Draft Assessment Report

Evaluation of Active Substances

Plant Protection Products

Prepared according to **Regulation (EC) 1107/2009**
as it applies in Great Britain (GB PPP)

Cinmethylin (BAS 684 H)

Volume 3 – B.6 (PPP) – BAS 684 03 H

Toxicology, Metabolism Data & Assessment of Risks for Humans

Great Britain

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

BAS 684 03 H is the representative formulation of the new active substance cinmethylin (BAS 684 H). This document reviews the toxicity and dermal absorption of BAS 684 03 H, an EC (emulsifiable concentrate) formulation containing 750 g/L (75 %) cinmethylin.

B.6.1. ACUTE TOXICITY OF PLANT PROTECTION PRODUCT

In accordance with Regulation 284/2013, the data requirements for the toxicological assessment of plant protection products offer the possibility to avoid animal testing where an alternative approach under Regulation (EC) 1272/2008 (CLP) can be justified by the applicant or other reliable methods (e.g. *in vitro* tests) are available. Since BAS 684 03 H is to be registered also outside Europe, the applicant performed toxicological vertebrate studies with the product to meet the regulatory requirements of those regimes. The applicant therefore presented both *in vivo* and *in vitro* toxicological tests with the product and predictions of its classification from the use of the calculation method, as allowed under Regulation (EC) No. 1272/2008. HSE has provided data protection for *in vivo* studies only when a decision on classification and labelling was made solely on the results of those studies.

Summary of acute toxicity:

Table 6.1-1. Predicted and tested acute toxicity of BAS 684 03 H

Endpoint	Product (BAS 684 03 H)			
	Predicted classification according to calculation method	**Study outcome and CLP classification**	**HSE Conclusion on classification**	**References**
Acute oral toxicity	LD_{50} > 2000 mg/kg bw. CLP classification: not required.	*In vivo:* LD_{50} > 2000 mg/kg bw. CLP classification: not required.	**CLP classification: not required.** Calculation method: LD_{50} > 2000 mg/kg bw *In vivo:* unnecessary – not relied upon.	[redacted], 2017a (2017/1156882)
Acute dermal toxicity	LD_{50} > 2000 mg/kg bw. CLP classification: not required.	*In vivo:* LD_{50} > 5000 mg/kg bw. CLP classification: not required.	**CLP classification: not required.** Calculation method: LD_{50} > 2000 mg/kg bw *In vivo:* unnecessary – not relied upon.	[redacted], 2017b (2017/1154823)
Acute inhalation toxicity	LC_{50} = 32.42 mg/L. CLP classification: not required.	*In vivo:* LC_{50} > 5.1 mg/L. CLP classification: not required.	**CLP classification: not required.** Calculation method: LC_{50} = 32.42 mg/L. *In vivo:* unnecessary – not relied upon.	[redacted], 2017 (2017/1198506)
Skin irritation	Not a skin irritant. CLP classification: not required.	*In vitro*: Skin Irrit. 2 (H315). *In vivo:* Skin Irrit. 2 (H315).	**CLP classification: Skin Irrit. 2 (H315).** Calculation method: not required.	*In* vitro - Remmele, 2017a (2017/1194114) SIT & SCT *In vivo* – [redacted]

Endpoint	Product (BAS 684 03 H)			
	Predicted classification according to calculation method	Study outcome and CLP classification	HSE Conclusion on classification	References
			In vitro: Skin Irrit. 2 (H315). *In vivo:* unnecessary – not relied upon.	[redacted] (2017/1154822)
Eye irritation	Causes serious eye damage. Eye Dam. 1 (H318).	*In vitro*: Eye damage / irritation (Category 1 or 2). *In vivo*: not an eye irritant.	**CLP classification: Eye Dam. 1 (H318).** *In vitro*: Eye damage/irritant (Category 1 or 2). + Calculation method: Eye Dam. 1 (H318). *In vivo:* unnecessary – not relied upon.	*In vitro* - Remmele, 2017b (2016/1193048) *In vivo* – [redacted], 2017a (2016/1345293) and 2017b (2017/1012902)
Skin sensitisation	Skin sensitiser. Skin Sens. 1 (H317).	*In vivo*: Skin sensitiser (Buehler test). CLP classification: Skin Sens. 1B (H317).	**CLP classification: Skin Sens. 1 (H317).** Calculation method: Skin Sens. 1 (H317). *In vivo*: unnecessary – not relied upon.	[redacted], 2017d (2017/1161446

Overall, BAS 684 03 H is of low acute toxicity by the oral, dermal and inhalation route on the basis of information on its components and the application of the calculation method of the CLP Regulation. It is a skin irritant requiring classification with Skin Irrit. 2 (H315) on the basis of *in vitro* skin irritation data available on the formulation. It is also meets the classification for classification for serious eye damage (Eye Dam. 1 H318) on the basis of information on its compoenents and the application of the calculation method of the CLP Regulation and indications of eye danage/irritation from an *in vitro* eye irritation formulation study. It is a skin sensitiser requiring classification with Skin Sens 1 (H317) on the basis of information on its components and the application of the calculation method of the CLP Regulation.

B.6.1.1. Oral

In vivo study

The acute oral toxicity of BAS 684 03 H has been investigated *in vivo* in a study in rats by the acute-toxic-class method.

The *in vivo* study has not been granted data protection due to sufficient data being available on its components allowing for the application of the calculation method of the CLP Regulation.

Table 6.1-2. Summary of the acute oral toxicity study of BAS 684 03 H

Method Guideline, GLP status, reference	Species, strain, sex, no./group	Test substance, dose levels, duration of exposure	LD_{50}	Remarks
OECD 423 (2001) (acute toxic class method) GLP compliant [redacted], 2017a (2017/1156882)	Rat, Wistar, females, 3 / group (6 animals total) Observation period: 14 days	2000 mg/kg bw	> 2000 mg/kg bw	No deaths. No clinical signs observed in the first group during the study period. However, clinical signs were observed in the second test group, which included: impaired general state and piloerection in all three animals, during the first hours after administration. Weight gain within the normal range for all animals throughout the study period. No adverse macroscopic necropsy findings.

In a GLP and guideline compliant acute toxic class study, 2000 mg/kg bw of the product BAS 684 03 H was administered to three fasted female rats. No deaths occurred in this group. This result was confirmed by administering the same dosage to another group of 3 females. Again, no deaths occurred.

No clinical signs were observed in the first test group. However, clinical signs were observed in the second test group, which included impaired general state and piloerection from hour 2 untill hour 3 after administration; this was indicative of general toxicity but did not indicate specific target organ toxicity. There were no macroscopic pathological findings in any of the animals. Weight gain was within the normal range for all animals throughout the study.

In this study, BAS 684 03 H was not acutely toxic by the oral route (LD_{50} > 2000 mg/kg bw) and thus did not meet the criteria for classification in accordance with Regulation EC (No) 1272/2008; however, the *in vivo* study

was not required (hence not relied upon) as robust conclusions could have been reached already based on the results of the calculation method.

Calculation method

Data on the acute oral toxicity of all of the formulation is available, with LD_{50} values > 2000 mg/kg bw in all cases. An LD_{50} > 2000 mg/kg bw can be calculated for the product (See Volume 4 for further details). Therefore, the product does not require classification for acute oral toxicity based on the calculation method.

Conclusion

Overall, no classification for acute oral toxicity in accordance with Regulation EC (No) 1272/2008 is required for BAS 684 03 H.

B.6.1.2. Dermal

In vivo study

The acute dermal toxicity of BAS 684 03 H has been investigated *in vivo* in a study in rats. The *in vivo* study has not been granted data protection due to sufficient data being available on its components allowing for the application of the calculation method of the CLP Regulation.

Table 6.1-3. Summary of the acute dermal toxicity study of BAS 684 03 H

Method Guideline, GLP status, reference	Species, strain, sex, no./group	Test substance, dose levels, duration of exposure	LD_{50}	Remarks
OECD 402 (1987) GLP compliant [redacted], 2017b (2017/1154823)	Rat, Wistar, 5/sex (10 animals in total) Observation period: 14 days	5000 mg/kg bw	> 5000 mg/kg bw	No deaths. Local effects; very sight to severe erythema (grade 1 to 4); slight oedema (grade 1 to 2); and incrustation and scaling – all observed within 10 days of application and reversible within the study duration of 14 days. No systemic effects observed.

In a GLP and guideline compliant acute dermal toxicity study, animals were exposed to a single dose of 5000 mg/kg bw of BAS 684 03 H for 24 hours under a semi-occlusive dressing. The area exposed to the test item totalled at least 10 % of the total body surface area. Following the 24-hour exposure period, the dressing was removed and the exposed area was rinsed with water. No deaths were recorded during the study period, nor were there any signs of systemic toxicity.

The following test item-related local effects were recorded during the course of the study; local effects occurred within 10 days after application, but recovered by the end of the observation period:

- Very slight to severe erythema (grade 1 to 4)
- Very slight to slight edema (grade 1 to 2)

- Incrustations
- Scaling

No macroscopic pathologic abnormalities were noted in any animal examined at the end of the study.

The body weight of the male and female animals increased within the normal range throughout the study period, with two exceptions. Two female animals showed stagnation of body weight during the first week, but both females gained weight in a normal range during in the second week. Due to the fact that stagnation or slight loss of body weight is commonly known for females after dermal applications, this stagnation is considered to be unspecific.

In conclusion, the median lethal dose (LD_{50}) of BAS 684 03 H after dermal application was found to be greater than 5000 mg/kg bw in male and female rats. BAS 684 03 H was not acutely toxic by the dermal route and thus did not meet the criteria for classification in accordance with Regulation EC (No) 1272/2008. Furthermore, HSE considers that this *in vivo* test was not required (hence not relied upon) and robust conclusions could have been reached based on the results of the calculation method.

Calculation method

Based on the calculation method, in accordance with Regulation EC 1272/2008, a dermal LD_{50} for the product of > 2000 mg/kg bw can be calculated (See Volume 4 for further details).

Conclusion

Overall, no classification for acute dermal toxicity in accordance with Regulation EC (No) 1272/2008 is required.

B.6.1.3. Inhalation

In vivo study

The acute inhalation toxicity of BAS 684 03 H has been investigated *in vivo* in a study in rats.

The *in vivo* study has not been granted data protection due to sufficient data being available on its components allowing for the application of the calculation method of the CLP Regulation.

Table 6.1-4. Summary of the acute inhalation toxicity of BAS 684 03 H

Method Guideline, GLP status, reference	Species, strain, sex, no./group	Test substance, dose levels, duration of exposure	LC_{50}	Remarks
OECD 403 (2014) GLP compliant [redacted], 2017 (2017/1198506)	Rat, Wistar, 5/sex Nose-only exposure Observation period: 14 days	5.1 mg/L air Mist (liquid aerosol) 4 hour exposure Mass median aerodynamic diameters. (MMADs): 1.5 µm	LC_{50} >5.1 mg/L	No deaths. Clinical signs: intermittent and labored respiration, abdominal respiration, respiration sounds and red encrusted nose, piloerection and substance-contaminated fur. The mean body weights of the animals decreased during the first post exposure observation day but increased thereafter. No adverse macroscopic necropsy findings.

In a GLP-compliant and guideline acute inhalation toxicity study (limit test) groups of 5 male and 5 female Wistar rats were exposed by nose-only for four hours to a liquid aerosol of BAS 684 03 H at a concentration of 5.1 mg/L (analytical concentration). The animals were observed for 14 days.

Clinical signs of toxicity comprised of intermittent and labored respiration, abdominal respiration, respiration sounds and red encrusted nose, piloerection and substance-contaminated fur. No abnormalities were detected in the female animals during the post-exposure observation period from study day 10 onwards. The mean body weights of the animals decreased on the first post-exposure observation day but increased thereafter. No gross pathological abnormalities were detected during the necropsy in the animals at the termination of the study.

Based on the absence of mortality in this study the acute inhalation LC_{50} was determined to be greater than 5.1 mg/L. Therefore, according to the classification criteria of Regulation 1272/2008, no classification is warranted for acute inhalation toxicity for BAS 684 03 H.

Calculation method

Data on acute inhalation toxicity was available for 82.64 % of the formulation. The calculated ATEmix for acute inhalation toxicity was 32.42 mg/L; therefore, the product does not require classification for acute inhalation toxicity based on the calculation method (See Volume 4 for further details).

Conclusion

In summary, based on the calculation method in accordance with Regulation EC 1272/2008, no classification for acute inhalation toxicity is required.

B.6.1.4. Skin irritation

An assessment of the skin irritation and corrosion potential of BAS 684 03 H was made in two *in vitro* assays. Additionally, an *in vivo* acute dermal irritation/corrosion study was performed in rabbits.

The *in vivo* study has not been granted data protection due to sufficient data being available from the calculation method and the *in vitro* assays.

Table 6.1-5. Summary of studies to investigate the skin irritation potential of BAS 684 03 H

Method Guideline, GLP status, reference	Test system	Test substance, dose levels, duration of exposure	Results
EpiDerm skin irritation test (SIT) OECD 439 (2015) GLP compliant Remmele, 2017a (2017/1194114)	Human reconstituted epidermis model	30 µL of BAS 684 03 H Exposure for 1 hour with 42 hours' post-incubation period Positive control: 5 % sodium dodecyl sulfate (SDS) in water	Tissue viability values: 1st test run: BAS 684 03 H = inconclusive results (due to non-concordant replicate measurements) Positive control = 2.3 % of the negative control values. 2nd test run: BAS 684 03 H = 18.5 % of negative control values Positive control = 2.5 % of the negative control values. Skin irritant under the conditions of this study
EpiDerm skin corrosion test (SCT) OECD 431 (2016) GLP compliant Remmele, 2017a (2017/1194114)	Human reconstituted epidermis model	50 µL of BAS 684 03 H Exposed for 3 minutes and 1 hour Positive control: 8-N potassium hydroxide solution (KOH)	Tissue viability values at 3 minutes: BAS 684 03 H = 116.7 % of the negative control value Positive control = 20.2 % of the negative control value Tissue viability values at 1 hour: BAS 684 03 H = 124.4 % of the negative control value Positive control = 5.2 % of the negative control value Not corrosive under the conditions of this study
Acute dermal irritation / corrosion in rabbits OECD 404 (2015) GLP compliant [redacted] 2017c (2017/1154822)	Rabbits, New Zealand White, 2 Females	0.5 ml of BAS 684 03 H Exposure period: 4 hours Observation period: 14 days	Mean scores over 24, 48 and 72 hours for each animal: Erythema = 2.3 and 3.0 Edema = 0.0 and 0.0 Not reversible in all animals within 14 days Potential skin irritant under the conditions of this study

Two *in vitro* EpiDerm assays were conducted with human reconstructed epidermis to assess the skin irritation and corrosion potential of BAS 684 03 H: a Skin Corrosion Test (SCT) and a Skin Irritation Test (SIT). Tissue viability was assessed by MTT assay and related to the respective negative controls (NC). Non-viable tissues were used to evaluate the ability of the test item to reduce the MTT-reagent directly.

In vitro SIT

The SIT experiment (OCED 439) was performed twice, due to inconclusive results in the first experiment evident by non-concordant replicate measurements. After 1-hour exposure followed by 42-hour recovery for the 2nd SIT experiment, the mean viability of the treated tissues was 18.5% (cut-off value <45% for irritant substances), based on individual values of 21.9 %, 21.7 % and 12.0 %.

Table 6.1-6. SIT results of the 1 h exposure on EpiDerm™ models followed by 42 h recovery with BAS 684 03 H

	Negative Control (NC)	**Test Item**	**Positive Control (PC)**
	viable tissue	**viable tissue**	**viable tissue**
Exposure: 1 h, 42 h recovery – 1st experiment			
OD570 tissue I	1.838	1.335	0.036
OD570 tissue II	1.826	0.053	0.043
OD570 tissue III	1.758	0.128	0.044
mean OD570	1.807	0.505	0.041
Viability (% of NC ± SD)	100 ± 2.4	27.9 ± 39.8	2.3 ± 0.3
Exposure: 1 h, 42 h recovery – 2nd experiment			
OD570 tissue I	1,806	0,366	0,046
OD570 tissue II	1,678	0,363	0,041
OD570 tissue III	1,523	0,201	0,041
mean OD570	1.669	0,310	0,043
Viability (% of NC ± SD)	100 ± 8.5	18.5 ± 5.7	2.5 ± 0.2

SD: relative standard deviation

Of the six tissues employed in this study, two tissues indicated non-corrosivity, four tissues indicated irritancy. Therefore, based on these results, BAS 684 03 H was a skin irritant in a GLP, guideline compliant EpiDerm skin irritation test (SIT).

In vitro SCT

OECD test guideline 439 cannot discriminate between skin irritation/corrosion categories 1 and 2, therefore an EpiDerm skin corrosion test (SCT) was conducted in accordance with GLP and OECD 431. After 3 minutes and 1-hour exposure, the mean viability of the treated tissues was 116.7 % (cut-off value 55 %) and 124.4 % (cut-off value 20 %), respectively. It is thus concluded that BAS 684 03 H was not corrosive under the conditions of this study.

Overall, on the basis of the *in vitro* data, BAS 684 03 H is therefore a skin irritant, but not corrosive and meets the criteria for classification for Skin Irritation category 2 (H315) in accordance with Regulation EC (No) 1272/2008.

In vivo skin irritation study

The acute dermal irritation and corrosion potential of BAS 684 03 H was also assessed *in vivo* in two rabbits. Mean scores over 24, 48 and 72 hours for each animal were 2.3 and 3.0 for erythema and 0.0 and 0.0 for oedema. At study termination (14 days), very slight erythema (grade 1) and scaling were observed in both animals on study day 14.

Table 6.1-7. Skin irritation in rabbits – Individual irritation scores

Readings	Animal	Erythema	Oedema	Additional findings
0 h	1	2	0	-
	2	2	0	48
1 h	1	2	0	48
	2	2	0	48
24 h	1	3	0	48
	2	3	0	48
48 h	1	2	0	48
	2	3	0	48
72 h	1	2	0	48
	2	3	0	48
7 d		2	0	S
		1	0	S
14 d	1	1	0	S
	2	1	0	S
Individual 24-48-72 h means	1	2.3	0.0	
	2	3.0	0.0	
Overall mean	-	2.7	0.0	

48 = Erythema beyond the application area; S = scaling

Thus, based on the results of this *in vivo* skin irritation test, classification as to Skin Irrit. 2 (H315) is warranted for BAS 684 03 H. HSE considers that this *in vivo* test was not required (hence not relied upon) as robust conclusions could have been reached based on the results of the *in vitro* tests.

Calculation method

Data on skin irritation potential are available for the entire product formulation. The active substance is not a skin irritant; however, the formulated product contains a component that is classified as skin irritation (category 2) which comprises 3.99 % of the composition. The remaining co-formulants are not classified as skin irritants. Therefore, the product would not require classification for skin irritation based on the calculation method of Regulation EC 1272/2008 (See Volume 4 for further details).

Conclusion

Overall, BAS 684 03 H is a skin irritant and requires classification with Skin Irrit. 2 (H315) in accordance with Regulation EC 1272/2008, based on the results of the available *in vitro* tests.

B.6.1.5. Eye irritation

The eye irritation potential of BAS 684 AL H (identical to BAS684 03 H) has been investigated in an *in vitro* EpiOcular Eye Irritation Test and in an *in vivo* study in rabbits. According to the applicant, the standard test strategy in case of a positive *in vitro* EpiOcular RhCE test (OECD 492) is to proceed with sequential *in vivo* eye irritation tests to check for the absence of eye-damaging properties. HSE considers that an *in vivo* test was not required, as taking a WoE approach, including indications of irritation/damage from the available *in vitro* test (see below), the skin irritancy of the product (see above) and the prediction of eye damage from the calculation method of the CLP Regulation (see below), a robust conclusion on the eye irritancy/damage potential of BAS684 03 H could be reached.

Table 6.1-8. Summary of the eye irritation studies with BAS 684 AL H (identical to BAS684 03 H)

Method Guideline, GLP status, reference	Test system	Test substance, dose levels, duration of exposure	Results
EpiOcular Eye Irritation Test OECD 492 GLP Compliant Remmele, 2017b (2016/1193048)	Two EpiOcular tissue samples	50µL of undiluted BAS 684 AL H Exposure period = 30 minutes Post-incubation period = 2 hours Positive control = methyl acetate Negative control = deionised water	Mean OD_{570} values (% of negative control: BAS 684 AL H = 31.4 ± 0.3 Negative control: 100 ± 12.8 Postive control: 27.2 ± 6.4 Potential eye irritant/damaging under the conditions of this study.
Acute eye irritation in rabbits OECD 405 (2002) GLP Compliant [redacted], 2017a (2016/1345293) and 2017b (2017/1012902)	Rabbit, New Zealand White, 3 females (step-wise procedure)	0.1 ml of undiluted BAS 684 AL H in one eye for 24 hours, followed by rinsing with tap water. Observation period = 28 days – no mention of total observation period	Mean scores (averaged over 24, 48 & 72 hours) for each animal: Corneal Opacity: 0.0, 0.0 and 0.0 Iris lesions: 0.0, 0.0 and 0.0 Conjuctiva Redness: 1.0, 1.3 and 1.3 Chemosis: 1.0, 1.3 and 1.3 All reactions reversible in all animals within 7 days BAS 684 AL H does not show an eye irritating potential under the conditions of this study

In a reconstructed human cornea model (OECD 492), BAS 684 AL H demonstrated an eye irritation/damage potential (mean tissue viability score ≤ 60 % of negative control = irritant/damage). The RhCE test method shows a certain number of false positive results (up to 37 %) and cannot resolve between eye irritation/damage (Categories 1 and 2). Additional information is required for classification purposes; therefore the applicant conduceted an *in vivo* eye irritation test in rabbits to investigate the eye irritation potential of BAS 684 AL H further.

However, it should be noted that validated *in vitro*/*ex vivo* eye corrosion OECD Test Guidelines (OECD 437 and 438) have been available since September 2009 for the detection of Category 1 eye damaging materials, and were revised in July 2013 to take account of new data showing they could identify non-irritants too. A combination of validated *in vitro* and *ex vivo* tests for eye irritation/corrosion should be conducted first, and may provide a definite classification for eye irritation/corrosion without the need for an *in vivo* test. HSE also notes that taking a WoE approach, including indications of eye irritancy/damage from the available *in vitro* test, the skin irritancy potential of the product (see above) and the prediction of eye damage from the calculation method of the CLP Regulation (see below), a robust conclusion on the eye irritancy/damage potential of BAS684 03 H could have been reached without the need to conduct an *in vivo* test.

In vivo test

In a GLP and guideline compliant eye irritation study, ocular reactions were reported from one hour until 72 hours after administration of the test material. The ocular reactions were reversible in one animal within 96 hours and in two animals within 7 days after application. Mean scores calculated for each animal over 24, 48

and 72 hours were 0.0, 0.0 and 0.0 for corneal opacity and for iris lesions and 1.0, 1.3 and 1.3 for redness of the conjunctiva and for chemosis.

Table 6.1-9. Eye irritation in rabbits – Individual irritation scores

Readings	Animal	Cornea		Iris	Conjunctiva			Additional Findings
		Area Involved	Opacity		Redness	Chemosis	Discharge	
1h	1	0	0	0	1	1	2	49
	2	4	1	1	2	2	3	49
	3	4	1	1	2	3	3	49
24 h	1	0	0	0	1	1	1	48, FL.neg.
	2	0	0	0	2	2	0	48, FL.neg.
	3	0	0	0	2	2	2	49, FL.pos.grade 1
48 h	1	0	0	0	1	1	0	48, FL.neg.
	2	0	0	0	1	1	0	48, FL.neg.
	3	0	0	0	1	1	0	48, FL.neg.
72 h	1	0	0	0	1	1	0	49
	2	0	0	0	1	1	0	49
	3	0	0	0	1	1	0	48, FL.neg.
96 h	1	0	0	0	1	1	0	48
	2	0	0	0	0	0	0	SD
	3	0	0	0	1	1	0	48
7 d	1	0	0	0	0	0	0	SD
	2	-	-	-	-	-	-	-
	3	0	0	0	0	0	0	SD
Individual 24-48-72 h means	1		*0.0*	*0.0*	*1.0*	*1.0*		
	2		*0.0*	*0.0*	*1.3*	*1.3*		
	3		*0.0*	*0.0*	*1.3*	*1.3*		
Total Mean			*0.0*	*0.0*	*1.2*	*1.2*		

Considering the described ocular reactions as well as the average score for irritation, BAS 684 AL H does not show an eye irritating potential under the test conditions chosen. No classification is required for eye irritation. HSE considers that this *in vivo* test was not required (hence not relied upon) as robust conclusions could have been reached based on the results of *in vitro* tests in combination with the calculation method of the CLP Regulation.

Calculation method

Data on the eye irritation potential of all the ingredients of the product are available. The active substance is not an eye irritant. However, one co-formulant is classified for severe eye damage (H318) and is present at a level of 3.99 %. Applying the calculation method, BAS 684 03 H would require classification for serious eye damage in Category 1 (H318) (See Volume 4 for further details).

Conclusion

In conclusion, on the basis of indications of eye irritation/damage in the EpiOcular RhCE test (OECD 492), the skin irritancy potential of the product and the predicted classification for serious eye damage by calculation, the product should be classified in category 1 for serious eye damage (H318).

B.6.1.6. Skin sensitisation

In vivo study

The skin sensitisation potential of BAS 684 AL H (identical to BAS684 03 H) has been assessed in the guinea pig Buehler test.

The *in vivo* study has not been granted data protection due to sufficient data being available on its components allowing for the application of the calculation method of the CLP Regulation, with positive classification (Skin Sens. 1; H317).

Table 6.1-10. Summary of skin sensitisation study with BAS 684 AL H (identical to BAS684 03 H)

Method, Guideline, GLP status, reference	Species, strain, sex, no/group	Test substance, dose levels, duration of exposure	Results
Buehler Test OECD 406 (1992) GLP Compliant [redacted], 2017d (2017/1161446)	Guinea pigs, Dunkin Hartley 30 females (10 for control group and 20 for the test group)	0.5mL applied Concentration: Induction phase = 75% (w/w) Challenge = 50% (w/w) Exposure period = 6 hours Observation period = 14 days Positive control: 85% α-hxyl cinnamaldehyde	No signs of systemic toxicity in the main test. In the test group, 10 animals in total showed the following skin findings after 24 and/or 48 hours: • Discrete erythema (grade 1) in 9 animals • Moderate erythema (grade 2) in 1 animal BAS 684 03 H has a sensitising effect on the skin.

The test item concentrations for the main test were selected based on the results of the pretest, in which 3 guinea pigs of the same animal strain in total were used. In the pre-test, the highest concentration that could be technically used was 100 % (w/w). Therefore, concentrations of 25 %, 50 %, 75 % and 100 % (w/w) preparations in deionised water were chosen.

In the pre-test, concentrations of 25 %, 50 %, 75 % and 100 % were analysed. At a concentration of 75 %, the test substance induced discrete erythema in 1/3 animals, whereas other concentrations tested did not revealed any cutaneous findings. Therefore, 75 % was used for induction and 50 % was used for challenge in the main test. Signs of systemic toxicity were not observed in the pre-test.

Table 6.1-11. Skin readings in the preliminary study

Animal	Readings at 1 hour				Readings at 24 hours				Readings at 48 hours			
	% test substance concentrations in deionised water											
	100	75	50	25	100	75	50	2%	100	75	50	25
A	1	0	0	0	1	0	0	0	1	0	0	0
B	1	0	0	0	1	1	0	0	0	0	0	0
C	0	0	0	0	1	0	0	0	1	0	0	0

Scoring:
0 = no visible change, 1 = discrete or patch erythema, 2 = moderate and confluent erythema, 3 = intense erythema and swelling

The main study was performed using 1 control group, which consisted of 10 animals and 1 test group, which consisted of 20 animals. The inductions were performed on days 0, 7 and 14. A challenge was carried out 14 days after the last induction.

In the main study, the animals did not show any signs of systemic toxicity. No local skin findings could be observed in the control group after the challenge. In the test group, 10 animals in total showed the following skin findings after 24 and/or 48 hours:

- Discrete erythema (grade 1) in 9 animals
- Moderate erythema (grade 2) in 1 animal

Table 6.1-12. The number of animals with skin findings following the challenge

Group	Challenge							
	Test item				Untreated skin			
	24h	48h	total	Percentage %	24h	48h	total	Percentage %
Control group	0/10	0/10	0/10	0	0/10	0/10	0/10	0
Test group	10/20	5/20	10/20	50	0/20	0/20	0/20	0

x/y: number of positive reactions/number of animals tested (reading at 24 h and/or 48 h after the removal of the patch).

Under the conditions of this GLP-compliant and guideline Buehler test, BAS 684 03 H showed skin sensitising potential (>15 % of test animals showed redness scores ≥ 1). As 50 % of treated animals responded using an induction concentration of 75 %, classification for skin sensitisation in Category 1B (H317) is required for BAS 684 03 H according to Regulation (EC) No. 1272/2008.

HSE notes that since the active substance (present at 82 % in the product) is a skin sensitiser (see below), according to the data requirements in Reg 284/2013, the calculation method of Regulation No. 1272/2008 should have been applied and the *in vivo* test should have not been performed. Therefore, this Buehler study was unnecessary and it is not relied upon. HSE also notes that a LLNA assay should have been conducted, or, as a minimum, a justification for a new/recent Buehler test should have been provided by the applicant.

Calculation method

The active substance, which is present in the product at a concentration of approximately 82 %, has been proposed to be classified as a skin sensitiser in category 1 (H317) (see Volume 3 CA B6 document). On the basis of this proposal and applying the calculation method of Regulation No. EC 1272/2008, BAS 684 03 H requires classification for skin sensitisation in Category 1 (H317) (See Volume 4 for further details).

Conclusion

Overall, based on the calculation method of Regulation No. 1272/2008, BAS 684 03 H requires classification with Skin Sens. 1 (H317).

B.6.1.7. Supplementary studies on the plant protection product

Not available and not required.

B.6.1.8. Supplementary studies for combinations of plant protection products

Not available and not required.

B.6.2. DERMAL ABSORPTION

The *in vitro* dermal penetration of BAS 684 H formulated as BAS 684 03 H through human skin has been investigated. The EFSA Guidance on Dermal Absorption (2017) was taken into account.

Table B.6.2.1 Summary of *in vitro* dermal penetration study

Table 6.2-1. Summary of *in vitro* dermal penetration study

Method, guideline, GLP status, reference	Species	Test substance, dose levels, duration of exposure	Results
In vitro dermal penetration OECD 428 (2004) GLP Compliant Fabian & Landsiedel, 2017 (2017/1137741)	Human abdominal skin, dermatomed (split thickness), thickness of 200-390 µm 5 donors Receptor fluid: ethanol / tap water Washing solution: mild soap solution: Estesol© HAIR&BODY 3% w:w in tap water.	BAS 684 03 H containing C14-labelled BAS 684 H, radiochemical purity > 98% High dose: formulation concentrate, (750 mg/mL; nominal dose 7500 µg BAS 684 H per cm²), 7 valid diffusion cells Low dose: 1:600 spray dilution (1.25 mg/mL; nominal dose 12.5 µg BAS 684 H per cm²,10 µg/cm², 8 valid diffusion cells Duration of exposure = 8 hours Duration of experiment = 24 hours	High dose concentrate = 0.4% Low-dose spray dilution = 11%

In an *in vitro* experiment the dermal penetration of BAS 684 H formulated as BAS 684 03 H through human skin was determined. For this a high dose (formulation concentrate (750 mg/mL; nominal dose 7500 µg BAS 684 H per cm²), and a low dose (1:600 spray dilution (1.25 mg/mL; nominal dose 12.5 µg BAS 684 H per cm²), was applied to human dermatomed skin at 10 µL/cm². The skin was mounted into Franz-type diffusion cells operated in flow-through mode with a continuous flow of 2.3 mL/h. The exposure of the skin to the test material lasted 8 hours under semi-occlusive conditions; thereafter the skin was thoroughly washed. Samples of the receptor fluid were taken in 1-hour intervals from 0 to 8 hours and in 2-hour intervals from 8 to 18 hours, and 3-h intervals from 18 to 24 hours after the start of the exposure, in order to determine kinetic parameters (lag phase, absorption rate and permeability constant). Dermal absorption estimates were derived following published EFSA recommendations.

Prior to the experiment, the skin sample integrity was determined by measurement of the trans-epidermal electrical resistance, the trans-epidermal water loss and visual inspection. At the end of the experiment, cells were assessed to be valid if total recoveries fulfilled guideline requirements (a total recovery per membrane of 100 ± 10%) and if clearly aberrant penetration kinetics and aberrant skin wash after the 8-hour exposure period could be excluded.

Six tape strips were taken, which were pooled into two samples for analysis: tape-strip sample 1 contained the first and second tapes, and tape-strip sample 2 contained the third to sixth tapes. The six collected tape strips were considered to represent the stratum corneum.

The mean recoveries of the different compartments are presented in the table below. Eight diffusion cells were used for the spray dilution, all of which yielded valid results.The applicant excluded cell #16, and the UK does not agree with this since the poor skin wash did not have any discernible effect upon the absorbed fraction; as the amount in the skin residue is within range of all other replicates, and the absence of radioactivity from the receptor fluid further indicates the cells' validity.

For the formulation concentrate, 8 cells were exposed and 7 cells provided valid results. The cell #3 was excluded from statistics due to an insufficient first skin wash of 97.76%; this value was below the mean value of the other cells minus almost twice their standard deviation. Furthermore, the residue detected in the post-stripped skin of cell #3 was significantly higher, at 2.01%, than the skin residue of all the other cells at 0.11% ± 0.09 (mean± SD); thus the skin residue of cell #3 is a 200% increase from the mean. Additionally, the other replicate (#4) from the same donor shows a profile more akin to all the other replicates. In conclusion, cell #3 was considered as an outlier.

The mean lag time for the onset of dermal penetration was 1.00 hour for the low dose. The low absorption of ^{14}C-BAS 684 H (Cinmethylin) in the high dose experiment did not allow the calculation of mean lag times and other kinetic parameters. In both groups absorption was essentially complete: after 12 hours.

In the high dose group, there were no quantifiable amounts of radioactivity (test substance) present in the receptor fluid during the exposure period for all cells. In the low dose group, the receptor media showed quantifiable amounts of radioactivity 2 hours after application for four valid cells. For three valid cells, the absorbed dose during the exposure period was too low for meaningful calculation of kinetic parameters.

Table 6.2-2. *In-vitro* dermal penetration of ^{14}C-BAS 684 H formulated as BAS 684 03 H through human skin – Recovery data

Dose group	**High dose (Formulation concentrate)**		**Low dose (Spray dilution 1:600)**	
Target concentration [mg/mL]	750		1.25	
Target dose [µg/cm²]	7500		12.5	
Mean actual applied dose [µg/cm²]	7089		13.4	
Number of cells used/Valid cells	8/7*		8/8	
	Recovery [%]		Recovery [%]	
	Mean	SD	Mean	SD
Dislodgeable dose				
Skin washing after 8 hours	99.94	1.11	79.81	4.04
Skin washing after 24 hours				
Donor chamber wash	0.57	0.68	6.64	1.68
Dose associated to skin				
Tape strips: 1st sample, strips 1 - 2	0.08	0.05	0.84	0.60
Tape strips: 2nd sample, strips 3 - 6	0.06	0.06	1.16	0.63
Skin preparation	0.11	0.09	2.30	1.61
Absorbed dose				
Sum receptor samples incl. wash out	0.00	0.00	0.00	0.00
Receptor fluid	0.00	0.00	0.00	0.00
Receptor chamber wash	0.14	0.10	6.16	2.76
Total recovery*	**100.85**	**0.81**	**96.67**	**1.76**
Absorption complete? (>75% absorption within half the study duration)	**Yes**		**Yes**	
Absorption estimates when absorption not essentially completed (= absorbed dose + dose associated to skin + tape strips sample 2)[a]	n/a		n/a	
Measure absorption (= absorbed dose + dose associated to skin)	0.24	0.17	8.47	2.98
Absorption estimate normalised[b]	n/a		n/a	
Relevant absorption estimate[c]	0.401		10.968	
Absorption estimates used for risk assessment[c]	0.4 %		11 %	

* cell 3 excluded from statistics due to insufficient first skin wash

a In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873) the radioactivity in the second tape-strip pool (3rd to 6th tape strip) is considered potentially absorbable if less than 75% of the absorption occurred in the first half of the study. Finally, the skin preparation is also considered potentially absorbable.

b Cells with insufficient recovery (<95%) were corrected by normalization of absorption estimate to 100% recovery if mean recovery was <95%.

c In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873) to address variability between replicates, a multiple of the standard deviation should be added to the mean dermal absorption value. This value was then rounded to the required number of significant figures.

n/a not applicable

Pro-rata calculations
The applicant tested the concentrate (750 g a.s./L) and one dilution (1.25 g a.s./L); the highest spray dilution (lowest active substance concentration) is 0.625 g a.s./L (250 g a.s./ha with 400 L water /ha). In accordance with the EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873), pro-rata correction is required in this instance, as the data are not available to cover the extremes of those recommended on the product label.

	Active content (g a.s./L)	**Proposed dermal absorption value (%)**
Concentrate (tested *in vitro*)	750	0.4
Tested dilution (1:600)	1.25	11
Highest in-use spray dilution (1:1200)	0.625	22

Conclusion

In conclusion, *in vitro* dermal absorption of ^{14}C-BAS 684 H formulated as BAS 684 03 H through human skin is low. The BAS 684 H dermal absorption estimates were 0.24 ± 0.17% for the formulation concentrate (750 mg a.s./mL), and 8.47 ± 2.98% of the 1:600 dilution (1.25 mg a.s./mL).

The dermal penetration estimates of BAS 684 H to be used for risk assessment were calculated to be 0.4% for formulation concentrate of BAS 684 03 H, 11% for the 1:600 spray dilution (1.25 mg/mL), and 22% for the 1:1200 in-use dilution (0.625 mg/mL), respectively.

B.6.3. AVAILABLE TOXICOLOGICAL DATA RELATING TO CO-FORMULANTS

Safety Data Sheets (SDS) have been submitted for all of the co-formulants listed in Vol 4, section C.1.4.5. Co-formulants classified for acute toxicity, skin and eye irritation and skin sensitisation have been considered above. No other classification is triggered by the co-formulants. However, for endpoints beyond acute toxicity, skin and eye irritation and skin sensitisation, it is proposed that the active substance should be classified for STOT-SE Category 2 (H371). As BAS 684 03 H contains the active substance cinmethylin (at 82.25 %) in excess of the generic concentration limit (GCL) (10 %) triggering classification for STOT-SE category 2 (H371), the product requires this additional classification.

For further details please see volume 4, section C.1.4.5.

Overall toxicological classification of BAS 684 H

Skin Irrit 2; H315 (Causes skin irritation)
Eye Dam 1; H318 (Causes serious eye damage)
Skin Sens 1; H317 (May cause an allergic skin reaction)
STOT-SE 2; H371 (May cause damage to the nervous system)

Classification of the lowest in-use dilution

The lowest in use dilution (5 g a.s./L = 0.5 % a.s.) does not require classification for any endpoint, including skin sensitisation. The skin sensitisation classification of the product is driven by the active substance. In the lowest dilution, the active substance is present at 0.5 %, which is below the GCL of 1 % for classification of a mixture for skin sensitisation.

B.6.4. EXPOSURE DATA

'BAS 684 03 H' is the representative formulation for the approval of the active substance BAS 684 H (ISO provisionally approved name: cinmethylin). A summary of the application parameters pertinent to the operator, bystander, resident and worker exposure assessment for 'BAS 684 03 H' are presented below.

Table B.6.4-1 Summary of 'BAS 684 03 H' application parameters pertinent to the operator, bystander, resident and worker exposure assessment.

'BAS 684 03 H'	
Formulation type	Emulsifiable Concentrate (EC), containing 750 g/L BAS 684 H (cinmethylin)
Use	Professional herbicide to outdoor winter wheat and winter barley
Application method	Tractor-mounted boom crop sprayer
Individual dose	0.333 - 0.666 L product/ha (250 - 500 g a.s./ha)
Number of applications	1 per year
Total dose	0.333 - 0.666 L product/ha/crop (250 - 500 g a.s./ha/crop)
Application volume	100 - 400 L/ha
Spray concentration range	0.625 - 5 g a.s./L
Latest time of application	Pre-emergence and post emergence, BBCH 00-29
Classification	H315 Category 2 – causes skin irritation H317 Category 1 – may cause an allergic skin reaction H318 Category 1 – causes serious eye damage H371 Category 2 – may cause damage to nervous system (STOT-SE 2)
Systemic AOEL	0.06 mg/kg bw/day
Systemic AAOEL	0.21 mg/kg bw/day
Oral absorption	100%
Dermal absorption	0.4% for the concentrate 11% for the spray dilution of 1.25 g a.s./L 22% for spray dilution of 0.625 g a.s./L
Vapour pressure	8.1×10^{-3} Pa at 20°C, 1.5×10^{-2} Pa at 25°C According to DAR04 Volume 3(AS) Section B2

Estimates of operator, worker, bystander and resident exposure have been conducted in line with the EFSA guidance[1] and the respective calculator (hereafter referred to as EFSA Calculator). Considering the proposed uses of the representative product, the higher application rate of 0.666 L product/ha intended for winter wheat is the critical GAP. This use is considered for this assessment and covers uses with the lower application rate of 0.333 L product/ha. This assessment would also provide a risk envelope for the use of winter oilseed rape at the same application rates for operator, bystander, resident and worker exposure.

B.6.4.1. Operator exposure

A Tier 1 estimate of operator exposure is presented based on the highest application rate and the highest dermal absorption values (worst case scenario). A summary of the estimated longer term operator exposure to BAS 684 H (cinmethylin) for the proposed uses of 'BAS 684 03 H' is provided in the following table, outputs of the EFSA Calculator are presented in Appendix 1 (Estimate 1).

[1] European Food Safety Authority (2014). Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products, EFSA Journal 2014;12(10):3874.

Table B.6.4.1-1 Estimated longer term operator exposure to BAS 684 H (cinmethylin) during the application of 'BAS 684 03 H' and comparison with AOEL

BAS 684 H (cinmethylin)			
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL (0.06 mg/kg bw/day)**
Scenario: Cereals / Outdoor / Downward spraying / Vehicle-mounted Formulation type: Emulsifiable Concentrate Work rate: 50 ha Season: Not relevant			
Application rate:		0.5 kg a.s./ha	
Spray application outdoor (AOEM; 75th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) mixing, loading and application	0.0184	31

Based on the EFSA Calculator the predicted level of longer term operator exposure to BAS 684 H (cinmethylin) is 31% of the systemic AOEL of 0.06 mg/kg bw/day for an individual applying the product via vehicle mounted sprayer to low crops and using no PPE. The estimated longer term operator exposure is within acceptable limits and no further risk assessment is required.

A summary of the estimated acute operator exposure to BAS 684 H (cinmethylin) for the proposed uses of 'BAS 684 03 H' is provided in the following table, outputs of the EFSA Calculator are presented in Appendix 1 (Estimate 1).

Table B.6.4.1-2 Estimated acute operator exposure to BAS 684 H (cinmethylin) during the application of 'BAS 684 03 H' and comparison with AAOEL

BAS 684 H (cinmethylin)			
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AAOEL (0.21 mg/kg bw/day)**
Scenario: Cereals / Outdoor / Downward spraying / Vehicle-mounted Formulation type: Emulsifiable Concentrate Work rate: 50 ha Season: Not relevant			
Application rate:		0.5 kg a.s./ha	
Spray application outdoor (AOEM; 75th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) mixing, loading and application	0.1065	51

Based on the EFSA Calculator the predicted level of acute operator exposure to BAS 684 H (cinmethylin) is 51% of the systemic AAOEL of 0.21 mg/kg bw/day for an individual applying the product via vehicle mounted sprayer to low crops and using no PPE. The estimated acute operator exposure is within acceptable limits and no further risk assessment is required.

The product 'BAS 684 03 H' is classified for human health effects:

- H315 – Causes skin irrigation
- H317 – May cause an allergic skin reaction
- H318 – Causes serious eye damage
- H371 – May cause damage to nervous system (STOT-SE 2)

The use of suitable protective gloves, suitable protective coveralls and face protection (faceshield) when handling the concentrate is therefore required.

B.6.4.2. Bystander and resident exposure

A Tier 1 resident and bystander exposure assessment is presented using the highest proposed application rate of 500 g a.s./ha, the lowest proposed water volume of 100 L/ha and the highest dermal absorption value of 22% (worst case scenario).
For exposure of residents and bystanders to vapour the EFSA Guidance specifies default values for the average concentration of active substance in the air 24 hours after application of the product. These values are based on the volatility of the active substance (preferably at 25 °C):

- Substances with low volatility having a vapour pressure of $< 5 \times 10^{-3}$ Pa (the default average concentration in air in the 24 hours after application is 1 µg/m³).
- Moderately volatile substances with a vapour pressure between 5×10^{-3} Pa and 10^{-2} Pa (the default average concentration in air in the 24 hours after application is 15 µg/m³).

BAS 684 H (cinmethylin) has a vapour pressure of 8.1 x 10^{-3} Pa at 20°C and 1.5 x 10^{-2} Pa at 25°C according to DAR04 Volume 3(AS) Section B2. The vapour pressure of BAS 684 H (cinmethylin) is therefore within the specified range for moderately volatile substances at 20 °C but marginally higher than the top limit of 10^{-2} Pa at 25 °C. It is considered that the top cut off point for moderately volatile active substances is a somewhat arbitrary value and the measurement of vapour pressures can be imprecise, with variation between different experiments.

The EFSA default average air concentration for moderately volatile substances of 15 µg/m³ is based on a surrogate air concentration value adjacent to treated crops from a study undertaken by the Californian Environmental Protection Agency [2]. In this study, a 24 ha orange orchard was treated with chlorpyrifos (vapour pressure 3.35 x 10^{-3} Pa at 25 °C, 1.43 x 10^{-3} at 20 °C) using a broadcast air-assisted sprayer. The maximum temperature during the trial was 42 °C. Chlorpyrifos air concentration adjacent to the orchard was monitored over 72 hours with the highest 24 hour time-weighted average concentration in air being 15 µg/m³. Although BAS 684 H (cinmethylin) has a slightly higher vapour pressure than chlorpyrifos, the temperature during application of 'BAS 684 03 H' to winter wheat and barley in the UK at growth stages of BBCH 00-29 is likely to be significantly lower than 42 °C. Given the above, it is considered that for the proposed application of 'BAS 684 03 H' in the UK the use of the default value of 15 µg/m³ for moderately volatile active substances is acceptable to estimate bystander and resident exposure to BAS 684 H (cinmethylin) vapour.

A summary of the estimated resident (longer term) exposure is provided in the following table, outputs of the EFSA Calculator are presented in Appendix 1 (Estimate 2).

Table B.6.4.2-1 Estimated resident (longer term) exposure to BAS 684 H (cinmethylin) from the uses of 'BAS 684 03 H' and comparison with AOEL

BAS 684 H (cinmethylin)			
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL (0.06 mg/kg bw/day)**
Tractor mounted boom spray application outdoors to low crops Buffer zone: 2-3 m Drift reduction technology: none DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 365 days Vapour pressure: moderately volatile substances with a vapour pressure between 5 x 10^{-3} Pa and 10^{-2} Pa			
Number of applications and application rate:		1 x 0.5 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0296	49
	Vapour (75th perc.)	0.0161	27
	Deposits (75th perc.)	0.0020	3

[2] California Environmental Protection Agency, Air Resources Board (1998). Report for the application and ambient air monitoring for chlorpyrifos (and the oxon analogue) in Tulare County during spring/summer 1996.

BAS 684 H (cinmethylin)			
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL (0.06 mg/kg bw/day)**
	Re-entry (75th perc.)	0.0186	31
	Sum (mean)	0.0486	81
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0071	12
	Vapour (75th perc.)	0.0035	6
	Deposits (75th perc.)	0.0007	1
	Re-entry (75th perc.)	0.0103	17
	Sum (mean)	0.0156	26

For proposed uses of the product 'BAS 684 03 H' the predicted exposure of a child and adult resident to BAS 684 H (cinmethylin) from spray drift, vapour, surface deposits, re-entry into treated crops and sum of all pathways is within acceptable limits.

A summary of the estimated bystander (acute) exposure is provided in the following table, outputs of the EFSA Calculator are presented in Appendix 1 (Estimate 3).

Table B.6.4.2-2 Estimated bystander (acute) exposure to BAS 684 H (cinmethylin) from the uses of 'BAS 684 03 H' and comparison with AAOEL

BAS 684 H (cinmethylin)			
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AAOEL (0.21 mg/kg bw/day)**
Tractor mounted boom spray application outdoors to low crops Buffer zone: 2-3 m Drift reduction technology: none DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: 365 days Vapour pressure: moderately volatile substances with a vapour pressure between 5 x 10^{-3} Pa and 10^{-2} Pa			
Number of applications and application rate:		1 x 0.5 kg a.s./ha	
Bystander child Body weight: 10 kg	Drift (95th perc.)	0.0673	32
	Vapour (95th perc.)	0.0161	8
	Deposits (95th perc.)	0.0059	3
	Re-entry (95th perc.)	0.0186	9
Bystander adult Body weight: 60 kg	Drift (95th perc.)	0.0182	9
	Vapour (95th perc.)	0.0035	2
	Deposits (95th perc.)	0.0023	1
	Re-entry (95th perc.)	0.0103	5

For proposed uses of 'BAS 684 03 H' the predicted acute exposure of a child and adult bystander to BAS 684 H (cinmethylin) from spray drift, vapour, surface deposits and re-entry into treated crops pathways are all within acceptable limits.

Local effect risk assessment for residents and bystanders

The representative product is classified as skin sensitizer (H317). Based on the proposed uses the highest in use product concentration is 0.7% (0.666 L product in 100 L water), which is lower than the threshold concentration of 1% that is required for the spray dilution to be classified for skin sensitization. On this basis, no local effects are expected for resident and bystanders.

B.6.4.3. Worker exposure

A Tier 1 estimate of worker exposure is presented based on the highest proposed application rate of 500 g a.s./ha and the highest dermal absorption value of 22%. A summary of the estimated worker exposure (longer term) is provided in the following table, outputs of the EFSA Calculator are presented in Appendix 1 (Estimate 4). It is noted that it is not currently possible to undertake an assessment of the acute exposure to workers using the EFSA Calculator.

Table B.6.4.3-1 Estimated worker (long-term) exposure to BAS 684 H (cinmethylin) and comparison with AOEL

BAS 684 H (cinmethylin)			
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL (0.06 mg/kg bw/day)**
Inspection, irrigation Outdoor Work rate: 2 hours/day DT_{50}: 30 days DFR: 3 µg/cm²/kg a.s./ha Interval between treatments: N/A			
Number of applications and application rate:		1 x 0.5 kg a.s./ha	
Body weight: 60 kg	Work wear (arms, body and legs covered) TC: 1400 cm²/person/h	0.0154	26

An acceptable (longer-term) systemic worker exposure equal to 26% of the systemic AOEL of BAS 684 H (cinmethylin) is predicted for a worker that undertakes crop inspection/irrigation activities wearing normal workwear (arms, legs and body covered).

B.6.5. EXPOSURE AND RISK ASSESSMENT

B.6.5.1 Operator exposure

Estimates of operator exposure to BAS 684 H (cinmethylin) for the proposed uses of the representative product 'BAS 684 03 H' have been calculated using the EFSA Calculator. An acceptable long-term systemic operator exposure equal to 31% of the AOEL of BAS 684 H (cinmethylin) and an acceptable acute systemic operator exposure equal to 51% of the AAOEL of BAS 684 H (cinmethylin) is predicted for an operator that applies the product 'BAS 684 03H' without using PPE.

The product 'BAS 684 03 H' is classified for human health effects:

- H315 – Causes skin irrigation
- H317 – May cause an allergic skin reaction
- H318 – Causes serious eye damage
- H371 – May cause damage to nervous system (STOT-SE 2)

The use of suitable protective gloves, suitable protective coveralls and face protection (faceshield) when handling the concentrate are therefore required.

B.6.5.2. Bystander and resident exposure

Exposure to bystanders and residents has been calculated using the EFSA Calculator. The exposure assessment for inhalation of vapour has been conducted using the EFSA Guidance default value for average concentration in air in the 24 hours after application of 15 µg/m³ for moderately volatile substances with a vapour pressure between 5×10^{-3} Pa and 10^{-2} Pa. BAS 684 H (cinmethylin) has a vapour pressure of 8.1×10^{-3} Pa at 20°C and

1.5 x 10^{-2} Pa at 25°C according to DAR04 Volume 3(AS) Section B2. The vapour pressure of BAS 684 H (cinmethylin) is therefore within the specified range for moderately volatile substances at 20 °C but marginally higher than the top limit of 10^{-2} Pa at 25 °C.

It is considered that for the proposed application of 'BAS 684 03 H' in the UK the use of the default value of 15 µg/m^3 for moderately volatile active substances is acceptable to estimate bystander and resident exposure to BAS 684 H (cinmethylin) vapour given that the top cut off point for moderately volatile active substances is a somewhat arbitrary value, and the vapour pressure of BAS 684 H (cinmethylin) is only marginally above this top cut off point. In addition, the temperature during application of 'BAS 684 03 H' to winter wheat and barley in the UK at growth stages of BBCH 00-29 is likely to be significantly lower than the maximum temperature of 42 °C measured in the surrogate Californian Environmental Protection Agency study that was used to support the default value for moderately volatile substances of 15 µg/m^3 .

A summary of the estimated bystander and resident exposure, as modelled using default values in the EFSA Calculator is provided in the table below. The proposed in-use spray dilutions are not classified for skin sensitisation therefore no local effects are expected for resident and bystanders.

Table B.6.5.2-1 Estimated resident (longer term) exposure to BAS 684 H (cinmethylin)

BAS 684 H (cinmethylin)		
Model data		**% of systemic AOEL (0.06 mg/kg bw/day)**
Tractor mounted boom spray application outdoors to low crops Buffer zone: 2-3 m Drift reduction technology: none DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha Interval between treatments: 365 days Vapour pressure: moderately volatile substances with a vapour pressure between 5 x 10^{-3} Pa and 10^{-2} Pa		
Number of applications and application rate:		1 x 0.5 kg a.s./ha
Resident child Body weight: 10 kg	Drift (75th perc.)	49
	Vapour (75th perc.)	27
	Deposits (75th perc.)	3
	Re-entry (75th perc.)	31
	Sum (mean)	81
Resident adult Body weight: 60 kg	Drift (75th perc.)	12
	Vapour (75th perc.)	6
	Deposits (75th perc.)	1
	Re-entry (75th perc.)	17
	Sum (mean)	26

Table B.6.5.2-2 Estimated bystander (acute) exposure to BAS 684 H (cinmethylin)

BAS 684 H (cinmethylin)		
Model data		**% of systemic AAOEL (0.21 mg/kg bw/day)**
Tractor mounted boom spray application outdoors to low crops Buffer zone: 2-3 m Drift reduction technology: none DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha Interval between treatments: 365 days Vapour pressure: moderately volatile substances with a vapour pressure between 5 x 10^{-3} Pa and 10^{-2} Pa		
Number of applications and application rate:		1 x 0.5 kg a.s./ha
Bystander child Body weight: 10 kg	Drift (95th perc.)	32
	Vapour (95th perc.)	8
	Deposits (95th perc.)	3
	Re-entry (95th perc.)	9
Bystander adult Body weight: 60 kg	Drift (95th perc.)	9
	Vapour (95th perc.)	2
	Deposits (95th perc.)	1
	Re-entry (95th perc.)	5

For proposed uses of 'BAS 684 03 H' the predicted exposure of a child and adult resident and bystander to BAS 684 H (cinmethylin) from spray drift, vapour, surface deposits and re-entry into treated crops pathways are within acceptable limits.

B.6.5.3. Worker exposure

For the proposed uses of the product 'BAS 684 03 H' an acceptable worker exposure equal to 26% of the AOEL of BAS 684 H (cinmethylin) is predicted for a worker that performs crop inspection / irrigation activities wearing normal workwear (arms, legs and body covered).

B.6.6. REFERENCES RELIED ON

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCP 7.1.1/1	[redacted]	2017a	BAS 684 03 H - Acute oral toxicity study in rats 2017/1156882 [redacted] yes Unpublished	Yes	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF
KCP 7.1.2/1	[redacted]	2017b	BAS 684 03 H - Acute dermal toxicity study in rats 2017/1154823 [redacted] yes Unpublished	Yes	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF
KCP 7.1.3/1	[redacted]	2017	BAS 684 03 H - Acute inhalation toxicity study in Wistar rats - 4-hour liquid aerosol exposure (nose only) 2017/1198506 BASF SE, Ludwigshafen/Rhein, Germany Fed.Rep. yes Unpublished	Yes	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF
KCP 7.1.4/1	Remmele M.	2017a	BAS 684 03 H - In vitro skin irritation and corrosion Turnkey testing strategy 2017/1194114 BASF SE, Ludwigshafen/Rhein, Germany Fed.Rep. yes Unpublished	No	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF
KCP 7.1.4/2	[redacted]	2017c	BAS 684 03 H - Acute dermal irritation / corrosion in rabbits 2017/1154822	Yes	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
			[redacted] yes Unpublished				
KCP 7.1.5/1	Remmele M.	2017 b	BAS 684 AL H - EpiOcular eye irritation test 2016/1193048 BASF SE, Ludwigshafen/Rhein, Germany Fed.Rep. yes Unpublished	No	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF
KCP 7.1.5/2	Remmele M.	2018 a	Amendment No. 1 to the report - BAS 684 AL H - EpiOcular eye irritation test 2018/1067901 BASF SE, Ludwigshafen/Rhein, Germany Fed.Rep. yes Unpublished	No	Yes	Data for first approva	BASF
KCP 7.1.5/3	[redacted]	2017 a	BAS 684 AL H - Acute eye irritation in rabbits 2016/1345293 [redacted] yes Unpublished	Yes	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF
KCP 7.1.5/4	[redacted]	2017 b	Amendment No. 1 to the report - BAS 684 AL H - Acute eye irritation in rabbits 2017/1012902 [redacted] yes Unpublished	Yes	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF

Data Point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Data protection claimed Y/N	Justification if data protection is claimed	Owner
KCP 7.1.6/1	[redacted]	2017 d	BAS 684 03 H - BUEHLER test in guinea pigs 2017/1161446 [redacted] yes Unpublished	Yes	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF
KCP 7.3/1	Fabian E., Landsiedel R.	2017	14C-BAS 684 H in BAS 684 03 H - Study of penetration through human skin in vitro 2017/1137741 BASF SE, Ludwigshafen/Rhein, Germany Fed.Rep. yes Unpublished	No	Yes	New data eligible for data protection according to SANCO/12576/2012	BASF

B.6.7. REFERENCE LIST

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

California Environmental Protection Agency, Air Resources Board (1998). Report for the application and ambient air monitoring for chlorpyrifos (and the oxon analogue) in Tulare County during spring/summer 1996.

APPENDIX 1: EXPOSURE CALCULATIONS

Estimate 1: EFSA Calculator estimate of exposure for operators applying 'BAS 684 03 H': field crop sprayer; no PPE

Model input

Substance name	BAS 684 H (cinmethylin) 750 g/L	
Product name	BAS 684 03 H	
Reference value non acutely toxic active substance (RVNAS)	0.06	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)	0.21	mg/kg bw/day
Crop type	Cereals	
Substance properties		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Miniumum volume water for application (liquids)	100	L/ha
Maximum application rate of active substance	0.5	kg a.s. /ha
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.40%	
Dermal absorption of in-use dilution	22.00%	
Oral absorption of active substance	100.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	moderately volatile substances with a vapour pressure between 5*10-3Pa and 10-2Pa	
Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Buffer strip	2-3	m
Number of applications	1	
Interval between multiple applications	365	days
Season (upward spraying orchards only)	not relevant	

Operator exposure for BAS 684 03 H outdoor spray applications

Application rate of active substance	0.5	kg a.s./ha	*i AppRate*
Assumed area treated	50	ha/day	*d AreaTreated*
Amount of active substance applied	25	kg a.s./day	*i AmoutAS*
Dermal absorption of the product	0.40%		*i AbsorpProduct*
Dermal absorption of in-use dilution	22.00%		*i AbsorInuse*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		
Indoor or Outdoor application	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Season	not relevant		

Outdoor/Soluble concentrates, emulsifiable concentrate, etc/Downward spraying/Vehicle-mounte

	Exposure values	µg exposure/day mixed and loaded		Reference	Comment
		75th centile	95th centile		
Mixing and loading	Hands	57881	218196	AOEM	
	Body	34276	183491	AOEM	
	Head	1297	7114	AOEM	
	Protected hands (gloves)	280	4952	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	412	3656	AOEM	
	Protected head (hood and face shield)	21	403	AOEM	
	Inhalation	10	31	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Water soluble bag	No		1	

	Exposure values	µg exposure/day applied		Reference	Comment
		75th centile	95th centile		
Application	Hands	3708	24212	AOEM	
	Body	2073	10688	AOEM	
	Head	98	296	AOEM	
	Protected hands (gloves)	243	4851	AOEM	
	Protected body (workwear or protective garment and sturdy footwear)	57	139	AOEM	
	Inhalation	5	19	AOEM	
	Protective Equipment	Select for inclusion		Penetration factor	Inhalation Protection factor
	Gloves	No			
	Clothing	Work wear - arms, body and legs covered		incl. in AOEM model	
	Head and respiratory PPE	None		1	1
	Closed cab	No		vehicle mounted upward spraying	

1. Total

	Without RPE/PPE	With RPE/PPE
Longer term		
Total systemic exposure from mixing, loading and application (mg a.s./day)	1.6821235	1.1030528
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0280354	0.0183842
% of RVNAS	46.73%	30.64%
Acute		
Total systemic exposure from mixing, loading and application (mg a.s./day)	9.4276712	6.3876881
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.1571279	0.1064615
% of RVAAS	74.82%	50.70%

Estimate 2: EFSA Calculator estimate of longer term exposure to residents

Resident exposure for BAS 684 03 H

Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Buffer strip	2-3	m
Application rate of the product	0.5	kg a.s./ha
Concentration of active substance (in-use dilution for liquid applications)	5	g a.s./l
Dermal absorption of product	0.40%	
Dermal absorption of in-use dilution	22.00%	
Oral absorption	100.00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	1.5	µg a.s./cm²
Vapour pressure of in-use dilution	moderately volatile substances with a vapour pressure between 5*10-3Pa and 10-2Pa	Pa
Concentration in air	0.015	mg/m³
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person
Exposure duration dermal	2	hours
Exposure duration inhalation	24	hours
Exposure duration entry into treated crops	0.25	hours
Light clothing adjustment factor	18.0%	
Breathing rate adult	0.23	m³/day/kg
Breathing rate child (1-3 year old)	1.07	m³/day/kg
Drift percentage on surface (75th percentile)	5.60%	
Drift percentage on surface (mean)	4.10%	
Turf transferable residues percentage	5.00%	
Transfer coeff. of surface deposits-adult	7300	cm²/hour
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm²/hour
Saliva extraction percentage	50.00%	
Surface area of hands mouthed	20	cm²
Frequency of hand to mouth activity	9.5	events/hour
Ingestion rate for mouthing of grass per day	25	cm²
Dislodgeable residues percentage transferability for object to mouth	20.00%	
Transfer coefficient for entry into treated crops (75th percentile) - adult	7500	cm²/h
Transfer coefficient for entry into treated crops (75th percentile) - child	2250	cm²/h
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm²/h
Transfer coefficient for entry into treated crops (mean) - child	1794	cm²/h

1. Total

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.2960540	0.1605000	0.0200760	0.1856250	0.4864135
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0296054	0.0160500	0.0020076	0.0185625	0.0486414
% of RVNAS	49.34%	26.75%	3.35%	30.94%	81.07%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.4244400	0.2070000	0.0449680	0.6187500	0.9350314
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0070740	0.0034500	0.0007495	0.0103125	0.0155839
% of RVNAS	11.79%	5.75%	1.25%	17.19%	25.97%

Estimate 3: EFSA Calculator estimate of acute exposure to bystanders

Bystander exposure for BAS 684 03 H

Croptype	Cereals	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Application rate of the product	0.5	kg a.s./ha
Buffer strip	2-3	m
Concentration of active substance (in-use dilution for liquid applications)	5	g a.s./l
Dermal absorption of product	0.40%	
Dermal absorption of in-use dilution	22.00%	
Oral absorption	100.00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	1.5	µg a.s./cm²
Vapour pressure of in-use dilution	moderately volatile substances with a vapour pressure between 5*10-3Pa and 10-2Pa	Pa
Concentration in air	0.015	mg/m³
Bystander dermal spray drift exposure - adult	1.21	ml spray dilution/person
Bystander dermal spray drift exposure - child	0.74	ml spray dilution/person
Bystander inhal. spray drift exposure - adult	0.00050	ml spray dilution/person
Bystander inhal. spray drift exposure - child	0.00112	ml spray dilution/person
Exposure duration	2	hours
Exposure duration entry into treated crops	0.25	hours
Light clothing adjustment factor	18.0%	
Breathing rate adult	0.23	m³/kg bw/day
Breathing rate child (1-3 year old)	1.07	m³/kg bw/day
Drift percentage on surface (90th percentile)	8.50%	
Turf transferable residues percentage	5.00%	
Transfer coeff. of surface deposits-adult	14500	cm²/hour
Transfer coeff. of surface deposits-child (1-3 year old)	5200	cm²/hour
Saliva extraction percentage	50.00%	
Surface area of hands mouthed	20	cm²
Frequency of hand to mouth activity	20	events/hour
Ingestion rate for mouthing of grass per day	25	cm²
Dislodgeable residues percentage transferability for object to mouth	20.00%	
Transfer coefficient for entry into treated crops - adult	7500	cm²/h
Transfer coefficient for entry into treated crops - child	2250	cm²/h

1. Total

1.1 1-3 year old child

	Spray drift	Vapour	Surface deposits	Entry into treated crops
Total systemic exposure (mg a.s./day)	0.6730800	0.1605000	0.0592450	0.1856250
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0673080	0.0160500	0.0059245	0.0185625
% of RVAAS	32.05%	7.64%	2.82%	8.84%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops
Total systemic exposure (mg a.s./day)	1.0939200	0.2070000	0.1355750	0.6187500
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0182320	0.0034500	0.0022596	0.0103125
% of RVAAS	8.68%	1.64%	1.08%	4.91%

Estimate 4: EFSA Calculator estimate of longer term exposure to workers

Worker exposure from residues on foliage for BAS 684 03 H

Crop type	Cereals	
Indoor or outdoor	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Worker's task	Inspection, irrigation	
Main body parts in contact with foliage	Hand and body	
Application rate of active substance	0.5	kg a.s./ha
Number of applications	1	
Interval between multiple applications	365	days
Half-life of active substance	30	days
Multiple application factor	1.0	
Dermal absorption of the product	0.40%	
Dermal absorption of the in-use dilution	22.00%	
Dislodgeable foliar residue (i_AppRate*i_DFR)	1.5	µg a.s./cm^2
Working hours	2	hr
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves
Total systemic exposure (mg a.s./day)	8.2500000	0.9240000	no TC available for this assessment
Total systemic exposure per kg body weight (mg/kg bw/day)	0.1375000	0.0154000	
% of RVNAS	229.17%	25.67%	