</td>
<td>0.0010</td>
<td>n.s.</td>
</tr>
<tr>
<td>TOTAL SC 3+</td>
<td>0.0683</td>
<td>0.0082</td>
</tr>
<tr>
<td>TOTAL DOSE SITE</td>
<td>0.2083</td>
<td>0.0115</td>
</tr>
<tr>
<td>Receptor fluid (0 - 12h)</td>
<td>0.0643</td>
<td>0.0310</td>
</tr>
<tr>
<td>Receptor fluid (0 - 24h)</td>
<td>0.2440</td>
<td>0.0540</td>
</tr>
<tr>
<td>Residual Rec Fluid</td>
<td>0.5108</td>
<td>0.0104</td>
</tr>
<tr>
<td>Receptor chamber</td>
<td>0.0000</td>
<td>0.0000</td>
</tr>
<tr>
<td>TOTAL DIRECT</td>
<td>0.75</td>
<td>0.06</td>
</tr>
</tbody>
</table>
**Document MCP – Section 7: Toxicological studies**

**Fluopicolide + Propamocarb-hydrochloride SC 687.5**

<table>
<thead>
<tr>
<th>Donor N°</th>
<th>X2014/3-7</th>
<th>X2014/1-1</th>
<th>X2014/2-1</th>
<th>X2014/1-20</th>
<th>608-01-0414-III-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>POTENTIAL (dose site+ receptor)</td>
<td>0.9636</td>
<td>0.0759</td>
<td>0.5814</td>
<td>2.3590</td>
<td>0.8450</td>
</tr>
<tr>
<td>POTENTIAL (skin+ receptor)</td>
<td>0.8953</td>
<td>0.0727</td>
<td>0.4504</td>
<td>2.0709</td>
<td>1.9619</td>
</tr>
<tr>
<td>TOTAL RECOVERY</td>
<td>94.48</td>
<td>96.37</td>
<td>94.61</td>
<td>97.83</td>
<td>97.32</td>
</tr>
</tbody>
</table>

**Evaluation according to EFSA Guidance**

<table>
<thead>
<tr>
<th></th>
<th>Group Human HD N° = 6</th>
<th>K N° = 1.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption &gt;75% within half of study duration?</td>
<td>No (include SC values except SC1 &amp; 2)</td>
<td></td>
</tr>
<tr>
<td>Recovery &lt;95%?</td>
<td>No correction needed</td>
<td></td>
</tr>
</tbody>
</table>

**Potential% Adjusted according to EFSA (2017)**

<table>
<thead>
<tr>
<th></th>
<th>Mean (%dose site + receptor) + (SD*1.2) = 2.0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD: standard deviation</td>
<td></td>
</tr>
<tr>
<td>n.d.: below limit of detection, n.s.: no sample; n.a: not applicable.</td>
<td></td>
</tr>
</tbody>
</table>

In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

Table 7.3-11: Distribution of radioactivity at 24 hours after dose application of \(^{14}C\)-propamocarb in a SC 687.5 formulation at the rates of 5 g/L to human skin samples (All cells).

| Sex | Donor N° | Cell N° | Skin wash 8h | Skin wash 24h | Surrounding swabs 24h | Total swabs | SC1 | SC2 | Total SC1+SC2 | Donor chamber | TOTAL NON-ABSORBED | Skin | Surrounding skin | Total skin | SC3 | SC4 | SC5 | SC6 | SC7 |
|-----|----------|---------|-------------|---------------|----------------------|-------------|-----|-----|----------------|--------------|-----------------|------|---------------|-----------|-----|-----|-----|-----|-----|-----|
| Female | X2014/4-10 | H07 | 85.87 | 0.23 | 0.0180 | 86.12 | 0.363 | 0.028 | 0.028 | 0.028 | 0.168 | 86.67 |
| Female | X2014/5-12 | H08 | 88.53 | 0.14 | 0.0288 | 88.69 | 0.022 | 0.037 | 0.037 | 0.037 | 0.614 | 89.40 |
| Female | TRA2001 B559 H09 | 81.99 | 0.04 | 0.0045 | 82.03 | 0.018 | 0.043 | 0.043 | 0.043 | 0.061 | 81.99 |
| Female | X2014/6-1 | H10 | 88.50 | 0.33 | 0.0073 | 88.84 | 0.119 | 0.047 | 0.047 | 0.047 | 0.152 | 89.22 |
| Female | H11 | 93.62 | 0.03 | 0.0022 | 93.65 | 0.011 | 0.008 | 0.008 | 0.008 | 0.096 | 93.76 |
| Female | H12 | 89.00 | 0.00 | 0.0003 | 89.01 | 0.003 | 0.003 | 0.003 | 0.003 | 0.543 | 89.57 |
| | MEAN | 87.92 | 0.00 | 0.0083 | 88.06 | 0.012 | 0.010 | 0.010 | 0.010 | 0.27 | 88.46 |
| | SD | 3.84 | 0.13 | 0.0083 | 3.83 | 0.13 | 0.14 | 0.14 | 0.14 | 0.24 | 3.85 |

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### Distribution of radioactivity (% dose applied)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Donor N°</th>
<th>SC8</th>
<th>SC9</th>
<th>SC10</th>
<th>SC11</th>
<th>SC12</th>
<th>SC13</th>
<th>Total SC3+</th>
<th>M</th>
<th>Receptor fluid (0 - 12h)</th>
<th>0.051</th>
<th>0.158</th>
<th>3.479</th>
<th>0.010</th>
<th>0.389</th>
<th>0.624</th>
<th>0.835</th>
<th>1.343</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>X2014/4-10</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
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#### Group Human HD

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#### Evaluation according to EFSA Guidance (2017)

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<th>Absorption &gt;75% within half of study duration?</th>
<th>No (include SC values except SC1 &amp; 2)</th>
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<tr>
<td>Mean Recovery &lt;95%?</td>
<td>Correction needed *</td>
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</table>

<table>
<thead>
<tr>
<th>Total % Potentially Absorbable adjusted according to EFSA (2017)</th>
<th>Mean (%dose site +%receptor) + (SD*1) = 3.6%</th>
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</thead>
</table>

* Normalisation was applied to all values as no specific sample type appeared to be responsible for the lower than 95% recovery from any of the “absorbed” fractions. Most probably due to losses during the skin swabbing procedures or an over-estimate of the amount applied.

SD: standard deviation; n: number of skin cells used for calculation
n.d.: not detected (below the limit of detection); n.a.: not applicable

In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

In the study report both Cells H07 and H09 were excluded from the reported cells due to “low recoveries”. However, looking at the cumulative absorption profile of all the cells it shows that cell H09 can be considered as outliers compared to other cells as shown in the graphs below.
Figure 7.3-1: Cumulative Absorption Profile after dose application of $^{14}$C-propamocarb in an SC 687.5 formulation at the nominal rate of 5 g/L to human skin (All cells)

Figure 7.3-2: Cumulative Absorption Profile after dose application of $^{14}$C-propamocarb in an SC 687.5 formulation at the nominal rate of 5 g/L to human skin (Reported cells)

Considering recovery all cells showed low recoveries (<95%) the results are presented normalized in the following table.
### Distribution of radioactivity at 24 hours after dose application of [14C]-propamocarb in an SC 687.5 formulation at the rate of 5 g/L to human skin samples (reported cells) normalized.

<table>
<thead>
<tr>
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<th></th>
<th></th>
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<td>H08</td>
<td>H10</td>
<td>H11</td>
<td>H12</td>
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<td>97.37</td>
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<td>Surrounding swabs 24 h</td>
<td>0.02</td>
<td>0.032</td>
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<td>97.23</td>
<td>96.49</td>
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<td>SC 1</td>
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<td>0.60</td>
<td>0.03</td>
<td>0.01</td>
<td>0.01</td>
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<td>SC 2</td>
<td>0.02</td>
<td>0.07</td>
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<td>Total SC 1 + SC 2</td>
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<td>Surrounding skin</td>
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<td>Total skin</td>
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<td>SC 9</td>
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<td>0.075</td>
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<td>SC 10</td>
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<td>SC 11</td>
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<td>TOTAL SC 3+</td>
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<td>TOTAL Dose SITE</td>
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<td>Receptor fluid (0 - 24h)</td>
<td>0.067</td>
<td>0.174</td>
<td>0.337</td>
<td>0.355</td>
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<td>Residual fluid (0-24h)</td>
<td>0.065</td>
<td>0.562</td>
<td>0.489</td>
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<td>% Ratio receptor fluid (12h/24h)</td>
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<td>56</td>
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<td>Residual fluid (0-24h)</td>
<td>0.07</td>
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<td>POTENTIAL (dose site+ receptor)</td>
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**Fluopicolide + Propamocarb-hydrochloride SC 687.5**

## Distribution of radioactivity (% dose applied)

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</table>

**Evaluation according to EFSA Guidance**

Absorption >75% within half of study duration? Yes

No. (include SC values except SC N° 2)

Recovery <95%? No

Total % Potentially Absorbable adjusted according to EFSA (2017) fully absorbed dose.

*: tape-strips excluding numbers 1 & 2 which are considered to be non-absorbed dose.

SD: standard deviation

n.d.: below limit of detection; n.s.: no sample; n.a: not applicable.

In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding differences resulting from the use of the spreadsheet program.

### Table 7.3-13: Distribution of radioactivity at 24 hours after dose application of [14C]-propamocarb in a SC 687.5 formulation at the rates of 0.3 g/L to human skin samples (All cells).

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<td>H16</td>
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<tr>
<td>Total swabs</td>
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<td>0.07</td>
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<td>Donor chamber</td>
<td>0.45</td>
<td>0.69</td>
<td>0.45</td>
<td>0.39</td>
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<td>Surrounding skin</td>
<td>0.06</td>
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<td>0.06</td>
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<td>0.152</td>
<td>0.039</td>
<td>0.082</td>
<td>0.087</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

**Distribution of radioactivity (% dose applied)**

**Group Human HD**

N = 5

K N° = 1.2

**Recovery <95%?**

No. (include SC values except SC N° 2)

**Correction applied**

| Mean (%dose site +%receptor) + (SD*1.2) = 2.9% |
| --- | --- |
| Recovery <95%? | Yes |

**Absorption >75% within half of study duration?**

Yes

**SD:** standard deviation

n.d.: below limit of detection; n.s.: no sample; n.a: not applicable.

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### Distribution of radioactivity (% dose applied)

<table>
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<th>N = 6</th>
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<td>SC13</td>
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<td>SC14</td>
<td>n.s.</td>
<td>0.128</td>
</tr>
<tr>
<td>SC15</td>
<td>n.s.</td>
<td>0.065</td>
</tr>
<tr>
<td><strong>Total SC3+</strong></td>
<td>3.30</td>
<td>2.15</td>
</tr>
<tr>
<td><strong>TOTAL DOSE SITE</strong></td>
<td>4.50</td>
<td>3.24</td>
</tr>
<tr>
<td>Receptor fluid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0 - 12h)</td>
<td>10.29</td>
<td>0.25</td>
</tr>
<tr>
<td>Receptor fluid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0 - 24h)</td>
<td>14.99</td>
<td>0.55</td>
</tr>
<tr>
<td>%Ratio</td>
<td>69</td>
<td>145</td>
</tr>
<tr>
<td>receptor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual Rec Fluid</td>
<td>0.507900</td>
<td>0.281400</td>
</tr>
<tr>
<td><strong>TOTAL DIRECT</strong></td>
<td>15.50</td>
<td>0.83</td>
</tr>
<tr>
<td>POTENTIAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(dose site+ receptor)</td>
<td>20.00</td>
<td>4.07</td>
</tr>
<tr>
<td>POTENTIAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(skin+ receptor)</td>
<td>16.70</td>
<td>1.92</td>
</tr>
<tr>
<td><strong>TOTAL RECOVERY</strong></td>
<td>100.09</td>
<td>42.35</td>
</tr>
</tbody>
</table>

### Evaluation according to EFSA Guidance (2017)

<table>
<thead>
<tr>
<th>Absorption &gt;75% within half of study duration?</th>
<th>No (include SC values except SC1 &amp; 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Recovery &lt;95%?</td>
<td>Correction needed*</td>
</tr>
<tr>
<td>Total % Potentially Absorbable adjusted</td>
<td>Mean (%dose site +%receptor) + (SD*1) = 14%</td>
</tr>
</tbody>
</table>

| SD: standard deviation; N: number of skin cells used for calculation; n.d.: not detected (below the limit of detection); n.a.: not applicable |

In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

# Normalisation was applied to all values as no specific sample type appeared to be responsible for the lower than 95% recovery from any of the “absorbed” fractions. Most probably due to losses during the skin swabbing procedures or an over-estimate of the amount applied.

In the study report both Cells H13 and H14 were excluded from the reported cells due to “high recovery” and “low recovery” respectively. However, looking at the cumulative absorption profile of all the cells it shows that cell H13 can be considered as outlier compared to other cells as shown in the graphs below whereas H14 has a comparable profile. Recoveries were quite low for all other cells and when normalized the data of the cell H14 are comparable to the other cells. In conclusion only the cell H13 has been excluded from the results.

---

**Document MCP – Section 7: Toxicological studies**

**Fluopicolide + Propamocarb-hydrochloride SC 687.5**

**Distribution of radioactivity (% dose applied)**

<table>
<thead>
<tr>
<th>Group Human HD</th>
<th>N = 6</th>
<th>K N° = 1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>SC12</td>
<td>0.088</td>
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<tr>
<td>SC13</td>
<td>1.952</td>
<td>0.087</td>
</tr>
<tr>
<td>SC14</td>
<td>n.s.</td>
<td>0.128</td>
</tr>
<tr>
<td>SC15</td>
<td>n.s.</td>
<td>0.065</td>
</tr>
<tr>
<td><strong>Total SC3+</strong></td>
<td>3.30</td>
<td>2.15</td>
</tr>
<tr>
<td><strong>TOTAL DOSE SITE</strong></td>
<td>4.50</td>
<td>3.24</td>
</tr>
<tr>
<td>Receptor fluid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0 - 12h)</td>
<td>10.29</td>
<td>0.25</td>
</tr>
<tr>
<td>Receptor fluid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(0 - 24h)</td>
<td>14.99</td>
<td>0.55</td>
</tr>
<tr>
<td>%Ratio</td>
<td>69</td>
<td>145</td>
</tr>
<tr>
<td>receptor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residual Rec Fluid</td>
<td>0.507900</td>
<td>0.281400</td>
</tr>
<tr>
<td><strong>TOTAL DIRECT</strong></td>
<td>15.50</td>
<td>0.83</td>
</tr>
<tr>
<td>POTENTIAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(dose site+ receptor)</td>
<td>20.00</td>
<td>4.07</td>
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<td>POTENTIAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(skin+ receptor)</td>
<td>16.70</td>
<td>1.92</td>
</tr>
<tr>
<td><strong>TOTAL RECOVERY</strong></td>
<td>100.09</td>
<td>42.35</td>
</tr>
</tbody>
</table>

In the study report both Cells H13 and H14 were excluded from the reported cells due to “high recovery” and “low recovery” respectively. However, looking at the cumulative absorption profile of all the cells it shows that cell H13 can be considered as outlier compared to other cells as shown in the graphs below whereas H14 has a comparable profile. Recoveries were quite low for all other cells and when normalized the data of the cell H14 are comparable to the other cells. In conclusion only the cell H13 has been excluded from the results.
Figure 7.3-3: Cumulative Absorption Profile after dose application of $[^{14}C]$-propamocarb in an SC 687.5 formulation at the nominal rate of 0.3 g/L to human skin (All cells)

Figure 7.3-4: Cumulative Absorption Profile after dose application of $[^{14}C]$-propamocarb in an SC 687.5 formulation at the nominal rate of 0.3 g/L to human skin (Reported cells)

Considering recovery, all cells showed low recoveries (<95%) the results are presented normalized in the following table.
Table 7.3-14: Distribution of radioactivity at 24 hours after dose application of \(^{14}\)C- propamocarb in an SC 687.5 formulation at the rate of 0.3 g/L to human skin samples (reported cells) normalized.

<table>
<thead>
<tr>
<th>Sex</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Group Human HD</th>
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<th>K N° = 15</th>
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<td>Donor N°</td>
<td>X2014/2-4</td>
<td>X2014/5-25</td>
<td>X2014/1-21</td>
<td>603-01-0414-V-1</td>
<td>598-01-0314-IV-1</td>
<td>MEAN SD</td>
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<td></td>
</tr>
<tr>
<td>Cell N°</td>
<td>H14</td>
<td>H15</td>
<td>H16</td>
<td>H17</td>
<td>H18</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin wash 8h</td>
<td>93.98</td>
<td>94.40</td>
<td>94.81</td>
<td>90.84</td>
<td>89.80</td>
<td>92.70</td>
<td>2.28</td>
<td></td>
</tr>
<tr>
<td>Skin wash 24h</td>
<td>0.48</td>
<td>0.36</td>
<td>0.28</td>
<td>0.32</td>
<td>0.84</td>
<td>0.24</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Surrounding swabs 24h</td>
<td>0.02</td>
<td>0.03</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>0.00</td>
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</tr>
<tr>
<td>Total swabs</td>
<td>94.48</td>
<td>94.78</td>
<td>95.11</td>
<td>91.19</td>
<td>93.16</td>
<td>93.28</td>
<td>1.41</td>
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<tr>
<td>SC1</td>
<td>0.10</td>
<td>0.04</td>
<td>0.07</td>
<td>0.14</td>
<td>0.14</td>
<td>0.14</td>
<td>0.03</td>
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</tr>
<tr>
<td>SC2</td>
<td>0.08</td>
<td>0.04</td>
<td>0.06</td>
<td>0.10</td>
<td>0.10</td>
<td>0.10</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Total SC1 + SC2</td>
<td>0.18</td>
<td>0.08</td>
<td>0.12</td>
<td>0.20</td>
<td>0.26</td>
<td>0.17</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Donor chamber</td>
<td>0.47</td>
<td>0.16</td>
<td>0.52</td>
<td>0.44</td>
<td>0.47</td>
<td>0.53</td>
<td>0.23</td>
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<tr>
<td>TOTAL NON-ABSORBED</td>
<td>95.12</td>
<td>95.67</td>
<td>95.75</td>
<td>91.83</td>
<td>91.24</td>
<td>91.34</td>
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<tr>
<td>Skin</td>
<td>1.24</td>
<td>0.02</td>
<td>0.08</td>
<td>0.06</td>
<td>0.06</td>
<td>0.06</td>
<td>0.45</td>
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</tr>
<tr>
<td>Surrounding skin</td>
<td>0.06</td>
<td>0.03</td>
<td>0.02</td>
<td>0.16</td>
<td>0.10</td>
<td>0.08</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Total skin</td>
<td>1.31</td>
<td>0.13</td>
<td>0.04</td>
<td>0.11</td>
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<td>0.09</td>
<td>0.47</td>
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</tr>
<tr>
<td>SC3</td>
<td>0.195</td>
<td>0.081</td>
<td>0.046</td>
<td>0.13</td>
<td>0.23</td>
<td>0.13</td>
<td>0.09</td>
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</tr>
<tr>
<td>SC4</td>
<td>0.167</td>
<td>0.055</td>
<td>0.036</td>
<td>0.024</td>
<td>0.024</td>
<td>0.024</td>
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<tr>
<td>SC5</td>
<td>0.234</td>
<td>0.067</td>
<td>0.055</td>
<td>0.235</td>
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<td>0.15</td>
<td>0.10</td>
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<td>SC6</td>
<td>0.226</td>
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<td>0.065</td>
<td>0.224</td>
<td>0.224</td>
<td>0.14</td>
<td>0.08</td>
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<tr>
<td>SC7</td>
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<td>0.086</td>
<td>0.075</td>
<td>0.202</td>
<td>0.156</td>
<td>0.19</td>
<td>0.16</td>
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<tr>
<td>SC8</td>
<td>0.4208</td>
<td>0.035</td>
<td>0.034</td>
<td>0.193</td>
<td>0.105</td>
<td>0.12</td>
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<tr>
<td>SC9</td>
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<td>0.057</td>
<td>0.046</td>
<td>0.055</td>
<td>0.144</td>
<td>0.13</td>
<td>0.07</td>
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<tr>
<td>SC10</td>
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<td>0.046</td>
<td>0.116</td>
<td>0.112</td>
<td>0.112</td>
<td>0.11</td>
<td>0.08</td>
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<tr>
<td>SC11</td>
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<td>0.043</td>
<td>0.095</td>
<td>0.098</td>
<td>n.s.</td>
<td>0.25</td>
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<tr>
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<td>0.040</td>
<td>n.s.</td>
<td>0.082</td>
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<td>0.04</td>
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<td>0.041</td>
<td>n.s.</td>
<td>0.077</td>
<td>n.s.</td>
<td>0.04</td>
<td>0.05</td>
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<td>0.153</td>
<td>0.045</td>
<td>n.s.</td>
<td>0.077</td>
<td>n.s.</td>
<td>0.05</td>
<td>0.06</td>
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</tr>
<tr>
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<td>n.s.</td>
<td>0.066</td>
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</tr>
<tr>
<td>Total SC3+</td>
<td>2.58</td>
<td>0.30</td>
<td>1.17</td>
<td>1.62</td>
<td>1.40</td>
<td>1.55</td>
<td>0.73</td>
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<tr>
<td>TOTAL DOSE SITE</td>
<td>3.89</td>
<td>0.65</td>
<td>1.27</td>
<td>2.24</td>
<td>2.30</td>
<td>2.23</td>
<td>1.14</td>
<td></td>
</tr>
<tr>
<td>Receptor fluid (0 - 12h)</td>
<td>0.09</td>
<td>2.44</td>
<td>1.85</td>
<td>3.81</td>
<td>4.18</td>
<td>2.52</td>
<td>1.57</td>
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</tr>
<tr>
<td>Receptor fluid (0 - 24h)</td>
<td>0.64</td>
<td>3.22</td>
<td>2.58</td>
<td>5.28</td>
<td>5.84</td>
<td>3.52</td>
<td>2.10</td>
<td></td>
</tr>
<tr>
<td>% Ratio Receptor fluid 12h</td>
<td>36.55</td>
<td>76</td>
<td>72</td>
<td>72</td>
<td>72</td>
<td>67</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Residual Rec Fluid</td>
<td>0.34</td>
<td>0.21</td>
<td>0.25</td>
<td>0.40</td>
<td>0.35</td>
<td>0.31</td>
<td>0.08</td>
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<tr>
<td>TOTAL DIRECT</td>
<td>0.99</td>
<td>3.44</td>
<td>2.83</td>
<td>5.68</td>
<td>6.19</td>
<td>3.83</td>
<td>2.13</td>
<td></td>
</tr>
<tr>
<td>POTENTIAL (dose site + receptor)</td>
<td>4.88</td>
<td>4.37</td>
<td>4.25</td>
<td>8.17</td>
<td>8.61</td>
<td>6.06</td>
<td>2.15</td>
<td></td>
</tr>
</tbody>
</table>
**Fluopicolide + Propamocarb-hydrochloride SC 687.5**

### Distribution of radioactivity (% dose applied)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Female</th>
<th>Female</th>
<th>Female</th>
<th>Female</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Donor No</td>
<td>X2014/2-4</td>
<td>X2014/5-25</td>
<td>X2014/1-21</td>
<td>603-01-0414-V-1</td>
<td>598-01-0314-JV-1</td>
</tr>
<tr>
<td>POTENTIAL (skin+ receptor)</td>
<td>2.30</td>
<td>3.79</td>
<td>2.94</td>
<td>6.37</td>
<td>7.13</td>
</tr>
</tbody>
</table>

**Group Human HD**

| N= 5 | K N° = 1.2 |

**TOTAL RECOVERY**

| 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

**Evaluation according to EFSA Guidance (2017)**

<table>
<thead>
<tr>
<th>Absorption &gt;75% within half of study duration?</th>
<th>No (include SC values)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Recovery &lt;95%?</td>
<td>Correction needed</td>
</tr>
</tbody>
</table>

**Total % Potentially Absorbable adjusted according to EFSA (2017)**

| Mean (%dose site +%receptor) + (SD*1.2) = 8.6% |

**SD:** standard deviation; **N:** number of skin cells used for calculation

**n.d.:** not detected (below the limit of detection); **n.a.:** not applicable

In the above table, the presented means do not always calculate exactly from the presented individual data. This is due to rounding-up differences resulting from the use of the spreadsheet program.

### Conclusion:

The dermal penetration through human dermatomed skin of [14C]-propamocarb in the propamocarb SC 687.5 formulation was investigated at three nominal concentrations corresponding to the neat product (625 g/L) and to two representative spray dilutions of 5 g/L and 0.3 g/L.

**Concentrate**

The mean percentage of propamocarb in the FLC+PCH SC 687.5 formulation that was considered to be potentially absorbable for the neat formulation applying the EFSA guidance (2017) to the study data was 2.0%.

**Intermediate Dose level (Spray dilution at 5 g/L)**

The mean percentage of propamocarb in the FLC+PCH SC 687.5 formulation that was considered to be potentially absorbable for the spray dilution at 5 g/L applying the EFSA guidance (2017) to the study data was 2.9%.

**Low Dose level (Spray dilution at 0.3 g/L)**

The mean percentage of propamocarb in the FLC+PCH SC 687.5 formulation that was considered to be potentially absorbable for the spray dilution at 0.3 g/L applying the EFSA guidance (2017) to the study data was 8.6%.

Therefore, the following dermal absorption values can be proposed for use in the non-dietary risk assessments for propamocarb in the FLC+PCH SC 687.5 formulation:

- 2.0% for the neat formulation (625 g/L)
- 2.9% for the intermediate dose (5 g/L)
- 8.6% for the low dose (0.3 g/L)
<table>
<thead>
<tr>
<th>Data Point:</th>
<th>KCP 7.3/03</th>
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<tbody>
<tr>
<td>Report Author:</td>
<td></td>
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<tr>
<td>Report Year:</td>
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<td>Report Title:</td>
<td>Dermal penetration in the rat propamocarb HCL</td>
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<tr>
<td>Report No:</td>
<td>A85147</td>
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<td>Document No:</td>
<td>M-157340-01-1</td>
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<tr>
<td>Guideline(s) followed in study:</td>
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<tr>
<td>Deviations from current test guideline:</td>
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</tr>
<tr>
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</tr>
<tr>
<td>GLP/Officially recognised testing facilities:</td>
<td>Yes, conducted under GLP/Officially recognised testing facilities</td>
</tr>
<tr>
<td>Acceptability/Reliability:</td>
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</tr>
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</table>

This study is an in vivo dermal absorption study in rats. This study is no longer relevant as an in vitro study through human skin is available which provides the best estimate of dermal absorption. Therefore, this study has not been considered further for this renewal.
CP 7.4 Available toxicological data relating to co-formulants

CONFIDENTIAL information – data provided separately (Document JCP).
Appendix 1 Critical GAPs for this assessment

Table of supported uses for this renewal.

The critical GAPs for the non-consumer exposure assessment are highlighted in grey.

<table>
<thead>
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<th>Crop and/or situation</th>
<th>Country</th>
<th>Flavour Group or I</th>
<th>Pests or Group of pests controlled</th>
<th>Formulation</th>
<th>Application</th>
<th>Application GAP per treatment</th>
<th>PHI</th>
<th>Remarks:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potato</td>
<td>EU</td>
<td>F</td>
<td>Phytophthora infestans (PHYTIN)</td>
<td>SC</td>
<td>FLC: 10</td>
<td>1 - 3</td>
<td>100 - 1000</td>
<td>FLC: 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>F</td>
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<td>FLC: 10</td>
<td>1 - 3</td>
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<td>FLC: 100</td>
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<td>PCH: 100 - 1000</td>
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<td>1 - 3</td>
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<td>F</td>
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<td>1 - 3</td>
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<tr>
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<td>EU</td>
<td>F</td>
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<td>FLC: 10</td>
<td>1 - 3</td>
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<td>Spraying / foliar</td>
<td>PCH: 100 - 1000</td>
<td>PCH: 1000</td>
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<td></td>
</tr>
<tr>
<td>Potato</td>
<td>EU</td>
<td>F</td>
<td>Phytophthora infestans (PHYTIN)</td>
<td>SC</td>
<td>FLC: 10</td>
<td>1 - 3</td>
<td>100 - 1000</td>
<td>FLC: 100</td>
</tr>
<tr>
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<td></td>
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<td>62.5 L</td>
<td>Spraying / foliar</td>
<td>PCH: 100 - 1000</td>
<td>PCH: 1000</td>
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<td>G</td>
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<td>100 - 1250</td>
<td>FLC: 100</td>
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<td>62.5 L</td>
<td>Spraying / foliar</td>
<td>PCH: 100 - 1000</td>
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</tr>
</tbody>
</table>

FLC: Fluopicolide
PCH: Propamocarb-hydrochloride
n.a.: not applicable

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## Appendix 2 Spreadsheets for exposure calculations

### Appendix 2.1 Operator exposure - Potatoes - 4 applications per crop*

No PPE work wear - arms, body and legs covered during mixing/loading and during application.

* This scenario also applies to the following:
3 applications a crop, 7 days between applications & 2 applications a crop, 7 days between applications.

### Fluopicolide

Operator exposure for FLC+PCH SC outdoor spray applications

<table>
<thead>
<tr>
<th>Application rate of active substance</th>
<th>0.1 kg a.s./ha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assumed area treated</td>
<td>50 ha/day</td>
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<tr>
<td>Amount of active substance applied</td>
<td>5 kg a.s./day</td>
</tr>
<tr>
<td>Dermal absorption of the product</td>
<td>0.26%</td>
</tr>
<tr>
<td>Dermal absorption of in-use dilution</td>
<td>13.00%</td>
</tr>
<tr>
<td>Formulation type</td>
<td>Soluble concentrates, emulsifiable concentrate, etc.</td>
</tr>
<tr>
<td>Indoor or Outdoor application</td>
<td>Outdoor</td>
</tr>
<tr>
<td>Application method</td>
<td>Downward spraying</td>
</tr>
<tr>
<td>Application equipment</td>
<td>Vehicle-mounted</td>
</tr>
<tr>
<td>Season</td>
<td>not relevant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mixing and loading</th>
<th>µg exposure/day mixed and loaded</th>
</tr>
</thead>
<tbody>
<tr>
<td>75th centile</td>
<td>18797</td>
</tr>
<tr>
<td>95th centile</td>
<td>52141</td>
</tr>
<tr>
<td>Reference</td>
<td>ADEM</td>
</tr>
<tr>
<td>Equipment</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Application</th>
<th>µg exposure/day applied</th>
</tr>
</thead>
<tbody>
<tr>
<td>75th centile</td>
<td>742</td>
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<tr>
<td>95th centile</td>
<td>2138</td>
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<tr>
<td>Reference</td>
<td>ADEM</td>
</tr>
<tr>
<td>Equipment</td>
<td>Vehicle mounted</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protective Equipment</th>
<th>Penetration factor</th>
<th>Inhalation Protection factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gloves</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Clothing</td>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>Head and respiratory PPE</td>
<td>None</td>
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</tr>
<tr>
<td>Water resistant bag</td>
<td>Yes</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure values</th>
<th>µg exposure/day mixed and loaded</th>
</tr>
</thead>
<tbody>
<tr>
<td>75th centile</td>
<td>16767</td>
</tr>
<tr>
<td>95th centile</td>
<td>62314</td>
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<tr>
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<td>ADEM</td>
</tr>
<tr>
<td>Equipment</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure values</th>
<th>µg exposure/day applied</th>
</tr>
</thead>
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<tr>
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<td>11058</td>
</tr>
<tr>
<td>95th centile</td>
<td>114960</td>
</tr>
<tr>
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<td>ADEM</td>
</tr>
<tr>
<td>Equipment</td>
<td>Vehicle mounted</td>
</tr>
</tbody>
</table>

### Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)

<table>
<thead>
<tr>
<th>Without RPE/PPE</th>
<th>With RPE/PPE</th>
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</thead>
<tbody>
<tr>
<td>Acute</td>
<td>0.0039030</td>
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<tr>
<td>Long term</td>
<td>0.2341771</td>
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</tbody>
</table>

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Propamocarb

Operators exposure for FLC+PCH SC outdoor spray applications.

<table>
<thead>
<tr>
<th>Application method</th>
<th>Vehicle-mounted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application equipment</td>
<td>Downward spraying</td>
</tr>
<tr>
<td>Indoor or Outdoor application</td>
<td>Outdoor</td>
</tr>
</tbody>
</table>

Exposure values [pg exposure/day] for various body parts:

- **Hands**: 9869 pg/day
- **Body**: 330,855 pg/day
- **Head**: 13,743 pg/day
- **Protective hands (gloves)**: 236 pg/day
- **Protective body (workwear or protective garment and sturdy footwear)**: 724 pg/day
- **Protective face mask**: 42 pg/day

Protection Equipment:
- **Face mask**: No
- **Inhalation**: No

Exposure values [pg exposure/day] for various body parts:

- **Hands**: 9869 pg/day
- **Body**: 330,855 pg/day
- **Head**: 13,743 pg/day
- **Protective hands (gloves)**: 236 pg/day
- **Protective body (workwear or protective garment and sturdy footwear)**: 724 pg/day
- **Protective face mask**: 42 pg/day

Protection Equipment:
- **Face mask**: No
- **Inhalation**: No

Total systemic exposure from mixing, loading and application (mg/kg bw/day) without RPE/PPE: 0.294 mg/kg bw/day

% of RVAAS: 15.99%

Total systemic exposure from mixing, loading and application (mg/kg bw/day) with RPE/PPE: 0.018 mg/kg bw/day

% of RVAAS: 0.018%

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Appendix 2.2

Operator exposure - Lettuce – Manual-Knapsack - 2 applications per crop*

No PPE work wear - arms, body and legs covered during mixing/loading and during application.

* This scenario also applies to the following:
1 application a crop

Fluopicolide

Operator exposure for FLC+PCH SC outdoor spray applications

<table>
<thead>
<tr>
<th>Application rate of active substance</th>
<th>0.1 kg a.s./ha</th>
<th>(Application)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assumed area treated</td>
<td>1 ha/day</td>
<td>(Assumed)</td>
</tr>
<tr>
<td>Amount of active substance applied</td>
<td>0.1 kg a.s./day</td>
<td>(Assumed)</td>
</tr>
<tr>
<td>Dermal absorption of the product</td>
<td>0.26%</td>
<td>(Product)</td>
</tr>
<tr>
<td>Dermal absorption of in-use dilution</td>
<td>13.00%</td>
<td>(Product)</td>
</tr>
</tbody>
</table>

**Formulation type**: Soluble concentrates, emulsifiable concentrate, etc.

**Indoor or Outdoor application**: Outdoor

**Application method**: Downward spraying

**Application equipment**: Manual-Knapsack

**Season**: not relevant

### Exposure values

#### Mixing and loading

<table>
<thead>
<tr>
<th>Exposure values</th>
<th>µg exposure/day mixed and loaded</th>
<th>75th centile</th>
<th>95th centile</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>9495</td>
<td>23482</td>
<td>AOEIM</td>
<td></td>
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<tr>
<td>Body</td>
<td>803</td>
<td>2107</td>
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<tr>
<td>Head</td>
<td>5</td>
<td>17</td>
<td>AOEIM</td>
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<td></td>
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<tr>
<td>Protected hands (gloves)</td>
<td>104</td>
<td>416</td>
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<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
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<td>158</td>
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</tr>
<tr>
<td>Protected head (hood and face shield)</td>
<td>5</td>
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</table>

**Inhalation**: 36 µg exposure/day

**Exposure values**

<table>
<thead>
<tr>
<th>Exposure values</th>
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<th>75th centile</th>
<th>95th centile</th>
<th>Reference</th>
<th>Comment</th>
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</thead>
<tbody>
<tr>
<td>Hands</td>
<td>1544</td>
<td>4213</td>
<td>AOEIM</td>
<td></td>
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<tr>
<td>Body</td>
<td>7038</td>
<td>21300</td>
<td>AOEIM</td>
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<td></td>
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<tr>
<td>Head</td>
<td>16</td>
<td>52</td>
<td>AOEIM</td>
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<tr>
<td>Protected hands (gloves)</td>
<td>52</td>
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<td>Protected head (hood and face shield)</td>
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<td>11</td>
<td>AOEIM</td>
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</tr>
</tbody>
</table>

**Protective Equipment**: Select for inclusion

**Gloves**

**Clothing**

**Inhaling**

**Head and respiratory PPE**

<table>
<thead>
<tr>
<th>Protective Equipment</th>
<th>Select for inclusion</th>
<th>Penetration factor</th>
<th>Inhalation Protection factor</th>
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<td>1</td>
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<td>N/A</td>
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### Application

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<th>95th centile</th>
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<th>Comment</th>
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<td>4213</td>
<td>AOEIM</td>
<td></td>
<td></td>
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<tr>
<td>Body</td>
<td>7038</td>
<td>21300</td>
<td>AOEIM</td>
<td></td>
<td></td>
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<tr>
<td>Head</td>
<td>16</td>
<td>52</td>
<td>AOEIM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
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<td>AOEIM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
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<td>120</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Protected head (hood and face shield)</td>
<td>5</td>
<td>11</td>
<td>AOEIM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Protective Equipment**: Select for inclusion

**Gloves**

**Clothing**

**Inhaling**

**Head and respiratory PPE**

<table>
<thead>
<tr>
<th>Protective Equipment</th>
<th>Select for inclusion</th>
<th>Penetration factor</th>
<th>Inhalation Protection factor</th>
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</thead>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Clothing</td>
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<td>N/A</td>
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<tr>
<td>Head and respiratory PPE</td>
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<td>1</td>
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</tbody>
</table>

### Total

#### Longer term

- Total systemic exposure from mixing, loading and application (mg a.s./day) 18.4951780
- No. of RVAAS 281.74%

#### Acute

- Total systemic exposure from mixing, loading and application (mg a.s./day) 18.4951780
- Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) 0.1972151
- % of RVAAS 281.74%

#### Exposure without RPE/PPE

- Total systemic exposure from mixing, loading and application (mg a.s./day) 18.4951780
- No. of RVAAS 281.74%
- Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) 0.1972151
- % of RVAAS 281.74%
Propamocarb

Operator exposure for FLC+PCH SC outdoor spray applications

<table>
<thead>
<tr>
<th>Application rate of active substance</th>
<th>1 kg a.s./ha</th>
<th></th>
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<tbody>
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<td>Assumed area treated</td>
<td>1 ha/day</td>
<td></td>
</tr>
<tr>
<td>Amount of active substance applied</td>
<td>1 kg a.s./day</td>
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</tr>
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<td>Dermal absorption of the product</td>
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<tr>
<td>Indoor or Outdoor application</td>
<td>Outdoor</td>
<td></td>
</tr>
<tr>
<td>Application method</td>
<td>Downward spraying</td>
<td></td>
</tr>
<tr>
<td>Application equipment</td>
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<tr>
<td>Season</td>
<td>not relevant</td>
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<table>
<thead>
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<th>Exposure values</th>
<th>ug exposure/day mixed and loaded</th>
<th>Reference</th>
<th>Comment</th>
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<td>Hands</td>
<td>9495</td>
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<tr>
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<tr>
<td>Head</td>
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<td>ADOM</td>
<td></td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
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<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
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<td>ADOM</td>
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<tr>
<td>Protected head (hood and face shield)</td>
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<td>ADOM</td>
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<tr>
<td>Inhalation</td>
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<td>ADOM</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Protective Equipment</th>
<th>Select for inclusion</th>
<th>Penetration factor</th>
<th>Inhalation Protection factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gloves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clothing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>head and respiratory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water-soluble bag</td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposure values</th>
<th>ug exposure/day mixed and loaded</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>1544</td>
<td>ADOM</td>
<td></td>
</tr>
<tr>
<td>Body</td>
<td>8886</td>
<td>ADOM</td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td>12</td>
<td>ADOM</td>
<td></td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td>5</td>
<td>ADOM</td>
<td></td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td>8903</td>
<td>ADOM</td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td></td>
<td>ADOM</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Protective Equipment</th>
<th>Select for inclusion</th>
<th>Penetration factor</th>
<th>Inhalation Protection factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gloves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clothing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>head and respiratory</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water-soluble bag</td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Total

<table>
<thead>
<tr>
<th>Systemic exposure from mixing, loading and application (mg a.s./day)</th>
<th>Without RPE/PPE</th>
<th>With RPE/PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total systemic exposure from mixing, loading and application (mg a.s./day)</td>
<td>8.0335</td>
<td>1.1609</td>
</tr>
<tr>
<td>Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)</td>
<td>0.133</td>
<td>0.016</td>
</tr>
<tr>
<td>% of RVAAS</td>
<td>46.17%</td>
<td>6.56%</td>
</tr>
</tbody>
</table>

2. Systemic exposure from mixing, loading and application (mg a.s./day) | 12.76 | 0.63 |
| Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day) | 0.21 | 0.105 |
| % of RVAAS                                                      | 4DV/01       | 2DV/01      |
### Operator exposure - Lettuce – Manual-Hand-held - 2 applications per crop

No PPE work wear - arms, body and legs covered during mixing/loading and during application.

* This scenario also applies to the following:
  1 application a crop

### Fluopicolide

**Operator exposure for FLC+PCH SC outdoor spray applications**

<table>
<thead>
<tr>
<th>Application rate of active substance</th>
<th>0.1 kg a.s./ha</th>
<th>0.1 kg a.s./ha (background)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assumed area treated</td>
<td>4 ha/day</td>
<td>4 ha/day</td>
</tr>
<tr>
<td>Amount of active substance applied</td>
<td>0.4 kg a.s./day</td>
<td>0.4 kg a.s./day (background)</td>
</tr>
<tr>
<td>Dermal absorption of the product</td>
<td>0.20%</td>
<td>0.20%</td>
</tr>
<tr>
<td>Dermal absorption of in-use dilution</td>
<td>13.00%</td>
<td>13.00%</td>
</tr>
<tr>
<td>Formulation type</td>
<td>Soluble concentrates, emulsifiable concentrate, etc.</td>
<td>Soluble concentrates, emulsifiable concentrate, etc.</td>
</tr>
<tr>
<td>Indoor or Outdoor application</td>
<td>Outdoor</td>
<td>Outdoor</td>
</tr>
<tr>
<td>Application method</td>
<td>Manual-Hand held</td>
<td>Manual-Hand held</td>
</tr>
<tr>
<td>Application equipment</td>
<td>Manual-Hand held</td>
<td>Manual-Hand held</td>
</tr>
</tbody>
</table>

#### Timing and loading

<table>
<thead>
<tr>
<th>Exposure values</th>
<th>ug exposure/day mixed and loaded</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>2999</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Body</td>
<td>2838</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Head</td>
<td>118</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td>342</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td>1140</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Protected head (hood and face shield)</td>
<td>58</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Inhalation</td>
<td>28</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

#### Protective Equipment

- Gloves
- Clothing
- Head and respiratory PPE

<table>
<thead>
<tr>
<th>Exposure values</th>
<th>ug exposure/day applied</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>4213</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Body</td>
<td>1127</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Head</td>
<td>13</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td>269</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td>6260</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
<tr>
<td>Head and respiratory PPE</td>
<td>1</td>
<td>95th centile</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

#### Total systemic exposure from mixing, loading and application

**Without RPE/PPE**

<table>
<thead>
<tr>
<th>mg/kg bw/day</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.7950999</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

**With RPE/PPE**

<table>
<thead>
<tr>
<th>mg/kg bw/day</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.3948068</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

**Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)**

<table>
<thead>
<tr>
<th>mg/kg bw/day</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1965850</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

**RVNAS**

<table>
<thead>
<tr>
<th>% of RVNAS</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>280.84%</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

**Acute**

<table>
<thead>
<tr>
<th>mg/kg bw/day</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.5902280</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% of RVAAS</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.21%</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>mg/kg bw/day</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3098368</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% of RVAAS</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1462975</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>mg/kg bw/day</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>#DIV/0!</td>
<td>ADEM</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% of RVAAS</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>#DIV/0!</td>
<td>ADEM</td>
</tr>
</tbody>
</table>
### Operator exposure for FLC + PCH SC outdoor spray applications

**Application rate of active substance**
1 kg a.s./ha

**Amount of active substance applied**
8 ha/day

**Dermal absorption of the product**
2.00%

**Dermal absorption of in-use dilution**
8.60%

**Formulation type**
Soluble concentrates, emulsifiable concentrate, etc

**Application method**
Downward spraying

**Application equipment**
Manual-Hand held

**Season**
not relevant

#### Mixing and loading

<table>
<thead>
<tr>
<th>Exposure values</th>
<th>50th percentile (μg exposure/day mixed and loaded)</th>
<th>95th percentile (μg exposure/day mixed and loaded)</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>34120</td>
<td>52376</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Body</td>
<td>9932</td>
<td>15683</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td>278</td>
<td>4353</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td>85</td>
<td>292</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td>81</td>
<td>292</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Protected head (hood and face shield)</td>
<td>81</td>
<td>292</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td>2.00%</td>
<td>5.13%</td>
<td>AOEM</td>
<td></td>
</tr>
</tbody>
</table>

#### Application

<table>
<thead>
<tr>
<th>Exposure values</th>
<th>50th percentile (μg exposure/day applied)</th>
<th>95th percentile (μg exposure/day applied)</th>
<th>Reference</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>4117</td>
<td>11235</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Body</td>
<td>23698</td>
<td>36535</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td>32</td>
<td>227</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td>13</td>
<td>59</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td>23741</td>
<td>167013</td>
<td>AOEM</td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td>69</td>
<td>69</td>
<td>AOEM</td>
<td></td>
</tr>
</tbody>
</table>

**Protective Equipment**
- Gloves
- Clothing
- Head and respiratory PPE

<table>
<thead>
<tr>
<th>Protective Equipment</th>
<th>Penetration factor</th>
<th>Inhalation Protection factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gloves</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clothing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head and respiratory PPE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Long-term exposure

**Total systemic exposure from mixing, loading and application (mg a.s./day)**

<table>
<thead>
<tr>
<th></th>
<th>Without RPE/PPE</th>
<th>With RPE/PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>21.3817/647</td>
<td>2.7617/037</td>
</tr>
<tr>
<td>Body</td>
<td>12.3910/029</td>
<td>1.6412/507</td>
</tr>
<tr>
<td>Head</td>
<td>2.2772/372</td>
<td>0.2772/372</td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td>0.3547/161</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td>0.3547/161</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Protected head (hood and face shield)</td>
<td>0.3547/161</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Inhalation</td>
<td>0.5953/585</td>
<td>0.2754/969</td>
</tr>
<tr>
<td>Closed cab</td>
<td>19.2910/029</td>
<td>1.9053/585</td>
</tr>
</tbody>
</table>

**% of RVNAS**

<table>
<thead>
<tr>
<th></th>
<th>Without RPE/PPE</th>
<th>With RPE/PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>122.34%</td>
<td>15.87%</td>
</tr>
<tr>
<td>Body</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protected head (hood and face shield)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Closed cab</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Longer term systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)**

<table>
<thead>
<tr>
<th></th>
<th>Without RPE/PPE</th>
<th>With RPE/PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>0.3547/161</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Body</td>
<td>0.2754/969</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Head</td>
<td>0.2754/969</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td>0.2754/969</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td>0.2754/969</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Protected head (hood and face shield)</td>
<td>0.2754/969</td>
<td>0.0400/24</td>
</tr>
<tr>
<td>Inhalation</td>
<td>0.5953/585</td>
<td>0.2754/969</td>
</tr>
<tr>
<td>Closed cab</td>
<td>19.2910/029</td>
<td>1.9053/585</td>
</tr>
</tbody>
</table>

**% of RVNAS**

<table>
<thead>
<tr>
<th></th>
<th>Without RPE/PPE</th>
<th>With RPE/PPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hands</td>
<td>122.34%</td>
<td>15.87%</td>
</tr>
<tr>
<td>Body</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protected hands (gloves)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protected body (workwear or protective garment and sturdy footwear)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protected head (hood and face shield)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Closed cab</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Appendix 2.3

Operator exposure - Cucumbers (glasshouse) - 3 applications per crop*
Dutch Glasshouse model - note that AOEL has been calculated based on 60 kg bw (not 70 kg bw stated in table) - Gloves and coveralls

**Fluopicolide**

<table>
<thead>
<tr>
<th>OPERATOR EXPOSURE</th>
<th>DUTCH GREENHOUSE MODEL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ACTION</strong></td>
<td><strong>APPLICATION IN</strong></td>
</tr>
<tr>
<td><strong>MANUAL SPRAYING</strong></td>
<td><strong>GREENHOUSES</strong></td>
</tr>
<tr>
<td><strong>FLORICID+PCH SC 687.5</strong></td>
<td><strong>Application including mixing and loading</strong></td>
</tr>
<tr>
<td><strong>a s</strong> Fluopicolide</td>
<td><strong>Parameter</strong></td>
</tr>
<tr>
<td><strong>Value</strong></td>
<td><strong>Unit</strong></td>
</tr>
<tr>
<td><strong>AR</strong> Application rate</td>
<td>0.1 kg a.s./ha/sum</td>
</tr>
<tr>
<td><strong>A</strong> Area treated</td>
<td>1 ha/day</td>
</tr>
<tr>
<td><strong>Inhalation Exposure</strong></td>
<td><strong>Surrogate Exposure Value</strong></td>
</tr>
<tr>
<td><strong>SV</strong> Surrogate Exposure Value</td>
<td>1 mg a.s./day</td>
</tr>
<tr>
<td><strong>Inhalation Exposure (without PPE)</strong></td>
<td><strong>IE (PPE) = (1/FFE factor) x IE</strong></td>
</tr>
<tr>
<td><strong>Dermal Exposure</strong></td>
<td><strong>Surrogate Exposure Value</strong></td>
</tr>
<tr>
<td><strong>SV</strong> Surrogate Exposure Value</td>
<td>20 mg a.s./day</td>
</tr>
<tr>
<td><strong>Dermal Exposure (with PPE)</strong></td>
<td><strong>IE (PPE) = (1/FFE factor) x IE</strong></td>
</tr>
</tbody>
</table>

---

**NOTE:** The above mentioned model is for spraying in greenhouses. For dusting of carnations the surrogate values should be changed: inhalation should be 20 mg/day instead of 1, and dermal should be 300 mg/day instead of 200.

Note: Only for gastorming/gaseous preparations and soil fumigation preparations: powered full-face filtering devices with filter type 2 (factor 20), powered full-face filtering devices with filter type 3 (factor 40).
### Propamocarb

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Unit</th>
<th>References, comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MANUAL SPRAYING in greenhouses</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AR</td>
<td>1</td>
<td>kg a.s./ha</td>
<td>Summary of intended use, Dutch model</td>
</tr>
<tr>
<td>A</td>
<td>1</td>
<td>ha/day</td>
<td></td>
</tr>
<tr>
<td><strong>Inhalation Exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV Surrogate Exposure Value</td>
<td>1</td>
<td>mg a.s./h</td>
<td></td>
</tr>
<tr>
<td>Inhalation Exposure (without PPE)</td>
<td>1</td>
<td>mg a.s./day</td>
<td></td>
</tr>
<tr>
<td><strong>Inhalation Exposure (with PPE)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPE-factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalation Exposure (with PPE)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dermal Exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV Surrogate Exposure Value</td>
<td>200</td>
<td>mg a.s./h</td>
<td></td>
</tr>
<tr>
<td>Dermal Exposure</td>
<td>200</td>
<td>mg a.s./day</td>
<td></td>
</tr>
<tr>
<td><strong>Dermal Exposure (with PPE)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPE-factor</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal Exposure (with PPE)</td>
<td>20</td>
<td>mg a.s./day</td>
<td></td>
</tr>
<tr>
<td><strong>Internal exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA Inhalation Absorption</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DA Dermal Absorption</td>
<td>17.4</td>
<td>mg a.s./day</td>
<td>Based on 70 kg bw</td>
</tr>
<tr>
<td><strong>Without PPE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA Inhalation</td>
<td>1 / 000</td>
<td>[mg a.s./day]</td>
<td></td>
</tr>
<tr>
<td>DA Dermal</td>
<td>1 / 000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>With PPE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA Inhalation</td>
<td>1 / 000</td>
<td>[mg a.s./day]</td>
<td></td>
</tr>
<tr>
<td>DA Dermal</td>
<td>1 / 000</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA Inhalation</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DA Dermal</td>
<td>17.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AOEL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA Inhalation</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DA Dermal</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>%AOEL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA Inhalation</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DA Dermal</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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## Appendix 2.4 Resident exposure – Potatoes - applications per crop*

* This scenario is worst case so also covers the following application rates:

- 3 applications a crop, 7 days between applications
- 2 applications a crop, 7 days between applications

### Fluopicolide

#### Resident exposure for FLC+PCH SC

<table>
<thead>
<tr>
<th>Crop type</th>
<th>Application method</th>
<th>Application equipment</th>
<th>Buffer strip</th>
<th>Application rate of the product</th>
<th>Concentration of active substance (in-usedilution for liquid applications)</th>
<th>Dermal absorption of product</th>
<th>Dermal absorption of in-usedilution</th>
<th>Oral absorption</th>
<th>Dislodgeable foliar residue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Root and tuber vegetables</td>
<td>Downward spraying</td>
<td>Vehicle-mounted</td>
<td>2-3m</td>
<td>Soluble concentrates, emulsifiable concentrate, etc</td>
<td>1g.a.s./ha.</td>
<td>0%</td>
<td>13.00%</td>
<td>100.00%</td>
<td>0.000%</td>
</tr>
</tbody>
</table>

#### Vapour pressure of in-use dilution

- Low volatile substances having a vapour pressure of <5 × 10⁻³ Pa

#### Concentration in air

- 0.001 mg/m³

#### Resident dermal spray drift exposure

- 75th percentile - adult: 0.0000017 ml spray dilution/person
- Exposed duration dermal: 2 hours
- Exposed duration inhalation: 24 hours
- Exposed duration entry into treated crops: 0.25 hours

#### Light clothing adjustment factor

- Adult: 18.0%
- Child (1-3 year old): 15.0%

#### Breathing rate

- Adult: 0.23 m³/day/kg
- Child (1-3 year old): 0.73 m³/day/kg

#### Drift percentage on surface

- 75th percentile: 5.60%
- Mean: 4.10%

#### Turf transferable residues percentage

- 5.00%

#### Transfer coefficient of surfacedeposits - adult

- 7,300 cm²/hour
- Child (1-3 year old): 2,600 cm²/hour

#### Transfer coefficient of surfacedeposits - child

- 500.00%

#### Transfer coefficient for entry into treated crops

- Adult (75th percentile): 7,500 cm²/hour
- Child (75th percentile): 2,250 cm²/hour
- Mean: 5,980 cm²/hour
- Adult (mean): 1,794 cm²/hour

#### Ingestion rate from mouthing of grass per day

- 25 cm³

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### Propamocarb

#### Resident exposure for FLC+PCH SC

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application method</td>
<td>Downward spraying</td>
<td>Vehicle-mounted</td>
</tr>
<tr>
<td>Application rate/kg</td>
<td>26.7 g a.s./ha</td>
<td></td>
</tr>
<tr>
<td>Application rate (75th percentile)</td>
<td>Adult</td>
<td>0.0062 kg a.s./day</td>
</tr>
<tr>
<td>Application rate (mean)</td>
<td>Adult</td>
<td>0.0030 kg a.s./day</td>
</tr>
<tr>
<td>Entry into treated crops</td>
<td>Adult</td>
<td>0.0030 kg a.s./day</td>
</tr>
</tbody>
</table>

#### Concentration in air

- **Residential spray drift exposure:**
  - 75th percentile: 0.0062 kg a.s./day
  - Mean: 0.0030 kg a.s./day

#### Dermal absorption of product

- Adult: 2.00%
- Child (1-3 year old): 8.60%

#### Oral absorption

- Adult: 100%
- Child (1-3 year old): 100%

#### Dislodgable foliar residue

- Adult: 3.00 g a.s./cm²
- Child (1-3 year old): 2.00 g a.s./cm²

#### Vapour pressure

- In-use dilution: low volatile substances having a vapour pressure of <5*10⁻³ Pa

#### Resident dermal spray drift exposure

- 75th percentile: 0.0018 ml spray dilution/person
- Mean: 0.0006 ml spray dilution/person

#### Exposed duration

- Dermal: 2 hours
- Inhalation: 0.25 hours
- Entry into treated crops: 0.25 hours

#### Light clothing adjustment factor

- Adult: 18.0%
- Child (1-3 year old): 18.0%

#### Breathing rate

- Adult: 0.23 m³/day/kg
- Child (1-3 year old): 1.07 m³/day/kg

#### Drift percentage on surface

- 75th percentile: 5.60%
- Mean: 4.10%

#### Transfer coefficient of surface deposits

- Adult: 730.0 cm/h
- Child (1-3 year old): 260.0 cm/h

#### Exposed duration on treated crops

- 75th percentile: 0.25 hours
- Mean: 0.25 hours

#### Surface area of hands and mouth

- Adult: 20 cm²
- Child (1-3 year old): 20 cm²

#### Frequency of hand to mouth activity

- Adult: 9.5 event/hour
- Child (1-3 year old): 9.5 event/hour

#### Ingestion rate of exposed grass per day

- Adult: 25 cm³/day
- Child (1-3 year old): 25 cm³/day

#### Dislodgeable residues transferability

- Object to mouth: 20.00%
- Crop to mouth: 20.00%

#### Transfer coefficient for entry into treated crops

- Adult: 7500 cm³/h
- Child (1-3 year old): 2250 cm³/h

#### Total exposure

- Adult: 0.23280 M(mg a.s./day) per kg body weight
- Child (1-3 year old): 0.23280 M(mg a.s./day) per kg body weight

---

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### Appendix 2.5 Resident exposure – Lettuces – 2 applications per crop*

* This scenario is worst case so also covers 1 application a crop

### Fluopicolide

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulation type</td>
<td>Soluble concentrates, emulsifiable concentrate, etc</td>
</tr>
<tr>
<td>Buffer strip</td>
<td>2-3 m</td>
</tr>
<tr>
<td>Application rate of the product</td>
<td>0.05 g/a.s./l</td>
</tr>
<tr>
<td>Concentration in air (Resident)</td>
<td>0.026%</td>
</tr>
<tr>
<td>Concentration in air (Resident dilution)</td>
<td>0.013%</td>
</tr>
<tr>
<td>Oral absorption</td>
<td>10000%</td>
</tr>
<tr>
<td>Dermal absorption of product</td>
<td>0.26%</td>
</tr>
<tr>
<td>Dermal absorption of dilution</td>
<td>13.60%</td>
</tr>
<tr>
<td>Dislodgeable foliar residue</td>
<td>0.03 pg.a.s./cm²</td>
</tr>
<tr>
<td>Vapour pressure of dilution</td>
<td>Low volatile substances having a vapour pressure of &lt;5*10⁻³ Pa</td>
</tr>
<tr>
<td>Concentration in air</td>
<td>0.001 mg/m³</td>
</tr>
<tr>
<td>Resident dermal spray drift exposure (75th percentile) - adult</td>
<td>0.00017 ml spray dilution/person</td>
</tr>
<tr>
<td>Exposed duration dermal</td>
<td>2 hours</td>
</tr>
<tr>
<td>Exposed duration inhalation</td>
<td>24 hours</td>
</tr>
<tr>
<td>Exposed duration entry into treated crops (75th percentile) - adult</td>
<td>0.000023 ml spray dilution/person</td>
</tr>
<tr>
<td>Exposed duration entry into treated crops (75th percentile) - child</td>
<td>0.000018 ml spray dilution/person</td>
</tr>
<tr>
<td>Exposed duration entry into treated crops (mean) - adult</td>
<td>0.000023 ml spray dilution/person</td>
</tr>
<tr>
<td>Exposed duration entry into treated crops (mean) - child</td>
<td>0.000018 ml spray dilution/person</td>
</tr>
<tr>
<td>Light clothing adjustment factor</td>
<td>0.0000000000000000017 ml spray dilution/person</td>
</tr>
<tr>
<td>Breathing rate adult</td>
<td>0.23 m³/day/kg</td>
</tr>
<tr>
<td>Breathing rate child (1-3 years old)</td>
<td>1.07 m³/day/kg</td>
</tr>
<tr>
<td>Drift percentage on surface (75th percentile) - adult</td>
<td>0.56%</td>
</tr>
<tr>
<td>Drift percentage on surface (75th percentile) - child</td>
<td>0.41%</td>
</tr>
<tr>
<td>Turf transferable residues percentage</td>
<td>5.00%</td>
</tr>
<tr>
<td>Transfer coefficient of surface deposits-adult</td>
<td>7.300 em³/hour</td>
</tr>
<tr>
<td>Transfer coefficient of surface deposits-child (1-3 years old)</td>
<td>2.600 em³/hour</td>
</tr>
<tr>
<td>Surface area of hands moulshed</td>
<td>20 cm²</td>
</tr>
<tr>
<td>Frequency of hand to mouth activity</td>
<td>9.5 events/hour</td>
</tr>
<tr>
<td>Ingestion rate for mouthing of grass per day</td>
<td>2.000 grams</td>
</tr>
<tr>
<td>Dislodgeable residues transferability for object to mouth</td>
<td>0.000%</td>
</tr>
<tr>
<td>Saliva extraction percentage</td>
<td>50.00%</td>
</tr>
<tr>
<td>Surface area of hand mouthed</td>
<td>20 cm²</td>
</tr>
</tbody>
</table>

### Transfer coefficients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total systemic exposure (mean)</td>
<td>0.0029100</td>
</tr>
<tr>
<td>Total systemic exposure (mean) - child</td>
<td>0.0025800</td>
</tr>
<tr>
<td>Total systemic exposure (mean) - adult</td>
<td>0.0033850</td>
</tr>
<tr>
<td>Total systemic exposure (mean) - child</td>
<td>0.0031600</td>
</tr>
<tr>
<td>% of RUIAS</td>
<td>0.0029100</td>
</tr>
<tr>
<td>% of RUIAS</td>
<td>0.0025800</td>
</tr>
<tr>
<td>% of RUIAS</td>
<td>0.0033850</td>
</tr>
<tr>
<td>% of RUIAS</td>
<td>0.0031600</td>
</tr>
</tbody>
</table>

### Additional notes

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### Propamocarb

#### Resident exposure for FLCP+PCH SC

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Application method</strong></td>
<td>Dowsed spraying</td>
<td></td>
</tr>
<tr>
<td><strong>Application equipment</strong></td>
<td>Manual-Knapsack</td>
<td></td>
</tr>
<tr>
<td><strong>Buffer strip</strong></td>
<td>2-3 m</td>
<td></td>
</tr>
<tr>
<td><strong>Concentration of active substance (in-use dilution)</strong></td>
<td>5 ga.s./l</td>
<td></td>
</tr>
<tr>
<td><strong>Dermal absorption of in-use dilution</strong></td>
<td>0.60%</td>
<td></td>
</tr>
<tr>
<td><strong>Dermal absorption of product</strong></td>
<td>10.00%</td>
<td></td>
</tr>
<tr>
<td><strong>Dissolvable foliar residue (1 Application)</strong></td>
<td>2.00%</td>
<td></td>
</tr>
<tr>
<td><strong>Vapour pressure of in-use dilution</strong></td>
<td>low volatile substances having a vapour pressure of ≤0.03 Pa</td>
<td></td>
</tr>
<tr>
<td><strong>Concentration in air</strong></td>
<td>0.001 mg/m³</td>
<td></td>
</tr>
<tr>
<td><strong>Resident dermal spray drift exposure 75th percentile - adult</strong></td>
<td>0.2225 mg/sqm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Resident dermal spray drift exposure 75th percentile - child</strong></td>
<td>0.0225 mg/sqm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Resident inhalation spray drift exposure - adult</strong></td>
<td>0.0001 mg/sqm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Resident inhalation spray drift exposure - child</strong></td>
<td>0.00001 mg/sqm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Resident dermal exposure mean - adult</strong></td>
<td>0.00001 mg/sqm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Resident dermal exposure mean - child</strong></td>
<td>0.000001 mg/sqm/year</td>
<td></td>
</tr>
<tr>
<td><strong>Dermal absorption of product</strong></td>
<td>2.00%</td>
<td></td>
</tr>
<tr>
<td><strong>Dermal absorption of in-use dilution</strong></td>
<td>8.60%</td>
<td></td>
</tr>
<tr>
<td><strong>Oral absorption</strong></td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td><strong>Dislodgeable foliar residue (1 Application)</strong></td>
<td>3 pgas./err/</td>
<td></td>
</tr>
<tr>
<td><strong>Vapour pressure of in-use dilution</strong></td>
<td>low volatile substances having a vapour pressure of ≤0.03 Pa</td>
<td></td>
</tr>
<tr>
<td><strong>Concentration in air</strong></td>
<td>0.001 mg/m³</td>
<td></td>
</tr>
</tbody>
</table>

#### Exposure duration

- **Dermal exposure:** 2 hours
- **Inhalation exposure:** 24 hours
- **Entry into treated crops:** 0.25 hours

#### Adjustment factors

- **Light clothing adjustment factor:** 18.0%
- **Breathing rate adult:** 0.23 m³/day/kg
- **Breathing rate child (1-3 years old):** 1.07 m³/day/kg

#### Drift percentage

- **On surface (75th percentile):** 5.60%
- **On surface (mean):** 4.10%

#### Transfer coefficients

- **Surface deposits - adult:** 7300 cm²/hour
- **Surface deposits - child (1-3 years old):** 2600 cm²/hour

#### Conversion factors

- **Surface area of hands mouthed:** 20 err/
- **Frequency of hand to mouth activity:** 9.5 event/V hour
- **Ingestion rate from mouthing of grass per day:** 25 g

#### Total systemic exposure

<table>
<thead>
<tr>
<th>Pathway</th>
<th>1,1-3 year old</th>
<th>1.2 Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>All pathways (mean)</td>
<td>0.00010700</td>
<td>0.00014921</td>
</tr>
<tr>
<td>All pathways (75th percentile)</td>
<td>0.00000382</td>
<td>0.00001064</td>
</tr>
<tr>
<td>Total systemic exposure</td>
<td>0.00038201</td>
<td>0.00010700</td>
</tr>
<tr>
<td>Entry into treated crops</td>
<td>0.00000382</td>
<td>0.00001064</td>
</tr>
<tr>
<td>Entry into treated crops (mean)</td>
<td>0.00000382</td>
<td>0.00001064</td>
</tr>
</tbody>
</table>

---

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### Fluopicolide + Propamocarb-hydrochloride SC 687.5

#### Appendix 2.6  Worker exposure – Potatoes - 4 applications per crop*

*This scenario is worst-case so also applies to the following:

- 3 applications a crop, 7 days between applications
- 2 applications a crop, 7 days between applications

### Fluopicolide

<table>
<thead>
<tr>
<th>Source of exposure</th>
<th>Total potential exposure (mg a.g./ha)</th>
<th>systemic exposure (mg a.g./kg bw/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>葉面</td>
<td>3.07E+05</td>
<td>2.30E-06</td>
</tr>
<tr>
<td>手、身体、身体と足</td>
<td>0.05E-01</td>
<td>0.01E-02</td>
</tr>
<tr>
<td>手、身体、身体と足</td>
<td>0.05E-01</td>
<td>0.01E-02</td>
</tr>
</tbody>
</table>

### Propamocarb

<table>
<thead>
<tr>
<th>Source of exposure</th>
<th>Total potential exposure (mg a.g./ha)</th>
<th>systemic exposure (mg a.g./kg bw/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>葉面</td>
<td>2.30E+05</td>
<td>0.04E+01</td>
</tr>
<tr>
<td>手、身体、身体と足</td>
<td>0.02E+00</td>
<td>0.01E+00</td>
</tr>
<tr>
<td>手、身体、身体と足</td>
<td>0.02E+00</td>
<td>0.01E+00</td>
</tr>
</tbody>
</table>

Inhalation: No for outdoor activities.
Appendix 2.7  Worker exposure – Lettuces - 2 application per crop*

* This scenario is worst case so also covers 1 application a crop

Fluopicolide

Worker exposure from residues on foliage for FLC+PCH SC

<table>
<thead>
<tr>
<th>Component</th>
<th>Application</th>
<th>Number of applications</th>
<th>Interval between multiple applications</th>
<th>Application rate of active substance</th>
<th>Main body parts in contact with foliage</th>
<th>Derma absorption of the in-use dilution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluopicolide</td>
<td>Downwards spraying</td>
<td>2</td>
<td>7 days</td>
<td>0.1 kg a.s./ha</td>
<td>Hand and body</td>
<td>0.26%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Body and legs</td>
<td>13.00%</td>
</tr>
</tbody>
</table>

Dermal absorption of the in-use dilution: 0.26% + 13.00% = 13.26%

Dislodgeable foliar residue: 0.3 g a.s./cm²

Working hours: 8 hr

Dermal transfer coefficient for automated applications: 5800 cm²/hr

Dermal transfer coefficient for cutting ornamentals: 2500 cm²/hr

Dermal transfer coefficient for sorting/bundling ornamentals: 580 cm²/hr

Inhalation transfer coefficient for automated applications: 0

Inhalation transfer coefficient for cutting ornamentals: 0

Inhalation transfer coefficient for sorting/bundling ornamentals: 0

Total systemic exposure (mg a.s./day): 3.3489673

Total systemic exposure per kg body weight (mg a.s./kgbw/day): 0.0558161

% of max tolerated dose (MID): 84.37%}

<table>
<thead>
<tr>
<th>Component</th>
<th>Potential exposure</th>
<th>Workwear and gloves</th>
<th>Working hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluopicolide</td>
<td>3.3489673</td>
<td>0.0558161</td>
<td>72.78</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Component</th>
<th>Formula</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermal-Potential</td>
<td>d_Derm遴</td>
<td>d_Derm遴选</td>
</tr>
<tr>
<td>Dermal-Workwear</td>
<td>d_Derm遴选</td>
<td>d_Derm遴选</td>
</tr>
<tr>
<td>Dermal-Working gloves</td>
<td>d_Derm遴选</td>
<td>d_Derm遴选</td>
</tr>
<tr>
<td>Inhalation</td>
<td>d_Inh遴选</td>
<td>d_Inh遴选</td>
</tr>
</tbody>
</table>

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### Propamocarb

#### Worker exposure from residues on foliage for FLC+PCH SC

<table>
<thead>
<tr>
<th>Crop type</th>
<th>Leaf vegetables and fresh herbs</th>
<th>Outdoor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indoor or outdoor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application method</td>
<td>Downward spraying</td>
<td></td>
</tr>
<tr>
<td>Application equipment</td>
<td>Manual-Knapsack</td>
<td></td>
</tr>
<tr>
<td>Worker's task</td>
<td>Reaching, picking</td>
<td></td>
</tr>
<tr>
<td>Main body parts in contact with foliage</td>
<td>Hand and body</td>
<td></td>
</tr>
<tr>
<td>Application rate of active substance</td>
<td>687.5 kg a.s./ha</td>
<td></td>
</tr>
<tr>
<td>Number of applications</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Interval between multiple applications</td>
<td>7 days</td>
<td></td>
</tr>
<tr>
<td>Half-life of active substance</td>
<td>30 days</td>
<td></td>
</tr>
<tr>
<td>Multiple application factor</td>
<td>3.9</td>
<td></td>
</tr>
<tr>
<td>Dermal absorption of the product</td>
<td>2.00%</td>
<td></td>
</tr>
<tr>
<td>Dermal absorption of the in-use dilution</td>
<td>8.60%</td>
<td></td>
</tr>
<tr>
<td>Dislodgeable foliar residue (<em>AppRate</em> <em>i_DFR</em>)</td>
<td>3.0 g a.s./cm²</td>
<td></td>
</tr>
<tr>
<td>Working hours</td>
<td>3 hours</td>
<td></td>
</tr>
<tr>
<td>Interval between multiple applications</td>
<td>7 days</td>
<td></td>
</tr>
<tr>
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<td>30 days</td>
<td></td>
</tr>
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<td>3 hours</td>
<td></td>
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<td>7 days</td>
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<td>2.00%</td>
<td></td>
</tr>
<tr>
<td>Dermal absorption of the in-use dilution</td>
<td>8.60%</td>
<td></td>
</tr>
</tbody>
</table>

#### Potential exposures

<table>
<thead>
<tr>
<th>Potential exposure</th>
<th>Workwear - arms, body and legs covered</th>
<th>Working wear and gloves</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total systemic exposure (mg a.s./day)</td>
<td>22.1547067</td>
<td>9.5494426</td>
<td>9.037207</td>
</tr>
<tr>
<td>Total systemic exposure per kg body weight (mg/kg bw/day)</td>
<td>0.3692451</td>
<td>0.1591574</td>
<td>0.0369245</td>
</tr>
<tr>
<td>% of RNAS</td>
<td>127.33%</td>
<td>46.88%</td>
<td>12.73%</td>
</tr>
</tbody>
</table>

#### Details

<table>
<thead>
<tr>
<th>Potential exposure</th>
<th>Workwear - arms, body and legs covered</th>
<th>Workwear and gloves</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermal Potential Exposure</td>
<td>22.1547067</td>
<td>9.5494426</td>
<td>9.037207</td>
</tr>
<tr>
<td>Dermal - Workwear - arms, body and legs covered</td>
<td>9.5494426</td>
<td>0.1591574</td>
<td>0.0369245</td>
</tr>
<tr>
<td>Dermal - Working wear and gloves</td>
<td>2.2154707</td>
<td>0.0369245</td>
<td></td>
</tr>
</tbody>
</table>

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Appendix 2.8  Worker exposure – Cucumbers (glasshouse) – 3 applications per crop

Fluopicolide + Propamocarb-hydrochloride SC 687.5

<table>
<thead>
<tr>
<th>Crop type</th>
<th>Application method</th>
<th>Application equipment</th>
<th>Worker's task</th>
<th>Main body parts in contact with foliage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruiting vegetables</td>
<td>Indoor or outdoor</td>
<td>Manual-Knapsack</td>
<td>Reaching, picking</td>
<td>Hand and body</td>
</tr>
</tbody>
</table>

**Fluopicolide**

**Worker exposure from residues on foliage for FLC+PCH SC**

- **Application rate of active substance (kg a.s./ha):** 0.1
- **Number of applications:** 3
- **Interval between multiple applications:** 7 days
- **Half-life of active substance:** 30 days
- **Dermal absorption of the product (%):** 0.26%
- **Dermal absorption of the in-use dilution (%):** 16.00%
- **Dislodgeable foliar residue (kg a.s./ha):** 15.00%
- **Working hours:** 8 hr
- **Dermal transfer coefficient - Total potential exposure:** 5800 cm²/hr
- **Dermal transfer coefficient - arms, body and legs covered:** 2500 cm²/hr
- **Dermal transfer coefficient - hands, arms, body and legs covered:** 580 cm²/hr
- **Inhalation transfer coefficient for automated applications:** 0.15 ha/hr

**Total systemic exposure (mg a.s./day):**
- **Workwear-arms, body and legs covered:** 5.73 mg a.s.
- **Workwear-arms, body and legs covered:** 2.47 mg a.s.
- **Workingwear and gloves:** 0.57 mg a.s.

**Inhalation transfer coefficient for cutting ornamentals:**
- **For re-entry 24 hours after application:** 0.0020000

**Percentage of RNAs:**
- **Total systemic exposure (mg a.s./day):** 13.87%
- **Total systemic exposure per kg body weight (mg/kg bw/day):** 0.0975581
- For re-entry 24 hours after application.
### Propamocarb

#### Worker exposure from residues on foliage for FLC+PCH SC

<table>
<thead>
<tr>
<th>Crop type</th>
<th>Fruiting vegetables</th>
<th>Indoor</th>
<th>Application method</th>
<th>Worker reentry - roof fogger</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application equipment</td>
<td>Manual-Knapsack</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Worker’s task</td>
<td>Reaching, picking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main body parts in contact with foliage</td>
<td>Hand and body</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Application rate of active substance</td>
<td>1 kg a.s./ha</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of applications</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interval between multiple applications</td>
<td>7 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Half-life of active substance</td>
<td>30 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple application factor</td>
<td>2.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal absorption of the product</td>
<td>2.00%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal absorption of the in-use dilution</td>
<td>8.60%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dislodgeable foliar residue ($i_{AppRate} \times i_{DFR}$)</td>
<td>ug a.s./cm²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Working hours</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal transfer coefficient - Total potential exposure</td>
<td>1 hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermal transfer coefficient - arms, body and legs covered</td>
<td>250 m²/ha/hr</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Dermal transfer coefficient - hands, arms, body and legs covered</td>
<td>2500 m²/ha/hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalation transfer coefficient (for automated applications)</td>
<td>0.015 ha/hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalation transfer coefficient for cutting ornamentals</td>
<td>0.015 ha/hr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalation transfer coefficient for sorting / bundling ornamentals</td>
<td>0.015 ha/hr</td>
<td></td>
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</tr>
</tbody>
</table>

####Potential exposure

<table>
<thead>
<tr>
<th>Formula</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{DermTcUCV} \times i_{DFR} \times i_{MAF} \times i_{Absorplnuse}$</td>
<td>Dermal-Potential</td>
</tr>
<tr>
<td>$\text{DermTcCV} \times i_{DFR} \times i_{MAF} \times i_{Absorplnuse}$</td>
<td>Dermal-Workwear-arms, body and legs covered</td>
</tr>
<tr>
<td>$\text{DermTcCV2} \times i_{DFR} \times i_{MAF} \times i_{Absorplnuse}$</td>
<td>Dermal-Working wear and gloves</td>
</tr>
<tr>
<td>$i_{AppRate} \times i_{lnhalTcAut} \times i_{WorkHr}$</td>
<td>Inhalation</td>
</tr>
</tbody>
</table>

#### Details

<table>
<thead>
<tr>
<th>Potential exposure</th>
<th>Workwear</th>
<th>Working wear and gloves</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total systemic exposure (mg a.s./day)</td>
<td>32.91</td>
<td>16.31</td>
<td>4.28</td>
</tr>
<tr>
<td>Total systemic exposure per kg body weight (mg/kg bw/day)</td>
<td>0.5336247</td>
<td>0.2413009</td>
<td>0.0713628</td>
</tr>
<tr>
<td>% of DNAP</td>
<td>184.01%</td>
<td>83.28%</td>
<td>24.80%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Potential exposure</th>
<th>Workwear</th>
<th>Working wear and gloves</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total systemic exposure (mg a.s./day)</td>
<td>30.81</td>
<td>15.3</td>
<td>3.56</td>
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<tr>
<td>Total systemic exposure per kg body weight (mg/kg bw/day)</td>
<td>0.5136247</td>
<td>0.2213009</td>
<td>0.0513625</td>
</tr>
</tbody>
</table>

For re-entry 16 hours after application