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Version history

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Date	Data points containing amendments or additions' and brief description	Document identifier and
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SANCO/10180/	2013 Chapter 4, 'How to revise an Assessment Report'.	
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CP 7 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/z), 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 thinito and Volare. FLC+PCH SC 687.5 was already a representative formulation of Bayer & G for the Annex Lanclusion of fluopicolide under Council Directive 91/414/EfC.

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 spectrum in the Domy etes fungi.

Fluopicolide has a long track record of safe use in a large number of largered crops within horticulture, e.g. cucumbers, lettuce and oncarable crops (e.g. potaro).

Fluopicolide is active against a write range of Opinyceto fungi, the cansal agents of devastating plant diseases of economic importance in EU27 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 termer.

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

The development of resistances of Comycetes 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, contribuing to effective and sustainable management of resistance development and preserving high level of protection against Oomycete diseases.

By reducing the Ootbycete 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 hopficultural produces for European consumer destinations and markets abroad, being it fresh of for the processing industo.

high-quality potatoes and hopficultural produces f abroad, being it fresh of for the processing industry.



CP 7.1 Acute toxicity

Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) is not acutely toxic *via* the oral route (LD₅₀ >2000 mg/kg bw), the dermal route (LD₅₀ >4000 mg/kg bw) or the inhalation route (QC_{50} >3195 mg/m³) and was not irritating to the skin or eyes. Fluopicolide + 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, Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) should be classified with skin sensitisation category 1B (H3+7).

Table 7.1- 1: Acute	toxicity studies with FLC+P	PCH SC 687.5	
Study Type	Species (sex)	Results 5	Reference O
Acute oral toxicity	Rat (M & F)	LD50 > 2000 mg/kg bw	<u>\$₩-2208\$3-02-1</u>
Acute dermal toxicity	Rat M & F)	LD50 > 4009 mg/kg/bw/d	<u>M-220889-022</u>
Acute inhalation toxicity	Rat (M & F) 🤹	$L_{c} 50 > 3.95 \text{ mg/m}^3$	<u>M-201342-01-1</u>
Acute skin irritation	Rabbit (M)	Biot irritating	<u>M224065-01-1</u>
Acute eye irritation	Rabbit (M)	Not instituting	<u>M-22465-01-67 5-000000000000000000000000000000000000</u>
Skin sensitisation	Guinea pig (M & F) 5	Non-sensitising	<u>M-237614-0181</u>
(modified Beuhler)			
Skin sensitisation (LLNA)	Mice (F)	Skin sensitise category 1B	<u>2376</u> <u>-01-1</u>

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 fluopicolide under Council Directive 91/414/EEC Please refer to the DAR and the Baseline Dossier of fluopicolide. One acute oral toxicity study is available for FLC+PCH SC 687.5, a short summary of which is presented below.

li l	
Data Point:	KCP\$7.1.1/01 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Report Author	
Report Year:	
Report Title?	AE BO66752 D4 SC6CA1-EXP11120A - Study for acute oral toxicity in rats
Report Nor	C036330 & A A A A
Document No:	<u>NA 220883-02-1</u>
Guideline(s) followed in	Directive 67/548/EEC, Annex V B, Part B, B.1; OECD 423 (1996); US-EPA 712-
study: 👸 🔬	C-98, 490, OPPTS 870.1100 (T998)
Deviations from current	6 animals (3 males and 3 females) were dosed concurrently rather than
test guideline 🖉	sequențially. A A A
Previous evaluation:	Oves, exaluated and accepted
E E	DAR 2005 OF ST ST
	for Propamocarb RAR June 2017
GLP Officially	Yes, conducted onder QLP/Officially recognised testing facilities
recognised testing	
facilities:	
Acceptability/Reliability?	

Executive Summary;

Three male and three female fasted rats were administered a single oral gavage dose of Fluopicolide + Propamocarb-hydrochlonde SC 687.5 (62.5+625 g/L), in demineralized water at a dose level of 2000 mg/kg b0. 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. Q_{μ}°

The acute oral LD₅₀ of Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) in rak 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 + Propamocarbehydrochloride SC 637.5 $(62.5+625)$ g/L)
Purity:	Fluopicolide 62.5 g/L, Propamocarb 6250g/L
Batch no.:	OP220159
2. Vehicle and/or po	ositive control
Vehicle:	Demineralized water w
3. Test animals	
C	
Species:	
	HSuc power of the second secon
Age. Weight at start:	$\sqrt[3]{105}$ 106 a malas 162 a 164 a Hamalas)
Source:	= 173 - 170 g marco, $102 = 104$ g marcos)
Acclimation period:	A Mays 'A G. A A A A A A A A A A A A A A A A A A
Identification	Cage Ords and index dual marking
Diet:	PROVIMICUIRA 3882 015 Switzerland
Water:	Available ad libum
Housing.	Polycarbonate cages , O' V , O'
Temperature:	$22^{\circ} \pm 2^{\circ} C \approx 0^{\circ} \sqrt{2} \sqrt{2}$
Humidity:	Approx. $\mathcal{D} \pm 5\%$
Air changes:	Approx 10 tipes/hour S S
Photoperiod	j12-hours by by by
.1	
Ĩ	
B. Study design 🔍	
1. In Jife dates: 6 🕅	overser 2002 to 22 Noversber 2002
2 Animal according	Stond Water &
2. Annual assignme	in size a 3 key
Dose(s)	\hat{c} \hat{c} \hat{c} \hat{c} \hat{c}
Expositive	A Once via gavage
Post exposure obser	vation period 14 days
Contraction of the second	

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 sacrified at the end of the observation period. All animals were subject to a gross necropsy.

1. Dose-response table (LD₅₀)

are symmarized in table 7,1.1-1 betow. The results of the study for acute oral toxicity in the f

Table 7.1.1- 1:	Dose response Q ⁴ 4 4 4 4 A A A A A A A
Dose (mg/kg bw)	Toxicological result* Duration of signs Time of death (14 days)
	$\mathcal{O}^{\mathcal{V}}$ $\mathcal{O}^{\mathcal{V}}$ Male rats $\mathcal{O}^{\mathcal{V}}$ $\mathcal{O}^{\mathcal{V}}$ $\mathcal{O}^{\mathcal{V}}$
2000	
	ry stemale pats of it of
2000	0/3/9 2 10 mins @ 3 hoars 2 2000

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

The LD₅₀ was therefore 200**0 / mg/kg b**w

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 bo Development in males or females.

4. Necropsy finding

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

III. Conclusion

The acute or a DED 50 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 + Propamocarbhydrochloride SC 687.5 (62.5+625 g/L).

Under the conditions of this study, Fluopicolide + Propamocarb-hydrochloride SC 687.5 ($62.5+62^{\circ}5$ 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 91/4/4/EEC. Please refer to the DAR and the Baseline Dossier of fluopicolide. One acute dermal toxicity study is available for FLC+PCH SC 687.50 a short overall summary of which is provided below.

Data Point:	KCP 7.1.2/01 0 4 6 6 6 6 4 4 6
Report Author:	
Report Year:	
Report Title:	AE B066752 04 SChr A1-EX011120X - Study for acute definal toxicity in sats
Report No:	C036532 & & & & & & & & & & & & & & & & & & &
Document No:	<u>M-220889-02-1</u> 0 7 7 8 8 8
Guideline(s) followed in	Directive 92/69/EEC, Agnex OPart B (1999), OE (402 (987); OS-EPA
study:	EPA @2-C9&192,: @PPT\$\$\$70.12@0(1998) O ~ ~ (1998)
Deviations from current	noné v v v v o
test guideline:	
Previous evaluation:	Ses, evaluated and accepted L S S
	DAR 2005 C C C C C
	for Propanocarb RAR June 2017 Y
GLP/Officially	Yes, conducted under GDP/Offreially recognised testing facilities
recognised testing	
facilities:	
Acceptability/Reliability.	$Y_{\mathbf{G}} = O^{\vee} \langle \langle \mathcal{O}^{\vee} \rangle \rangle \langle \mathcal{O}^{\vee} \rangle \langle \mathcal{O}^{$
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	

# 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 secluded 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 faily 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 a 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 day 8 of the study only. There were no unusual gross necropsy findings in any animal. The acute dermal  $UD_{50}$  of Fluopicolide Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) in rats was greater than 4000 mg/kg by. Classification for acute dermal toxicity in accordance with regulation (EC) No. 1272/2008 a 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	Ĺ	1

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

### 3. Test animals

Batch no.:	OP220159
2. Vehicle and/or po	sitive control
Vehicle:	None
3. Test animals	
Species:	Rat Q o d d d
Strain:	HsdCpb:WU $Q^{0}$ $\gamma$ $Q^{1}$ $Q^{2}$ $Q^{2}$
Age:	9 weeks (males) & 12 weeks (females)
Weight at start:	227-239g (males) & 200-221g (females)
Source:	
Acclimation period:	5 days
Identification:	Cage cards and individual markings , O , O , S , C
Diet:	PROVIMI KLAPA 3883.0.15 Switzerland
Water:	Available advibitum
Housing:	Housed individually in polycarlonate coges 2 2 2
Temperature:	$22^{\circ} \pm 2^{\circ}$
Humidity:	Appro% 55 ± 5% 28 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2
Air changes:	Approx. 10 dimes/lateur 2
Photoperiod:	12-Mours
Ó	
B. Study design	
1. In-life dates: Nove	mber 13, 2002 to November 27, 2002
• • • • <b>• °</b> •	
2. Animal assignmer	it and treatment v 0 v v v v
No. of animals (grou	$\mathcal{D}^{SIZe}$ $\mathcal{D}^{Y}$ $\mathcal{D}^{Y}$ $\mathcal{D}^{Y}$ $\mathcal{D}^{Y}$ $\mathcal{D}^{Y}$ $\mathcal{D}^{Y}$
Dose(s)	) $(Y + 0) = (Kg) = (K$
Exposure	attan normal Marker of the second sec
rost exposure observ	an here an as a factor of the second se

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 frem was left in place for 24 hours, after which the area was washed with soap and water.

#### K) 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)

· Dusc-respons			((	
Dose (mg/kg bw)	Toxicological result*	Duration of signs	Time of death	LD ₅₀ (mg/kg bw)
		Male rats		
4000	0/0/5	- Ø	- 4	× >4000 × 5
		Female rats	Ŕ	
4000	0/1/5	5 days to 1, days		jo ≫ <b>4</b> 000 jo ky

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

## The $LD_{50}$ 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 o 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  $LD_{50}$  of Fluopicolide + Proparnocarb-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 if therefore not required.

# Assessment and conclusion by applicant

The study is realid 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 ( $LD_{50} > 4000$  mg/kg b%), 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 fluopholide under Council Directive 91/414/EEC. Please refer to the DAR and the Baseline Dossier of fluopholide. One source inhalation study is available for FLC+PCH SC 687.5, a short overall summary of which is provided below.



Data Point:	KCP 7.1.3/01	
Report Author:		
Report Year:	2003	
Report Title:	AE C638206 and Propamocarb SC 62,5 + 625 - Study on acute inhalation in ras according to OECD No. 403	
Report No:	C032394	
Document No:	<u>M-231342-01-1</u>	
Guideline(s) followed in study:	Directive 92/69/EEC., B2 (1992); OECD 403 (1981; US-EPA 712C-98-193, OPPTS 870.1300 (1998)	Î,
Deviations from current test guideline:	None	Ļ
Previous evaluation:	yes, evaluated and accepted DAR 2005 for Propamocarb RAR June 2017	,° ≯
GLP/Officially	Yes, conducted under GLP/Officially recognised testing facilities	
recognised testing		
facilities:		
Acceptability/Reliability:	Yes A & Q Q O' Q' A	

## **Executive Summary:**

The acute inhalation toxicity of FbC+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 thour continuous nose-only exposure. The target concentration was the limit concentration 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 to 4 µm with a geometric standard deviation (GSD) of 1.5 to 3 (2.96±2.43 µm).

Animals were then subject a 44-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 days 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 tospiratory tract).

There were no deaths of 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 FLC PCH SC 688,5). there were no unusual findings on gross necropsy.

The 4-hour acute inhabition  $PC_{50}$  of FLC+PCH C 68/25 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. A Fluopeolide Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) Purity: Fluopicolide 62.5 g/L, Propamocarb 625 g/L Batch no

# 2. Xenicle and/or positive control

Vehicle.

None



## 3. Test animals

Species:	Rat $\mathbb{Q}^{\circ}$
Strain:	HsdCpb:WU
Age:	Approximately 2 months
Weight at start:	Weight range was within $\pm 10\%$ of the mean
Source:	
Acclimation period:	5 days
Identification:	Cage cards and individual markings
Diet:	PROVIMI KLIBA 3883.0.15, Switzerland
Water:	Available <i>ad libitum</i>
Housing:	Housed individually in convertional Makrolon type III cages
Temperature:	$22^\circ \pm 2^\circ C$
Humidity:	Approx. 40-60%
Air changes:	Approx. 10 times/hour & @
Photoperiod:	12-hours
B. Study design	
1 In-life dates: Nove	ember 20, 2002 December 22, 200 , a start of a
1. In me dates. 1000	
2. Animal assignmer	it and treatment of a gradient of the second s
No. of animals (grou	p size) 5/sex 5/sex 4 A A A A A
Dose(s)	$\odot$ 0 (control) and 5000 mg/kg by Ctarget concentration)
Exposure	A fours prose-opty of a grad
Post exposure observ	vaction petrod 34 days & ~ ~ ~
The second strates 1	

The acute inhalation toxicity of FSC+PCFI SC 687.5 was investigated by exposing groups of five male and five female rate to a Daeros of atmosphere of the sest substance for a hour continuous nose-only exposure. The target concentration was the limit concentration 5000 mg/m3; however, the maximum technically obtainable concentration was 3495 mg/m3. Animals were then subject a 14-day observation period, following which the animals were sacrificed and a full gross recropsy was performed.

 $\bigcirc$ 

# Table 74,3-1: Concenterions of the test substance

Mean concent	ation Normal concentration MMAD ± GSD	Resp. fraction
(mg/m ³ )	$(\mu m)$	$(\% < 3 \ \mu m)$
3103	2.96 ±2.43	50.8
A		

The mass median aerodynamic diameters (MMAD) was in the recommended range of 1 to 4  $\mu$ m with a geometric standard deviation (GSD) of 1,5 to 3, 2.96±2.43  $\mu$ m). 

# C. Methods

# 1. Observations

The animals were examined for mortality and clinical signs several times on the day of exposure and at least once don'y 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 below. A

. Dose-response	e table (LD ₅₀ )	Ś	Å.	
Target concentration (mg/m ³ )	Toxicological result*	Duration of signs	Time of death	
		Malorats		
0	0/0/5	- <u> </u>	0, 7, 0	
5000	0/0/5		\$ - \$	>5000
		A Female rats		
0	0/0/5			
5000	0/0/5			5000

* Number of animals which died /number of animals with shens / total number of animals , '

The LD₅₀ was therefore > 3195 mg/m

## 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 gaid in treated females, during the observation period, was considered to be incidental and not air effect of treatment with EDC+PCH SC 687.5

# 4. Necropsy finding

s in animals sacrificed at the end of the observation period. There were no unas

# III Conclusion

The 4-hour acute inhalation  $\mathcal{R}C_{50}$  of FLQ  $\mathcal{P}CH$  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 applicant?

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 (LC₅₀ >  $3195 \text{ mg/m}^3$ , and classification for acute inhalation toxicity is not required.

# **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.

Data Point:	KCP 7.1.4/01
Report Author:	
Report Year:	2003
Report Title:	AE B066752 04 SC61 A1 (EXP11120A) - Acute derma Firritation in rabbits
Report No:	C038035
Document No:	<u>M-224065-01-1</u>
Guideline(s) followed in	Directive 92/69/EEC, B.4 (1992) DECD 404 (1992)
study:	
Deviations from current	none of the of t
test guideline:	
Previous evaluation:	yes, evaluated and accepted
	DAR 2005 $($ $)^{\circ}$ $)^{\circ}$ $($ $)^{\circ}$
	for Propamocarb RAB June 🔊 17 🔬 🖉 🖉
GLP/Officially	Yes, conducted under GLP Officially recognised testing facilities
recognised testing	
facilities:	
Acceptability/Reliability:	Yes Q V V V V V V V V

## **Executive Summary:**

The potential of FLC+PCH SC 687.5 to instate 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 flanks of three animals, via application onto a gauze pad, and held *in situ* with a semi-occusive cressing for four hours. The intreated 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 son was examined approximately 3-, 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 bours 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 crythema observed, had recovered by day 2 of the observation period in all animals.

Therefore, FLC+PCH SC 687 s is not ritating to the skin of rabbits following a 4-hour exposure period and no classification for derival irritation is thus required.

I. Marerials and Methods

# A. Materials

1. Test materiat

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

2. Vehicher and/or positive control

Vehicle:

None



# 3. Test animals

Species: Strain:	Rabbit 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 $\sqrt{2}$ $\sqrt{2}$
Temperature:	18 ± 3°C
Humidity:	30 to 70%
Air changes:	Approximately 12 cycles $\beta^{\circ}$ $\gamma^{\circ}$ $\gamma^{\circ}$ $\gamma^{\circ}$ $\gamma^{\circ}$
Photoperiod:	12 hours light/12 hours dark
1	
B. Study design	
1. In-life dates: Not s	stated
<b>.</b>	
2. Animal assignmer	it and treatment of the Real o
No. of animals (grou	p size) 3 mates
Dose(s)	
Exposure	Y A Hours semi-occlusive a grad
Post exposure observ	ration petiod 4 days
Approximately 24-h	urs prior to the atment both Manks of each animal were shorn with electric clippers
and the skin example	d and a study. The undiluted test
item (0 5mL) was apr	the to the right flank of 3 animals, via approximition onto a gauze pad, and held in
situ with a sero-occli	Sive dressing for 4 hours. The untreated skin served as a control. After the 4-hour
exposure period the	tressings were reproved and the area wined with a moistened cotton had
C. Methods	
1. Observations	
The treated shin was	exampled approximately 24-, 24-, 48- and 72-hours following removal of the
dressing. Local derm	al irrotation was evoluted for each animal using the following numerical scale:
la construction de la constructi	

# Erythema and Eschar formation

No erythema No erythema No erythema	0
Very slight rythema (bacely perceptible)	1
Well-defined ergthema	2
Moderate to severe grythena	3
Severe erythema (beet redness) to slight eschar formation	4
(injuries in depth) preventing	



### Oedema formation

No oedema	0	° r
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	4	
the area of exposure)	L, '	
II. Desults and Discussion	Õ ^v	
11. Results and piscussion		

#### 1. Dermal reactions

The observed dermal reactions for each animal, and the mean scores for 24,048 and 72 hours for each animal are provided in the table below:

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Table 7.1	.4-1: Derr	nal irritation so	cores	°~	N 💊	× A	×.	
Animal No.		e	Sco 1 h	ores after 24 4	treatmen 48,h	t * ⁵ 72 h	Mean scores (24, 2 h)	Reversible (day)
287	Erythema Oedema	Q.						
288	Erythema Oedema	9 Ch			б ФО			2
289	Erythema Oedema							2

# Table 7.1.4-1: Dermal irritation scores

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

III. Conclusion

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

# Assessment and conclusion by applicant?

The study is galid 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 ^(C) Eye irritation ^(C)

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



Data Point:	KCP 7.1.5/01
Report Author:	
Report Year:	
Report Title:	AE B066752 04 SC61 A1 (EXP11120A) - Acute eye irritation in rabbits
Report No:	C038025
Document No:	<u>M-224035-01-1</u>
Guideline(s) followed in	EC Directive No. 92/69/EEC,, B.5 (1992); OECD 405 (1987)
study:	
Deviations from current	A systemic and topical analgesic was not applied
test guideline:	$\dot{\mathcal{O}}$ $\dot{\mathcal{A}}$ $\dot{\mathcal{A}}$ $\dot{\mathcal{A}}$
Previous evaluation:	yes, evaluated and accepted $\sqrt[\infty]{}$
	DAR 2005
	for Propamocarb RAR June 2017
GLP/Officially	Yes, conducted under GLP Officially recognised resting facilities
recognised testing	
facilities:	
Acceptability/Reliability:	Yes O' & A A
<b>Executive Summary:</b>	

# **Executive Summary:**

The eve irritating potential of FLC+PCH SC 687 S was investigated in three male New Zealand White rabbits only animals without irritation, ocular defects or pre-existing njury were used). A single dose (0.1 mL) of the undiluted test item was installed into the compunctival sac of the left eye of each animal. No irrigation of the eyes was performed. The untreated (right) eyeserved as the control

The eyes were examined 1-, 20, 48 and 22-hours following administration of the test item. Conjunctival reactions, initis and cornear opacity were evaluated daily for each animal; the detection of the presence or absence of corneal opacity was added with fluorescein. The ocular reactions were assigned a numerical score.

48 and 12 hours were 1.0, of and 1.0 for conjunctivae The mean scores for each animal over 24, 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 opacito. A

Very slight chemosis (grade 1 of 2) and very sught 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 3/3 animals of day bonly.

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

# J. Materials and Methods A. Materials 1. Test materia Fluspicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L) Test substan FüropiceTide 62.5 g/L, Propamocarb 625 g/L Purity Batch OP220159 ŝ 2. Vehicte and/or positive control

Vehicle:

None



## 3. Test animals

Species:	Rabbit 🔊 🐁
Strain:	New Zealand White
Age:	2-4 months old
Weight at start	$29 \pm 0.3 \text{ kg}$
Source:	2.7 ± 0.5 Kg
A colimation noriod:	At least 5 days
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:	$18 \pm 3^{\circ}\mathrm{C}$
Humidity:	30 to 70%
Air changes:	Approximately 12 cycles $\beta^{\circ}$ $\beta^{\circ}$ $\beta^{\circ}$ $\beta^{\circ}$ $\beta^{\circ}$
Photoperiod:	12 hours light/12 hours dark a hours and hours light/12 hours dark a
I	
B. Study design	
D. Study design	
1. In-life dates: Not s	stated $\mathcal{L}^{O'} \stackrel{\sim}{\sim} \sim$
2. Animal assignmer	it and treatment
No. of animals (grou	$p size) \ll 3 mates a a a a a a a a a a a a a a a a a a a$
Dose(s)	6 O ^v 0.13mL O ^v V A ^v A ^v
Exposure	Single instillation in conjunctival sac

Irrigation Post exposure observation period 4 days

Approximately 20 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 installed into the conjunctival sac of the left exe 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

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control C. Methods 1. Observations The eyes were examined 1-24-, 48- and 72-hours following administration of the test item. Conjunctival reactions initis and corneal opacity were evaluated daily for each animal; the presence or observe of corneal opacity were evaluated daily for each animal; the presence or observe of corneal opacity were evaluated daily for each animal; the presence or observe of corneal opacity were evaluated daily for each animal; the presence or observe of corneal opacity were evaluated daily for each animal; the presence or observe of corneal opacity oper evaluated daily for each animal; the presence of observe of corneal opacity oper evaluated daily for each animal; the presence of observe of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence of corneal opacity oper evaluated daily for each animal; the presence oper evaluated daily for each animal; t absence of corneal opacity was and ed with a Liv lamp following the addition of one or two drops of 0.5% sodium fluorescein to the eve (performed on day 1 and day 2 in animal 287 and 288 and on day 1

0.5% socium nuorescentro the eye (performed on day 1 and day 2 in animal 287 and 288 and on day 1 in animal number 289). The beular reactions were assigned a score in accordance with the following numerical scate:



Chemosis (lids and/or nicititating membranes):       0         No swelling       0         Any swelling above normal (includes nicititating membranes)       1         Obvious swelling with partial eversion of lids       2         Swelling with lids half closed       4         Redness (refers to palpebral and bulbar conjunctivae, contea and iris):       0         Blood vessels normal       0         A number of blood vessels definitely hyperemic (injected)       1         Diffuse, crimson colour, individual vessels not early discernible       2         Discharge       0         Absence of discharge       0         Slight discharge       0         Discharge with moistening of lids and hairs adjacentob lids       2         Discharge of discharge       0         Normal       2         Markedly deepened rugae congestion, swelling, moderate circum ebreal       1         Normal       0         Statemet or officiscarges       0         Degree of opacity:       0         No reaction to light       0         Scattere for on opacity       0         Scattere for officiscarges       1         Opaque cornea, fris no discertible forough the opacity discertible       3         Opaque cornea, fris no discert	Conjunctival lesions and discharge		
Redness (refers to palpebral and bulbar conjunctivae, cortea and iris):       0         Blood vessels normal       0         A number of blood vessels definitely hyperemic (injected)       1         Diffuse, crimson colour, individual vessels not early discernible       2         Diffuse, crimson colour, individual vessels not early discernible       3         Diffuse, crimson colour, individual vessels not early discernible       3         Discharge:       0         Absence of discharge       0         Discharge with moistening of lids and hairs and active of disconnective of disconnectiv	Chemosis (lids and/or nictitating membranes): No swelling Any swelling above normal (includes nictitating membranes) Obvious swelling with partial eversion of lids Swelling with lids half closed Swelling with lids more than half closed		
Discharge: Absence of discharge Slight discharge Discharge with moistening of lids and hairs and accent to lids Discharge with moistening of lids and hairs on wide area around eyes <u>Iris lesions</u> Normal Markedly deepened rugae congestion, swelling, moderate circum-corneal Normal Markedly deepened rugae congestion, swelling, moderate circum-corneal No reaction (any combination), icts still reacting to light No reaction to light <u>Corneal lesions</u> Degree of opacity: No ulceration or opacity Scattered or diffuse areas of opacity details of iris clearly visibly Lasily discernible translucent area details of iris slightly observed Nacreous areas, no details of iris visible, size of puptibarely discernible Opaque cornea, fris not discernible through the opacity Area of opacity One quarter (or less) but not zero No uncertainty of the size of the	Redness (refers to palpebral and bulbar conjunctivae, corrier and iris): Blood vessels normal A number of blood vessels definitely hyperemic (injected) Diffuse, crimson colour, individual vessels not easily discernible Diffuse, beefy red		
Corneal lesions       0         Degree of opacity:       0         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 observed       2         Nacreous areas, to details of iris visible, size of puptiblarely discernible       3         Opaque cornea, iris no discernible through the opacity       4         Area of opacity       1	Discharge: Absence of discharge Slight discharge Discharge with moistening of lids and hairs adjacent to lids Discharge with moistening of lids and hairs on wide area around eyes <u>Iris lesions</u> Normal Markedly deepened rugae congestion, swelling, moderate circum-corneal hyperemia, or injection (any combination), ins still reacting to light No reaction to light		J ^y G ^y
Greater than one had but less than three quarters 3 Greater than three quarters up to whole area 4	Corneal lesions Degree of opacity: No ulceration or opacity Scattered or diffuse areas of opacity details of iris clearly visible Easily discernible translucent area, details of iris slightly observed Nacreous areas, no details of iris visible, size of pupil barely discernible Opaque cornea, iris no discernible through the opacity Area of opacity One quarter (or less) but not zero Greater than one quarter but less than a half Greater than one half but less than three quarters Greater than three quarters up to whole area	0 1 2 3 4 1 2 3 4	

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:



Animal			Scor	es after	treatm	ent *	Mean	Reversible	
No.	Region of eye	Description	1 h	24 h	48 h	72 h	scores (24-72 h)	(day)	j G
287	Conjunctiva	Chemosis Redness	2	2	1	0	<ul> <li> ⁰/₂, 1.0         ⁰/₂, 0.3     </li> </ul>		F
		Discharge	1	1	0	0	0.3		
	Iris	Lesions		$\bigcirc_1^0$	0				Ì
	Cornea	Opacity intensity Opacity area		1		0			
288	Conjunctiva	Chemosis Redness Discharge					0.7 0.3 0.3		
	Iris	Lesions			Q [°]		0.00		
	Cornea	Opacity intensity Opacity area							
289	Conjunctiva	Chemosis & & Redness Discharge					₩.0 0.3 0.3	⋧ 3	
	Iris	Lestons of C			60	. O	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$		
	Cornea	Opacity intensity Opacity area					0.0 0.0		

Table 7.1.5-1. Ocular irritation scores

The mean scorec for each animal over 24, 48 and 72 hours were 1.0, 9.7 and 1.0 for conjunctivae chemosis, 0.3 9.3 and 0.3 for conjointive redness, 0.0 0.0 and 0.0 for iritis and 0.3, 0.0 and 0.0 for Ĩ corneal opacity. L

Very slight chemosis (grade 1 or 2) and very slight redness (grade V) 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  $i_{D}^{2/3}$  animals off day 1/only

# III Conclusion

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

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# 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 eve initiation 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.  $Q_{\mu}^{\circ}$ 

Data Point:	KCP 7.1.6/01
Report Author:	
Report Year:	2003
Report Title:	AE B066752 04 SC61 A1 (EXP11120A) - Skin sensitization test in Quinea Digs
	(Modified Buehler test: 9 applications)
Report No:	
Document No:	<u>M-224078-01-1</u>
Guideline(s) followed in	EC Directive No. 96/54/EEC@B.6 (1996); OECD 406 (1992)
study:	
Deviations from current	none Q A A A A A
test guideline:	
Previous evaluation:	yes, evaluated and accepted O 2 2 2 2 2 2
	DAR 2005 $\mathcal{A}$ $\mathcal{A}$ $\mathcal{A}$ $\mathcal{A}$ $\mathcal{A}$
	for Propamocarbe RAR forme 2017
GLP/Officially	Yes, conducted under GLP/Officially (ecognised testing facilities 🖉 🖉
recognised testing	
facilities:	
Acceptability/Reliability:	Yes $Q'$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$ $\sim$

## **Executive Summary:**

A preliminary test was conducted in which the sest iters was applied at concentrations of 100% and 50% (w/w) to the shaved flanks of 2 male and 2 female Hartley guines pigs (4 applications).

The highest concentration selected for the induction phase of the main study should cause weak/moderate skip reactions, whilst the highest concentration for the challenge phase should cause no irritant effect; therefore as no dermakeffects were noted with 50% (w/w) and only mild irritation effects were noted with undiffered test substance, the undifference (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, & 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 feft 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 challing 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 sensitiser, therefore no classification for skin sensitisation is warranted.



# A. Materials

# 1. Test material

	Q° >>
Test substance: Purity:	Fluopicolide + Propamocarb-hydrochloride SC 687.5 (62.5+625 g/L)
Batch no.:	OP220159
2. Vehicle and/or po	sitive control
Vehicle [.]	Purified water
3. Test animals	
~ .	
Species:	Guinea pigs
Strain:	Hartley Crl: (HA) BR
Age:	1 to 2 months old in the second
Weight at start:	$453 \pm 30$ g (matos) and $432 \pm 32$ g (females)
Source:	
Acclimation period:	At least 5 days
Identification:	Individual ear tattoo of fr of for for for for the
Diet:	106 perfeted diet, SAFE, Villemoisson, France
Water:	Provided addibitune of a management of the second s
Housing:	Housed individually in polycarbonate cages with statuless steel lids
Temperature:	$22 \pm 2^{\circ}$ $2^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$ $3^{\circ}$
Humidity:	30 to 78% 2 , s 2 O & 2 , y
Air changes:	Approximately 12 hours 2 2 0
Photoperiod:	120 hours the hours clark and a second se
D. Studu danian	
B. Study design	
1. In-life dates: Nove	endber 18 2002 $\infty$ January 3, 2003 $\sqrt{2}$ $^{\vee}$
2. Animal assignmen	nt and treatments y y O >>
No. of animals (grou	$p$ (gize) $\sqrt{2}$ (gize a substance group) 15 and 15 female guinea pigs
	Vehicle control group: 5 male and 5 female guinea pigs
Range finding	Yes (preliminary study with 2 male and 2 female guinea pigs)
Exposure	tion(s), no of miduction phase: 100% on days 1 & 3 and 50% (w/w) on days 5.
applications)	2 . 8. 10. 12. 150 17 and 19
	Charlenge Y: 100% on day 29
Ĩ. Ŋ	$\mathcal{O}^{\vee}$ Challenge 2: 50% (w/w) on day 44
Reliability che	Regularly assessed with Mercaptobenzothiazole
For the preliminar	ad man tasts, the availingtion sites of each animal ware aligned and should the day
before application of	the induction phase and challenge phase and again before the 18 hour reading of
the challenge nucleo	Appropriate concentrations of the test substance were loaded on to a filter paper
the unangenze parase.	¹ appropriate concentrations of the test substance were readed on to a filler paper

(approximated) 8 cm² which was applied to the shaved skin of the flank and held in place with an occlusive dressing for 6 hours. For the meliminary 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

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



2 3

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 Mank whilsto vehicle only was applied to the posterior left flank of the same animal As equivocal reactions 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 fank and vehicle to the right flan No residual test item was noted on removal of the dressing for the induction or challenge phases.

## C. Methods

## 1. Observations

Animats were Animals were observed at least once daily for mortality and Pinical the day of group allocation, and on days 3**% and 46 of** 

## 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

Discrete or patchy erythema Moderate and confibent erythema

Intense ervehema

In addition, any observed geogram of other lesions were recorded. Any reactions in the treated group (score  $\geq$  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 suration of those in the control animals are considered positive.

Discussion A. Results

# 1. Clinical sign

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

# 2. Dermal reactions

In the proximinary 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 study of g table below.

Table 7.1.0-	1. Scorm	g of uer	mai reac	uon uur	mg the k	Hanenge	: phage	of the m	ang sinuy-	, <i>°</i>
		24 hours				» 48 ho	ouro		Totabil	imber of
					A	4		° A		
				After f	inst chall	enge న	°≈ ⊘			
	Ma	ale	Fem	ale 🖇	Â.	ale	Fe	male 🤇	Male	Female
	LF	RF	LF	RF	jif ,	RF Q	[©] ۲۴ 🤅	RF	Ő g	
Control	0/5	5/5	0/5	€ 1/5 [∧]	0/5	200	Q73	≈¶/5	لا 5/5	K K
Treated	0/10	6/10	0/10.2	3/10/	0710	A10	€0/10 č	2/10	650	Q _{4/10}
			<u>A</u>	After se	cond cha	llenge		No.		2
Control	0/5	0/5	0/5	\$ 0/5 ₀	0/5	03	×0/5	0/5	0/5	0/5
Treated	0/10	0/10	0/10	000	0/10	0/10	0/100	0/10	ؕ10	0/10
40 T 1 0 1			. ~~	~ ¥	OMA DU LU			1 0. 4	for I a	· ·

		CA		
Table 716 1. Scoring of derma	l reaction during	the eballence	nham ^v af tha	main otudy
Table 7.1.0-1. Scoring of definal	i i cacuon uuring	the remaininge	phase of the	manestudy

*Number of animals with positive derma responses for core of 1-3) /number of animals in dose group, or = Left flank (vehicle), RF = right flank (test item)

Following the first challenge apprentien, discrete ersthemag(grade 1) was observed at the 24-hour reading in 6/10 and 9/200 of the control and breated groups respectively persisting until the 48-hour reading in 3/10 and 6010 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.

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II. Conclusion

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Under the conditions of this modified Benner 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. Ø

# 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 and the second se skin sensitisation is therefore not required on the basis of this study.



Data Point:	KCP 7.1.6/02	
Report Author:		
Report Year:	2004	
Report Title:	EXP11120A (AE B066752 04 SC61 A1) (AE C638206 62.5 g/l + propamocard	Ş
	HCl 625 g/l) - Evaluation of potential dermal sensitization in the local lymph node	J.
	assay	
Report No:	C046056	
Document No:	<u>M-237614-01-1</u>	
Guideline(s) followed in	OECD 429 (2002)	2
study:		C
Deviations from current	None $\nabla $ $O$ $O'$ $V'$	Å
test guideline:		0
Previous evaluation:	yes, evaluated and accepted $\sqrt[6]{2}$	<i>y</i>
	DAR 2005	
	for Propamocarb RAR Juge 2017	
GLP/Officially	Yes, conducted under GLP/Officially to cognised testing facilities '	
recognised testing		
facilities:		
Acceptability/Reliability:	$Yes \qquad \swarrow \qquad \checkmark \qquad \checkmark \qquad \checkmark \qquad \land \qquad \land \qquad \land \qquad \land \qquad \land \qquad \land \qquad \land$	

# **Executive Summary:**

The skin sensitising potential of FLC+FCH SC 687,5 was investigated in a morse local lymph node assay (LLNA). Groups of 4 female CBA mice were topically administered control item of test substance at concentrations of 10, 25, 50 or 100 %; 16 aqueous Plutonic acid provided the vehicle/vehicle control whilst p-Benzoquinone 0.4% 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 of days 6/1 and 2 of the study. The test site was examined for dermal reactions and annuals were examined daily for mortality and clinical signs; body weights were becorded at the start of the study and at sacrifice. Following injection with ³H methyl thyniding the nodes of each group of mice were reproved and pooled and prepared for the determination of provideration indices. A proliferation index of 23 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 15, 25, 50 and 100% respectively. As the simulation index at 100% was >3 FLC+PCH SC 687.5% 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 887.5 should be classified for skin sensitisation category 1B (H317).

1	
A. Materials	
l. Test material 🔏	
Test substance,	Kluopicolide Propanocarb-hydrochloride SC 687.5 (62.5+625 g/L)
Purity: 🖉 🔨	Flugpicolide 62.5 g/L, Propamocarb 625 g/L
Batch no 2 5	
2. Vepicle and/or po	jsitive 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 <i>ad libitum</i>
Housing:	Individually housed in suspended, stainless steel, wire most cages
Temperature:	20°C to 24°C
Humidity:	40% to 70%
Air changes:	10 to 15 changes per hour 2 0 0 2 0 2
Photoperiod:	12 hours light/12 hours darko
B. Study design	
1. In-life dates: Octo	ber 20. 2004 October 26. 2004 20 20 20 20 20 20 20 20 20 20 20 20 20
2. Animal assignmen	it and treatment of the second s
No. of animals (grou	p sizes 0 4 temate/geoup
Range finding	
Exposure (concentration	tron(s), no. of v (vehicle control), 40, 25, 50 & tou% and 0.1% p-Benzoquinone
applications)	y in a 50:50 fest substance: venicle/mixture
Each mouse was opi	callo dosed on the dorsal surface of each ear, once daily on days 0,1 and 2 with
25µl of the test substa	the using an Eppendorf pipette; the applied dose remained on the ear reflecting
realistic exposure to t	pe test substance. V & & &
, Q	
C. Methods 🦒	
2	
1. Observations	
The animals were ex	amined daily for mortality and elinical signs of toxicity. Body weights were
recorded at the start o	f the test and at secrifice
, a '	
	Y A A A A
2. Dermal observation	$\operatorname{Dns} \mathcal{S}^{\prime} \mathcal{S}^{\prime} \mathcal{Q} \mathcal{S}^{\prime}$
The site of application	n was examined for signification
	was examined for signs of local initiation.
3 Proliferation acca	
On day 5 of the study	the tax vein of each mouse was injected with 250 μ l of sodium chloride (0.9%)
containing 20µCi of	'H methyl thymidine; the mice were retained in a plastic cage for 5 hours. The
nodes torm each grou	p of 4 mice were pooled in a tube of physiological saline and disaggregated with
a plastic piston to obt	ain a connective-tissue-free cell suspension.
Cell suspensions were	e washed with 10 mL of 0.9% physiological saline, centrifuged for 20 minutes at
1800 rpm. The result	ing pellets were resuspended in 4 L of 5% trichloroacetic acid (TCA) and stored
1	



overnight at approximately $+4^{\circ}V$. 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 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 consentration of the test substance results in an increase of ³H-TdR incorporation of 3-fold or greater (Re. 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.

II. Result

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 reatment site in the treated negative control or positive control groups.

3. Proliferation assa

Table 5.1.6-2: mean DPM and simulation index

Group No.	Concentration Man DPM &	Simulation index
	Control the grand and gran	-
2		0.96
3	23% 5% 20 5% 27 524	0.66
4	30% 1 2 ⁵ 2 ⁷ 2 ⁶ 1261 7	1.6
5		6.3
6	Positive control * Q Q 391	4.4
A		•

*1% Aqueous Pluronic acico **0.1% p-Benzoquinone in 50% yest 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 of 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 securitisation 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 sensitiser, and classification for skin sensitisation category 1B (H317) is appropriate.

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

No such studies are necessary since there are no concerns arising, e.e. from potential synergistic SC 68' additive effects exerted by the active substance(s) or other components in FLC+ CH would require further investigations.

Supplementary studies for combinations of plant projection products e necessary since FLC+PCH SO 687. S is not intended for a second structure in the second structure in the second sec CP 7.1.3 Suplementary studies for cambinations of 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 arros, 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 estidents also covers bystanders; therefore, exposure estimates for bystanders are also considered acceptable for all intended uses of FLC+PCH SC 687.5, provided normal 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 trom combined long-term exposure to fluopic for and propanocarb. Propanocarb and tluopic for a combined acute exposure risk assessment is not reeded.

FLC+PCH SC 687.5 is a fungicide for the control of bomycete phytopathogens, especially in potato plants, but also in vegetables (indoors and outdoors) It combines fluopicolide (ELC), a fungicide with a novel mode of action and propanocarb-bydrochtoride (PCH), a well-known anti-fungal 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 foliat, 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 lettices 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.

Crop	Application maximation formulation (Lepa)	ntion rate	Spray Addition water (L/ha)	Application equipment	Number of applications
A.		Field Grops			
Potato			100-1000	Field Crop Sprayer	1-4
Potatoes treate	dewith a tractor boom (Field Cr	Sprayer). AO	EM model used	l.	
This scenario	also covers positoes treated with	h 1-3 applications	s and 1-2 applic	ations per crop.	
Lettuce		1	200-1000	Handheld Sprayer	1-2
Lettuce toated	with a manual hand-held and k	napsack sprayer.	AOEM model	used.	
This scenario a	lso covers lettuces treated with	only 1 applicatio	n per crop.		

Table 7.2-01: Summary of critical pres patterns (i.e. worst case) of FLC+PCH SC 687.5



			Greenhouse Crop)		
Cucumber (high tech glasshouse)	1.6	0.1	1	1000-1250	Handheld Sprayer	1-25
Cucumbers tre The Dutch gre	ated with manuated with manuated with manuated with a second second second second second second second second s	al sprayer, and vulue of the sprayer, and volume of the sprayer of	worker re-entry aft ors and AOEM mo	er roof-fogger del used for w	. Up to 3 applicat	tions per crep?
Estimations of hydrochloride predictive mod	<u>potential oper</u> using the list c lels:	ator exposure of intended use	have been under es (Appendix 2 o	taken for flu f this docom	picolide and pro-	opanocarb®
Field crops: T	he current EFS	SA modelling	tool on the asses	smept of exp	osure of operato	rs, workers,
residents, and	bystanders, wa	is used to estin	nate the respective	expositives	from the applica	ation of
FLC+PCH SC	687.5 on pota	toes and lettuc	ces. The AOEM@	alculator rel	eased of 030 May	rch 2045
supports the E	FSA guidance	document in	m was last upgate	a on 24 Apr		
Glasshouse cro	ops: The Dutch	n greenhouse n	nodel has been u	sýd ² .		× Č
Dermal absorr	tion and AOE	L values	$\mathcal{D}_{\mathbf{x}}$ $\mathcal{D}_{\mathbf{x}}$ $\mathcal{D}_{\mathbf{x}}$	N D		. L
The estimation	is of human de	rmal penetrati	on of fluopicolid	eand propar	nocarb which ar	e the active
substances in t	he mixed form	natation FLC+	PCH SC 087.5 4	ere obtained	from two in vin	o dermal
absorption stu	dies using hun	ian skin conde	reted by	2063; M-2	2382001-1, and	
<u>; 2015; M-5</u>	<u>16805-01-1</u>	spectwely. Th	e proposed value	s including t	he AOEL values	sare
summarised be	elow. The vap	outpressures	of both actives a	below 5x1	0 [®] Pa.	
Table: 7.2-02: assessment.	Proposed va	Mes for EU o	ndpoints used of	n the non-di	etary human ri	sk
Endnoints us	<u> </u>		A	<u>(6)</u>		
	ed in risk assess	sment &	Fluopicolide		Propamo	carb
	ed ûn risk assess	sment &	Fluopicolide Vermatipenetratio	n o v	Propamo	carb
Concentrate	ed (in risk assess) (g/L of active)	sment &	Fluopicolide Vermal penetratio	∑ 0 ⁷ 5 n 0 0 ₽ 5	Propamo 2% (625	carb g/L)
Concentrate %	ed in risk assess (g/L of active)	ment 4	Fluopicolide <u>Vermat penetration</u> 0.26 % (62.5 g/L ** (0.1 PL outdoor	n O O v v v v v v v v v v v v v v v v v v v	Propamo 2% (625 8.6%** (1 g/L o	carb g/L) utdoor use)
Concentrate Spray dilution	cd ûn risk assess (g/L of active) % (g/L of active)	ment 4 13.8 13.8 13.8 13.8 13.8 13.8 13.8 13.8 13.8 13.8 13.8 13.8 13.8 13.8 13.8 14 15 15 15 15 15 15 15 15 15 15	Fluopicolide <u>Fluopicolide</u> <u>9ermal penetration</u> 0.26 % (62.5 g/L %* (0.4 9 L outdoo %* (608 g/L outdoo	n O O n O O or uses or uses or uses	Propamo 2% (625 8.6%** (1 g/L o 8.6%** (0.8 g/L	carb g/L) utdoor use) indoor use)
Concentrate Spray dilution Reference	ed in risk assess (g/L of active) % (g/L of active)	ment (4) 13.0 5 5 5 5 5 5 5 5 5 5 5 5 5	Fluopicolide <u>Fluopicolide</u> <u>Vermal penetration</u> <u>0.26 % (62.5 g/L</u> * (0.4 g/L outdoo * (608 g/L) hdog * (608 g/L) hdog * (608 g/L) hdog * (608 g/L) hdog	n O O n O O or use) or use) or use)	Propamo 2% (625 8.6%** (1 g/L o 8.6%** (0.8 g/L Study M-516805- humai	carb g/L) utdoor use) indoor use) 01-1 <i>in vitro</i> n
Concentrate Spray dilution Reference	ed in risk assess (g/L of active) % (g/L of active)	ment 4 T 13.2 5 5 5 5 5 5 5 5 5 5 5 5 5	Fluopicolide <u>Vermal penetratio</u> 0.26 % (62.5 g/L ** (0.4 pL outdoo ** (608 g/L) indoo ** (608 g/L) indoo	n O O v O v O v v V v v v v v v v v v v v v v v v v v v v	Propamo 2% (625 8.6%** (1 g/L o 8.6%** (0.8 g/L Study M-516805- human	carb g/L) utdoor use) indoor use) -01-1 <i>in vitro</i> n
Concentrate &	(g/L of active) % (g/L of active)	ment 4 T 13.8 Study	Fluopicolide <u>Vermal penetratio</u> 0.26 % (62.5 g/L ** (0.1 pL outdoo ** (608 g/L indoo ** (608 g/L indoo	n O O O O O O O O O O O O O O O O O O O	Propamo 2% (625 8.6%** (1 g/L o 8.6%** (0.8 g/L Study M-516805- human 0.29	carb g/L) utdoor use) indoor use) -01-1 <i>in vitro</i> n
Concentrate Spray dilution Reference	ed un risk assess (g/L of active) % (g/L of active) % (g/L of active) body weight da	ment T T T T T T T T T T T T T	Fluopicolide Vermal penetratio 0.26 % (62.5 g/L ** (0.1 pL outdoo ** (608 g/L indoo ** (608 g/L indoo	study (Propamo 2% (625 8.6%** (1 g/L o 8.6%** (0.8 g/L Study M-516805- human 0.29 EFSA Scientific I 78, 1-8	carb g/L) utdoor use) indoor use) .01-1 <i>in vitro</i> n Report (2006) 0)

¹ Guidane on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874)

 $^{2}\ Available\ from\ Ctgb\ \underline{https://english.ctgb.nl/documents/assessment-framework-ppp/2016/10/27/calculation-model-operator-nl-greenhouse}$



AAOEL (mg/kg bw	/day)	None pro	pposed for the renewal of fluopicolide	of Not set
*Pro-rata calculation for	r the highest in-use	dilution from	m a value derived from the	e tested dilution (50.25g/L with a granal
absorption of 5.1% **Tested dilution was 0	.3 g/L therefore no	pro-rata adj	ustment needed	
<u>Summary of estim</u>	ates		Č,	
Exposure assessme	nts pertinent to t	the assess	ment of non-dietary e	xposare are summarized below.
Crop	Model		Summary ~	
Potatoes (Field)	AOEM	4	Can be used safety wi Dormal Work wear is w	the vehicle mount of sprayers provided
Lettuce (Field)	AOEM	 	Acceptable tisk to by	tanders and esidents. the manual hand-bed spravers and
			manual knapsack sprä worn arms legs, tors	vers provided pormal workwear is o covered).
		, , ,	Acceptable risk bys	standers and residents.
Cucumber (glasshouse)	Dutch Greenho (operators)	ouse C	, Can be used safely war workers wear gloves a	In hand-held sprayers provided and protective coveralls.
	AOEM (work	ers)	San be used safely for	worker to entry following roof
			covered) and gloves	re worn.
			Acceptable risk for bys	standers and residents.
Overall conclusion		°, 40		
Exposureestimate	s predict accep	table risk	s for all the intende	use of FLC+PCH SC 687.5 as
long as pormal wo	rkwear (arms,	legs, tors iv on wat	o covered) is worn fo ors and workers in c	or all uses and in addition
protective gloves s				
A. C.				
		Ŷ Ŷ	₹	
Č ^{O*}				



CP 7.2.1 Operator exposure

CP 7.2.1.1 Estimation of operator exposure

CP 7.2.1.1 Estimation	on of operator exposure	
Table 7.2.1-01:Input param	eters considered for the estimation	of operator exposure for particles &
AOEM EFSA calculator	رم. ريم	La L
Product name and code	FLC+PCH SC 687.5	
Formulation type	SC soluble or suspension	
Category	Fungicide	
Crop type	Potatoes & 6° S	
Indoor/outdoor	Outdoor	
Application method	Downward spraying	A. Or & G
Application equipment	Vehicle-Hounter	
Minimum water volume	100 Lana & ~ ~ ~ ~	
DT50	30 days of of of	
DFR	Şμg/cm2	
Buffer strip	2-3 metres J O	
Number of applications	14 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	
Interval between multiple	7 days 5 5 7 0	
Assumed area treated	\$0 ha/day	
Active substance(s)	Fluopicolide (FLC)	Propamocarb (DCH) 625 g/L
Maximum application are of active substance	0.1 kg /ha	1 kg/ha
AOEL systemic 🖏 🐴	£507 mg trg bw/day	0.29 mg/kg bw/day
AAOEL OV Č	Nontes of or or	None
Inhalation absorption		100%
Oral absorption		100%
Dermal absorption	Conventrate 026% Dilution: 03%	Concentrate:2%Dilution:8.6%
	For more information please refer to section 7.3	For more information please refer to section 7.3

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

Ś



Table 7.2.1-02: Estimated operator exposure to fluopicolide (FLC) and propamocarbhydrochloride (PCH) on potatoes

Model data	Level of PPE	Fluopic Total absorbed dose (mg/kg	olide % of AOEI	Propamo	carb			
Poteto Field Cron An	nligation vohiala mounted	bw(day)		bw/day)				
Application rate 1.6 L	Application rate 1.6 L/ha PPP (0.1 kg/ha FLC and P0 kg/ha PCH)							
Body weight 60 kg	4							
4 applications a crop,	7 days between application	ns*	jor d		Å «			
AOEM 75 th percentile longer term systemic exposure	no PPE; work wear - arus, body and legs covered during mixing/loading Cand during applications		3.65.2		2 0 0 15.66			
AOEM 75 th percentile acute systemic exposure	no PPE work wear sarms body and legs covered during mixing/bading and during application.	64 0 60197.5 5 5 5 5 5 5 5 5 7	NA S		N/A			
* This scenario also a 3 applications a grop, 7 2 applications & crop	pplies to the following: days between applications days between applications			Ø J				
Lettuce								
Table 7.2.1-03: Input	parameters considered	for the estimat	tion of ope	rator exposure	for lettuce			
AOEM EFSA calculat								
Formulation turns	FIC+PCH SC 08		<i>t</i> a					
Catagor	Sc solutie of suspe		lle					
Crop Fine	I struce	y						
Indoor/outdoor @	Qutdoor	1						
Application nothod	Downward spravin	g						
Application	Manual-Knapsack	e and Manual Han	id-held					
Minimum water Voluma	1000 L/ha							
DT 50 DT	<u>مَحْمَّ</u> 30 days							
DFR 5	3 μg/cm2							
Buffer strip	2-3 metres							
Number of applications	1-2							



Interval between multiple applications	7 days	
Assumed area treated	1 ha/day for manual-knapsack 4 ha/day for manual hand-held	
Active substance(s) (incl. content)	Fluopicolide (FLC) 62.5 g/L	Propamocarb (PCH)
Maximum application rate of active substance	0.1 kg/ha	
AOEL systemic	0.07 mg/kg bw/day	DD9 mg/kg bwstay
AAOEL	none	nones of the the
Inhalation absorption		
Oral absorption		
Dermal absorption	Concentrate: A 0.26% Dilution: 13% For more information please weier to section 7.3	Concentrate: 29 Diffation: \$.6% For nore information please refer to section 7.5

The scenario of a manual-knapsack sprayer, and manual hand-head sprayer in low crops (lettuces) was assessed and the defaults settings of the EESA 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.

output pages from the calculator Table 7.2.1-04: Estimated operator exposure to fluopicolide (FLC) and propamocarbhydrochloride (PCH) on lettuce

Fuopicolide C	Propamocarb	
Model data Devel of PPE A A A A A A A A A A A A A A A A A A A	Total absorbed dose (mg/kg bw/day)	% of AOEL
Lettuce Field Crop Application		
Application rate 1.6 L/ha PPP (04 kg/ha PLC and 1.0 kg/ha PCH)		
Body weight 60 kg		
2 applications a crop 7 days between applications whese scenarios also cover 1 a	application a cro	p)
Manual-knapsack sprayer 1 ha day 🖉		



					1	1
AOEM 75 th percentile	Potential exposure (no clothing)	0.197	281.74	0.1339	46.17°°	al de la companya de la compa
longer term systemic exposure	no PPE: work wear - arms, body and legs covered during mixing/loading and during application.	0.0239	34.18			
AOEM 75 th percentile	Potential exposure (no clothing)	0.308		9.2128 9.2128 9.2128		
acute systemic exposure	no PPE: work wear - arms, body and legs covered during mixing/loading during application.					
Manual hand-held 4	ha/day					
AOEM	Potential Exposure (no crothing)	2 0,1966		0.3548	122.34	
Ionger term systemic exposure of the systemic exposure of the systemic exposure of the systemic and legs covered du mixing/loading during application	no PPE: work wear - arms, body, and legs covered during mixim/loading & and during application	5 50.0222 5 6 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	\$3.21 ×	© Ø 0.0460	15.87	
AOEM 75 th percentile	Potential exposure (nor clothing)	67 £7 7 0,50998	N/A	0.5955	N/A	
acute systemic posure	no PPE: work wear - arms, bod and legs covered during mixing/loading during application	0.1463	N/A	0.2755	N/A	
A A						

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: Table 7.2.1 05: Input parameters considered for the estimation of operator exposure for cucumbers grown under glass

Dutch Glasshouse Model

Product name and code	FLC+PCH SC 687.5			


Formulation type	SC soluble or suspension concentrate
Category	Fungicide
Crop type	Cucumber
Indoor/outdoor	Indoor
Application method	Spraying
Application equipment	Manual sprayer
Minimum water volume	1000 L/ha
Number of applications	
Interval between multiple applications	7 days A^{0}
Assumed area treated	1 ha/day (k) $(b)^{\circ}$ $(c)^{\circ}$ (c)
Active substance(s) (incl. content)	Fluopicolide (FLC) A C C Propamocarti (2.5 g/L A C A C C C C C C C C C C C C C C C C
Maximum application rate of active substance	0.1 kg/ba
AOEL systemic	0.07 mg/kg bw/day & D 29 mg by/day >
AAOEL	mone in the first of the first
Inhalation absorption	100% β β 0 4 100% β 0
Oral absorption	100% & J J J J J J J J J J J J J J J J J J
Dermal absorption	Concentrate: 0.26% Concentrate 2% Dilution: 16% Dilution: 8.6% For more information please refer to For more information please refer to
· · · · · · · · · · · · · · · · · · ·	section 7.3

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 flupicolide (FLC) and propamocarb-**hydrochloride (FCH) or cucumber of the summary results from the calculator.

	i V o V			
	Fluopico	lide	Propai	nocarb
Model data	Total absorbed dose (mg/kg bw/day)	% of AOEL	Total absorbed dose (mg/kg bw/day)	% of AOEL
Cucumber glasshouse application, manual-knaps Application rate 1.64 /ha PPP (0.1 kg/ha FLC an Body weight 60 kg 3 applications a crop, 7 days between application	sack sprayer d 1.0 kg/ha PCH s*)		



DUTCH GLASSHOUSE MODEL longer term systemic exposure	None	0.055	78.6	0.30	104.6 °	
	Gloves and coveralls	0.007	10	0.0453) , (
* This scenario also a 2 applications a crop, 7 1 application a crop	oplies to the following: days between applications					, S

Overall conclusion on operator exposure

Exposure estimates predict acceptable risks for all the intended use of FLC PCHSC 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 with 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 wrift and by inhalation of dotting spray droplets. Handheld application is considered to be worse case compared to held grop sprayer.

Residents may live or work near 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 and 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+PCF 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 EFSACOEM model

Potatoes

Table 7.2.2-01: Input parameters considered for the estimation of resident	¢&po	osur@for	potatoes
--	------	----------	----------

AOEM EFSA calculator	
Product name and code	FLC+PCH0SC 6870.5
Formulation type	SC solutive or suspension concentrate of o
Category	Fungicide S Of O S S S
Crop type	Potatoes & & & & & & & & & & & & & & & & & & &
Indoor/outdoor	Outdoor a strand of strand
Application method	Downward spraxing
Application equipment	Vehicle-mounted
Minimum water volume 🗸	100 L/ha
DT50	Avdays a construction of the construction of t
DFR A	β μg/cm2 c c c c c c c c c c c c c c c c c c
Buffer strip	2 metres & O
Number of applications Q	$\overline{\mathfrak{F}}^{4}$ $\overline{\mathfrak{C}}$ $\overline{\mathfrak{T}}$ $\overline{\mathfrak{F}}$
Interval between multiple	7 dravs
Assumed area treated	So ha/day
Active substance(s)	Flutopicolide (ELC) (2.5 g.C)
Maximum application rate of active substance	0.1 kg/ha
AOEL sostemic	0.07 mg/kg bw/day
AAQÉL O' ô' ò	none
Inhalation absorption	100%
Oral absorption	100%
Dermal absorption	Concentrate:0.26%Dilution:13%



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 on 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 propamocarbhydrochloride (PCH) on potatoes

nyur ochior luc (r Cri	j on potatoes		<u>^</u>	1	
Model data	Exposure route	Fluopia Fluopia Total absorbed dose dose dose bw/da	colide	Propa	mocarb Q Q Mocarb Q Q Q M M M M M M M M M M M M M M M M
Potato Field Crop Ap Application rate 1.6 L Body weight 60 kg	ly plication, vehicle-providented /ha PPP (0.1 kg/ba FL & ar	sprayer ind 1.9 kg/ha PC	H) L 2		
4 applications a crop,	7 days between application	\$* ^~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~			1 1
	Spray drift &	0.0035	5.01	0.0233	8.03
AOEM	Vapour 2	0,0011	4,53	0.0011	0.37
75 th percentile	Surface deposits	0.0009	° [™] 1.2 %	∿0.0066	2.27
1-3-year-old child	Entry intertreated crops	00070 20070	10.00	0.0463	15.96
	All pathways (mean)	0.0092	§ 13.17	0.0557	19.19
	Spray driff	0.6008	1.20	0.0055	1.91
AOEM	Vapous (\$0.0002 ⁵	0.33	0.0002	0.08
75 th percentile	Surface deposits	0.0003	0.40	0.0019	0.64
Adult	Entry into treated crops	0.0039	5.55	0.0257	8.87
	All pathways (mean)	0,0039	5.62	0.0247	8.53
* This scenario is wor	est case so also applies to th	e fottowing app	lication rates:	:	
3 applications a crop, 7	days between applications				
2 applications a crop	days between applications	Ý.			

Lettuce

Table 7.2 203: Input parameters considered for the estimation of resident exposure for lettuce

AOEM CFSA calculator	Ø *
Product name and code	FLC+PCH SC 687.5
Formulation type	SC soluble or suspension concentrate
Category	Fungicide
Crop type	Lettuce



Indoor/outdoor	Outdoor
Application method	Downward spraying
Application equipment	Manual-Knapsack and Manual Hand-held
Minimum water volume	200 L/ha
DT50	30 days
DFR	3 µg/cm2
Buffer strip	2-3 metres
Number of applications	
Interval between multiple applications	7 days 2^{4} 2^{4} 2^{4} 2^{4} 2^{4} 2^{4} 2^{4}
Assumed area treated	1 ha/day for manual-knapsack
Active substance(s) (incl. content)	Fluopicolide (FLC) 62.5 g/L 2 + 2 + 2 + 2 + 2 + 2 + 2 + 2 + 2 + 2
Maximum application rate of active substance	0.1 kg/ha
AOEL systemic	0@07 mg/kg bw/day
AAOEL	hone of a hone of
Inhalation absorption	
Oral absorption	
Dermal absorption	Concentrate 0,26% Concentrate: 2% Dilution: 13% 9 9 Dilution 8.6%
	For more information please refer to section 7.3

The scenaryo of a manual knapseck sprayer, and manual hard-held sprayer in low crops (lettuces) was assessed and the defaults settings of the EESA calculator was used with no refinements. The following





Table 7.2.2-04: Estimated resident exposure to fluopicolide (FLC) and propamocarbhydrochloride (PCH) on lettuces

Model data	Exposure route	Fluopicolide		Propamocarb		and and a
Wiouci uata	Exposure route	Total absorbed	4- 	Total absorbed C		, Ô,
		dose	% of	dose 🔊	% of	
		(mg/kg	AUE	(mg/kg		Å
		bw(day)		bw/day)		\$
Lettuce Field Crop A	pplication - manual-knapsa	ck sprayer	Q' g°	Å 4		U
Application rate 1.6 L/I	ha PPP (0.1 kg/ha FLC and 1	Heg/ha PCH)	\sim \sim			
2 applications a crop, 7	days between applications (this scenario is	vorst case so	uso cover 1 app	reationa	
		0.001	2.51	00116		0
	Spray drift		2.51	\$		
AOEM	Vapour				, 0,37 '	
75 th percentile systemic exposure	Surface deposits	0.000S	0.72	20.00380 [°]	1.32	
1-3-year-old child	Entry into treated grops	0700941	530	0.0269 2	≫ 9.26	
	All pathways (means	0.0056	8.06	0.0317	10.94	
	Spray drift	0.0004	0.60	\$¥ 0,0 62 8	0.96	
AOEM	Wapout O	0.00020	\$ 0.33 0	\$00002	0.08	
75 th percentile systemic exposure Adult	Surface deposits	0.00002	0.23	0.0011	0.37	
	Entry into treated crops	~0,0023	3.22	0.0149	5.15	
ð á	All pathways (mean)	0.0003	3.35	0.0142	4.91	
<u> </u>			Z.O			-

Cucumber

Resident exposure to cucumber grown in grasshouses will not occur so no exposure estimate is necessary.

À

Overall conclusion on resident expositive

Exposure estimates product 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 FUC 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.

ching of the second of the sec



AOEM EFSA calculator	
Product name and code	FLC+PCH SC 687.5
Formulation type	SC soluble or suspension concentrate
Category	Fungicide
Crop type	Potatoes
Indoor/outdoor	Outdoor
DT50	30 days
DFR	$3 \mu g/cm^2$
Buffer strip	2-3 metres
Number of applications	
Interval between multiple applications	7 days
Work rate per day	2 hours/day in the second seco
Active substance(s) (incl. content)	Fluopheolide
Maximum application rate of active substance	0.1 kg/ha
AOEL systemic	0.07 mg/kg bw/day
AAOEL &	Anone & A A A N ON none
Inhalation absorption	
Oral absorption &	100% & ~ ~ ~ ~ ~ 100% ~
Dermal absorption	Dilution: 13% (worst case)
	$\mathcal{A} \stackrel{\sim}{\longrightarrow} \mathcal{A} \stackrel{\sim}{\longrightarrow} \mathcal{A} \stackrel{\sim}{\longrightarrow} section 7.3$

Table 7.2.3-01: In	put parameters	considered for th	e estimation of	worker exi	posure for 1	ootatoes
1 abic 7.2.5-01. 11	put parameters	constact cu for th	ic commanion of	WULKEL CA	JUSUIC IUI	Jorarous

The scenario of inspection and infiguration in low crops was assessed and the defaults settings of the EFSA





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

1						
Model data	Level of PPE	Fluopio Total absorbed dose (mg/kg	colide % of AOE	Propa Total absorbe d dose (mg/kg	mocarb ^A ^A ^A ^A ^A ^A ^A ^A	
		bw/day)		bw/day)	Q A K	\checkmark
Potato Field Crop Ap Application rate 1.6 L	plication, worker inspection //ha PPP (0.1 kg/ha FLC an	n, irrigation 2 l 41.0 kg/ha PC	iours of	Â, Ô		ĩ
Body weight 60 kg			$\mathcal{P}' \mathcal{L}' \mathcal{I}$	Ø D		
1 applications a aron	7 dave hotwoon annligation		<u>~</u> ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			
4 applications a crop,	/ days between application		Q O	o ô		
AOEM	Potential exposure to clothing)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	⁷ 74.05 ² 6 ⁴		× 0 × 0 × 18.25	
exposure		"0" A	Û ^V Ø	, O	8	
	Workwear Overing arms body, and legs	0:0058 0:0058	829	0.0384	13.24	
* This scenario is your	st case so also applies to the	e following app	lication rates;	7 7 n		
3 applications a crop, 7	days between applications	N N	O S			
2 applications a Prop, 7	days between applications					
Lettuce	ulation has been used to a	Stimate exposi	The to worker	rs for reachi	ng and nicking	
The following assured	tions were made *		The to worker		ig und picking.	
The following assumption of th	tions were stade: Ny to the state of the sta					
\bigcirc						



AOEM EFSA calculator	_ °
Product name and code	FLC+PCH SC 687.5
Formulation type	SC soluble or suspension concentrate
Category	Fungicide
Crop type	Lettuces
Indoor/outdoor	Outdoor
DT50	30 days
DFR	3 µg/cm2
Buffer strip	2-3 metres Q^{0} Q^{0} Q^{0} Q^{0} Q^{0}
Number of applications	
Interval between multiple applications	7 days
Work rate per day	8 hours/day in the second seco
Active substance(s) (incl. content)	Fluopfeolide
Maximum application rate of active substance	0.1 kg/ha
AOEL systemic	0.07 mg/kg bw/day 0.29 mg/kg bwoday
AAOEL	none none in
Inhalation absorption	
Oral absorption &	100% ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Dermal absorption of the	Difation: A 3% (worst case) Dilution: 8.6% (worst case)
	For more information lease for to F For more information please refer to section 7.3 F

Table 7.2.3-03: Ir	nnut	parameters	considered	for the	estimation	of worker	exposure fo	or lettuces
1 4010 7.2.0 00.11	put	parameters	constacted	ior the	commution	or worker	caposul e la	/ ictuces





Table 7.2.3-04: Estimated worker exposure to fluopicolide (FLC) and propamocarb-hydrochloride (PCH) on lettuces

Model dete		Fluopie	colide	Propa	mocarb	
Model data		Total absorbed dose (mg/kg by/day)	% of 4 AOE	Total absorbed dose (mg/kg bw/day)	À Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â Â	
Lettuce Field Crop A Application rate 1.6 L Body weight 60 kg	oplication, worker reaching /ha PPP (0.1 kg/ha FLC an &	g and picking 8 APT.0 kg/ha PC	hours of fry of the second sec	p p p		<i>'</i> J
2 applications a crop,	7 days between application	is* L	Dr Dr	N N		0
AOEM longer term systemic exposure	Potential exposible (nor clothing) Workwear covering arms, body, and logs	₩ ₩ ₩ ₩ ₩ ₩ ₩ ₩ ₩ ₩ ₩ ₩ ₩ ₩	299.74 2 299.74 2 2 3 4 3 4 3 4 3 4 3 4 3 4 3 4 3 7 4 4 3 7 4 3 7 4 3 7 4 3 7 4 5 7 4 5 7 7 7 7 7 7 7 7 7 7 7 7 7	0.1592 4 0.1592 4 0.1592 4 0.1592 4 0.1592 4 0.1592 4 0.1592 4 0.1592 1 1 1 1 1 1 1 1 1 1 1 1 1	54.88	
C. C	Workwear overing arms, body and legs and protective glokes	59 57 300056,59 57 57	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	ج 0.0369	12.73	
* This scenterio is wor 1 application a crop	st case so also applies to the	E following app	lication rates:	:		

<u>Cucumbers</u> The AOEM BSA calculator has been used to estimate exposure to workers where the product is applied





cucumbers grown under gra	22
AOEM EFSA calculator	<u>v</u> °
Product name and code	FLC+PCH SC 687.5
Formulation type	SC soluble or suspension concentrate
Category	Fungicide
Crop type	Cucumber
Indoor/outdoor	Indoor
DT50	30 days
DFR	3 µg/cm2
Number of applications	
Interval between multiple applications	7 days O C C C C C C C C C C C C C C C C C C
Work rate per day	8 hours/day of the the second se
Active substance(s) (incl. content)	FluopieQide
Maximum application rate of active substance	Gri kg/ha di kg/ha
AOEL systemic	0.0 Ding/kg Dw/day
AAOEL	trone of the one of the one
Inhalation absorption	
Oral absorption	100% 2 2 2 400%
Dermal absorption	Concentrate: 0.26% Concentrate: 2% Dilution: 16% O Dution: 8.6%
	For more information please refer to For more information please refer to section 7.3

Table 7.2.3-05: Input parameters considered for the estimation of operator exposure for ananmhara grawn undar glass

The scenario of reaching and picking fulting vegetables in glasshouse crops was assessed and the

The scenario of reaching and picking thiting vegetables in glasshouse crops was assessed and the defaults settings of the ERSA 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-

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.

Measurement of worker exposure **CP 7.2.3.2** 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 proparnocar for current of the study may be used to refine the default DFR.



Data Daint:	V CD 7 2 2 2/01	I
Data Folili.		
Report Author:		
Report Year:	2013	
Report Title:	Determination of the dislodgeable foliar residues (DFR) of fluopicolide and	
	propamocarb in/on cucumber after spraying of fluopicolide & propamocarb x	d i
	hydrochloride SC 687.5 in the greenhouse in Italy - FLC+RCH SC 62,5+65 GU	-
	WW S & S	
Report No:	12-2903	~
Document No:	<u>M-460022-01-1</u>	Q 1
Guideline(s) followed in	US EPA OCSPP 875.2100 Foliar Dislodgeable Residue Dissipation	
study:	(formerly US EPA Pesticide Assessment Guidelines Subdivision K:	L.
	Reentry Protection, Series 132(1 (a))	, Oʻ
Deviations from current		×
test guideline:		
Previous evaluation:	yes, evaluated and accepted	
	fluopicolide DAR 20%6, \mathcal{O}° , $\mathcal{O}^{$	
GLP/Officially	Yes, conducted under GLP/Officially recognised testing facilities	
recognised testing		
facilities:		
Acceptability/Reliability:	Yes of the of the second secon	

Executive Summary:

The GLP study is valid and acceptable to determine the dislodgeable foliar reside 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 Peaves was 1.1 µg/cm² per kg a.s./ha for fluopicolide and $0.2 \ \mu g/cm^2$ per kg a.s./ha for propamocarb. The DFR from this study may be used to refine the detault DFR value in

default DFR value in exposure assessments if a higher tier assessment is required

Materia and Method

A. Materials

Fuopiconde + propanjocarb hydrochloride SC 687.5 (62.5+625 g/L) 1. Test material Test substance: 🖉 Fluoptrolide 62.5 g/D, Propamocal 625 g/L Purity: EV\$9000 Batch no .:

B. Study design

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

Location	I-Q0050 Palidoro-Fiumicino, Italy
Type of total of C 5	Ty Indoor, glasshouse
Crop D G A S	Cucumber, Marketmore
Date of planting	12-09-2012
Date of Parvest	01-10 to 30-11 2012
Number of plants per ha	11110
Soil	Sand

1. Trial dates, location, crop and plot size



Plot size 194.4 m ² divided into 3 sub-plots of 64.8 m ² each

Application type	Spraying
Nozzle type	Albuz AVI ISO 11003, size 110 03
Pressure	5.0 bar
Date of application	05-10-2012, 15-10-2012 and 25-10-2012 (3 applications with 10-day interval between spraying)
Water	750 L/ha
Crop height	0.45, 0.8, and 1.2 meters at 1 st , 2 nd and 3 rd application respectively
Application rate	0.125 kg/ha fluopicolide
Concentration of active substance (%) in spray dilution	0.0167% fuopicolide
Growth stage [BBCH]	61, 63, 71 at 1st, 2nd and 3rd apple ations respectively
Air temperature °C	30, 25, 30 at 1% 2 nd and 3 rd applications respectively
Relative humidity [%]	36, 64, 43 at 1st, 2nd and 3th applications respectively

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 5 cm². A sample was collected from each of the three sub-plots to provide three replicates at 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 cesidue collection

Dislodging we performed not later than 4 hours after sample collection. Samples were dislodged by adding a 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

 \searrow

Unspiked intreated control samples were collected using the same method as for the treated leaf samples and the same method as for the treated leaf

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 $1.0 \,\mu\text{g/cm}^2$ of test substance (corresponding to 20, 200 and 2000 $\mu\text{g/L}$ respectively). Dislodgeable residue was collected from the leaves in the same manner as described for treated crop. In addition,



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. (3013), 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.

Spiked leaf wash sample recoveries showed acceptability of the analytical method. For flyppicolide mean recovery was 93% at the LOQ of 0.01 µg/cm². For propartocarb mean recovery was 98% at the LOQ of 0.01 μ g/cm². Ø O

Mean recovery of spiked field samples were 92% and 83% for thopic and propamocarb respectively which is within acceptability writeria (of 70 to 110%). Relative standard deviation was 11.5% for fluopicolide and 12.8% for propamocarb samples with is within a comparative levels (of $\leq 20\%$).

The residues from field samples are shown in the table below. To convert to DPR a correction for the application rate the values of the DER are expressed in µg/cm² per kg a.s./ha.

punch was	ning specin	nens 🔊	<u>, </u>		6	
DA1.T	DA2.T	[»] DA3. ۳	Fluopicolide 🔊	DKK	Propamocarb	DFR
	ja karakarakarakarakarakarakarakarakaraka	Å . Č	µg/cm	Fuopicalide	µg/cm ²	Propamocarb
	N.			µg/cm ² per		µg/cm² per kg
				kg_a.s./ha 🔊	Ź	a.s./ha
0	ð S		0.373 🗸 👸	2,2834	Z 150	2.52
1	0. Ø		0.262	20096	M.370	1.096
3	Ĩ		0.230	1.84	0.277	0.2216
7			0.084 ° ° °	0.672	0.075	0.06
10	~		0.0180	ØKJ44 🔊 🖉	0.018	0.0144
10	0 3	.4 Ø	0.289	Q.312	1.825	1.46
11	1 🦉		0, 201 3 🔪 💭	1.70 4	0.562	0.4496
13	30	N E	0184_0`0`	1.472	0.180	0.144
17	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		x0.0920 0 0	0792	0.061	0.0488
20	10		0.038	0.304	0.020	0.016
20	10 🗞	% %	0.228	1.824	1.312	1.0496
21	11 🔊	1 4	0.183	1.464	0.410	0.328
23	13	3 5	0.14Q S	1.128	0.188	0.1504
27	17	70 50	0.29	0.952	0.212	0.1696
34	24	\$14 Ø	<u></u> ¢00079 √Q	0.632	0.060	0.048
Geometric	Mean 🔿		0.134	1.072	0.239	0.191

Table 7.2.3-07: Dislodgeable foliar residues of flugpicolide and propanocarb in cucumber leaf

DA(1.)T = Days after (first) @atment

DA(2.)T Days after (second) treatment. DA(3.)T Days after (third) treatment; LO Q^{24} 0.01 Qg cm 2^{24}

Approximate was @125 kg/ha fluopicolide and 1.25 kg/ha propamocarb

Q

The mem 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.



kg â.

per

 $.1 \ \mu g/cm^2$

III. Conclusion

Under the conditions of this study, the mean DFR for fluopicolide was $1.1 \ \mu\text{g/cm}^2$ per kg a.s./ha and the mean DFR for propamocarb was $0.2 \ \mu\text{g/cm}^2$ 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 reside (DFR) of luoppolide and propamocarb on cucumber leaves.

Under the conditions of this study, the mean DFR for fluopicolide was

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 xposure assessment 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 probamocarb 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

Scenario & S	Active Substance	Estimated exposure / AOEL (RVNAS) (HQ) ³				
Crop: Potatoes (Field)	Crop: Potatoes (Field) $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$					
application rate. Da kg/ha juopopliae						
Operators, normal workwear	Fluopicotice	0.0365				
For detail please refer to 7.2.1 Only	Propapocarby	0.1566				
the work case scenario is presented	Cumulation risk Operators (HI) ²	0.1931				
Adult Strength	QuopicQide	0.0562				
For details please refer to 7.22. Only	Propimocarb	0.0853				
the worst case scenario is presented 4	[♥] @umulative risk Resident-Adult (HI) ²	0.1415				
Resident - Child'	Fluopicolide	0.1317				
For details please refer to 7.2.2. Only	Propamocarb	0.1919				
the vorst-case scenario is presented	Cumulative risk Resident-Child (HI) ²	0.3236				
Workers, with Workwear	Fluopicolide	0.0829				
For details please refer to 7.2.3. Only	Propamocarb	0.1324				
the worst-case scenario is presented	Cumulative risk Workers (HI) ²	0.2153				



ð

- 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 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 .r

		Estimated experiesure
Scenario	Active Substance	A QEL (RANAS)
		(HQ) ³
Crop: Lettuces (Field)		
Application rate: 0.1 kg/ha fluopicolide	/ 1 kg/ha propunocarlo 🖉 💍	
Applied by manual hand-held sprayer		
Operators , normal workwear	Fluopicolide , , , , , , , , , , , , , , , , , , ,	\$ \$3321 \$
For details please refer to 7.2.1. Onl	Propamocarty S	0.1583
the worst-case scenario is presented	Gumulative rist Operators (HD)2	0.4908
Resident – Adult ⁷	Fluopicolide	% % 9 .0335
For details please refer to 7.2.2. Quy	Propamocarb @	0.0491
the worst case scenario is presented	Cumustive risk Resident-Adult (H1)2	<u>م</u> م 0.0826
Resident – Child'	Fluopicolide	0.0806
For details please effer to 7.2.2. Only	Propamocarb 2 0	0.1094
the worst-case scepario is presented	Cumulative wisk Resident Child (H)2	0.1900
Workers, with Workwear	Fluopicolifae	0.3437
For details please refer to 7.2.3 Only	Propamocarb	0.5488
the worst-case scenario is presented	Cumulativerisk Workers (HI)2	0.8925
¹ The higher exposure galue either from	the 75" percentile of each of the four path	ways (spray drift, vapour,
surface deposits, entry into treated cite	ps) of the sum of the mean exposure values i	s taken into consideration
I HI = Hazar Index		

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.



Ø)

Table 7.2.3-10: Long-term risk assessment from combined exposure to fluopicolide and propamocarb on cucumbers

· ·		
Scenario	Active Substance	Estimated expositive / 8 AOEL (RV&AS) 6 (HQ)
Crop: Cucumbers (Indoor)	.1	
Application rate: 0.1 kg/ha fluopicolide	/ 1 kg/ha propamocarb 🏹	
Applied by manual-knapsack sprayer	Č Á	L ~ 5
Operators , with gloves and coveralls during mixing and loading and	Fluopicolide	
application.	Propamocarb Q 2	L 0.156 C
For details please refer to 7.2.1. Only the worst-case scenario is presented	Cumulative risk Operators (H)	0.256
Resident – Adult ¹	Fluopfeolide	N/A A
For details please refer to 7.2.2. Only the worst case scenario is presented	Propamocarb Cumulative right Resident-Adult (HI)	NAS ÚY
Resident – Child ¹	Flugpicolide 2 2	N/AQ
For details please refer to 7.2.2. Only	Bropamægarb & S	Ĩ N¥Ă
the worst-case scenario is presented	Cumulative ask Resident Field (HI) ²	°°° [⟨] ∕N/A
Workers, with workwear and &	Flopicolide @	٥.1651
For details please refer to 7.23	Propanocarb & S	0.2461
the worst-case scenario s presented	Cumulative risk Worker (HI)2	0.4112
 ¹ The higher exposure after either from surface deposits, entry into treated error into treated error into the surface deposits, entry into treated error into the surface deposits and the surface deposits into the surface deposits and the surface deposite deposit	m the 75 th percentile of each of the four bath ops) or the sum of the mean exposure values i	ways (spray drift, vapour, is taken into consideration

For lettice uses the Hazard price is $\gtrsim 1$. Therefore, the combined exposure to all active substances in FLC+PCH SC 687 S is not expected to present wrisk for operators, workers, bystanders, and residents. FLC+PCH SC 68 rg/is not expressed to specified.

Overall conclusion on combined expessive

N N N N N N 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



CP 7.3 Dermal adsorption

Fluopicolide

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

]	Cable 7.3-1: Dermal absorption	rates for fluopicolide in	Ļ	FLC+PCH	687.5	
			7	~		2

	💎 fluopicolifie	Å 39	
	Value Value		
	(% of dese applied)		
Concentrate	© .26%) ~~~~
Dilution	5,7% @0.25 g/L		
(dilution factor)			
		Ŷ _ĸ , Ĝ	
Instification for proposed value			Č,
Justification for proposed valu			0

Justification for proposed values – Ruopicolide 🛫

The proposed dermal absorption rates for fluopicolide are based or an in stiro homan skin dermal absorption study using the FLC+PCH SC 687 \$ 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 assemblent Ø Q

Table 7.3-2: Summary of the results of supplitted derma absorption studies for Fluopicolide

Test	Concentrate	Spray dilution Formulation Justification provided on	Reference
		(dilution factor) in study representativity of study	
	No. C	D' Y' V Y Y tormulation for current	
		y y y product	
In vitro	Human:	Ruman: FLC+RCH Not required	<u>M-222382-01-1</u>
(rat/human)	Ø.26% 🔍	5.1% SC 87.5 0	
	ڻ ک	(1 in Q50) (1 in Q5) (1 in Q50)	2003.
<i>K</i> [™]	~		
	<u>~</u>		
Data Point:	<u> </u>	KCB7.3/01/0 ~~ ~~ ~~	
Report Auth	<u> 26 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 </u>		
Report Year	: *		
Report Title		(14CDEXP1720A Comparative in vitro dermal penetration st	tudy using human
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	and sat skin S	
Report, No:	<u> </u>	QQ37214 0 2 2 2	
Document N	lo:	<u>×1-2223×2-01</u>	
Guideline(s)	followed in	EU Directive 91/414/EEC Annex III, Section 7.3; OECD 417, 4	428 (draft) (2002)
study:	S A	V J V	
Deviations f	rom current	avene Q	
test guidelin	ë:		
Previous eva	uluation:	yes valuated and accepted	
de la companya de la comp	8 A	DAR (2005)	
GLP Officia	Øy 🖓	Ses, conducted under GLP/Officially recognised testing facilities	es
recognised	esting 4		
facilities			
Acceptabilit	y/Reliability:	Yes	



#### Material and methods:

Rat:	Q° ~
Species, strain:	Rat, Sprague-Dawley CD
Source:	Charles River (UK) Ltd, Margate, Kent, UK.
Sex:	Male.
Number:	6
Anatomical site:	Dorsal $\mathcal{A}$ $\mathcal{O}$ $\mathcal{O}$ $\mathcal{O}$
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 2
	electric clippers and the skin removed. Connective tissue, blood and any &
	residual fat were removed from the demais using absorbent tissue. The
	resulting full thickness skin membrane was then wiped brefly with 70%
	ethanol/water to remove residual far and blood, wiped dry and re-
	hydrated with distilled water ready for dermatoming A mini dermatome
	was used to cut slices of skin which contained epidermis and softer
	dermis
Human skin:	Source: International Institute for the Advancement of Stedicine, USA
	Anotomical rogide Dool
	Thickness anthrowing the way and a second se
Test Material:	
Non-radiolabelled:	Batch: PAN02/02.
	Parity = 9.3% 3 /w. 0
Radiolabelled:	phenyl-U-14CP-fluopicolides
$\approx$	Bately: SEL 200. O o o o o
Ű	Specific activity 25.50 MBq/mg.
S, v	Sadioputity of the formulation: 99,8%.
Formulation	The formulation when every mentioned in this every mentioned in the severiment was the Eluonicolide + propamocarb
	hydrochloride. 687 5. formulation (EXP11120A specification N°
	(102000011067) containing fluopicolide at a concentration of 62.5 g/L. It was
	used at two nominal concentrations of Duopicolide: neat, 62.5 g/L and 0.25
	g/D. The same formulations were used concurrently in the in vivo dermal
J.	study BAG/389. O S
	THE A STATE
Test system:	The Scott Dick How-through diffusion cell (Lockley Roper Howes and
Å	Williams, 1997) was constructed from stainless steel and permitted the
Ö, ^y	contents of the receptor chamber to be continuously stirred. The skin
	membranes were maintained at approximately 32°C using a water-heated
	manifold. The flow are of 1.5 mL/hr allowed approximately 6 receptor
an a	chardber content changes per hour. The receptor fluid used was physiological
5 A	same, 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
J Z A	then fixed in place providing an exposure area of 0.64 cm ² skin and the
	assembled diffusion cell inserted in-line in the flow-through set-up. The
4	receptor chamber was warmed by a constant circulation of warm water which
Č ^{O*}	maintained the receptor fluid at $32 \pm 2^{\circ}$ U (close to the normal skin temperature). The recentor fluid was pumped through the recentor showher
-	at a rate of 1.5 mL/h and stirred continuously whilst in the recentor chamber
	by means of a magnetic bar
	- ,



Skin intoquity.	
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 $[{}^{14}C]$ -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 flowrate of approximately 1.5 mL/ 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 overage to a sub-
	Tritiated water was used as an indicator for the skin memoranes, as a number
	of the samples fulfilled the exclusion criterion of having a permeability
	absorption data from/skin membranes with kin values greater them 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 30 x 10/3
	cm/hr, in the same group, the data from the evells would be acceptable
	Two human cells (kells 1 and 7) from the high tose Group Vand one cell
	(cell7) from the kniman low dose group Group 3.55 the for values were
	greater than 3.0 x 10 ⁻³ cm/hr
	Calle (2) and 12 from the bat high days group (arche 2) wars avaluded
	because of poor recoveries of radioactivity
	a a a a a a a a a a a a a a a a a a a
Treatment: 🔬	Priocto dosing, the flow rate was checked (approximately 1.5 mL/hr) by
Ű,	weighing the receptor fluid passed over a measured period of time and
S.	dijusted accordingly. Samples of receptor fluid were taken and analysed for
Ô ð	background radioactivity (residual triffated water). All cells used had
ð S	acceptably row ranoactivity levers (< 30 dpm) in the receptor huid prior to
, Φ	The dose preparation was applied to the kin membrane with a calibrated
	$\frac{1}{2}$ positive displacement pipele at the rate of approximately 10 µL/cm ² exposed
	skin area (6.4 aL dose, un-occluded). The actual amount of [ ¹⁴ C]-
	Fluopic lide applied was determined using quality control (QC) checks taken
ġ "ć	before, during and after dosing each dose group.
Sampling: 0	The receiptor flow passing through the receptor chamber was collected into
4	Mastie Scintillation wals here in a fraction collector. The fraction collector
J. C	was moved on after dose application for each group was complete. Samples
	were then collected houry for the duration of the experiment (24 hours).
	$\frac{1}{2}$
	"At 8 nours after appreciation, the skin was swabbed with 1 % $V/V$ 1 ween 80 in
A A	aqueous solution control (0.9 g/L) until no further factoactivity was
Ő ÁS (	At the end of the study, the skin membranes were tape stripped using 3M
J & A	Scotch "Magic" tape. The initial two tape strips (1 and 2) were collected
	separately into glass vials and represented residual surface (non-
	subsorbed) dose. Subsequent tape strips containing the stratum corneum
Č ⁰	were pooled in balances of three and analysed separately (6 to 12 strips for human skin). The remaining skin was retained separately
	numan skinj. The remaining skin was retained separately.



0

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 liquid scintillation counting (LSC)

#### **Findings:**

Fluopicolide was demonstrated to be sufficiently soluble in the receptor fluid to avoid any isk of a diffusion.

Measurements of the homogeneity of the three concentrations of formulation applied  $\widehat{M}$  dicated that 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 rates of 62.5 g/L to human skin samples (All cells).

Dose Level:	الد			, o	~~ Ś	Group	Human HD
62.5 g/L	Distri	y butiôn of ra	boactivery (	% abose app	died),	K	N≈5 N°∕= 1.2
Donor N°	₩Q>	°≯ H1	f f i	H2	H2	ð Å	1
Sex	Female	Female	Female	Female ~	Female	ĮQ.	
				Ő ^Y «.		MEA	
Cell N°				<u> </u>	<u>&amp; 6 %</u>	Ň	SD
Skin wash 8h	<u> </u>	~&2.55	~~ 92,302	@95.32	89.96	92.02	6.48
Total swabs	99,95	82.55	92.32	S 95.32	89.96	92.02	6.48
Total SC 1 + SC 2	0.07 ⁽	<b>0 € 4 3 2</b>	<u>مَنْ 2.18</u>	0.21	1.15	0.79	0.89
Donor chamber	k.d.	, n.d.Ĉ	n.d.	0 n. <b>¢</b>	n.d.	n.d.	n.a.
TOTAL	. 6	A A	Ô [°] 4				
ABSORBED	<b>A 100.02</b>	82.87	94(50	A95.53	91.11	92.81	6.40
Total skin 🔊 🛓	0,097	× 0.01.0	1.823	۵.043	0.050	0.33	0.73
SC3-5 0 0	0.076	0.098	<u>0</u> 0.1080	0.086	0.085	0.09	0.01
SC6-8	o and	Q n.d.	0,039	n.d.	0.036	0.02	0.03
SC9-1	Q061	0 ng.	\$0.088	0.036	n.d.	0.04	0.04
SC12+15	0.048	Øn.d.	🔊 n.d.	n.d.	n.d.	0.01	0.02
TOTAL SC 3+ a	0 9. <b>9</b> 85	0.098	0.255	0.122	0.121	0.16	0.06
TOTAL DOSE SITE	<b>0.19</b>	0.108	0.264	0.134	0.133	0.17	0.06
Receptor third		~Ŷ					
(0 - 240)		0.015	0.007	0.016	0.017	0.01	0.01
%Retrio receptor	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
Residual receptor fluid	n.d.	n.d.	0.000	n.d.	0.001	0.00	0.00
Receptor chamber	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.a.
TOTAL DIRECT	0.006	0.015	0.007	0.016	0.018	0.01	0.01



Dose Level:						Group	Human HD					
62.5 g/L	Distrib	oution of rad	dioactivity (	% dose app	lied)	K	N=5 $N^{\circ}=1.2$ $O^{\circ}$	~				
POTENTIAL (dose site+ receptor)	0.20	0.12	0.27	0.15	0.15	> 0 18		ð				
	0.20	0.12	0.27	0.15	0.15			\$				
(skin+ receptor)	0.01	0.03	0.02	0.03	03	0.02	\$ ~0.01	Ô				
TOTAL RECOVERY	100.02	82.99	94.77 <i>č</i>	is 95.67	×91.26	92.9	× × 6.4Č	U [*]				
Evaluation according & FESA Cuidéras												
Evaluation according to EFSA Guidance												
Abcomption $>75\%$ within helf of tudy duration $(in M de Seriel (20))$												
Absorption >75% within half of study duration (include S@value)												
		4	Recovery <	95%? <u>7</u> 50r	rection nee	2000 d "		p				
Total % Potentially	Absorbable	adjusted ac	cording to	EFSA Me	an (%dos	e site +9	%receptor)#					
			× v (	<u>2019)   (Sas</u>	<u>r 1.2)⊊ 0.</u>		× [×]	1				
* Normalisation was applied to any of the "absorbed" fraction	all values as no s. Most probabl	o specific samp Que to losses	le type appeare during the skin	to be respons swabbing pro	ible for the lo	over than g	% recovery from ate of the amount					
applied.	, A	, "O"		A C	ÌÌ DÌ							
SD: standard deviation		. L ³ 0			ð	~~ «						
n.d.: below limit of detection; n	.s.: no sample; r	n.a. not applical	ble. " ^{()"}	Y Ö ^ş		0	Ϋ́					
In the above table, the presente	ed means do por	always calcula	to xactly from	the presented	individual da	ta. Théois d	ue to rounding-up					
amerences resulting from the u	se of the spread	sneegorogram.				<u> </u>		J				

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

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

Dose Level:	ku _{ku}			õ "V		Group	Human HD
62.5 g/L~y	Distri	bution of ra	dieactivity	% dose app	lied)	I K N	N = 5 $N^{\circ} = 1.2$
Donor N°	\$ \$7 H1 ≪	an .	У HA	H2	H2		
Sex S	Fernale	Female	Female 2	» Female	Female		
						MEA	
Cell N° $\sqrt[\infty]{0}$	0 1~		× 35	5	6	N	SD
Skin wast 8h	<b>9</b> 9.95	<b>99.4</b> 7	×97.41	99.63	98.58	99.01	1.03
Total swabs	4 ^{999.95}	99.47.	9 <b>7.4</b> 1	99.63	98.58	99.01	1.03
Total SC 1 + SC 2	0.07	~ 0. <b>3</b> \$	2.30	0.22	1.26	0.85	0.94
Donor chambe	n.d	Qi.d.	n.d.	n.d.	n.d.	n.d.	n.a.
TOTAL NON-							
ABSORBED ~~~	100.02	<b>99.86</b>	99.72	99.85	99.84	99.86	0.11
Total skin 🖉 🤬	~~0.006	0.012	0.009	0.013	0.013	0.01	0.00
SCS &	× > 0.076	0.118	0.114	0.090	0.093	0.10	0.02
SC6-8	n.d.	n.d.	0.062	n.d.	0.039	0.02	0.03
SC9-M	0.061	n.d.	0.093	0.038	n.d.	0.04	0.04
SC12-15	0.048	n.d.	n.d.	n.d.	n.d.	0.01	0.02



Dose Level:						Group	Human HD N= 5	
62.5 g/L	Distril	bution of ra	dioactivity (	% dose app	lied)	Kľ	$N^{\circ} = 1.2$ $Q^{\circ}$	8
TOTAL SC 3+ ^a	0.185	0.118	0.269	0.128	0.133	0.17	29.06	Ĩ
TOTAL DOSE SITE	0.19	0.13	0.28	0.14	0.15	0.18	0.06	2
Receptor fluid					<i>.</i> 4			Ĩa
(0 - 24h)	0.006	0.018	0.007	0.017	×0.019	0.01	0.01	
%Ratio receptor 12h/24h	n.a.	n.a.	n.st.	n.a	n.a.	Ju.a.	ý p.g.	
Residual receptor fluid	n.d.	n.d.	Ø.000	n.d.	0.001	^س 0.00	8.00	K ^O
Receptor chamber	n.d.	n.d.	n.d.	n.d.	\$° n€	કરા.	na	
TOTAL DIRECT	0.01	0.02	©0:01	~ ⁰ 0.92	<b>@</b> 02	<b>∂0.01</b> %	<b>0.01</b>	
POTENTIAL (dose site+ receptor)	0.197	0 ³ 0148	0.2 <b>86</b>	<b>4</b> ,157	0.165		and the second	0
POTENTIAL			Z SZ	à À				1
(skin+ receptor)	0.01	0.03	≪0.02 [°] ^	× 0,03	0.03	0.02	0.01	
TOTAL RECOVERY	100:02	0 00.00	^م رکم 1 <b>00</b> .00	2100,00	2 100.00		× × 0.01	_
	Evéla	S O	A RES					
\$		ation accord				ž,		1
Abso	rption >75%	ewithin Balf	of Judy dur	ation (inc	Jude SC 🖗	ues)		
J.			Recovery <	95%? Not	applicable	e – data no	ormalised	
Total % Potentially	Absorbable	adjusted ac	cording to	FSA Me	an@%doso *1.2) = 0.2	e site +% 26%	receptor) +	
SD: standard deviation	KU KI	A						
n.d.: below kinnit of detection;	: no sample; n.a	a got applicable				TT1 · · · ·		
In the above table, the presented differences resulting from the use	means do not a	iways calculate	exactly tronvth	e presented inc	lividual data.	This is due	to rounding-up	

Table 7.3-5: Distribution of radioactivito 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).

Dose Leves		Distopution	of radioactiv	vity (% dose :	applied)		Grou Human N= ( K N° :	1p   HD  6  = 1
Donor N°	HAL	ØHI Á	) Н1	H1	H2	H2		
Sex of A	Female *	Female	Female	Female	Female	Female		
Cell N°		~92	3	4	5	6	MEAN	SD
Skin wastern	<b>90</b> .74	80.91	93.37	86.92	82.49	90.19	85.77	5.26
Total swabs	80.74	80.91	93.37	86.92	82.49	90.19	85.77	5.26
Togal SC 1 SC 2	1.33	4.96	4.15	5.11	4.81	1.84	3.70	1.68
Donor mamber	0.966	1.847	2.588	1.233	0.746	0.506	1.31	0.78
TOTAL NON-ABSORBED	83.03	87.72	100.11	93.26	88.05	92.54	90.78	5.88
Total skin	0.22	0.40	0.59	0.47	0.65	0.29	0.44	0.17



0.25 g/L       N= 6 $(5 \times 10^{\circ})$ Distribution of radioactivity (% dose applied)       N = 6 $(5 \times 10^{\circ})$ SC3-5       1.151       0.985       0.843       1.734       2.395       0.904       1.36       0.61         SC6-8       0.259       0.230       0.235       0.413       1.003       0.695       0.447       0.50         SC9-11       0.155       0.266       0.332       0.135       0.288       0.349       0.25       0.09         SC12-15       n.s.       0.117       n.d.       n.s.       6.142       0.142       0.07       0.07         TOTAL SC 3+ a       1.57       1.60       1.417       2.28       3.83       2.09       3.13       0.60         Receptor fluid       0.621       0.899       1.818       0.903       1.160       0.016       2.00       6.45         %Ratio receptor 12h/24h       n.a.											
SC3-5       1.151       0.985       0.843       1.734       2.395       0.904       1.36       0.61         SC6-8       0.259       0.230       0.235       0.413       1.003       0.695       0.47       930         SC9-11       0.155       0.266       0.332       0.135       0.288       0.349       0.255       6.09         SC12-15       n.s.       0.117       n.d.       n.s.       6.142       0.142       0.00       0.074         TOTAL SC 3+ "       1.57       1.60       1.416       2.28       3.83       209       213       1630         Receptor fluid       0.621       0.899       1.818       0.903       1.160       0.646       3.00       645         %Ratio receptor 12h/24h       n.a.       n.a.       0.39       0.002       6008       0.005       0.91°         Receptor fluid       0.009       0.021       0.039       0.002       6008       0.005       0.91°         %Ratio receptor 12h/24h       n.a.       n.a.       0.39       0.002       6008       0.005       0.91°         Receptor chamber       n.d.       0.201       0.039       0.002       6008       0.005       0.91°     <											
SC6-8       0.259       0.230       0.235       0.413       1.003       0.695       4.47       9.50         SC9-11       0.155       0.266       0.332       0.135       0.288       0.349       0.025       0.09         SC12-15       n.s.       0.117       n.d.       n.s.       9.442       0.142       0.06       0.07         TOTAL SC 3+ a       1.57       1.60       1.412       2.28       3.83       209       2.13       0.09         TOTAL DOSE SITE       1.78       2.00       200       2.75       4.48       2.38       2.56       1.00         Receptor fluid       0.621       0.899       1.818       0.903       1.160       0.046       21.00       6.45         %Ratio receptor 12h/24h       n.a.											
SC9-11       0.155       0.266       0.332       0.135       0.288       0.349       0.25       0.09         SC12-15       n.s.       0.117       n.d.       n.s.       0.142       0.07       0.07         TOTAL SC 3+ a       1.57       1.60       1.417       2.28       3.83       209       2.13       000         TOTAL SC 3+ a       1.57       1.60       1.417       2.28       3.83       209       2.13       000         Receptor fluid       0.621       0.899       2.15       0.60       0.0616       2.00       0.645         %Ratio receptor 12h/24h       n.a       n.a.       n.a. <t< td=""></t<>											
SC12-15       n.s.       0.117       n.d.       n.s.       0.142       0.07       0.07         TOTAL SC 3+ a       1.57       1.60       1.412       2.28       3.83       209       13       030         TOTAL SC 3+ a       1.78       2.00       200       2.75       4.48       2.38       2.56       1.00         Receptor fluid       0.621       0.899       1.818       0.903       1.160       0.676       2.00       645         %Ratio receptor 12h/24h       n.a       n.a       0.39       0.002       9.008       0.005       0.92       0.91°         Receptor fluid       0.009       0.021       0.039       0.002       9.008       0.005       0.92       0.91°         %Ratio receptor 12h/24h       n.a											
TOTAL SC 3+ a       1.57       1.60       1.41%       2.28       3.83       200       2.13       050         TOTAL DOSE SITE       1.78       2.00       200       2.75       4.48       2.38       2.56       1.00         Receptor fluid       0.621       0.899       1.818       0.903       1.160       0.616       2.00       0.445         %Ratio receptor 12h/24h       n.a       n.a       0.039       0.002       9008       0.005       0.912         Receptor chamber       n.d.       0.201       0.039       0.002       9008       0.005       0.912         Receptor chamber       n.d.       9.031       0.402       9.035       0.402       9.008       0.005       0.912         Receptor chamber       n.d.       9.039       0.002       9.008       0.005       0.912       0.912         POTENTIAL       0.63       1.12       9.86       0.92       1.36       0.62       1.08       0.47         POTENTIAL       0.43       9.44       9.45       9.45       9.45       1.19       9.45       1.19         POTENTIAL       0.43       9.45       9.45       9.45       9.45       1.19       9.45 <td< td=""></td<>											
TOTAL DOSE SITE       1.78       2.00       2400       2.75       4.48       2.38       2.56       1.00         Receptor fluid       0.621       0.899       1.818       903       1.160       0.666       9.00       645         %Ratio receptor 12h/24h       n.a.       n.a.       0.621       0.899       1.818       903       1.160       0.666       9.00       645         %Ratio receptor 12h/24h       n.a.       n.a.       0.02       9.039       0.022       9.008       0.005       0.91°         Residual receptor fluid       0.009       0.021       9.039       0.022       9.008       0.005       0.91°         Receptor chamber       n.d.       0.021       9.039       0.022       9.008       0.005       0.91°         TOTAL DIRECT       0.63       1.12       9.866       0.92       9.035       0.62       1.08       0.47         POTENTIAL       3.42       3.86       3.67       5.82       3.900       3.65       1.19         POTENTIAL       3.42       3.86       3.67       5.82       3.900       3.65       1.19											
Receptor fluid       0.621       0.899       1.818       903       1.160       0.666       9.00       9.45         %Ratio receptor 12h/24h       n.a.       n.a.       6a.       1.66       0.62       0.899       0.62       0.62       n.a.       n.a.       n.a.       1.60       0.666       9.00       9.45         %Ratio receptor 12h/24h       n.a.       n.a.       6a.       1.60       0.62       9.08       0.005       0.91       0.91°         Residual receptor fluid       0.009       0.021       0.039       0.602       9.08       0.005       0.91°       0.91°         Receptor chamber       n.d.       0.031       n.d.       n.d.       0.185       n.d.       0.062       9.091°         TOTAL DIRECT       0.63       1.12       4.86       0.92       1.36       9.62       1.05       0.47         POTENTIAL       0.63       1.12       3.86       3.67       5.82       3.90       3.65       1.19         POTENTIAL       0.41       3.42       3.86       3.67       5.82       3.90       3.65       1.19         POTENTIAL       0.41       3.42       3.86       3.67       5.82       3.90       3.6											
(0 - 24h)       0.621       0.899       1.818       903       1.160       0.616       3.00       645         %Ratio receptor 12h/24h       n.a.       n.a.       6a.       n.a.       n.a.       6a.       n.a.											
%Ratio receptor 12h/24h       n.a.											
Residual receptor fluid         0.009         0.021         0.039         0.002         0.002         0.005         0.005         0.012         0.012           Receptor chamber         n.d.         0.01         n.d.         n.d.         0.185         n.d.         0.025         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.012         0.											
Receptor chamber         n.d.         \$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$\$											
TOTAL DIRECT         0.63         1.12         4.86         0.92         1.36         0.62         1.08         0.47           POTENTIAL (dose site+ receptor)         2.41         3.86         3.86         3.67         5.85         390         43.65         1.19											
POTENTIAL (dose site+ receptor)         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q         Q <t< td=""></t<>											
$\begin{array}{c c c c c c c c c c c c c c c c c c c $											
$\begin{array}{c c c c c c c c c c c c c c c c c c c $											
TOTAL RECOVERY \$5.45 0 90.93 104.00 \$6.93 93.970 95.54 94.45 6.2											
Evaluation according to EFSA Guidance											
No. Or y No. Or											
Absorption >/5% within half of study durations (include SC values)											
Keevery 595%? Correction needed "											
Total % Potentially absorbably adjusted according to EKSA (2017) (SD*1) = 4.8%											
* 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: stands deviation											
n.d.: below limit of detection n.s.: po samplezora: not applicable y											
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 spreadshop program.											
The mean recovery of cells is below 95% therefore the data were normalized for all cells except cell 3.											
Table 7.3-6: Distribution of radioactivity at 24 hours after dose application of [14C]- fluopicolide											
in a SC 58/.5 formulation at the rates of 0.25 g/b to human skin samples (All cells), Normalized											
Dose Level:											
0.25 g/L Distribution of radioactivity (% dose applied) K N° = 1											
Donor N° AHI HI HI H2 H2											
Sex Female Female Female Female Female											
Cell N° 2 3 4 5 6 MEAN SD											
Skin vash 8h 57 94,44 89.08 93.37 89.67 87.87 94.40 91.48 2.94											
Takal swaps 9449 89.08 93.37 89.67 87.87 94.40 91.48 2.94											
Total Se P+ SC 2 1.55 5.46 4.15 5.27 5.12 1.93 3.91 1.75											
Donor chamber         1.13         2.03         2.59         1.27         0.79         0.53         1.39         0.78											
TOTAL         NON-           ABSORBED         97.17         96.57         100 11         96 22         93 79         96 86         96 79         2 03											



Dose Level:							Group	Human HD
0.25 g/L		Distribution	of radioacti	vity (% dose	applied)	-	K	$\frac{N^{\circ} = 1}{N^{\circ}}$
Total skin	0.25	0.44	0.59	0.48	0.69	0.30	0.46	0.17
SC3-5	1.35	1.08	0.84	1.79	2.55	0.95	1.43	0.65
SC6-8	0.30	0.25	0.24	0.43	1.07	13	0.50	~ . 633
SC9-11	0.18	0.29	0.33	0.14	0.31	0.37	0.2	\$ 0.09
SC12-15	n.s.	0.13	n.d.	Č49.S.	0.15	0.15	×0,07	0.08
TOTAL SC 3+ ^a	1.83	1.76	1.41	₹2.35	4.08	2.19	2.27	9 ×0.95
TOTAL DOSE SITE	2.08	2.20	2.00	2.84	Q4.77	° 2.49	2.73	0 1.04
Receptor fluid $(0, 24b)$	0 727	0.000		۳″ م° ۵ ۵ ۵ ۲۵				
%Ratio receptor 12h/24h	0.727 n a	n.a.	n.a. \$		n.a.	n.a.	- 1.00 ×	, n.a.
Residual receptor fluid	0.01	0.02	× × ×		, <b>Q</b> .01	20 20 20 0.0 14	× × 0,0×	0.01
Receptor chamber	n.d.	1921 1921	n.e	n.d.	0.20	r nga.	9.07	۵.11
TOTAL DIRECT	0.74		n (k) Ni.86	0.99	¥.44	0.65 ⁽	6 ⁰ k ₁ 4	0.46
POTENTIAL (dose site+ receptor)	2. <b>8</b> D	0 3.43		۲۵ 3.78 م		3.14 s	ر بر 3.87	1.21
POTENTIAL (skin+ receptor)	≫ ∞0.99		2.45	20 27.43	2.1%		1.60	0.61
TOTAL RECOVERY	<u> 100-90</u>	200.00	9 AQ4.00	<u></u>		~~ 	100.66	1.62
<u> </u>		- Exalua	ationaccordin	to EFSA Gui	dayaçe »	Ĵ,		
Ť.	S V	Alsorption ⁴	×75% with⊮n ha	lf <b>Ar</b> study dura	tion?	ude SC value	s)	
		3 E		Recovery <	Not	applicable –	data normal	lised correction
Tota	Potentially	Aberbablea	Ö 🗸 djusted æcord	ing to EFSA (2	Mea 2017) 5.19	n (%dose sit %	e +%recept	tor) + (SD*1) =
*: tape-strips excluding SD: standard deviation n.d.: below limit det In the above table, the differences resulting fre	number V & 2 ectifut; n.s.: ro presented bea om the use of th	sample: n/a: not ns do not alway ne specadsheet p	idered to be not applicable calculate exa rogram	reabsorbed tose	e. presented ind	ividual data.	This is due	to rounding-up

**Conclusion:** The dermal penetration through human dermationed skin of [¹⁴C]-fluopicolide in the fluopicolide SC 687.5 formulation was investigated at two minal concentrations corresponding to the neat product (62.5 g/L) and a representative spray dilution of 0.25 g/L. ~Q

Concentrate (6

The precentage of thopicolide 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 rist assessments for fluopicolide in the FLC+PCH SC 687.5 formulation: risk f

	Human Skin	
Concentrate (62.5 g/L)	0.26%	Ĉŝ
Low dose (0.25 g/L)	5.1%	Ţ

Assessment and conclusion by applicant:

Propanceard A summary of the dermal absorption rates for propanocation in the fluenceolidest propanocation as a resented by the following tables of the derma absorption rates for propanocation in the fluenceolidest propanocation. HCI SC 687.5 (FLC+PCH SC 687.5) formulation is presented by the following tables of the derma absorption rates for propanocation in the fluenceolidest propanocation. HCI SC 687.5 (FLC+PCH SC 687.5) formulation is presented by the following tables of the derma absorption rates for propanocation. HCI SC 687.5 (FLC+PCH SC 687.5) formulation is presented by the following tables of the derma absorption rates for the derma



#### Table 7.3-7: Dermal absorption rates for propamocarb in FLC+PCH SC 687.5

	Propamocarb						
	Value (% of dose applied)	<b>~</b> .					
Concentrate	2.0%	- A	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				
Dilution	2.9% @ 5 g/L	A »					
(dilution factor)	8.6% a 0.3 g/L						

#### Justification for proposed values – Propamocar

The proposed dermal absorption rates for propamocarb are based on an *invitro* numan skin dermal absorption study using the FLC+PCH SC 6805 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	f submitte	dermal	absorption	studies fô	r Propamocarb
J			S. ∎∕		alv (🔊

Test	Concentrate	Spray dilution Formulation Justification J Beterence
		(dilution factor) in study > provided on
		Contraction in the second seco
		study formulation
		for current product of
In vitro	2.0%	2.9% A FLC PCH Not required 2015; M-
(Human)	Í.	$\mathbb{P}(1 \text{ in } \mathbb{Q}^{5})$ $\mathbb{Q}^{5} = \mathbb{Q}^{5} \mathbb{Q}^{5}$
		in 2083) ( , , , , , , , , , , , , , , , , , ,
	<u> </u>	
Data Poir	itsy	×4KCP * 3/02 ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~
Report A	athor:	
Report Y	ear:	$\frac{1}{2003}$ $\frac{1}{\sqrt{2}}$ $\frac{1}{\sqrt{2}}$ $\frac{1}{\sqrt{2}}$ $\frac{1}{\sqrt{2}}$ $\frac{1}{\sqrt{2}}$
Report Ti	tle:	In vive dermal absorption in the male rat Code: (14C)-EXP11120A
Report N	o: 🖗	
Documen	t No: 🖉 🔬 🖉	∑ [™] <u>M¢222384Q01-1</u> 0 [°] 0 [°] 0 [°]
Guideline	(s) followed in	DECD Guideline of Testing of Chemicals,
study:	4	Toxicokinetics, 417, Adopted April 1984 using
, K	Ç′	the latest draft of the OECD, Test Guideline 427
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	and the respective DECDQ uidance Documents
	₩,	for the conduct of in vivo skin absorption studies (April 2002).
Deviation	is from current	(prinone) V O
test guide	line:	
Previous	evaluation: 🚽	yes, evaluated and accepted
	<u> S</u>	(2005) (2005)
GLP/Offi	éjally 🛇	Yes, conducted under GLP/Officially recognised testing facilities
recognise	d testing	
facilities:		
Acceptab	iling/Reliability	/: Wes

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.



Data Point:	KCP 7.3/04
Report Author:	
Report Year:	2015
Report Title:	FLC + PCH SC 687.5 [14C]-propamocarb HCl - In vitro dermal absorption study
	using human skin
Report No:	SA 14050
Document No:	<u>M-516805-01-1</u>
Guideline(s) followed in	OECD 428 (2004); OECD Assessment No 28, (2004); EFSA Panel on Plan
study:	Protection Products and their Residees (PPR), : Gridance on Derval Absorption
Deviations from current	None A O' A O' A
Previous evaluation	No. not previously submitted
GLP/Officially	Yes, conducted under GLP/Officially recognised testing facilities
recognised testing	
Acceptability/Reliability:	Yes X A A A
Material and methods:	
Human skin:	Source: Bløpredie, Rennes & Xenometrics, Begenheim, France.
	Number and sea: minum @4 domors per dose level, female.
	Anatomical region: Abdomen.
	Thickness: 365 to 491 µm.
Test Material:	
Non-radiolabelled:	Batch EK1C000430. A a a a a
\$	Purity = 70.9% (www). γ
Radiolabelled:	[1-°C]-propamocarb
	Batch; RML 9864.
	Specific activity: 3.75 MB@mg. 5 0 5
	Radiopurity of the formulation >98.5%.
Formulation:	The formulation used in this experiment was the fluopicolide +
	propamocarb HCl SC 6875 formalation (specification N° 102000013376)
	containing fluopeolide 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
ġ j	dilutions of a g/L and 0.3 g/L.
a Sy	
Test system:	A flow through diffusion celosystem (Franz's cell modified, Gallas, France)
· A	was used to study the absorption of the test substance (exposure area of 1 cm^2
	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
	predium supplemented with 5% bovine serum albumin and gentamycin (50
a, `	mg/k) at a αH of βa 7.4. The receptor chamber was warmed by a constant
× 1	circulation of warm water which maintained the receptor fluid at $32 \pm 2^{\circ}C$
	Gose to the formal 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
Ĉ	measuring the trans-epidermal water loss (1EWL) 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 μ L/cm² aposed 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.

The receptor fluid passing through the receptor chamber was collected in a Sampling: 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-apprication, the skin was swabbed with freshly prepared 1% of Tween 80(in PB\$ (phosphate buffer saline) using precision wipes (Kindech Sciences from Kimberts-Clark° professional), in order to remove and retain the non absorbed dose, until no radioactivity was detected with a Geiger-Muller 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 kin sample was tape-strigged to remove the stratum corneum. This involved the application of Monaderm adhesive tape (Monaderm Monaco) for Oseconds before the tape was carefully removed against the direction of haid growth. This procedure/was continued untita 'shiny' appearance of the epidermis was sevident, which indicated that the stratum corners had been removed. The taperstrips 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 Getained for analysis.

Radioassay

The amounts of radioactivity in the various comples were determined by liquid sentillation counting (CSC). Sample's were counted for 10 minutes or for 2 sigma s in an appropriate sentillation cocktail using a Packard 1900 TR counter with on-line computing facilities. Quenching effects were determined using an external standard and spectral quench parameter (tSIE) method. Effreiency correlation cucies were prepared for each scintillation cocktail and were regularly checked by the use of [14C-n-hexadecane standards. The sentillation counter was recalibrated when a deviation of greater than 22 was abserved 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 4

The study results are presented in the following Table.



Table 7.3-9: 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 (All cells).

		Distribution of radioactivity (% dose applied)							
						608-01-	Group I Ha	lumaan	Ĩ
Donor N°	X2014/1-6	X2014/3-7	X2014/1-1	X2014/2- 1	X2014/1-20	0414-111-	No.	3. 5	0
Sex	Female	Female	Female	Female	Female	Female			
Cell N°	H01	H02	H03	H04	H05	H06 -	MEAN O	S SD 🖌	Ŝ,
Skin wash 8h	78.47	93.40	96.26	Ø 93.70	52 .58	96.25	91.78	6.69	a.
Skin wash 24h	0.0041	0.0441	0.0033	0.1090	9.2875	0,0195		Å.11	6
Surrounding swabs 24 h	0.0014	0.0055	0.0086	0.0045	0.0897	0.0039	0.02		Y
Total swabs	78.48	93.45	96.27	93.82	92.96	Q 96,30	91-88	¢72	
SC 1	0.0023	0.0166	0.0016	0,0994	× 1.1055	0.096	\$0.21	£0.44	
SC 2	0.0013	0.0092	0 0.065	0.0221	0.9960	Ø.0337	ر 0.0 <u>3</u>	0.040	
Total SC 1 + SC 2	0.0036	0.0258	- • 0 0079 <i>∧</i>	0.1215	<u>1.2015</u>	0.0633	×	@ .47	
Donor chamber	n.d.	0.0441	€ € 0.02	0,0877	1.3134	0,0\$28	ي 0.31	0.56	
TOTAL NON-		Q 4					ŝ, ĉ	D	
ABSORBED	78.48	93.52	°~96.29	× 94.02°	95.47	<u>) 96.48</u>	92.38	6.91	
Skin	0.0027	× 0,42,14	<u>6</u> 0.0040	0,4541	0 0.802	0.0014	[*] >0.25	0.31	-
Surrounding skin	0.001	<u>≈</u> 0.0191	0.00034	0.0021	Q <u>0.3942</u>	09.0092	0.07	0.16	-
Total skin	0.0039	<u>()</u> 0.14(5)	0.0083 (<u>∂</u> 0.1562⁄∕	°4) ,1964	<u>© 0.4106</u>	0.32	0.45	
SC3	<u></u>	0,00068	0.0021	0,1056	≪J [♥] 0.166€	0:0440	0.05	0.07	
SC4	0.0012	©0.0050 (<u>) 699911</u>	©0.0156%	0.1278	<u>0</u> 0.0515	0.03	0.05	
SC5	n.s.	<u>(~ 0.00</u> 64)		0.0098	©″ n.s. 4	0.0184	0.01	0.01	
SC6	O ^V n.§	\$ 0122	n.s	Ön.s.	ne ne	n.s.	0.00	0.00	
SC7	n.s.	× 0.0069	n.s.	n.s	ý Wh.s.	n.s.	0.00	0.00	
SC8	n.s.	0.0310	n.s.	× Q.	n.s.	n.s.	0.01	0.01	-
TOTAL SC-3+4	× 0.0108	\$10683	0.0032	@1310	0.2881	0.0839	0.10	0.10	-
TOTAL OOSE SITE	0.0047	[©] 0.2088	00115	× 0.2872	1.4845	0.4945	0.42	0.55	-
Receptor fluid $(0 - 12h)$	0.0270		~ 0.03Q	AQ 0375	0.0552	0.0445	0.043	0.014	
Recentor fluid	5	\$0013 \$0 %			0.0002	0.0115	0.015	0.011	
(0 - 24h)	D	°∼ 0,2¥40	°≫0 0548	0 0692	0 1967	0 1105	0 120	0.082	
%Ratio receptor 12h/24h	C AC	A 26	B. G	54	28	40	44	15	
Residual K CFluid %	0.0925	0.510	2 20104	0.0441	0.4323	0.0974	0.18	0.23	1
Receptor chamber	201 560	0.0000	0.0000	0.1809	0.2455	0.1434	0.12	0.10	
TOTAL DIRECT	0.2128	0.7548	0 0.0644	0.2942	0.8745	0.3513	0.43	0.32	
POTENTIAL	\ [√]	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Y						
(dose site+ receptor)	2275	× <u>0.9636</u>	0.0759	0.5814	2.3590	0.8458	0.84	0.82	
POTENTIAL (skin+ recentor)	0,2,487	0.8953	0.0727	0.4504	2.0709	0.7619	0 74	0.72	
TOTALRECOVERY	28.71	94.48	96.37	94.61	97.83	97.32	93.2	7.2	
		Evaluation	according to E	FSA Guidan	ce		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		1
A A	- AB			July Survey	No.				1
Č	Abso	rption >75% wi	thin half of stuc	ly duration?	(include SC values except SC1 &2)				
			Reco	very <95%?	Yes (due to H	I01) correction	n needed		
Total % Potentially Absorbable adjusted according to EFSA (2017)						the next table	•		



^a: 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 roughing-up differences resulting from the use of the spreadsheet program.

differences resuring means 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.

Distribution & radioactionity (% Dose applied) L. 808-01-Group Human HD X2014/2n [∛] N=*b*y[,] KN⊗1.2 Ø C X2044/1-1 Donor N° X2014/3-7 -20 0414-III Ø Female Female Sex Female Female \mathbb{O}_{SD} H03 MEAN Cell N° H02 104 H05% ≈H06 096.26 93 70 93.40 962 Skin wash 8h 94.44 1.71 0.0441 0.003 0.10 0.000 Skin wash 24h Ô 0.287 Q0775 0.11 @0045 0.6897 0.02 0.0039 Surrounding swabs 24 h 0055 0,0026 0.04 <u>ڳؤ</u> 26,33 92.96 93,45 **Total swabs** 93.80 94.56 1.61 0<u>7</u>029<u>6</u> Ô 0 1.1055 SC 1 0.0166 0.0046 0.0994 94.56 1.61 ð0.022 t 0.0960 0.0063 0.032 0.25 SC 2 0.48 G.0<u>079</u> 0.0633 0.0258 0.03 Total SC 1 + SC 2 1.2015 0.04 0.1215 K j Ò 0.0828 0 0441 0.0213 1.3154 1877 Donor chamber à 0.28 0.51 ABSORBED 96.29 96.48 94.88 TOTAL NON 93.52 94.02 98.47 1.36 0.802¥ 0.154 Skin 0.0049 0.4014 0.30 0.32 0.1214 0 Surroundingskin 0.0034 0.0191 0.3942 0.0092 0.09 0.0021 0.17 \bigcirc °√,1964 Total skin 10,0083 0.1562 0.4106 0.1405 0.38 0.48 ۵<u>.1603</u> 0,4056 0.0068 0.002 SC3 0.0140 0.058 0.071 0.0011 0.0156 SC4 9.0050 0.1278 0.0515 0.040 0.053 0 O 0.0098 SC5 0.006 0.0184 0.007 0.008 n.s. n.s. n.s SC6 Q(0)122 0.002 0.005 n.s. n.s. n K j 0.0069 0.003 SC7 0.001 มัร n.s. n.s. n.s. 0.0310 0.006 0.014 SC8 n.s n.s. n.s. n.s. Q, TOTAL SC 3+ a 0.0683 0.0032 0.1310 0.2881 0.0839 0.11 0.11 0.9115 TOTAL DOSE SIDE 0.2088 0.2872 1.4845 0.4945 0.50 0.58 X, Receptor fluid 0.0310 0.013 0.0375 0.0552 0.0445 0.047 (0 - 12h)x0₆43 Receptor fuid (0 -0.2440 0.0540 0.0692 0.1967 0.1105 0.135 0.082 26 57 54 28 40 41 14 12h/24 ARSTIN receiption Residual Rec Fluid 0.5108 0.0104 0.0441 0.4323 0.0974 0.22 0.23 Receptor chamber 0.0000 0.0000 0.1809 0.2455 0.1434 0.11 0.11 TOTAL DIRECT 0.75 0.06 0.29 0.87 0.35 0.47 0.34

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



	Distribution of radioactivity (% dose applied)								
			X2014/2-		608-01-	Group Human HD			
Donor N°	X2014/3-7	X2014/1-1	1	X2014/1-20	0414-III-1	$K N^{\circ} = 1.2$	ð		
Sex	Female	Female	Female	Female	Female		Ş		
POTENTIAL					Ĵ.				
(dose site+ receptor)	0.9636	0.0759	0.5814	2.3590	0.8458	0.97 0.85	1		
POTENTIAL (skin+ receptor)	0.8953	0.0727	0.4504	2.0709	7 7619	Q95 0.75	<i>Ŋ</i>		
TOTAL RECOVERY	94.48	96.37	94.61	97.83	97.32	396.12 1.55	e R		
Evaluation according to EFSA Guidance									
Absorption >75% within helf of study duration? (implude Stevalues except SCI & 2)									
			Rec	cover	No correction	inceded of a			
Total % Pot	entially Absorb	able adjusted	according to	EFSA (2007)	Mean (%de (\$1)*1.2) = 2	site +%receptor) +	p		
^a : tape-strips excluding numbers	1 & 2 which are	considered to t	e non-absorb	ed dose.	1 8				
SD: standard deviation									
n.d.: below limit of detection; n.	s.: no sample; p	not applicabl							
In the above table, the presented	means do por a	lways calculate	exactly from	the presented	dividual data.	This due to founding-up			
differences resulting from the use	e of the spreadsh	ieetorogram. V V							

Table 7.3-11: Distribution of radioactivity at 24 hours after dose application of [140]- propamocarb in a SC 687.5 formulation at the rates of 5 g/L to human stein samples (All cells).

Distribution of ratioactivity (% doseapplied								
Sex &	Febrale	Female	Female	Female 0	Female	Female	Group H	uman HD
		X2014/2-	×2014/5-	TRA2001		7	K N	° = 1
Donor N°	Ox2014/4-10	-0 [%] &		B \$559	SSB2014/2 ℃	X2014/6-1		
Cell N°	Ĥ197	H08	F109	A1010		H12	MEAN	SD
Skin wash 8h	85.85	8853	⁰ 81.99	<u> </u>	93.62	89.00	87.92	3.84
Skin wash 24h	Ø <u>\$</u>	0.14	>` 0.0	≪ _{0.33 %}	0.03	0.00	0.13	0.13
Surrounding swabs 24 h 🍣	0.0180	© 0.0 288	0 0045	0.0073	0.0022	0.0083	0.01	0.01
Total swabs	A 86,4	\$\$8 .69	مریکی 82.03	,	93.65	89.01	88.06	3.83
SC1		× 0.056	0 000	0.119	0.005	0.012	0.10	0.14
SC2	0.022	0.00	0.022	0.115	0.011	0.003	0.03	0.04
Total SC1	\$ 138	Ø.09	0.04	0.23	0.02	0.02	0.13	0.15
Donor chamber	1 0.168	0.614	6.08	0.152	0.096	0.543	0.27	0.24
TOTAL NON-		y Q	Å,					
ABSORBED	86,67	\$9.4 0	82.14	89.22	93.76	89.57	88.46	3.85
Skin A	×	0.09	Q* 0.21	1.20	0.02	0.16	0.44	0.51
Surrounding skills	0.175	, 05283	0.042	0.028	0.007	0.386	0.15	0.16
Total skin		0.37	0.25	1.22	0.03	0.54	0.59	0.49
SC3	0.028	0.050	0.033	0.091	0.009	0.002	0.035	0.032
SCA ST O	0.025	0.043	0.035	0.120	0.008	0.011	0.040	0.041
SC5 SO	n.s.	0.061	0.032	0.127	0.020	n.s.	0.040	0.048
SC6	n.s.	0.033	0.031	0.102	0.025	n.s.	0.032	0.037
SC7	n.s.	0.484	n.s.	0.108	0.022	n.s.	0.102	0.191



	Distribution of radioactivity (% dose applied)									
Sex	Female	Female	Female	Female	Female	Female	Group Hu	Group Human HD N= 6 or °		
Donor N°	X2014/4-10	X2014/2- 3	X2014/5- 12	TRA2001 B559	B2014/2	X2014/6-1	K Nº			
SC8	n.s.	n.s.	n.s.	0.104	0.020	Ö n.s.	0.021	0.042		
SC9	n.s.	n.s.	n.s.	0.067	0.018	n.s.	0.014	10.027		
SC10	n.s.	n.s.	n.s.	0.051	0.021	n.s.	0 12	S0.021	þ	
SC11	n.s.	n.s.	n.s.	0087	0.018	n.s.	0.017	0.03		
SC12	n.s.	n.s.	n.s.	0.055	Q16	n.Ø	0.00	Ø.922	Ň	
SC13	n.s.	n.s.	n.s.	n.s.	<i>√</i> 0.076		0.913	0.000	1	
Total SC3+	0.05	0.67	0.13	0.91	× 0,23	Q 0.01	0.34	0.37		
TOTAL DOSE SITE	1.19	1.04	0.38	_ ∘ 2.14	¥ ¥.28	ര ത്ര	.0.93	9 .69		
Receptor fluid (0 - 12h)	0.051	0.158	0 3.473		0.30	0.624	م م الا	1.30°		
Receptor fluid		Å			A	Ô, "	Д,	Ű.		
(0 - 24h)	0.058	0.005	°¥.007	@ 0.51¥	0.463	g , \$ 08	A.02	5 ¹ .48		
%Ratio receptor 12h/24h	89	۵ ⁹ 56	\$.85	\$ 60	Ø "N	S 77	Ž 73 🔊	14		
Residual Rec Fluid	0.057	Q 0.029	0 0.029	0.04	0.024	Č 0.02	0,034	0.013		
Receptor chamber	0.21	0.466	00.162	S 0,648	0.166	7 29839	\$ 0.300	0.205		
TOTAL DIRECT	1.33	0.78	\$ 4,20	0.71	Q [*] .0.65	1.47	0° _{1.36}	1.44		
POTENTIAL (dose site+ receptor)	× 1.52	ري 1.82	\$ ⁴ .58	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.93×	\$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$ \$	2.29	1.28		
POTENTIAL (skin+ receptor)		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		↓ 0 ¹	0 ×	2.01	1.95	1.32		
TOTAL RECOVERY	88.2	94.2	86.7	Q 924	ه 94.7	Ø 91.6	90.7	2.9		
Č,		Evaluation a	coording to	EFSA Guidan	ce (2017)	ý.				
	Absorpt	ion >75% wil	thin half@f st	udy duration?	No (in Øade S	C values excep	t SC1 & 2)			
		? A	Mean Rec	overy <95%?	Çofæction ne	eded #			1	
Total % Potent	ialy Absorbab	le adjusted a	ccording	EFSA:(2017)	Quean (%dose	e site +%recepto	or) + (SD*1)	= 3.6%]	
* Normalisation was apped	* 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 "absolved" fractions. Nost probably diffeto losse during the skin swabbing procedures or an over-estimate of the amount applied. Ċ 6

SD: standard deviation; B number of skiir cells used for calculation

n.d.: not detected (below the limit of deaction) and : 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 coulting from the use of the spreadsheet program.

In the study report both Cells 107 and HO were excluded from the reported cells due to "low In the study report both Cells 1107 and H09° were excluded from the reported cells due to "low recoveries". However, looking at the camulative absorption profile of all the cells it shows that cell H09 can be considered as autilier compared to other cells as shown in the graphs below.



Figure 7.3-1: Cumulative Absorption Profile after dose application of [¹⁴C]-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 [14Ct propamocarbon an SC 687.5 formulation at the nominal rate of 5 g/L to human skin (Reported tells)




Table 7.3-12: Distribution of radioactivity at 24 hours after dose application of $[^{14}C]$ -
propamocarb in an SC 687.5 formulation at the rate of 5 g/L to human skin samples (reported
cells) normalized.

ells) normalized.	1							, 1
	Di	istribution of r	adioactivity	(% dose applie	d)		J.	S
			TRA200		Â	Group Hu	manOMD	10.
Donor N°	X2014/4-10	X2014/2-3	1B559	B2014/2	X2014/6-1C	K N°	- 1 42 _ ~~	0
Sex	Female	Female	Female	Female	Female	<u>S</u>		Ô
Cell N°	H07	H08	H10	H11	¥Ú/2 ⁷	MEAN	s SÓ	K, ^s
Skin wash 8h	97.37	97.05	96.13	98.86	97.17	97.31	0.90	p"
Skin wash 24h	0.26	0.15	036	0.03	∑ ¥ 0.00	× 0.14	Q715	٩ پ
Surrounding swabs 24 h	0.020	0.032	20.008	0.002	م 0.009° <u>م</u>	0.01	0.01	Ŵ
Total swabs	97.65	97.23	<i>2</i> 96.49	\$\$8.90	. 0 97.18	0 97.49	\$ \$ \$ \$	
SC 1	0.41	0.06	, ¢		× 0.01	0.13	Ø.17	
SC 2	0.02	0.04	×0.12	Č với	0.00	Q.04	A 0.05c	0
Total SC 1 + SC 2	0.44	× 9 .10	°~ 0.25		A 0.02	0.17 4	6	ſ
Donor chamber	0.19	0.67	Ø16	. ~ 0.16	2 20.59	Q 0.54	27	
TOTAL NON-ARSORRED	98.27	S de ai	\$ 96.91 ⁴		07 70¢		© 0.76	
Skin	1 000		1.20			0.54	0.70	1
Surrounding skin	a 20	0.10				0.10	0.01	
	(<u>9.20</u>		0,03		0.42	0,19	0.10	
	× 1.29			0.010	0.59	0.73	0.57	
803		~~0.055	0.099	0.010*	× 0.002	<u> </u>	0.04	
<u>SC4</u>			09,131	0,008	~~0.012	× 0.05	0.05	
SC5	n.s.	0.067	~ 0.138 S		0^{N} $n_{\text{rs.}}$	0.05	0.06	
SC6		¥ 0.036		0.027	n.s.	0.03	0.05	
SC7	n.s.	0:530	0.118	~~~~ 0.0 24	n.s.	0.13	0.23	
SC8	O n.s.C	n.s.	0.1130	2 <u>20</u> 22	@ n.s.	0.03	0.05	
SC9	figs.	<u>, n.</u>	0.0073	0.019	9 n.s.	0.02	0.03	
SC10	n.s.	n.s.	Ø.055	<u> </u>	n.s.	0.02	0.02	
SCI1	N ms	n.s.	× 0.094	0.018	n.s.	0.02	0.04	
SC12	Da.s.	🔊 n,\$Ø	0.960	0.017	n.s.	0.02	0.03	
SC13	n.s. e	Ø .s.	S n.s.	9 0.080	n.s.	0.02	0.04	
TOTAL SC 3	0.460		> 0.991	0.268	0.014	0.41	0.43	
TOTAL DOSE SITE	° ,⊋.35	A 1,14	J 2.32	0.30	0.60	1.14	0.78	
Receptor fruid	Ŷ,							
(0 - 12h)	0.058	0.174	0.337	0.355	0.681	0.32	0.24	
Receptor fluid		, ^s	2 A					
(0 - 24h)	0.065	© 642	0.562	0.489	0.882	0.46	0.30	
%Ratio recept@12h/24h	\$ 89	2 , 56	60	73	77	70	9	
Residual Reg Fluid	D	°♀ [−] 0.03	0.04	0.02	0.03	0.04	0.02	
Receptor chamber, 4	0.25	0.51	0.16	0.18	0.70	0.36	0.24	
TOTAL DIRECT	0.38	0.85	0.77	0.69	1.61	0.86	0.46	
ROTENTAL	\$ 7							
(dose sign receptor)	1.73	1.99	3.09	0.99	2.21	2.00	0.76	
POTENTIAL	1.65	1.01	2.10	0.70	2.20	1.00	0.01	
(skin+ receptor)	1.67	1.26	2.10	0.72	2.20	1.59	0.61]



	D	istribution of r	adioactivity	(% dose applie	ed)		
			TRA200			Group Human HD	
Donor N°	X2014/4-10	X2014/2-3	1B559	B2014/2	X2014/6-1	$N=5$ $K N^{\circ} = 12$	ð
Sex	Female	Female	Female	Female	Female		Å
TOTAL RECOVERY normalized	100.00	100.00	100.00	100.00	100.00		
	E	valuation acco	rding to EFS	5A Guidance	4	22 2 2	<i>Č</i> a
				<i>⊳</i> ∧	No		K,
	Abso	rption >75% wi	thin half of s	uay duration?	(include SC v	alues except SC1 & 2)	ſ
			Rec	covery <95%?	Correction ap	plied S	. 8
			, O'	Å	Mean (%dq	se site +%receptor) +	
Total % Pot	entially Absorb	able adjusted	according to	EFSA (2017)	(SØ*1.2) = 2	9% 4	
^a : tape-strips excluding number	rs 1 & 2 which a	re considered to	o be non-abşo	orbed dose.			
SD: standard deviation		Ő					0
n.d.: below limit of detection;	n.s.: no sample;	n.a: not applica	able w	v Q		ĨĨ Â Â Â	-
In the above table, the presente	ed means do not	always ealculat	é exactly from	n the presented	individual@ata.	This is due to rounding ap	

differences resulting from the use of the spreadshoed program. Table 7.3-13: Distribution of radioactivity at 24 yours after dose application of [10]propamocarb in a SC 687.5 formulation at the rates of 0.3 g/L to forman skin samples (All cells).

		Distribu	fion of radio	activity (% dø	seapplicity	20° _0°		
Sex	Female 🔏	Female	Female	Female	Fepfale	Female	Group I	Human HD
	608-01	X2014/2-	32014/5	X20141-	603-01	598-01-		$N^{\circ} = 1$
Donor N°	04149,0121	4 (0414- %-1	0304-1V-1	/	
Cell N°	<u>∢</u> HJ13 ∡	₩H14Ô	HQS	[™] H16 [™]	A 47	H18	MEAN	SD
Skin wash 8h	78.07	28.45	@ 85.53	\$ \$5.01	81.7®	\$\$5.45	82.38	3.48
Skin wash 24h	0.84	م م الم الم	<i>* *</i> 0 ,33	م 0.26 ف	\$ 29	0.79	0.65	0.61
Surrounding swabs			\$0.02 ^{\$}		1 0 02 V	0.02	0.02	0.00
Total swabs	79.93		8588	85.28	82.11	86.27	83.06	3.21
SC1	0.10	\$ 0.00	0.04	~ 0.0G	×0.09	0.13	0.09	0.03
SC2		%_0 .07	0.03 [°]	¢ © 0.05	0.09	0.11	0.08	0.03
Total SC1 + SC2	0.20	0.15	× 9207	0 ⁰ 0.11	× 0.18	0.24	0.16	0.06
Donor chamber	0.45	§* 9.99	\$70.69	S 45	0.39	0.45	0.47	0.11
TOTAL SON- ABSORBED	80258	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	8644	85.86	82.68	86.96	83.69	3.26
Skin	ي © 1.14	5 1. 6	3 .29	۰.07 v	0.48	0.81	0.64	0.43
Surrounding skin	~~~ 0 <u>.0</u> 6	×06	0.03	0.03	0.14	0.09	0.07	0.04
Totalškin	A .20	مُ 1.09	<u>)</u>	0.10	0.62	0.90	0.70	0.44
SC3	0.125	V QAS	0.028	0.043	0.150	0.207	0.12	0.07
SC4	A 0.08	0.156	Ø 0.050	0.056	0.183	0.282	0.14	0.09
SC5	9.113	S 0.195	0.035	0.040	0.212	0.209	0.13	0.08
SC6	0.139	0.189	0.051	0.058	0.112	0.215	0.13	0.07
SC7	Š 0174	0.384	0.078	0.049	0.182	0.148	0.17	0.12
sca g	6 .177	0.174	0.032	0.030	0.177	0.100	0.12	0.07
SC9	0.146	0.189	0.060	0.041	0.139	0.137	0.12	0.06
SC10	0.168	0.199	0.042	0.043	0.105	0.107	0.11	0.06
SC11	0.132	0.152	0.039	0.812	0.087	n.s.	0.20	0.00



		Distribu	tion of radio	activity (% do	se applied)			
Sex	Female	Female	Female	Female	Female	Female	Group I	Human HD J−6 °
Donor N°	608-01- 0414-III-1	X2014/2- 4	X2014/5- 25	X2014/1- 21	603-01- 0414-V-1	598-01- 0314-IV-1	K	$N^{\circ} = 1$
SC12	0.088	0.072	0.037	n.s.	0.074	Ô.	0.05	0.00
SC13	1.952	0.087	0.037	n.s.	0.070	Øn.s.	0.36	0,00
SC14	n.s.	0.128	0.040	n.s.	0.070	n.s.	0.0	2 .05
SC15	n.s.	0.065	n.s.	nČs	0.059	n.s.	×0,02 /	0.03
Total SC3+	3.30	2.15	0.53	1.17	1.62	1.40	© 1.70 🍣	0.25
TOTAL DOSE SITE	4.50	3.24	0.85	1.27	\$24	2.30	2.40	Q.33
Receptor fluid (0 - 12h)	10.29	0.25	2.21	1.66	3.43	2° 2.98	3.64	220
Receptor fluid			×				* `~	, K
(0 - 24h)	14.99	0.55	2.92	× 23Ô	4.76	5.35	548	∽ 5.13 °
%Ratio receptor 12h/24h	69	45		72		2 4 7 2 C	72	A O
Residual Rec Fluid	0.509700	0.28140	0.194700	J.221100	0.357300	0.332800	Ø.72	0.11
Receptor chamber	n.d.	n.d.	n.d.	y wy n.d.		n.d.	§n.d. ≮	n.a.
TOTAL DIRECT	15.50	0.83	3	2.54	5 \$12	5.89	5,50	5.23
POTENTIAL (dose site+ receptor)	20.00	م ب <u>لا</u>	^{3.96}	0 ⁷	~ 7. 3 6	6 8.19	7.90	6.22
POTENTIAL (skin+ receptor)	\$ 16.70	<u> </u>		2.64	5.74	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	6.20	5.47
TOTAL RECOVERY	100.6	83 .5	90.6	897	0 90.0 %	375.2	91.59	5.77
		Baluatio	according	to EESA Guio	ance (2017)	~~ 		
, Î	Absorpt	ion >75% wit	hin half of st	udy duration	No (in and s	alues except	t SC1 &2)	
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		0	Mean Rec	overy <96%?	Correction ne	∼ eded [#]		
Total & Potent	ially Absorbab	le adjusted a	cording	EFSA 2017)	Mean (%dose	site +%recepto	r) + (SD*1)	= 14%
SD: standard deviation	n; N: wimber?	¢skin cels	used for cal	cultation				
n.d.: not detected (belo	w the limit of	detection);	n a?: not ap	plicable	Å			
In the above table, the due to rounding-up of	presented me ferences resul	ar® do not a trig from th	ways carcu e use of the	late Ractly	fom the present or ogram.	nted individua	l data. This	s is
# Normalisation was a	polied to all	alues as no	specific san	O ple type app	eared to be res	sponsible for t	he lower th	ian
95% recovery from a procedures an over-	ny of the "al	osorbed" fr	Otions. Mo	st probably	due to losses	during the sl	kin swabbi	ng
				×~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				
<u> </u>	S'A	· A		<u>,</u> ,				]

In the study report both Cells HD and H14 were excluded from the reported cells due to "high recovery" and "low recovery" respectively. However, booking at the cumulative absorption profile of all the cells it shows that Cell H43 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.

has been excluded from the results.



Figure 7.3-3: Cumulative Absorption Profile after dose application of [¹⁴C]-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 [14CP propamocarb in an SC 687.5 formulation at the nominal state of (0.3 g/L to human skin (Reported cells)



Considering ecovery all 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	5 fo	rmulation at t	he 1	ate	of 0.3 g/	/L to h	uman	skin samples	(rej	ported
cells) normaliz	zed.										aı°

cells) normalized.						1	·
	D	istribution of r	adioactivity	(% dose applie	ed)		
Sex	Female	Female	Female	Female	Female	Group Hu	man HOD
			X2014/1-	603-01-	598-01-	K N°	= f.¥
Donor N ^o	X2014/2-4	X2014/5-25	21	0414-V-1	0314-IV-1	,	Ŷ
Cell N°	H14	H15	H16	H17 《今	H18 📞	MEAN S	s SD S
Skin wash 8h	93.98	94.40	94.81	90.84	Ø.80	92.7	[♥] 2.28 @°
Skin wash 24h	0.48	0.36	0.28	0.32	♥0.84	<u>42,476</u>	
Surrounding swabs 24 h	0.02	0.03	0.02	0.02	Q 0.02	<u> </u>	<u>C0.00</u>
Total swabs	94.48	94.78	<b>955</b> 11	91.19	<b>20.</b> 66	· 93.24	<u>© 2.14</u>
SC1	0.10	0.04	0.07	ÔŬ ÔŬ	0.14		<u>8</u> .94
SC2	0.08	0.04	0.66	Č0.10	<u>0' 612</u>	0°0.08	0.03 °
Total SC1 + SC2	0.18	0.08	°∼ <b>0</b> /12	<u>~ 0.20</u>	0.26	<b>0.17</b>	© 0.02
Donor chamber	0.47	<b>6</b> ,76	× 0.52	Q ^V . 1944	0.47		
TOTAL NON- ABSORBED	95.12	ب چ 95.630	9575	S 91.83	291.39	5 93.9 <del>4</del>	2.15
Skin	1.24	QQ2	Q 0.08	ð 🕉	0.85	¢.60 ×	0.45
Surrounding skin	0:0C>	°≫0.03	0.09	× 0.16	Q 0.10	0.08 ×	0.05
Total skin	1.31	\$ 0.30	<b>A</b> 11	@ 0.69 ⁵	0.95 •	0.68	0.47
SC3	°∼y0.198₄	0.931	\$0.048	\$ _ <b>0</b> 5467	€ 0.217S	Q.13	0.09
SC4	× 0.1×	Q0.055	0.00	0.204	Ø.296	°∼ ^{0.16}	0.10
SC5	0.234	N 0.03	<b>1</b> 0045	0.235	Q.220	0.15	0.10
SC6	0.226	0.056	∽ 0.065	Q (724	~ 0.22¢	0.14	0.08
SC7	0,460	0.086	0.053	0.202	0.156	0.19	0.16
SC8	×9/208	0.035	\$0.034	S 0.19	× 0.105	0.12	0.08
SC9	0.22	0:067	0.046	£155	0.144	0.13	0.07
SC10	0 0.238	0.046	<u>\$ 0.648</u>	≪ ^y 0.119	0.112	0.11	0.08
SC11	9.181	× 0,093	<b>\$0</b> .905	0.096	n.s.	0.25	0.38
SC12	0.086	0.040	К ng	0.082	n.s.	0.04	0.04
SC13	0 [°] 0005	°∼0.041C	[™] , Ω.s.	@ ^v _{0.077}	n.s.	0.04	0.05
SC14	0.153	0.005	n.s.	0.077	n.s.	0.05	0.06
SC15	\$ 0.0 <del>8</del>	Ø _{n.s.}	n hs	0.066	n.s.	0.03	0.04
Total SC3+	<u></u> 2.58	0.53	°	1.62	1.40	1.55	0.73
TOTAL DOSE SITE	3.89	× 1985	<b>1.27</b>	2.24	2.30	2.23	1.14
Receptor Ofluid	¢29	2.44	1.85	3.81	4.18	2.52	1.57
Receptor fluid							
(0 - 24h)	0 0 D	3.22	2.58	5.28	5.84	3.52	2.10
%Ratio receptor 10 24h	45	76	72	72	72	67	12
Residual Rec Rouid	0.34	0.21	0.25	0.40	0.35	0.31	0.08
Receptor	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.a.
TOTAL DIRECT	0.99	3.44	2.83	5.68	6.19	3.83	2.13
POTENTIAL (dose site+ receptor)	4.88	4.37	4.25	8.17	8.61	6.06	2.15
• • /							



Õ

	D	istribution of r	adioactivity	(% dose applie	ed)			
Sex	Female	Female	Female	Female	Female	Group Hu	man HD	
Donor N°	X2014/2-4	X2014/5-25	X2014/1- 21	603-01- 0414-V-1	598-01- 0314-IV-1	K N° :	= 1.2	
POTENTIAL (skin+ receptor)	2.30	3.79	2.94	6.37	7.13	4.51	× 2.14	/
TOTAL RECOVERY	100.0	100.0	100.0	100.0	100.0 «	100.0	a a a	6
		Evaluation ac	cording to El	FSA Guidance	(2017)			
	Abso	rption >75% wi	thin half of st	udy Waration?	No (include S	C values)		¢.
		•	Mean Reg	overy <95%?	Confection ne	eded 🖉 🗴		Ő¥
			4		Rean (%dos	e site +%receptor)	+ (SD*1.2)	/
Total % Pote	ntially Absorb	able adjusted	accordingto	EFSA (2017)	, 8.6%	<u>Q'</u>	è a a	L
SD: standard deviation; N	: number of s	kin cells used	forcalculat	ion° 🖓				
n.d.: not detected (below t	he limit of de	tection); n.a. :	not applica	ble	à số	θ L	4	
In the above table, the pro-	esented mean	s do not alwa	vs calculate	exactly from	the presented	andividual data.	This is due to	
rounding-up differences re	esulting 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 topresentative spray dilutions of 5 g/L and 0.3 g/L.  $\bigcirc$ 

#### Concentrate

The mean percentage of propandocarb in the FEC+POH SC F87.5 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

 $\bigcirc$ 

The mean percentage of propamocade in the FLC PCH Sc 687 formulation that was considered to be potentially absorbable for the spray dilution at 5 g/L applying the EESA guidance (2017) to the study data was 2.9%.

Dose level (Spray dilution at 0,3 g/I

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

Therefore, the following derma absorption values can be proposed for use in the non-dietary risk assessments for propand carb in the FUC+PCA SC 687.5 formulation:

- 2.0% for the neat formulation (625
- 8.6% for the 40w dose (0.3 g/L) 2.9% for the intermediate dose (5



Data Point [.]	KCP 7 3/03
Report Author:	
Report Year	1994
Report Title:	Dermal penetration in the rat propamocarb HCL
Report No:	A85147
Document No:	M-157340-01-1
Guideline(s) followed in	
study:	
Deviations from current	none
test guideline:	
Previous evaluation:	yes, evaluated and accepted DAR 2005
	for Propamocarb RAR June 2017
GLP/Officially	Yes, conducted under GLP Officially recognised fasting facilities
recognised testing	
facilities:	
Acceptability/Reliability:	Yes O V C Q A
This study is an <i>in vivo</i> of	lermal absorption study in rate This study to no langer relevant as an in vitro
study through human skir	nic available which provide the best estimate of termal who refer to the and the second
this study has not been a	angidered frother for this reasons and a second second second from the second
this study has not been ed	
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Appendix	1 Cri	tic	al GAPs for th	his as	ssessment				°₹ ₽	- - 	CTJ 32	đ.	regj	The out of
The critical	GAPs for	use or t	s for this renewa	al. er exp	oosure assess	ment are l	highlighted in g	grey. P	ALC.	2 Prope	e Ste	20 ^t 10 th	Shill Shill	, Ç. Ĝ , }, 2
Crop and/ or situation	Country	F G or I	Pests or Group of pests controlled	F	ormulation		Appliea			Applicatio		eatment CO	<b>YPHI</b>	Remarks:
(a)		(b)	(c)	Type (d-f)	Conc. of a.s. (i)	Method kind Š (f-h)	Tuming / Growth stage of crop & season (j)	Number min - max (kÖ	Interval between applications min	g a.s./hL	Water L/ha	g a.s./ha	Days	(m)
Potato	EU	F	Phytophthora infestans (PHYTIN)	SC	FLC: 62.5 g/L PCH: 625 g/L	Spraying© foliat	BBCH 24 589	1 Ale	29 ⁰ ro	PCH: 10 - 100 C PCH: 100 J000	100 - 1000	FLC: 100 PCH 1000	7	1 in 2 years
Potato	EU	F	Phytophthora infestans (PHYTIN)	SC	FL 6 62.5 g/L DEH: 625 g/L	Spraying / foliar	BBCH 21 - 89C	1-4	7 COD	FLC: 0 100 PCD: 100 - 1000	100 - 1000	FOC: 100 PCH: 1000	7	1 in 3 years
Potato	EU	F	Phytophthora infestans (PHYTIN)	80°	FLC: 62.02/L PCH: 625 g/L	Spraving/ fonar	BBCH 24 - 89			FLC: 10 - 200 PCH: 100 - 1000	100 - 1000	FLC: 100 PCH: 1000	7	1
Potato	EU	F	Phytophthora Sinfestans (NATIN)	SC	PCH: 62.5 g/L	Spraying /	BBCH 21 - 399			FLA: 40 - 100 ( RCH: 100 - 2000	000 - 1000	FLC: 100 PCH: 1000	7	1 in 2 years
Potato	EU	F	Phytophthora infestans (PHYTIN)	SC &	PCH. 625 g/L	Spraying / Poliar				PCHO 00 - 1000	100 - 1000	FLC: 100 PCH: 1000	7	1 in 3 years
Potato	EU	Г Г	infestans (PHYTIN)		PCH: 62.5 g/L	folia				PCH: 100 - 1000	100 - 1000	PCH: 1000	7	1 in 2 years
Potato	EU	г F	infestans (PHOTIN)	sc vol?	PCH: 625 g	foliar	BBCOM 89 AG	1 - 2 - Wa.		PCH: 100 - 1000 PCH: 100 - 1000	100 - 1000	PCH: 1000	7	1 in 2 years
Lettuce	FU	F	infesting (PHYTIN)	SC &	PCH 625 g/L	Koliar	BBCH 4 K 49		7	$\frac{PCH: 100 - 1000}{FLC: 10 - 50}$	200 - 1000	PCH: 1000 FLC: 100	7	
Lettuce	FU		(BREMLA)	ŝ	PCH: 625 91	foliar	BROH 13 - 49		n a	PCH: $100 - 500$ FLC: $10 - 500$	200 - 1000	PCH: 1000 FLC: 100	7	
Cucumber	EU	G	(BREMLA)	SC 1	POH: 625 g/L	Spraving	BBCHI 21-89	1-3	7	PCH: 100 – 500 FLC: 10 - 100	1000 - 1250	PCH: 1000 FLC: 100	1	High tech greenhouse.
FLC: Fluopico	lide	5	cubensis (RSPECU)	2027	PCH: 025 g/L	fotial	Leo.				1200	PCH: 1000		soil-based
PCH: Propamo a.a.: not appli	carb-hydroc cable	e C	ALEALIY COM ALEAL COM WITH	DUEL	the p	2012.102	*							



#### 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 application Fluopicolide Operator exposure for FIC+PCH SC outdoor come in the

Operator ex	mosure for ELC+PCH SC outdo	or sprav applicati	ons		4	(		Ô
Application rate	of active substance		kg a s /ha	i AnnRate		000	r .Q	L.
Assumed area t	reated	50	ha/day	d Arealindated	L.	4	s V s	ý
Amount of activ	ve substance applied	5	kg a.s./dav	i Andratates		$\sim$	S O	"Q
Dermal absorpt	ion of the product	0.26%	<b>.</b> . ,	i_AbsorpProduct	Q. a	) //	S 45	Å.
Dermal absorpt	ion of in-use dilution	13.00%		;[AbsorInuse	_0* <ĭ			U,O
Formulation typ	oe Soluble concer	ntrates, emulsifiable co	oncentrate, etc.	7)1	Å .0	~	i o s	
Indoor or Outdo	oor application	Outdoor	4	, d		L.	U U	,W
Application me	thod	Downward spraying	°°°'	×		Ô [¥]		1
Application equ	upment	Vehicle-mounted	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	× ×				
Season		not relevant	la			<b>`</b>		
-		OutdoorSoluble conc					×	
	Exposure values	μg exposure/day i	mixed end loaded	Reference	Somment O	L	4	0
		75 centile	95 centile			0″		1
	Hands	16767	62344	AOEM V		_		
	Body	11058 🔍	114850			~		
	Head	259 🖉	1, 1423	ADEM	O XI S	**		
							0	
ing	Protected hands (gloves)	980 ¥	990 4 8	ADEINI			Ô	
oad	Protected body (workwear or	×	10° ° Y			1	K.	
p	protective garment and sturdy		/31	AUEM			l≪y ¯	
ıga	footwear)					1.	Ŷ	
lixir	Protected head (hood and face	4 %	81 0	AQEM	R S	*		
Σ	shield)			· · · · · · · · · · · · · · · · · · ·		O		
	Inhalation	× .	0 30-5	ADEM Y				
	Protective Equipment	<u> </u>	Select focunclusion	Penetration factor	Antialation Protection factory	, ,		
	Gloves	A Q	Ne Ne					
	Clothing	Work wear warms, b	ody and legs cover	Incl. in ADEM moder				
	Head and respiratory PPE	S 19	- Ohe					
	Water soluble bag							
		6 × ~C	y N	N OI	·			
		م 🖉 µg exposinge,	/day applied	9 6				
	Exposure values			Reference	C Somment			
		75° cetorile	99 centile					
	Hands 🖉 📿		7449	O ADEM	<i>a</i> ,			
	Body O	A15 4	2000		1,4,9			
	Head S	20 00 "	59	ACCEM				
ы 🌾	Protected hands (gloves)	102	4021	N NOEM O	1			
Cati	Protected body (workwear or							
ild	protective garmen and sturdy	× (	D #,"	AOENAS				
A	footwear)	N N	R	0´				
	Inhalation	2	. 1	AQEM				
	Protective Equipment		Select for inclusion	Penetration factor	Inhalation Protection factor			
	Gloves 0 0 C			"0"				
	Clothing 0	Work wear - arms, b	by and legs overed	Soci. in AOEM model				
	Head and respiratory PPE		None None	1	1			
	a cab	N ar	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	vehicle mounted				
j.				upward spraying only				
		· ~ .	<del>y .9</del>				1	
1. Total, Ѡ	1 A A	~~~~						
		<u>~</u> ~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Withou	It RPE/PPE	With RPE/PPE			
		s a.	A.					
Longerterm			$\mathcal{O}_{\mathcal{I}}^{\nu}$					
Longerterm	AA		¥					
Total systemic e	exposure from mixing loading a the	plication (mg	0.2	2/1771	0 1522575			
a.s./day)			0.2	541771	0.1532575			
Total systemic e	er of sure from this ing, load of and ap	plisation per kg body		220220	0.0005540			
weight (mg/kg	wy/day)	0	0.0	039030	0.0025543			
% of RVNAS		Ž	5	58%	3 65%			
				.30%	3.05%			
Acut	o 'o sy							
	Q ^a							
Total systemic	osure from mixing, loading and ap	plication (mg		EE70E1	1 1044534			
a.s./day) 🔘	7		1.7	357051	1.1044524			
Total systemic e	exposure from mixing, loading and ap	plication per kg bodv						
weight (mg/kg	bw/day)		0.0	292618	0.0197409			
% of RVAAS			#0	0IV/0!	#DIV/0!			
-							4	



Operatorex	<pre>kposure for FLC+PCH SC out do</pre>	or spray applicati	ons				
Application rat	e of active substance	1	kga.s./ha	i_AppRate			
Assumed area	treated	50	ha/day	d_Area Treated			
Amount of acti	ve substance applied	50	kga.s./day	i_Amo utAS			
Dermal absorpt	tion of the product	2.00%		i_AbsorpProduct			
Dermal absorpt	tion of in-use dilution	8,60%		i_Absorin use	li l		
Formulation tv	pe Soluble concer	trates, emulsifiable o	oncentrate, etc.		(	Or I	l Oi A
Indoor or Outd	oor application	Outdoor			-C	1	
Application me	athod	Downward spraving			1 Alian A		
Application ag	viewont	Vohiclo mounted			0		
Sancacionieq	upment	not relevant			1		
Season		notrelevant					
		1		8			
	Exposure values	μg exposure/day	mixed and loaded	Reference	Comment		
		75 ^{°°} centile	95" centile	1 AVA	<u> </u>		
	Han ds	98691	374323	ACEM		Ó	
					04	1	
	Body	55794	224425	AOEM			
	Head	2594	14228	AOEM		$\mathcal{O}$	
	Protocol ( January)	100	0000			$\forall$	
<u>.</u>	Protected hands (gloves)	439	9903	ADEM			
9	Protected body (workwear or			1			
2	protective garment and sturdy	762	7313 🛛	AOEM 🥢			
E E	footwear)		<b>%</b> .	l là sĩ		Q	
뿓	Protocological based (based on different			a si		L.	
Aixi	- Forected nead (nood and face	42		AOEM		10°	
2	shield)						
	Inhalation	12	A 22 0	A OF			
	Description Factoria	12	A The A	A VICENT		,	
	Protective Equipment		Select for Aclusion	recetration factor	r inhalation Plotection factor	×	
	Gloves	, n	V No	Q' A		L'	
	Clothing	Work wear - amp	ody and legs covered	Ing. in AOEM andel		Ű	
	Head and respiratory PPE	<u> </u>	Nong	N ACY			
	Water soluble bag		No.No.			?	O O
		Ň	10° - 19		Y Or A		NY W
		exposure	day applied			P	r 🔊
	Exposure values			Reference ON	Comment	g	<i>v</i>
		centile €	95" deneile	S OF			6
				10°		Or	
	Hands	7416	A0226	AOEM		-	0
	Body	4 <u>47</u> .	21376	AQEM	N N N		
		i i i i i i i i i i i i i i i i i i i				Q	Ď
	Head		591	AOEM		×,	8
5	Protected hands (gloves)	a 355 🔍	5250			$\sim \sim$	
i t	Protected body (workwear or	A &					
j	protected body (workwear of	Q″ 114. Q	Q ₇₉	A 20544			
Ap	protective gament and story	y w			0 3 3	?	
	rootwear			<u> </u>			
	Inhalation		28 ~	NOEM OF			
	Protective Equipplient		Select for inclusion	<ul> <li>Penetration factor</li> </ul>	Inhalation Protection actor		
	Gloves 🔊 🔰		No No				
	Clothing_O	Work wear Carms, b	ody and logs covered	Incl. in AOEM model			
	Head and espiratory P	Ň	1. O Nether		1		
			× à	vehicle nounted			
	Closed Cab			upwarts praying only			
	6	2		0			
		N m	» <u>O</u> ″		× '0'		
1. Total A	, Č,		d		× ×		
		N. C.	Without		With RPF/DDF		
K Y		1					
	Č, Č,		O [×] J [×]	Ka A	/		
Longer term	y v	A SA					
	~ 4	U ×	0				
Total systemic	exposure froghixing, loading and ap	plication (mg			2.72/591/		
a.s./day)		S AU			2.7243014		
Total systemic	exposure on mixing beding and ap	lication per kg body	0,0	0	0.000		
weight (mg/kg	bw/sco O		× × 900	95342	0.0454097		
			d Ø	_0'			
% of RVNAS	A O	20 1	M 6 23	.98	15.66%		
(7)		N al					
Acute		.O		*			
- Q	~~~····	× ~	A AN	/			
Total systemic	exposure from mixing, bading and ap	plication (mg	ay only	6720.97	11 5105467		
a.s./day	KY AY	, °° ,	¥7.6	0/200/	11.510646/		
Total							
weight (mel)	bw(day)	price of the rest	<b>0.2</b> 9	944535	0.1918441		
weight (mg/ kg	Bw/day)	at u					
% of RVAAS			L Q #D	IV/0!	#DIV/0!		
			Q)				
× Å	y"						
<u>َ</u> 0_	<i>v</i>						
Ű							
~							



## **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

% of RVAAS



#DIV/0!

#DIV/0!



Operator exp	posure for FLC+PCH SC outdo	or spray applicati	ons			
pplication rate	of active substance	1	kg a.s./ha	i_AppRate		_
ssumed area tr	eated	1	ha/day	d_Area Treated	s. 4	
mount of active	e substance applied	1	kg a.s./day	i_AmoutAS		6
Dermal absorpti	on of the product	2.00%		I_AbsorpProduct	The second secon	- ج
ormulation type	on of in-use dilution	8.00% stratos, omulsifiablo o	oncontrato oto	I_Absorinuse	S L	
ndoor or Outdo	or application	Outdoor		l	0' 1	
application met	hod	Downward spraving		2		y O
application equi	ipment	Manual-Knapsack		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	K V
eason		not relevant	Ĉ	S.		S.
		OutdoorSoluble conce				
	Exposuro valuos	µg exposure/dayı	mixed and loaded	Profession of		
	exposure varues	75 th centile	<b>⊗</b> centile	Receivence		
	Hands	9495	25482			, Qi
	Body	803	0 2787		Q, O A	
	body	000				
	Head	5		AOEM 0		×
ള	Protected hands (gloves)	18	0 164	AOEM	S . A	
adir	Protected body (workwear or	, ,	K Û			۰ م
Ha Ha	protective garment and sturdy	A		AQEM 2		
anc	footwear)					
ling	Protected head (bood and face				E & D	
Mb	shield)			AOEM		
		O ^V V,	Q Y		S S A	
	Inhalation	<u> </u>		ACENT		
	Protective Equipment	à à	Selector indusion	Pen tation factor	Inhal cion Protection factor	
	Gloves	KI O		× õ	~0 <i>(</i>	
	Clothing	Work wear - arms, b	ody ord legs covered	Ince the AOEM model		
	Head and respiratory PP		None			
	water soluble bag		Y IONNO			J
			(day and )			1
		<ul> <li>µg exposure,</li> </ul>		( Poforonco	Commont	
		75 th centifie	O 95 th centile	Nelelelice		
				AUEIVI		
	Body	\$\$\$8868	37007	AOEM		
	Head A	( 12 V	L 85 ~	AOEN		
Ę	Assected ballas (glovea)			ADEM		
atio	Dratasta Reductivas				+	
Ó blic	protective garment and sturde	A. 8003	\$2630 a.	A DEM		
Ap	footwear)					
EG.	Inhalation Qu	25	O all			
«\Y	Drotoction Calinment		Soloct for inducio	Depatration factor	Inhalation Dratastian factor	J
	Gloves			Penetration ractor	Innaration Protection factor	1
	Clothing A	Work wear - arms, b	ody and legs coreved	Incl. in AOFM model		
	Head and respiratory PPE	10 °a	A None	1	1	
			O O	vehide mounted		
~	Besed cabo		No No	upward spraying only		
a			<u> </u>		•	•
A h			*			
. Total	<u>_</u>					
~			Withou	IT RPE/PPE	WITH RPE/PPE	
			1			
ongerterm		. A 04				
otal systemic -	unglika from mixing lasting and	Oution (may				
oral systemice	Approved the more making, to approve and app	proceeding (1982)	8.0	335240	1.1409740	
instrudy		plicatio Carlos haste				
voight (mg/kab	w/dava	pricacies per kg body	0.1	338921	0.0190162	
Carlence (111Back p		V				
6 of RAMAS			46	.17%	6.56%	
- AN						
any a						
. V all						
	ve ocure from mixing loading and an	nlication (mg	(27	609200	6.3197280	
otal system ce	xposure nonninxing, ioaunig and ap	prication (mg	1//	030300	and a strated	
otal systemice i.s./dayO	xposure from mixing, loading and ap	photon (mg	12.7			
otal systemic e i.s./davO	xposure from mixing, loading and ap	plication per kg body	127	139305	0.4052222	
otal systemice otal systemice veight (mg/kg b	xposure from mixing, loading and ap w/day)	plication perkgbody	0.2	128305	0.1053288	



### **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

Fluo

<b>scenario</b> cation a ci	also applies to the fo	ollowing:				
olide	νομ				ð	D .
Operator ex	posure for FLC+PCH SC outdo	or spray application	ons		in the second se	$\langle \langle \langle \rangle \rangle$
Application rate	e of active substance	0.1	kg a.s./ha	i_AppRate	4 \$	- C
Assumed area t Amount of activ	reated ve substance applied	4 0.4	na/day kg a.s./day	i_Arrea Ireated	$\rightarrow$ $\sim$	<u>, 0</u>
Dermal absorpt	ion of the product	0.26%	Č	i_AbsorpProduct	\$\" F	S S
Dermal absorpt	ion of in-use dilution Soluble concer	13.00% htrates, emulsifiable co	oncentrate, etc.	i_AbsorInuse		
Indoor or Outdo	por application	Outdoor	L.	, O'Y	× 2	
Application me	thod	Downward spraying Manual-Hand held	, C	Ő . ·		
Season	apinent	not relevant	6			
			pixed and loaded			
	Exposure values	75 th centile	95 Centile	Reference	Component ~	
	Hands	2399	8719	ODEM ~		
	Body	173	5519	Q AOEM		
	Head	21	114	AOEAT	O ^v «,	
gu	Protected hands (gloves)		Ø 79 🔍 🔨	AOEM V		Jan Star
loadi	Protected body (workwear or			CALCENA O		
and	footwear)	<u> </u>			J & J	3
xing	Protected head (hood and face			p		
Ξ	shield)	L' O	5	ADEM (		
	Inhalation	Y and	28	ADEM		
	Protective Equipment		Select for inclusion	Penetration factor	Inglation Protection factor	- I
	Clothing S. O	Wear - arns, b	ody and legs covered	Incl. in A@EM modek		
	Head and respiratory PPE	A St	Notes			
	Water soluble bag	<u>þ</u>				J
		@Ag exposure	day applied		4	
	Exposure values	5 th cențile	A Centile	Reference	Comment	
6	Hands	1500	4213 N	COFM 2		
~O	Body		13/282	AOFM		
0°	Head	12 0	- Co	O ADER		
, Ôg	Protected hands (gloves)	A 5 0	0°22 @,	ROEM		
licati	Protected ordy (workwear or		\$ .\$	N N		
Appl	protecti@garment and sturdy	890%	<b>⊖</b> ″ 626 <b>3€</b> ∪″			
	Infredation	° 0 26 ℃	×** ·	AOEM		
	Protective Equipment		Selector inclusion	Penetration factor	Inhalation Protection factor	
	Gloves	Work weak arms h	And less one red	Incl. in AOEM model		
, Ø	Head and respirato PE		None	1	1	
Ŷ	Closed cab	0, 0	No No	vehicle mounted		
A			× ·	upward spraying only		
			N N			
™sotal			)) Withou	It RPE/PPE	With RPE/PPE	
Longer term		7, 6				
Total systemic	exposure from mixing arrow	plication (Q				
a.s./day)	AGV		11.7	950999	1.3948068	
Total semice	exposure from maning, loading and ap	plication per kg body	0.1	965850	0.0232468	
weiger (mg/kg		ν				
RVNAS			28	0.84%	33.21%	
Acute						
TotoQuerani		plication (mg				
a S. day)	exposure tronks from and ap	plication (mg	18.5	902080	8.7778527	
Jotal systemic e	exposure from mixing, loading and ap	plication per kg body		009269	0.4450000	
weight (mg/kg	bw/day)		0.3	805050	0.1462975	
% of RVAAS			#D	0IV/0!	#DIV/0!	



	Operator exp	posure for FLC+PCH SC outdo	or spray applicati	ons					
	Application rate	of active substance	1	kg a.s./ha	i_AppRate			a,°	
	Assumed area tr	eated	4	ha/day	d_Area Treated				Or .
	Amount of active substance applied 4 k		kg a.s./day	i_AmoutAS				y"	
	Dermal absorpti	on of the product	2.00%		i_AbsorpProduct	*	(	65° 0	2
	Dermal absorpti	on of in-use dilution	8.60%		i_AbsorInuse	Ŭ,	Ø		
	Formulation typ	e Soluble concer	ntrates, emulsifiable co	oncentrate, etc.		-Q	L		
	Indoor or Outdo	or application	Outdoor			10°	"		
	Application met	hod	Downward spraying			4			2
	Application equi	ipment	Manual-Hand held					6 14	<i>"</i>
	Season		not relevant	(e	×A		° A		
			OutdoorSoluble con o				N	ar i	. W
		Exposure values	µg exposure/day r	mixed and loaded	Reference 💭	Commen	Q	× v	S
		· · · · · · · · · · · · · · · · · · ·	75''' centile	95" centile	04	*	pr		), C
		Han ds	14120	523	AOEM	l o 4		0' 🔊	,
		Body	9452	107 43	AOE		C		
	Lload	209		ANOFM (		Ro			
		neau	200	- QQ ⁴¹⁵⁰					
	쯑	Protected hands (gloves)	85	792 0	AOEM Y			4 X	
	adi	Protected body (workwear or			1 L				
	olb	protective garment and sturdy	81		AO PA		2	0	
	an	footwear)	4				-O		
	cing	Protected head (hood and face					Ő	U U	
	Δ.	shield)	3	64	AOEM		Ĩ	AS I	
	_		ar and a second s	v oʻ	Å Å			45	
		Inhalation		í 🕸	AO EM		(	ρ	
		Protective Equipment		Select of indusion	Penetration factor	Inhalation Protection Secon	Ĉo		
		Gloves	S O	- No No					
		Clothing	Work wear - arms, b	ody and legs overed	Incl ADAOEM model				
		Head and respiratory PPE	ľ "Q	None			ſ		
		Water soluble bag		O No					
		Y			Y OV				
		~	μg expositre/	/day applied	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~				
		Exposure values	0 75 th cefitie	95 th centile	Reference	Commer@			
		Hands 2	4117	\$`_ <u>1</u> @	AQEM				
		Body	236981	Q352 %	AGEM (				
				S di		× 4, [×]			
		Head		Nº 21 N		<i>V</i>			
	.u	Protected ands (gloves)		5%O	AOEM	Ŵ			
	at	Protected body (workwear or			N O	~Q			
	ild	protestive garment and sturdy	23741	10 013	AREM	K) (			
	A	fo@twear)		S 8					
		Inhalation 🔗 🖌	69	69					
	Ô	Protective Equipment	A C	Select for indusion	@Penetration factor	Inhalation Protection factor			
	°~	Gloves	<u>o</u> ř	Ng Ng					
	<u>s</u> Q*	Clothing	Work wear - arms, b	ody and legs covered	Yncl. in Appy model				
	k~y`	Head and respiratory PPE		None	Ň	1			
			× . 0″	SI SING	velate mounted				
			× ×	<u>r O'</u> NO	upward spraying only				
			× ×	j	0*			l	
					y y				
	1. Total				۲ 			1	
	4			<b>Withou</b>	t RPE/PPE	With RPE/PPE	<b></b>		
	A	<u> </u>							
	Longer tern	' e S							
				1 North Contraction of the second sec					
	Total systemice:	xposure from mixing, loading and ap	plication (mg	_ ~Q [°] 21.2	877647	2,7617037			
	a.s./day)		r U			217021057			
	Total systemice:	xposure from mixing, leading and 🐅	plication proig body	03	47961	0.0460284			
	weight (mg/kg b	w/day) 0° C		)	AI 301	0.0400204			
	% of RVNAS			12	24%	15 87%			
	20 OT RVINAS		<u> </u>	124	1.3470	13.0770			
	Acuto	0'~``\$	N ()						
	Atule							l .	
	Total systemice	xposure from mixing loading and to	plication (mg						
	a.s./day)			35.7301052		16.5298130		l .	
		NA NY	alianting a solution t						
	notal systemice:	xioure from moving, load nevand ap	plication perkgbody	0.59	955018	0.2754969			
	weight (mg/ kg l							l .	
4	RVAAS O	) i i i i i i i i i i i i i i i i i i i		#D	IV/0!	#DIV/0!		l –	
	× Å								
	e Y a								



### 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



Note: Only for gasforming/gaseous preparations and soil fumigation preparations: powered full-face filtering devices with filtertype 2 (factor 20), powered full-face filtering devices with filtertype 3 (factor 40)















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

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

#### Fluopicolide





Resident exposure for FLC+PCH SC			
Croptype	Leaf vegetables and fresh herbs	0	
Application method	Downward spraying	i AnnEquin	ð
Formulation type Soluble cor	icentrates, emulsifiable concentrate, etc.	i_FormVal	Ž
Buffer strip	2-3 m	i_Buffer	
Application rate of the product Concentration of active substance (in-use dilution for liquid	1 kg a.s./ha	I_AppRate	
applications)	5 g a.s./I	d_concAs	
Dermal absorption of product	2.00%	i_AbsorpProduct	
Dermal absorption of in-use dilution Oral absorption	8.60% 100.00%	i Absorptiouse	
Dislodgeable foliar residue (i_AppRate*i_DFR)	³ µg а.ş./cm ²		
Vapour pressure of in-use dilution	low volatile substances having a vapour	C Cipvolat	,O
	pressure of <5" 10-3Pa		\$
Concentration in air Resident dermal spray drift exposure 75th percentile - adult	0.0/fL mg/m"		J
Resident dermal spray drift exposure 75th percentile - child	40.527 ml spray dilution/per		
Resident inhal. spray drift exposure 75th percentile - adult	0.00010 ml spray dilution/pers		
Resident inhal, spray drift exposure 75th percentile - child Resident dermal spray drift exposure mean - adult	0.22318 ml spray dilution perso		
Resident dermal spray drift exposure mean - child	0.18 rRI spray dilutton/perso		
Resident inhal, spray drift exposure mean - adult	0.00% mi spray diversion/persu		
Resident innal, spray drift exposure mean - child Exposure duration dermal	Light mispraverution/pers	Aperpour A o	
Exposure duration inhalation	1 10 24 hold Q		
Exposure duration entry into treated crops	0.25 mayrs	d_ExpDurTrectorop	
Light clothing adjustment factor Breathing rate adult			
Breathing rate child (1-3 year old)			
Drift percentage on surface (75th percentile)	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		
Drift percentage on surface (mean)	$\mathcal{L}$ $\mathcal{O}'$ $\mathcal{O}'^{4.106}$ $\mathcal{O}'$ $\mathcal{O}'$		
Turf transferable residues percentage Transfer coeff, of surface deposits-adult			
Transfer coeff. of surface deposits-child (1-3 year old)		d gettch	
Saliva extraction percentage		d Saugert	
Surface area of hands mouthed	20 cm ² 4	Orea HM	
Frequency of hand to mouth activity	9.5 events/hour		
Dislodgeable residues percentage transferability for over to			
mouth		d_DRP	
Transfercoefficient for entry into treated crows (75th percev(the)- ad		d_ToEntryAd	
Transfer coefficient for entry into treated (1956 (75th per ) tile) - ch	2250 sh h O	d_TcEntryCh	
Transfer coefficient for entry into treated ops (meap) - adult	5 598(Spr /h	d_TdEntryAd	
Transfer coefficient for entry into treased crops (mean) - child		d_TcEntryCh	
		×	
111-3 year old child		<i>Q</i> [*]	
Spray Gift (75th percentile)	Vapour (75th pert tile) Surface deposits (75th	Entry into treated (rops (75th percentile) Entry into treated All pathways (mean)	
Total systemic exposure 0.1364002	0 0.0107000 ~ 0.0382052	0.2685781 0.3171326	
(mg a.s./day)			
per kg body weisyn		. 0.0268578 0.0317133	
% of RVN AS 4.01% 7		9.26% 10.94%	
1.2 Adult			
C Say drift	C Ospour O' Surface depo	sits Entry into treated All pathways (mean) crops	
Total systemic exposure 0.166220 (mg a.s./day)	0.0138000 0.0650635	0.8952602 0.8543999	
per kg body weigh	0.0010844	0.0149210 0.0142400	
% of RVNAS	0.37%	5.15% 4.91%	
	r O' Y		
, o C.			
A A S	J ^y ··· ·· ·· ·· ·· ·· ·· ·· ·· ·· ·· ·· ·		
	Č V		
	~Q		







#### Worker exposure – Lettuces - 2 application per crop* Appendix 2.7

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

# Fluonicolide

This scenario is worst case		i application a c	lop	a s
Fluopicolide				
Worker exposure from residues of	on foliage for FLC+P	сн sc	~	
Crop type	Leaf	vegetables and fresh herb	s 47	
Indoor or outdoor		Outdoo	r "Ø"	
Application method		Manual Knapsac		
Worker's task		Reaching niskin	\$\$ [*]	
Main body parts in contact with foliage		Hand and und		
Application rate of active substance		¥ 0.	1 kg a.s./ha	AppRate S &
Number of applications		L	2 ≪	
Interval between multiple applications		«O"	7 days	i_AppInt
Half-life of active substance		3	D days 😽 🖉	d_HadiifeAS
Multiple application factor				
Dermal absorption of the product		0.269		Absorptrotect
Dislodgeable foliar residue (i AppRate*i D	FR)		Augas / Ar	d DER
Working hours	,	, v O	shr O O	d Warthr
Dermal transfer coefficient - Total potentia	l exposure	\$580	⁰ cm ² /h ² 4	d_DermTcUCV
Dermal transfer coefficient - arms, body an	d legs covered	250	v∰/hr (→ 、O′ s	dpDermTcCV1
Dermal transfer coefficient - hands, arms, b	ody and legs covered	, N , O 58	¢m²/hr O v v	d_DermToS/2
Inhalation transfer coefficient for automate	ed applications Q		(ha/hr*10^(-3)	d_InhdiNeAut
Inhalation transfer coefficient for cutting of	rnamentals ()*		A ha/h#010^(-3)	d_leventcCut
Innaration transfer coefficient for softing /				
1. Total				
	Potential exposure	Work wear Oarms, body	Werking wer and gloves	Comments
Total systemic exposure (mg a.s./day)	3.3499673	1.4435204 O	A3348967	ta
Total systemic exposure perkg body weigh				<b>J</b>
(mg/kg bw/day)	0.0558161		0.00558269	
% of RVNAS	79.7400	<u> </u>	<u> </u>	
2 Dotaile		&	O O A	
2. Details	Stylem	ic exposure	le de la companya de	Common da
	([mg a.s. /day]	[mg a.s./kg ww/day]	y Formula	Comments
ODermal-Obtentia	3.3489673	Ø <b>6/0558161</b>	d_DecriteUCV*d_werkHr*i_DFR*i_M	
Dermal - Work wear - arms, party and los			DermTaCy WorkHr*d DFR*d	
Covered Covered	4435204	0.024058	MAF/1000*i_AbsomInuse	
Dermal-Working wear and glove	s <b>0.33489</b>	0.0055816	d_DepoTCV2*d_WorkHr*d_DFR*d_ #AF/1000*i_Absorptnuse	
halation				Na for outdoor activities
		<u>, 0 0 0 0</u>		
		y g g	/	
Š Å				
a ta	NO O			
	. × ~, £			
Q1	~ @	£		
A A		4		
	, v			
	Õ			
N & A	G.			
	J			
× AV				
Ŭ				



Worker exposure from residues o	n foliage for FLC+F	PCH SC		0	
Crop type	Leaf ve	egetables and fresh herbs		2 8	F
Indoor or outdoor		Outdoor			/
Application method		Downward spraying	~	ST O	
Application equipment		Manual-Knapsack	Č,	<u> </u>	
Worker's task		Reaching, picking	S		
Main body parts in contact with foliage		Hand and body	"Or		
Application rate of active substance		1	kga.s./ha	i_App(R)te	
Number of applications		2	× "	LADYNO NO	
Interval between multiple applications		<u> </u>	days	Appint Y	Ø
Half-life of active substance		30	days Q	d_HalflifeAg 🖌	1
Multiple application factor		1.9		d_MA	
Dermal absorption of the product		د¶ ^۲ 2.00%		i_Abs or product	
Dermal absorption of the in-use dilution		8.60%		i Aps orpinuse	
Dislodgeable foliar residue (i_AppRate*i_D	FR)		yuga.s./ 🐨 🌾 🔪		
Working hours		, ^v , ° , 0°	hr 🖉 🧷 🖓	d_Warking	
Dermal transfer coefficient - Total potential	exposure 2		cmt/hr	d_DermTcUCV	
Dermal transfer coefficient - arms, body and	l legs covered	2500	co /hr	de GermTcCV12	
Dermal transfer coefficient - hands, arms, b	ody and legs cove <u>r</u> ed	<u> </u>	Qm²/hr	@DermTcc	
Inhalation transfer coefficient for automate	d applications 🔊 🏾		ha/hr*10^(-3)	d_InhalTcAvit	
Inhalation transfer coefficient for cutting or	namentals 🎊 , 🕅	V QI ANA	ha/b(*10^(-3) >	d_IntrolificCut	
Inhalation transfer coefficient for sorting / k	oundlingonamentak		ha/hr*10^(-3)	d AbalTcSort	
			O S S		
1. Total	<u>~~ '0'</u>			ž K	
	Potential exposure	Work wear arms, body	Working wear and gloves	Comments	
Total systemic exposure (mg a s /day)	22 1547067	549442	2 2154707	*	
Total systemic exposure per kg body weight				O	
(mg/kg bw/day)	9.3692451	0.15970774	0.0369245		
% of RVNAS	127.39%	<b>54.88%</b>	12 20 12		
v v					
2. Details		O N (			
	Stem	ic posure	Formula	Comments	
	22 1547067	[mg as(/kg bw/dgy]	d @ermTcU@C*_WorkHr*i_DFR		
Dormal Work way arms and or		0:50524545	MAF/\$000*i_Absorptnuse		
cowered	9.5494426	0.1591574	*d_M4/1000*i_AbsorpInuse		
Dema Working wear add gloves	2.2154707	0.0369245	d_lpgmTcCV2*d_WorkHr*d_DFR ~\$g_MAF/1000*i_AbsorpInuse		
			¢″	Na for outdoor	
		KY K A'		activities	
6 A					
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	$\sim$	à à			
A. O'	S'AV.	ð "O			
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Appendix 2.8 Worker exposure – Cucumbers (glasshouse) – 3 applications per crop

Roof-fogger worker re-entry

Fluonicolide

Fluopicolide	y					ð
• Worker exposure from residues or	n foliage for FLC+F	РСН SC		~	5	5
Crop type		Fruiting veg	etables			
Indoor or outdoor			Indoor	°		
Application method		Worker rentry -roo	f fogger	2		'n
Application equipment		Manual-Ki Roaching	napsack	K, Y		
Main body parts in contact with foliage		Reaching, Hand a	Č,	Å.	N N N	a
Application rate of active substance		nana a	V 0.1	kg a.s./ha	PAppRate 2	L.
Number of applications		L	3	,O ^v «	j_AppNo	0"
Interval between multiple applications		ש۲	7	days 🔗 🛛 💭		1
Half-life of active substance		A	30	days 🌂 🌀 🎢	d_HodujeAS	
Multiple application factor		Q0	2.6		C-OF Q Q'	
Dermal absorption of the product		lu Pa	0.26%	Ø 47 . Ø ?	MbsorpProduct	
Dislodgeable foliar residue (i AppRate*i DE	R)	N ON	10.00%		d DER	
Working hours	,	, w	Ŭ,	hr of of	d Warthr	
Dermal transfer coefficient - Total potential	exposure 🦯		5800	cm²/hł 4	d_DermTcUCV	
Dermal transfer coefficient - arms, body and	legs covered	$\sim \sim \sim$	2500	m ² /hr	dj_DermTcCV1	
Dermal transfer coefficient - hands, arms, bo	dy and legs covered		580	¢m²/hr 🔿 🖌	d_DermToS/2	
Inhalation transfer coefficient for automated	d applications			ha/hr*10^(-3)	d_InhaTrAut	
Inhalation transfer coefficient for cutting or	namentals () *	a si		ha/http://www.ha/http://www.ha/http://www.ha/http://www.ha/http://www.ha/http://www.ha/http://www.ha/http://www	d_leastTcCut	
Innalation transfer coefficient for sorting / b			NA			
1. Total						
	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	Work wear Oirms	, body		× ·	
\$		and legs cover	ed	working wor and gloves	Comments	
Total systemic exposure (mg a.s./day)	5,8594849	2,5913297	0°	A 6933485	Ê2	
Total systemic exposure per kg body weight	0.0975581	0.0431/88		0.011555	p	
(mg/kg bw/day) //	120 2700		. Ô	16 51%		
	× × · 139.300					
2. Details			Ŷ	a. 0. 4		
	([mg a.s./day]	nic exposure	day] 🕎	Formula	Comments	
Opermal Optential	5,7324849	Ø/0955581		d_DecolcUCV*d_workHr*i_DFR*i_M		
Dormal Work wood arms in wand in			Ŷ,	AF/1000*i_Absorplnuse		
covered	<b>713297</b>	0.0411888	," 	MAE/1000*i_Absorptnuse		
Derra - Working wear an gloves	0.573348	0.0095558	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	d_Dere TCV2*d_WorkHr*d_DFR*d_ AF/1000*i_AbsorpInuse		
Subalation	0.4200000		~	AnoRate*d InhalTcAut*d WorkHr	For re-entry 16 hours after	
			/		application	
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		ô ^g				
		Q ^Y				
	Q ¥					



Worker exposure from residues o	n foliage for FLC+I	PCH SC		0	
Crop type		Fruiting vegetables	)	Q	ð
Indoor or outdoor		Indoor			Ş
Application method		Worker rentry -roof fogger	~	6 6	ř
Application equipment		Manual-Knapsack	, Or	υ´ δ	
Worker's task		Reaching, picking	Ŕ		
Main body parts in contact with foliage		Hand and body	l l		
Application rate of active substance		1	kga.s./ha	i_AppRov	2
Number of applications		ČA -	L L	LAPPAGO SA C	
Half life of active substance			days		,Ø
Multiple application factor		y 50 C 36	uays o	d MAE	Ñ
Dermal absorption of the product		2.0		i Absorrenduct	
Dermal absorption of the in-use dilution		8 60%	$Q' \sim \zeta$	i Absorninuse	
Dislodgeable foliar residue (i AppRate*i Di	FR)	~0 [*] ~3	ugas./m	OFR CO	
Working hours		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	hr 🛇 🔊 🔊	WorkHK	
Dermal transfer coefficient - Total potential	exposure	& 0° .~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~			
Dermal transfer coefficient - arms, body and	legs covered	ວ້ , 🥙 🏂 2500	may/hr of m	d_DermTcCV1	
Dermal transfer coefficient - hands, arms, b	ody and legs covered		0tm²/hr	CermTcCV2	
Inhalation transfer coefficient for automate	d applications	°~ ~ .0.15	ha/hr <u>#1</u> 0^(-3)	d_InhalTcA	
Inhalation transfer coefficient for cutting or	namentals 🏑		ha/bc*10^(-3	d_InhalTcCut	
Inhalation transfer coefficient for sorting / b	oundling orn ad ental		ha@r*10^(-\$)	d_InjectcSort	
	A C			O' A	
1. Total	L O				
	Potential exposure	Work weak - arms, body	Working wear and gloves	<b>%</b> mments	
	a w	and covered	× ~ ~	Q	
Total systemic exposure (mg a.s./day)	32.0174815	124833972	4.2817481	Å	
Total systemic exposure per kg body weiget	Ø.5336247	J. 0.2413900	°~0.0713626		
(mg/kg bw/day)				Þ	
% OT RVNAS	184.01	86.24%			
2 Details		S ~ O			
<u> </u>	See (Ster	micered sure		Comments	
Dential	30.8174815	A 5136247	d_&ermTcUCV @WorkHr*i_DF @I_MAF/10 #i_Absorptouse		
Dermal - Work weaparms, boy and legs	10833972	0.221 200	Derm TcCV1 *d_WorkHr*d_DF		
Derma Working wear and gloves	Q 3.081741	0.0023625	d_Ddm_TcCV2 *d_WorkHr*d_DF R*MAF/1000*i_Absorptnuse		
			AppRate*d InhalTcAut*d W	For re-entry 16 hours	
A A A A A A A A A A A A A A A A A A A	1.2090000	0.0200000	orkHr	after application	
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