Section A5 (Annex Point)

Effectiveness against target organisms and intended uses

Official use only

5.3 Effects on target organisms, and likely concentration at which the active substance will be used (IIA5.3)

References:

A5.3/01:

Fisher, J.P., Robinson, J., Debray, P.H. (1983): WL85871 – A new multipurpose insecticide. Proceedings of 10th International Congress of Plant Protection, Brighton, England, 20–25 November 1983, Vol. 1, pp 452–459 (published), BASF DOC ID: 1983/1002038.

Alphacypermethrin (identified by its development code WL85871) has been evaluated as insecticide, for non-crop uses, in tests carried out by tropical applications against a range of representative species (*Aedes aegypti*, *Musca domestica*, *Blatella germanica* and *Periplaneta Americana*) :

Mean LD_{50} (24h) ≤ 0.48 µg/g insect varying by species (Mean LD_{50} (24h) ≥ 1.1 µg/g insect with other active substances).

An additional example of efficacy after surface treatment on *M.domestica*, is reported : 100 % mortality was achieved for a period of 24 days after application of a 50 g a.i./kg product (wettable powder formulation) at an application rate of 0.01 g a.i./m².

Alphacypermethrin is a fast acting insecticide, active at very low rates compared to other active substances against some crawling and flying insects.

A5.3/02:

Jung, R. (2008): Biological test report: Insecticide efficacy of Fendona SC, various surfaces, several test insects. BioGenius GmbH, Bergisch Gladbach, Germany, report no. Bio035/08, May 15, 2008 (unpublished), BASF DOC ID: 2008/1032683.

Efficacy tests with Alphacypermethrin,(in Fendona SC formulation, containing 60 g a.i./L) against 2 cockroach species (*Blattella germanica* and *Periplaneta americana*, at 5th larval stage):

A. Residual efficacy:

For both cockroach species: 100% Knock-down/mortality is achieved up to 2 weeks within 2h (on glazed tiles and plywood). Longer time is needed on PVC. Control mortality was invariably 0 %.

B. Efficacy of freshly treated surfaces (still moist):

For both cockroach species: 100% KO/mortality is achieved within 2h.

A5.3/03:

Lüpkes, K.-H. (2008): Residual efficacy of various products: Residual efficacy of products based on various actives against cat fleas and bed bugs. BioGenius GmbH, Bergisch Gladbach, Germany, report no. BIO055/08, August 13, 2008 (unpublished), BASF DOC ID: 2008/1052708.

Efficacy tests with Alphacypermethrin,(in Fendona SC formulation, containing 60 g a.i./L) against cat fleas (*Ctenocephalides felis*) : On carpets, 100% KO is achieved within 8h and up to 3 weeks. On fabric, alpha-cypermethrin has a lower effectiveness but still acceptable.

5.3.1 Effects on target organisms

Alphacypermethrin provides rapid knock-down and kill of insect imagos. The affected insect shows uncoordinated movements and finally dies.

In general, excellent efficacy of Alphacypermethrin against the specified target insects is demonstrated by the above references, extensively summarised in Table A5-1 below. However, residual efficacy against cat fleas on carpet or fabric is slightly reduced, nevertheless still resulting in 100 % knock-down on carpet up to three weeks and 80–90 % on fabric. This may still be regarded as good or very good performance.

Section A5 Effectiveness against target organisms and intended uses
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5.3.2	Likely concentrations at which the A.S. will be used	
	PT 18	Concentration of Alphacypermethrin in the representative biocidal product: 30 g/l. 25–50 mL b.p. diluted in 5 l water give the application solution, resulting in a final application concentration of 150–300 mg a.s./l (0.5–1.0 % b.p, v/v).
5.4	**Mode of action (including time delay) (IIA5.4)**	**References:** **A5.4/01:** van Heemstra-Lequin EAH, van Esch GT (1992) Alphacypermethrin. Environmental Health Criteria 142, WHO ICPS, Geneva, Switzerland (published), BASF RDI No.: AL-901-012. **A5.4/02:** Tomlin C (1994) Alphacypermethrin. In: The Pesticide Manual, 10th Edition, BCPC, Farnham, UK (published), BASF RDI No.: AL-905-069.
5.4.1	Mode of action	Alphacypermethrin is a synthetic pyrethroid and as such does not depend on conversion or degradation to an active form in order to exert its insecticidal activity. It acts by preventing transmission of impulses along nerves. This effect is brought about by blocking the passage of positive sodium ions through sodium channels in nerve membranes, thus preventing action potentials passing down axons. Typically, this intoxication results in a rapid "knockdown" and resultant mortality.
5.4.2	Time delay	Rapid knockdown and death upon contact or ingestion.
5.5	**Field of use envisaged (IIA5.5)**	
	MG03: Pest control	PT 18
	Further specifications	Insecticide for domestic and public hygiene (indoor use)
5.6	**User (IIA5.6)**	
	Industrial	Not envisaged
	Professional	Pest controls operators (PCOs): Application to hard surfaces, cracks and crevices, areas behind furnishings and equipment etc. by low-pressure spraying (< 2 bar).
	General public	Not envisaged

Section A5 **Effectiveness against target organisms and intended uses**
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5.7	**Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies (IIA5.7)**	
5.7.1	Development of resistance	Resistance to pyrethroids has been reported for a number of pests in Europe and around the world. A comprehensive summary of these reported cases of resistance is provided by the Insecticide Resistance Action Committee's (IRAC) resistance database, available online at http://www.pesticideresistance.org/DB. In the version of this database (updated 2004-10-08, accessed 2005-12-02) relevant at the time of original submission of this dossier (April 2006), three insect species exhibiting specific resistance to Alphacypermethrin, all of them agricultural pests, were recorded. For the current dossier amendment, the resistance database lists five insect species with known resistance, all of them agricultural pests, i.e. *Aphis gossypii* (melon and cotton aphid), *Bactrocera oleae* (olive fruit fly), *Bemisia tabaci* (sweetpotato whitefly), *Halotydeus destructor* (redlegged earth mite), and *Helicoverpa armigera* (cotton bollworm). For details see Figure A5- 1 below. According to this permanently updated source, the target insects in domestic and public pest control (cockroaches and fleas, see 5.2.1 above) are to date not affected by resistance to Alphacypermethrin. Furthermore, a recent literature search (Appendix 1 to Doc. III-A) revealed no relevant information about resistance of the target organisms as specified under 5.2.1 above, i.e. cockroaches and fleas. The mechanisms of development of resistance against pyrethroids like Alphacypermethrin in insects in general can be discussed as follows (according to the results of the literature search): Activities of esterase (Est) and glutathione S-transferase [glutathione transferase] (GST) in resistant strains of the green peach aphid (*Myzus persicae*) were significantly higher than in susceptible strains (see pp 21–22 of the literature search). In mosquitoes of the genera *Anopheles* and *Culex*, selection for a "kdr-allele" was identified to potentially confer resistance to Alphacypermethrin (p. 13 of the literature search). In conclusion, pyrethroid resistance appears to be a consequence of the overproduction of esterase isoenzymes. This is supported by a study on enzyme activity in dependence of Alphacypermethrin concentration, showing a "positive relationship between concentrations of Alphacypermethrin and inhibiting time effect on acetylcholinesterase (AChE) activities of *Blattella germanica* (susceptible) in 144 h and mortality rate of *B. germanica* in 72 h. It is concluded that AChE activity may be one of the indices for determining resistance to pyrethroid insecticides" (p. 21–22 of the literature search). *Culex pipiens pallens* of a permethrin-resistant strain was found to

Section A5 **Effectiveness against target organisms and intended uses**
(Annex Point)

			Official use only
		exhibit cross resistance to deltamethrin and Alphacypermethrin (p. 20 of the literature search). **Conclusion:** Development of resistance against Alphacypermethrin is in principle possible in a wide range of insect taxa. Due to the common mode of action of pyrethroids cross-resistance may be of importance. However, actual resistance (including cross-resistance) has to date only been observed in agricultural pest insects, which are the targets of large-scale applications of insecticides, thus increasing the likelihood of resistance development. Biocidal treatments, in contrast, are typically targeted on relatively small populations of pest insects forming more or less closed populations. Good treatment practice will most likely results in high control levels which in turn reduces the likelihood of resistance development. In the literature search, *Blattella germanica* is identified as susceptible to Alphacypermethrin, with no indications of resistance (p. 70 of the literature search). Any records related to *Periplaneta americana* or to fleas (Siphonaptera) were not identified by the literature search. This suggests that both the American cockroach and the whole order of fleas (Siphonaptera) resistance has to date not been detected. In conclusion, resistance against Alphacypermethrin has to date not been observed in the organisms to be controlled (cockroaches, fleas), and the probability of development of resistance currently appears to be low.	
5.7.2	Management strategies	Whilst resistance has occurred and is a real problem in agricultural use, its expression is by no means uniform. The continued threat of resistance must be managed in order to prevent its build in species where it has already developed and in order to minimise the risk of resistance developing in species which have not yet developed resistance to the synthetic pyrethroids. For this reason, strategies such as alteration of insecticides with different modes of action, mixtures of insecticides with different modes of action and avoidance of frequent and repeated use are standard practice.	
5.8	**Likely tonnage to be placed on the market per year (IIA5.8)**	Data on produced/ imported tonnages are considered to be commercially sensitive and are therefore to be treated as CONFIDENTIAL. These data are provided separately in Appendix 1 to Document III-A (confidential information).	

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	*17/12/2013*
Materials and methods	The efficacy against cockroaches and fleas are supported by recent laboratory test performed in 2008 (Studies A5.3/02 and A5.3/03). 15 × 15 cm tiles made of PVC, plywood, or glazed tiles (for efficacy tests against cockroaches - *Blattella germanica* and *Periplaneta americana,* at 5th larval stage) and made of carpet or fabric tiles (for efficacy tests against cat fleas - *Ctenocephalides felis*) were treated with the product at rate of 50 mL/m² (= 15 mg a.i./m²) applied by spraying. Residual efficacy and mortality is observed.
Results and discussion	With *Blattella germanica*, on freshly treated **(15 mg a.i./m²)** surfaces , 100% mortality was achieved in 18,5 min on non-porous surfaces and in 1h13 on porous surfaces. *Blattella germanica* seems to be more resistant than *Periplaneta Americana.* With Ctenocephalides felis,on carpet and fabric treated with 15 mg a.i./m², 100% mortality was achieved within 8h up to 3 weeks.
Conclusion	Clear evidences are presented for the efficacy of AlphaCypermethrin against cockroaches and fleas. This test demonstrates a good efficacy of AlphaCypermethrin at an application rate of 50 mL/m² (= 15 mg a.i./m²) applied by spraying. More efficacious activity is achieved on non-porous surfaces.
Reliability	2
Acceptability	Acceptable
Remarks	The first study, based on the product WL85871, suggested that alpha-cypermethrin is effective against *Blattella germanica* and *Periplaneta Americana.* But, due to insufficient information on the methodology, this study not a key study for this dossier. It's an old and sparsely documented, publication. Nevertheless, as it's one of the first published records of this new (at that time) insecticide, this information should not be ignored. That's why this information was reported for a purpose of clarity.
	COMMENTS FROM ... ***(specify)***
Date	*Give date of comments submitted*
Comments	*Discuss if deviating from view of rapporteur member state*
Summary and conclusion	*Discuss if deviating from view of rapporteur member state*

Table A5-1: Summary table of experimental data on the effectiveness of Alphacypermethrin against target organisms. Generally, the substance functions as an insecticide (PT 18) and the envisaged field of use is pest control (MG 03).

Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference
Alphacypermethrin (identified by its development code WL85871)	*Aedes aegypti*, ad. ♀♀ *Musca domestica*, ad. ♀♀ *Blatella germanica*, ad. ♂♂ *Periplaneta americana*, final instar nymphs Furthermore, a wide range of agricultural pest insects were tested which are, however, omitted from this summary for lack of relevance in a biocidal context.	LD_{50} tests by topical application	Only the tests against non-crop pest insects are summarised here. 24-hour LC_{50} tests by topical application in comparison to other insecticides; no further details were reported.	Mean 24-h LD_{50} [µg/g insect] *A. aegypti* 0.02 *M. domestica* 0.16 *B. germanica* 0.48 *P. americana* 0.26 Mean LD_{50} values for the other active substances permethrin, propoxur, and fenitrothion were in range of 1.1 to 32 µg/g insect, varying by species. As an additional example of efficacy, mortality rates of *M. domestica* on mortar 1, 3, 7, 14, 24, 38, 59, and 87 days after surface treatment using a wettable powder (w.p.) formulation at an application rate of 0.01 g a.i./m² were reported. 100 % mortality was achieved for a period of 24 days after application of a 50 g a.i./kg product formulation, and over 14 days (except 90 % mortality after 7 days) after application of a 200 g a.i./kg product formulation. Alphacypermethrin was superior compared to Cypermethrin (0.1 g a.i./m²), Permethrin (0.1 g a.i./m²), Deltamethrin (0.03 g a.i./m²) and Fenitrothion (0.1 g a.i./m²) applied as the same formulation type (w.p.), respectively.	A5.3/01

(continued on next page)

Table A5-1: Summary table of experimental data on the effectiveness of Alphacypermethrin against target organisms. Generally, the substance functions as an insecticide (PT 18) and the envisaged field of use is pest control (MG 03).

Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference
Alphacypermethrin, in Fendona SC formulation, containing 60 g a.i./L	In the context of the current application only the following two test organisms are summarised: *Blattella germanica*, 5th larval stage *Periplaneta americana*, 5th larval stage Results on *Aedes aegypti*, *Culex quinquefasciatus*, *Musca domestica*, *Lasius niger*, *Lepisma saccarina*, and *Cimex lectularius*, are not referred to, for lack of relevance	15 × 15 cm tiles made of PVC, plywood, or glazed tiles, treated with the product at rate of 50 mL/m² (= 15 mg a.i./m²); application by low-pressure spraying (2.0 bar) from 25–30 cm distance. A) Residual efficacy 1, 2, 3, 4, 8, 15, 22, and 29 days post treatment B) Efficacy of freshly treated surfaces (still moist) Crawling insects like cockroaches were placed on the tiles in talcumed glass rings (Ø 9.5 cm, height 5.5 cm), several rings piled on top of each other if necessary. Mortality (knock-down) observations at A) 15, 30, 60 min, 2, 3, 4, 5, 6 8, 24 and 48 hours. B) Continuously up to 2 hours, then at 24 and 48 hours.	*Temperature:* A) 22–25 °C B) 21–21 °C *Rel. humidity:* A) 70–75 % B) 42–45 % *Light regime:* A) Darkness B) Artificial light/darkness	A) Residual efficacy 100 % knock-down after min/hours (or x % knock-down with mortality 24 h later): *Blatella germanica*: **Days: 1 2 3 4 8 15 22 29** P 2 h 60' 2 h 2 h 4 h 4 h 24 h 80 % 24 h LK 60' 30' 30' 30' 30' 60' 60' 60' H 2 h 60' 60' 60' 60' 2 h 60' 2 h *Periplaneta americana*: **Days: 1 2 3 4 8 15 22 29** P 60' 60' 60' 60' 3 h 24 h 3 h 24 h 80 % LK 60' 30' 30' 60' 60' 2 h 60' 60' H 60' 60' 60' 60' 60' 2 h 60' 60' B) Efficacy of freshly treated surfaces (still moist) Per cent knock-down after hours, minutes, seconds: *Blatella germanica*: **Days: 20 % 100 %** LK 11'40'' 18'30'' H 26'00'' 1h13' *Periplaneta americana*: **Days: 20 % 100 %** LK 5'40'' 13'50'' H 20'00'' 46'00'' Surface codes: P – PVC, LK – glazed tile, H – plywood Control mortality was invariably 0 %.	A5.3/02

(continued on next page)

Table A5-1: Summary table of experimental data on the effectiveness of Alphacypermethrin against target organisms. Generally, the substance functions as an insecticide (PT 18) and the envisaged field of use is pest control (MG 03).

Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference
Alphacypermethrin, in Fendona SC formulation, containing 60 g a.i./L Formulations containing Alphacypermethrin and Flufenoxuron, Deltamethrin, or Chlorpyrifos were tested in parallel; however, the corresponding results are omitted here for lack of relevance	Cat flea (*Ctenocephalides felis*) Bedbug (*Cimex lectularius*); results on this species are, however, not referred to in this summary, for lack of relevance in the context of the current application	15 × 15 cm patches of carpet (velour synthetic) and fabric (cotton), treated with the product at rate of 50 mL/m² (= 15 mg a.i./m²); application by low-pressure spraying (2.0 bar) from 25 cm distance. Residual efficacy 1 day, 1, 2, 3, and 4 weeks post treatment Fleas were placed on the ptaches in talcumed glass rings (Ø 9.5 cm, height 5.5 cm), several rings piled on top of each other if necessary. Mortality (knock-down) observations at 15, 30, 60 min, 2, 3, 4, 5, 6 8, and 24 hours.	*Temperature:* 22–23 °C *Rel. humidity:* 40–50 % *Light regime:* Artificial light, photoperiod 10:14 h (L:D)	100 % knock-down after min/hours (or x % knock-down with mortality 24 h later): *Ctenocephalides felis*: **Time: 1 d 1 wk 2 wk 3 wk 4 wk** CP 8 h 5 h 6 h 6 h 24 h 90 % FB 24 h 90 % 24 h 24 h 80 % 24 h 80 % 24 h 90 % Surface codes: CP – carpet, FB – fabric Control mortality was invariably 0 %.	A5.3/03

(continued on next page)

Table A5-1: Summary table of experimental data on the effectiveness of Alphacypermethrin against target organisms. Generally, the substance functions as an insecticide (PT 18) and the envisaged field of use is pest control (MG 03).

Test substance	Test organism(s)	Test method	Test conditions	Test results: effects, mode of action, resistance	Reference
~~Tenopa SC, biocidal product containing 30 g/L Alphacypermethrin and 30 g/L Flufenoxuron~~	~~In the context of the current application only the following two test organisms are summarised:~~ ~~*Blattella germanica*, 5th larval stage~~ ~~*Periplaneta americana*, 5th larval stage~~ ~~Results on *Aedes aegypti*, *Culex quinquefasciatus*, *Musca domestica*, *Lasius niger*, *Lepisma saccarina*, and *Cimex lectularius*, are not referred to, for lack of relevance~~	~~15 × 15 cm tiles made of PVC, plywood, or glazed tiles, treated with the product at rate of 50 mL/m² (= 7.5 +7.5 mg a.i./m²); application by low-pressure spraying (2.0 bar) from 25–30 cm distance.~~ ~~A) Residual efficacy 1, 2, 3, 4, 8, 15, 22, and 29 days post treatment~~ ~~B) Efficacy of freshly treated surfaces (still moist)~~ ~~Crawling insects like cockroaches were placed on the tiles in talcumed glass rings (Ø 9.5 cm, height 5.5 cm), several rings piled on top of each other if necessary.~~ ~~Mortality (knock-down) observations at~~ ~~A) 15, 30, 60 min, 2, 3, 4, 5, 6 8, 24 and 48 hours.~~ ~~B) Continuously up to 2 hours, then at 24 and 48 hours.~~	~~*Temperature:*~~ ~~A) 22–25 °C~~ ~~B) 21–21 °C~~ ~~*Rel. humidity:*~~ ~~A) 70–75 %~~ ~~B) 42–45 %~~ ~~*Light regime:*~~ ~~A) Darkness~~ ~~B) Artificial light/darkness~~	~~The current study reports residual insecticidal efficacy and speed of knock-down of Alphacypermethrin in combination with Flufenoxuron. Due to the limited relevance for evaluation of Alphacypermethrin the results are only briefly summarised as follows:~~ ~~*Blatella germanica*:~~ ~~Duration of efficacy (100 % mortality): 2 to > 4 weeks~~ ~~Degree of speed (to achieve 100 %): 30' - 5 h~~ ~~*Periplaneta americana*:~~ ~~Duration of efficacy (100 % mortality): 3 d to > 4 weeks~~ ~~Degree of speed (to achieve 100 %): 30' - 24 h~~	A5.3/04

Search, Active Ingredient Profile http://www.pesticideresistance.org/search/22/92/

cypermethrin-alpha

Profile

MOA: Sodium channel modulators, Pyrethroids, Pyrethrins, DDT

Group: PYR **CAS #:** 67375308 **Shaugnessy Code:** 209600

Reported Resistance

Species	Order	Family	Common Name(s)	Group	Host
aphis gossypii	homoptera	aphididae	melon and cotton aphid	AG	cotton, vegetables
bactrocera oleae	diptera	tephritidae	Olive Fruit Fly	AG	Olives
bemisia tabaci	homoptera	aleyrodidae	sweetpotato whitefly	AG	cotton
halotydeus destructor	acari	pentatomidae	redlegged earth mite	AG	
helicoverpa armigera	lepidoptera	noctuidae	cotton bollworm	AG	cotton, corn, sorghum, tomato

Other Reference

Google Search for cypermethrin-alpha

Figure A5- 1: Results of a recent search for resistance to Alphacypermethrin in the pesticide resistance database.

Section A6.1.1 Acute oral toxicity in rats

Annex Point IIA 6.1.1

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.1/01:** [redacted] (1993) FASTAC technical: Acute oral and dermal toxicity in rat, skin and eye irritancy in rabbit and skin sensitisation potential in Guinea pig. [redacted], Report no. SBTR.92.033, April 01, 1993 (unpublished), BASF RDI No.: AL-410-003.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes EC method B.1 (84/449/EC)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	As given in Section A2.
3.1.1	Lot/Batch number	02156
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Off white powder
3.1.4	Purity	95.6%
3.1.5	Stability	Stable for the duration of the study.
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain / Stock	Crl: CD.BR
3.2.3	Source	Charles River, U.K.
3.2.4	Sex	Male and female
3.2.5	Age	5–6 weeks

Section A6.1.1 Acute oral toxicity in rats

Annex Point IIA 6.1.1

3.2.6	Weight at study initiation	Males (day 1): 177–239 g Females (day 1): 130–187 g
3.2.7	Number of animals per group	5 males and 5 females per group
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Oral
3.3.1	Post-exposure period	14 days
3.3.2	Type	Gavage
3.3.3	Concentration	33, 46, 64, 90 and 126 mg/kg bw
3.3.4	Vehicle	Corn oil
3.3.5	Concentration in vehicle	Not stated.
3.3.6	Total volume applied	10 mL/kg
3.3.7	Controls	None
3.4	**Examinations**	
3.4.1	Mortality	Observation up to 14 days after treatment.
3.4.2	Clinical signs	Observations were made at least 8 times on the day of dosing and twice daily thereafter for the remainder of the 14 day observation period.
3.4.3	Body weights	The body weight of each animal was recorded the initial day (day 1), day 8 and day 15 of the study.
3.4.4	Macroscopical findings	At the end of the study on day 15.
3.5	**Method of determination of LD_{50}**	Calculation using a method based on probit analysis (Finney, 1977).
3.6	**Further remarks**	None

Section A6.1.1 **Acute oral toxicity in rats**
Annex Point IIA 6.1.1

4 RESULTS

4.1	**Clinical signs**	Mortalities occurred between four hours after dosing and day 3. There were deaths among rats dosed at 46 mg/kg and at all higher dose levels. All rats receiving 126 mg/kg bw Alphacypermethrin died. Hunched posture, piloerection, diarrhoea, an unkempt appearance and staining (yellow) of the anogenital fur were common clinical signs at all dose levels. The female decedent dosed at 46 mg/kg b.w. and the majority of the rats treated at higher dose levels developed a splayed gait, trashing and a bloody discharge from the mouth and nose. Those rats dosed at 64 mg/kg bw and above commonly showed twitching, tremor fasciculations, convulsions, vasodilatation and salivation. Other overt responses to treatment included pallor of the eyes, especially among rats dosed 126 mg/kg bw, and isolated cases of lachrymation, chromodacryorrhoea, lethargy, abasia, vocalisation (distressed noises), hypothermia, cyanosis, bradypnoea and prostration. These latter clinical signs were generally apparent in animals that died shortly afterwards. Results see table Table A6.1.1- 1.
4.2	**Pathology**	Examination at necropsy of the decedents revealed to pallor or a darkened appearance of the liver, kidneys and spleen, lung congestion and abnormal contents (gaseous or yellow liquid) of the stomach and small intestines. Two female rats dosed at 33 mg/kg bw and killed at the end of the study showed pallor of the liver. No other macroscopic changes were apparent during necropsy.
4.3	**Other**	All rats had gained weight relative to their day 1 bodyweights by the end of both the first and second weeks of the 14 day observation period.
4.4	**LD_{50}**	Males: 57 mg/kg bw (95% CI = 36–81 mg/kg bw) Females: 71 mg/kg bw (95% CI = 58–87 mg/kg bw) Combined: 64 mg/kg bw (95% CI = 53–77 mg/kg bw)

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute oral toxicity of Alphacypermethrin was tested in rats according to EC method B.1 (84/449/EC). Groups of 5 male and 5 female rats received 33, 46, 64, 90 and 126 mg/kg bw of test substance by gavage. After exposure the animals were observed for 14 days.
5.2	**Results and discussion**	The acute oral LD_{50} of Alphacypermethrin in rats (male and female) was 64 mg/kg bw (95% CI = 53–77 mg/kg bw). Thus, according to the requirements specified by Directive 67/548/EC and subsequent regulations, Alphacypermethrin requires classification with the symbol "T" and with R25 "toxic if swallowed" (LD_{50}, oral, rat; 25 < $LD_{50} \leq 200$ mg/kg).

Section A6.1.1 **Acute oral toxicity in rats**
Annex Point IIA 6.1.1

5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Ad 5.1. it should have been mentioned that the test material was dispersed in corn oil and administered by oral gavage at 10 ml/kg Applicant's version adopted
Results and discussion	
Conclusion	LD_{50} = 57 mg/kg in rats
Reliability	acceptable
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A6.1.1- 1: Acute toxicity in rats.

Group	Dose level [mg/kg]	Mortalities			Time of death	Observation
		Males	Females	Total		
1	33	0/5	0/5	0/10	–	Lethargy, hunched posture, pallor of eyes, piloerection, diarrhoea, unkempt appearance, anogenital fur stained yellow, swollen jaw/snout.
2	46	3/5	1/5	4/10	Day 1 to 2	Trashing, abasia, splayed gait, lethargy, hunched posture, piloerection, diarrhoea, unkempt appearance, bloody discharge around mouth, epistaxis, cyanosis, hypothermia, anogenital fur stained yellow.
3	64	3/5	0/5	3/10	Day 2 to 3	Convulsion, fasciculations, tremors, twitching, prostrate able to move, trashing, abasia, splayed gait, hunched posture, salivation, lachrymation, pallor of eyes, piloerection, diarrhoea, unkempt appearance, chromodacryorrhea, bloody discharge around mouth, epistaxis, vasodilatation, anogenital fur stained yellow
4	90	3/5	5/5	8/10	Day 1 to 2	Clonic convulsion, convulsion, fasciculations, tremors, twitching, prostrate able to move, trashing, abasia, splayed gait, vocalisation, hunched posture, salivation, lachrymation, pallor of eyes, piloerection, diarrhoea, unkempt appearance, chromodacryorrhea, bloody discharge around mouth, epistaxis, cyanosis, bradypnoea, vasodilatation, anogenital fur stained yellow.
5	126	5/5	5/5	10/10	Day 1 to 2	Clonic convulsion, convulsion, fasciculations, twitching, trashing, splayed gait, vocalisation,hunched posture, salivation, pallor of eyes, piloerection, diarrhoea, unkempt appearance, bloody discharge around mouth, epistaxis, cyanosis, vasodilatation, anogenital fur stained yellow.

Section A6.1.1 **Acute oral toxicity in rats**
Annex Point IIA 6.1.1

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.1/02:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute oral toxicity study in rats. [redacted] Report no.: 10A0563/041083, May 18, 2005 (unpublished), BASF Doc-ID: 2005/1011568.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 423 (2001) EC B.1 tris (2004) OPPTS 870.1100 (2002)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000166
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Solid white powder
3.1.4	Purity	99.3%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain / Stock	Wistar/ HanRcc:WIST(SPF)
3.2.3	Source	RCC Ltd Laboratory Animal Services, Füllinsdorf, Switzerland
3.2.4	Sex	Female

Section A6.1.1 Acute oral toxicity in rats

Annex Point IIA 6.1.1

3.2.5	Age	8–12 weeks
3.2.6	Weight at study initiation	Mean body weights (day 0): 172–188 g
3.2.7	Number of animals per group	Groups of 3 females at 50 and 300 mg/kg bw 2 groups (total 6 animals) at 2,000 mg/kg bw
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Oral
3.3.1	Post-exposure period	14 days
3.3.2	Type	Gavage
3.3.3	Concentration	50, 300, 2,000 mg/kg bw
3.3.4	Vehicle	0.5% CMC-solution (cleaned sodium carboxymethylcellulose)
3.3.5	Concentration in vehicle	0.5, 3 and 20 g/100 mL The correctness of the concentration of the test substance preparation in the vehicle for the first administration was confirmed by analysis.
3.3.6	Total volume applied	10 mL/kg
3.3.7	Controls	None
3.4	**Examinations**	
3.4.1	Mortality	A check for any dead or moribund animal was made twice each workday and once on Saturdays, Sundays and on public holidays.
3.4.2	Clinical signs	Observations were made several times on the day of administration and thereafter at least once each workday for the remainder of the 14 day observation period.
3.4.3	Body weights	The individual body weights were recorded shortly before administration (day 0), weekly thereafter and at the end of the study.
3.4.4	Macroscopical findings	Necropsy with gross-pathology examination on the last day (day 14) of the observation period.
3.5	**Method of determination of LD_{50}**	Classification according to the globally harmonized classification system (GHS).
3.6	**Further remarks**	None

Section A6.1.1 **Acute oral toxicity in rats**
Annex Point IIA 6.1.1

4 RESULTS

4.1	**Clinical signs**	No mortalities occurred in the administration groups. No clinical signs were observed.
4.2	**Pathology**	No macroscopic pathologic abnormalities were noted in the treated animals.
4.3	**Other**	Over the study period all rats gained weight relative to their individual body weights at day 0.
4.4	**LD_{50}**	LD_{50} > 2,000 mg/kg bw

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute oral toxicity of Alphacypermethrin was tested in female Wistar rats according to OECD 423 (2001), EC B.1 tris (2004) and OPPTS 870.1100 (2002). Groups of 3 female rats received 50 and 300 mg/kg bw and 6 females were administered 2,000 mg /kg bw of test substance by gavage. After exposure the animals were observed for 14 days. No deviations from the methods prescribed by the guidelines were reported.
5.2	**Results and discussion**	Administration of the test material moistened with 0.5% CMC-solution caused no mortality among the test animals. Under the conditions of this study the acute oral LD_{50} of Alphacypermethrin was found to be greater than 2,000 mg/kg bw in rats.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Applicant's version adopted
Results and discussion	Applicant's version adopted
Conclusion	LD_{50} > 2000 mg/kg $_{bw}$ in rats
Reliability	acceptable
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A6.1.1 **Acute oral toxicity in rats**
Annex Point IIA 6.1.1

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.1/03:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute oral toxicity study in rats. [redacted] Report no.: 10A0562/041081, May 20, 2005 (unpublished), BASF Doc-ID: 2005/1011604.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 423 (2001) EC B.1 tris (2004) OPPTS 870.1100 (2002)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000165
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Solid white powder
3.1.4	Purity	98.8%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain / Stock	Wistar/ HanRcc:WIST(SPF)
3.2.3	Source	RCC Ltd Laboratory Animal Services, Füllinsdorf, Switzerland
3.2.4	Sex	Female

Section A6.1.1 Acute oral toxicity in rats

Annex Point IIA 6.1.1

3.2.5	Age	8–12 weeks
3.2.6	Weight at study initiation	Mean body weights (day 0): 178–185g
3.2.7	Number of animals per group	Groups of 3 females at 50 and 300 mg/kg bw 2 groups (total 6 animals) at 2,000 mg/kg bw
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Oral
3.3.1	Post-exposure period	14 days
3.3.2	Type	Gavage
3.3.3	Concentration	50, 300, 2000 mg/kg bw
3.3.4	Vehicle	0.5% CMC-solution (cleaned sodium carboxymethylcellulose)
3.3.5	Concentration in vehicle	0.5, 3 and 20 g/100 mL The correctness of the concentration of the test substance preparation in the vehicle for the first administration was confirmed by analysis.
3.3.6	Total volume applied	10 mL/kg
3.3.7	Controls	None
3.4	**Examinations**	
3.4.1	Mortality	A check for any dead or moribund animal was made twice each workday and once on Saturday, Sundays and on public holidays.
3.4.2	Clinical signs	Observations were made several times on the day of administration and thereafter at least once each workday for the remainder of the 14 day observation period.
3.4.3	Body weights	The individual body weights were recorded shortly before administration (day 0), weekly thereafter and at the end of the study.
3.4.4	Macroscopical findings	Necropsy with gross-pathology examination on the last day (day 14) of the observation period.
3.5	**Method of determination of LD_{50}**	Classification according to the globally harmonized classification system (GHS).
3.6	**Further remarks**	None

Section A6.1.1 **Acute oral toxicity in rats**
Annex Point IIA 6.1.1

4 RESULTS

4.1	**Clinical signs**	No mortalities occurred in the administration groups. No clinical signs were observed.
4.2	**Pathology**	No macroscopic pathologic abnormalities were noted in the treated animals.
4.3	**Other**	Over the study period all rats gained weight relative to their individual body weights at day 0.
4.4	**LD_{50}**	LD_{50} > 2,000 mg/kg bw

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute oral toxicity of Alphacypermethrin was tested in female Wistar rats according to OECD 423 (2001), EC B.1 tris (2004) and OPPTS 870.1100 (2002). Groups of 3 female rats received 50 and 300 mg/kg bw and 6 females were administered 2,000 mg /kg bw of test substance by gavage. After exposure the animals were observed for 14 days. No deviations from the methods prescribed by the guidelines were reported.
5.2	**Results and discussion**	Administration of the test material moistened with 0.5% CMC-solution caused no mortality among the test animals. Under the conditions of this study the acute oral LD_{50} of Alphacypermethrin was found to be greater than 2,000 mg/kg bw in rats.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Applicant's version adopted
Results and discussion	Applicant's version adopted
Conclusion	LD_{50} > 2000 mg/kg $_{bw}$ in rats
Reliability	acceptable
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A6.1.1 Acute oral toxicity

Annex Point IIA6.1.5 – Supportive data –

The following reference is considered to contain additional information concerning acute oral toxicity in rats and is thus presented in tabular format as supportive data (non-GLP study):			
Reference	**Title**	**System**	**Results**
A6.1.1/04: [redacted] (1982) Report no. SBGR.82.130, June 04, 1982 (unpublished), BASF RDI No.: AL-411-004.	Toxicology of pyrethroids: The acute oral and percutaneous toxicity of cis-2-Ripcord comparison with Ripcord.	10 rats, male and female	LD_{50} ranging between 3170 and > 5000 mg/kg b.w.; administered in aqueous suspension or DMSO

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Rats and mice (m+f)
Results and discussion	If administered in corn oil (5% m/v), LD_{50} ranging between 26 and 116 mg/kg (mice). If administered in aqueous solution (50% m/v), LD50 ranging between 434 and 1074 mg/kg (mice); LD_{50} ranging between 2815 and 5000 mg/kg (rats). If administered in DMSO (40% m/v), LD_{50} ranging between 514 and 3162 mg/kg (mice); LD50 is 4000 mg/kg (rats).
Conclusion	
Reliability	1
Acceptability	acceptable
Remarks	confidential
	COMMENTS FROM ...
Date	
Materials and methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A6.1.2 **Acute dermal toxicity in rats**
Annex Point IIA 6.1.2

Official use only

1 REFERENCE

1.1	**Reference**	**Cross-reference to A6.1.1/01:** [redacted] (1993) FASTAC technical: Acute oral and dermal toxicity in rat, skin and eye irritancy in rabbit and skin sensitisation potential in Guinea pig. [redacted], Report no. SBTR.92.033, April 01, 1993 (unpublished), BASF RDI No.: AL-410-003.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex IA.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes EC method B.3 (84/449/EC)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	As given in Section A2.
3.1.1	Lot/Batch number	02156
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Off white powder
3.1.4	Purity	95.6%
3.1.5	Stability	Stable for the duration of the study.
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain / Stock	Crl: CD.BR
3.2.3	Source	Charles River, U.K.
3.2.4	Sex	Male and female
3.2.5	Age	5–6 weeks

Section A6.1.2 Acute dermal toxicity in rats

Annex Point IIA 6.1.2

3.2.6	Weight at study initiation	Males (day 1): 220–244g Females (day 1): 166–184g
3.2.7	Number of animals per group	Main study: 5 males and 5 females
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Dermal
3.3.1	Area covered	6 × 8 cm
3.3.2	Occlusion	Occlusive
3.3.3	Vehicle	Test substance was moistened.
3.3.4	Concentration in vehicle	2000 mg/mL
3.3.5	Total volume applied	Not stated.
3.3.6	Duration of exposure	24 hours
3.3.7	Removal of test substance	With warm dilute detergent solution.
3.3.8	Observation period	14 days
3.3.9	Controls	None
3.4	**Examinations**	
3.4.1	Mortality	Observation up to 14 days after treatment.
3.4.2	Clinical signs	Observations were made at least 7 times on the day of dosing and twice daily thereafter for the remainder of the 14 day observation period.
3.4.3	Body weights	The body weight of each animal was recorded the initial day (day 1), day 8 and day 15 of the study.
3.4.4	Necropsy	At the end of the observation period on day 15.
3.5	**Method of determination of LD_{50}**	None (limit test)
3.6	**Further remarks**	Limit test

4 RESULTS

4.1	**Clinical signs**	No mortalities occurred. Common signs of systemic reaction to treatment were salivation, hypersensitivity to stimuli and hyperactivity. These signs were apparent from day 2 but had resolved by day 4. Two females showed yellow staining of the anogenital fur on day 3 only. Sites of application of the test material were discoloured (white) after removal of the dressings on day 2. This effect of the test material resolved by day 5.

Section A6.1.2 Acute dermal toxicity in rats

Annex Point IIA 6.1.2

4.2	**Pathology**	All animals showed minor vascular congestion of the sites of application of the test material.
4.3	**Other**	Over the 14 day study period all animals gained weight.
4.4	**LD_{50}**	Male: > 2000 mg/kg Female: > 2000 mg/kg

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute dermal toxicity of Alphacypermethrin was tested in Sprague-Dawley rats according to EC method B.3 (84/449/EC). A dose of 2000 mg/kg b.w. test substance was applied as supplied and once only, by the cutaneous route.
5.2	**Results and discussion**	Administration of the moistened test material caused no mortality among the test animals. LD_{50} > 2000 mg/kg Thus, with respect to dermal toxicity, Alphacypermetrin does not require classification according to the requirements specified by Directive 67/548/EC and subsequent regulations.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and Methods	Applicant's version adopted
Results and discussion	Applicant's version adopted
Conclusion	Ad 5.3. it should have been mentioned that with respect to dermal toxicity, Alphacypermetrin does not require classification according to the requirements specified by Directive 67/548/EC and subsequent regulations.
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM APPLICANT
Date	29 April 2009
Materials and Methods	
Results and discussion	
Conclusion	Please note that according to the standard formats provided by the TNsG on dossier preparation headline 5.3 is associated with a "non-entry field". Furthermore, since the classification conclusion is presented in chapter 5.2, repetition of this statement one cell further below would not be very useful. In view of this the CA's remark may be reconsidered.
Reliability	
Acceptability	
Remarks	
	COMMENTS FROM RAPPORTEUR MEMBER STATE
Date	May 2009
Materials and Methods	Applicant's version adopted
Results and discussion	Applicant's version adopted
Conclusion	Applicant's version adopted.
Reliability	Applicant's version adopted
Acceptability	acceptable
Remarks	

Section A6.1.2 Acute dermal toxicity in rats

Annex Point IIA 6.1.2

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.2/01:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute dermal toxicity study in rats. [redacted], Report no.: 11A0563/041084, May 18, 2005 (unpublished), BASF Doc-ID: 2005/1011569.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex IA.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 402 (1987) EC B.3 (1992) OPPTS 870.1200 (1998)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000166
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Solid white powder
3.1.4	Purity	99.3%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain / Stock	Wistar / HanRcc:WIST(SPF)
3.2.3	Source	RCC Ltd Laboratory Animal Services, Füllinsdorf, Switzerland
3.2.4	Sex	Male and female

Section A6.1.2 Acute dermal toxicity in rats

Annex Point IIA 6.1.2

3.2.5	Age	Males: 8–10 weeks Females: 12–14 weeks
3.2.6	Weight at study initiation	Males (day 0): 251–272 g Females (day 0): 214–229 g
3.2.7	Number of animals per group	5 males and 5 females
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Dermal
3.3.1	Area covered	About 40 cm^2 (corresponding to at least 10% of the body surface).
3.3.2	Occlusion	Semi-occlusive
3.3.3	Vehicle	0.5% CMC-solution (cleaned sodium carboxymethylcellulose)
3.3.4	Concentration in vehicle	50 g/100 mL
3.3.5	Total volume applied	4.0 mL/kg
3.3.6	Duration of exposure	24 hours
3.3.7	Removal of test substance	With warm water
3.3.8	Observation period	14 days
3.3.9	Controls	None
3.4	**Examinations**	
3.4.1	Mortality	A check for any dead or moribund animal was made twice each workday and once daily on Saturdays, Sundays and on public holidays.
3.4.2	Clinical signs	Observations were made several times on the day of administration and thereafter at least once each workday for the remainder of the 14 day observation period.
3.4.3	Scoring of skin findings	30–60 minutes after removal, weekly thereafter and at the end of the study. Assessment of skin findings according to Draize, J.H. (1959).
3.4.4	Body weights	Individual body weights were recorded shortly before application (day 0), weekly thereafter and at the end of the study, and at death or sacrifice, respectively.
3.4.5	Necropsy	Necropsy with gross-pathology examination on the last day (day 14) of the observation period. Necropsy of all animals that died before as early as possible.
3.5	**Method of determination of LD_{50}**	None (limit test)
3.6	**Further remarks**	Limit test

Section A6.1.2 **Acute dermal toxicity in rats**
Annex Point IIA 6.1.2

4 RESULTS

4.1	**Clinical signs**	No mortalities occurred in the male dose group. One animal of the female dose group was found dead on study day 13. However, this was considered to be due to a abscess of the lower jaw and not test substance related. No systemic clinical signs were observed and no local effects occurred.
4.2	**Pathology**	In the female animal that died a green to yellow pasty abscess of the right lower jaw was observed upon macroscopic pathological examination. In the animals examined at termination of the study no macroscopic pathological abnormalities were noted.
4.3	**Other**	Over the 14 day study period all animals gained weight.
4.4	**LD_{50}**	Both sexes combined: > 2000 mg/kg Male: > 2000 mg/kg Female: > 2000 mg/kg

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute dermal toxicity of Alphacypermethrin was tested in Wistar rats according to OECD 402 (1987), EC B.3 (1992) and OPPTS 870.1200 (1998). A single dose of 2,000 mg/kg bw was applied via the dermal route.
5.2	**Results and discussion**	Administration of the moistened test material caused no treatment-related mortality among the test animals. LD_{50} > 2000 mg/kg
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and Methods	Applicant's version adopted
Results and discussion	Applicant's version adopted
Conclusion	LD_{50} > 2000 mg/kg bw
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A6.1.2 Acute dermal toxicity in rats

Annex Point IIA 6.1.2

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.2/02:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute dermal toxicity study in rats. [redacted], Report no.: 11A0562/041082, May 20, 2005 (unpublished), BASF Doc-ID: 2005/1011605.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex IA.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 402 (1987) EC B.3 (1992) OPPTS 870.1200 (1998)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000165
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Solid white powder
3.1.4	Purity	98.8%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain / Stock	Wistar / HanRcc:WIST(SPF)
3.2.3	Source	RCC Ltd Laboratory Animal Services, Füllinsdorf, Switzerland
3.2.4	Sex	Male and female

Section A6.1.2 Acute dermal toxicity in rats

Annex Point IIA 6.1.2

3.2.5	Age	Males: 8–10 weeks Females: 12–14 weeks
3.2.6	Weight at study initiation	Males (day 0): 248–272 g Females (day 0): 212–221 g
3.2.7	Number of animals per group	5 males and 5 females
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Dermal
3.3.1	Area covered	About 40 cm^2 (corresponds to at least 10% of the body surface).
3.3.2	Occlusion	Semi-occlusive
3.3.3	Vehicle	0.5% CMC-solution (cleaned sodium carboxymethylcellulose)
3.3.4	Concentration in vehicle	50 g/100 mL
3.3.5	Total volume applied	4.0 mL/kg
3.3.6	Duration of exposure	24 hours
3.3.7	Removal of test substance	With warm water
3.3.8	Observation period	14 days
3.3.9	Controls	None
3.4	**Examinations**	
3.4.1	Mortality	A check for any dead or moribund animal was made twice each workday and once daily on Saturdays, Sundays and on public holidays.
3.4.2	Clinical signs	Observations were made several times on the day of administration and thereafter at least once each workday for the remainder of the 14 day observation period.
3.4.3	Scoring of skin findings	30–60 minutes after removal, weekly thereafter and at the end of the study. Assessment of skin findings according to Draize, J.H. (1959).
3.4.4	Body weights	Individual body weights were recorded shortly before application (day 0), weekly thereafter and at the end of the study.
3.4.5	Necropsy	Necropsy with gross-pathology examination on the last day (day 14) of the observation period.
3.5	**Method of determination of LD_{50}**	None (limit test)
3.6	**Further remarks**	Limit test

Section A6.1.2 **Acute dermal toxicity in rats**
Annex Point IIA 6.1.2

4 RESULTS

4.1	**Clinical signs**	No mortalities occurred. No systemic clinical signs were observed and no local effects occurred.
4.2	**Pathology**	No macroscopic pathological abnormalities were noted.
4.3	**Other**	Over the 14 day study period all animals gained weight.
4.4	**LD_{50}**	Both sexes combined: > 2000 mg/kg Male: > 2000 mg/kg Female: > 2000 mg/kg

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute dermal toxicity of Alphacypermethrin was tested in Wistar rats according to OECD 402 (1987), EC B.3 (1992) and OPPTS 870.1200 (1998). A single dose of 2,000 mg/kg bw was applied via the dermal route.
5.2	**Results and discussion**	Administration of the moistened test material caused no treatment-related mortality among the test animals. LD_{50} > 2000 mg/kg
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and Methods	Applicant's version adopted
Results and discussion	Applicant's version adopted
Conclusion	LD_{50} > 2000 mg/kg bw
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Section A6.1.3 Acute inhalation toxicity in rats

Annex Point IIA6.1.3

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.3/01:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute inhalation toxicity study in Wistar rats. [redacted] Report no.: 1310563/047013, August 05, 2005 (unpublished), BASF Doc-ID: 2005/1015687.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 403 (1981) EC B.2 (92/69/EC) OPPTS 870.1300 (1998)
2.2	**GLP**	Yes
2.3	**Deviations**	None

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000166
3.1.2	Specification	As given in Section A2.
3.1.3	Purity	99.3%
3.1.4	Description	Solid white powder
3.1.5	Stability	Expiry date: November 01, 2006
3.2	**Test animals**	
3.2.1	Species	Rat
3.2.2	Strain	Wistar / HanRcc: WIST(SPF)
3.2.3	Source	RCC Ltd Laboratory Animal Services, Füllinsdorf, Switzerland
3.2.4	Sex	Male and female

Section A6.1.3 Acute inhalation toxicity in rats

Annex Point IIA6.1.3

3.2.5	Age at study initiation	Males: 8–9 weeks Females: 11–12 weeks
3.2.6	Weight at study initiation	Males (mean): 262.4–287.5 g Females (mean): 202.0–207.0 g
3.2.7	Number of animals per group	5 males and 5 females
3.2.8	Control animals	No
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Concentrations	*Nominal concentrations* Group 1: 4.9 mg/l air Group 2: 7.7 mg/l air *Analytical concentrations (gravimetric determination)* Group 1 (mean concentration): 0.42 mg/l air (SD: 0.03) Group 2 (mean concentration): 1.16 mg/l air (SD: 0.25)
3.3.2	Particle size	Mass median diameter of the aerosol particles [µm] (geometric standard deviation [µm]): Group 1: 2.6 µm (3.7) Group 2 (sample 1): 2.8 µm (2.9) Group 2 (sample 2): 2.6 µm (2.8)
3.3.3	Type or preparation of particles	The test atmosphere was generated by means of a dosing-wheel dust generator.
3.3.4	Type of exposure	Head-nose inhalation system
3.3.5	Vehicle	Aerosil® 200 (to improve dust formation)
3.3.6	Concentration in vehicle	1% (w/w)
3.3.7	Duration of exposure	4 hours
3.3.8	Observation period	14 days
3.3.9	Controls	No
3.4	**Examinations**	Clinical examinations Body weights Gross pathology
3.4.1	Clinical signs	Twice a day on workdays and once daily on weekends and public holidays. Detailed clinical observations were recorded for each animal separately several times during exposure and at least once on each workday of the observation period. Additionally, clinical observations were carried out on one weekend for both test groups.
3.4.2	Body weights	Body weight was determined just prior to exposure, weekly thereafter and at the end of the observation period and additionally in animals that died from study initiation onward.

Section A6.1.3 **Acute inhalation toxicity in rats**
Annex Point IIA6.1.3

3.5	**Method of determination of LC_{50}**	LC_{50} by probit analysis following Finney (1971). For results of the type "LC_{50} greater than", "LC_{50} approx." or "LC_{50} smaller than", the binominal test according to Snedecor (1989) was used.
3.6	**Further remarks**	None

4 RESULTS

4.1	**Clinical signs**	No mortalities occurred following exposure to the test material at 0.42 mg/l. At 1.16 mg/l, no males but two out of five females died after exposure to test material. Details are presented in Table A6.1.3- 1. Clinical signs of toxicity in animals exposed to 0.42 mg/l comprised visually accelerated respiration, squatting posture, piloerection and smeared fur. Incidences of clinical signs of toxicity increased from 0.42 mg/l to 1.16 mg/l in males and females. Clinical signs of toxicity in animals exposed to 1.16 mg/l comprised visually accelerated respiration, squatting posture, tremor, abdominal position, staggering, high-stepping gait, startle reflex, piloerection and smeared and contaminated fur. Moreover, reddish discoloration in the anogenital region and around the snout was observed in one high dosed female. Findings were observed from hour 0 of exposure until including study day 6. Details are presented in Table A6.1.3- 2.
4.2	**Pathology**	0.42 mg/l: No gross pathological findings 1.16 mg/l: No gross pathological findings
4.3	**Other**	The mean body weight of the low dosed males and the high dosed males and females increased throughout the study period. The mean body weight of low dosed females decreased slightly during the first week post-exposure, and then increased slightly during the second half. This effect is observed sometimes in the rat strain used, because in the required age range the female animals have already reached the phase of slow growth.
4.4	**LC_{50}**	Combined: 1.33 mg/l air (probit analysis) Males: > 1.16 mg/l air (binominal test) Females: 1.21 mg/l air (probit analysis)

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute inhalation toxicity of Alphacypermethrin was tested in Wistar rats according to OECD 403 (1981), EC B.2 (92/69/EC) and OPPTS 870.1300 (1998). Groups of 5 male and 5 female rats were exposed to Alphacypermethrin with an average solid dust concentration of 0.42 or 1.16 mg/l air for 4 hours.

Section A6.1.3 Acute inhalation toxicity in rats

Annex Point IIA6.1.3

5.2	**Results and discussion**	Two out of five females died following exposure to the test material at 1.16 mg/l. Animals exposed to Alphacypermethrin concentrations of 0.42 mg/l and 1.16 mg/l air showed signs of toxicity. These effects were more pronounced in the 1.16 mg/l exposure group. The combined LC_{50} was determined to be 1.33 mg/l (males: > 1.16 mg/l; females: 1.21 mg/l). Thus, according to the requirements specified by Directive 67/548/EC and subsequent regulations, Alphacypermethrin requires classification with the hazard symbol "Xn" and with R20 "harmful by inhalation" (LD_{50}, inhalation, rat, for aerosols or particulates $1 < LC_{50} \leq 5$ mg/l/4h).
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Applicant's version adopted
Results and discussion	Ad 4.2. it should have been mentioned that no gross pathological abnormalities were detected in the two female animals that were found death after the exposure to 1.16 mg/l
Conclusion	LC_{50} =[> 1.16 – 1.21] mg/l
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A6.1.3- 1: Mortality.

Dose [mg/l]	Cumulated mortality		Time interval of deaths
	Males	Females	
0.42	0 / 5	0 / 5	–
1.16	0 / 5	2 / 5	d0 – d1

Table A6.1.3- 2: Maximum incidence and duration of clinical findings.

Symptom	0.42 mg/l 5 males	1.16 mg/l 5 males	0.42 mg/l 5 females	1.16 mg/l 5 females
Respiration, visually accelerated	5 (h0 – d1)	5 (h0 – d3)	5 (h0 – d1)	5 (h0 – d3)
Squatting posture	5 (d0)	5 (d0 – d3)	5 (d0)	3 (d0 – d3)
Tremor	0	5 (d0)	0	4 (d0)
Abdominal position	0	2 (d0)	0	1 (d0)
Staggering	0	3 (d0)	0	3 (d0)
High-stepping gait	0	5 (d1 – d3)	0	3 (d1 – d2)
Startle reflex	0	5 (d1 – d3)	0	3 (d1 – d3)
Reddish discoloration in the anogenital region and around the snout	n.d.	n.d.	0	1 (d0)
Piloerection	5 (d0 – d2)	5 (d0 – d6)	5 (d0 – d2)	4 (d0 – d3)
Fur, smeared	5 (d0)	5 (d0)	5 (d0)	4 (d0)

h = hour
D = day
d0 = post-exposure on exposure day
n.d. not determined

Section A6.1.3 Acute inhalation toxicity in rats

Annex Point IIA6.1.3

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.3/02:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute inhalation toxicity study in Wistar rats. [redacted] Report no.: 1310562/047014, August 08, 2005 (unpublished), BASF Doc-ID: 2005/1013246.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 403 (1981) EC B.2 (92/69/EC) OPPTS 870.1300 (1998)
2.2	**GLP**	Yes
2.3	**Deviations**	None

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000165
3.1.2	Specification	As given in Section A2.
3.1.3	Purity	98.8%
3.1.4	Description	Solid white powder
3.1.5	Stability	Expiry date: November 01, 2006
3.2	**Test animals**	
3.2.1	Species	Rat
3.2.2	Strain	Wistar / HanRcc: WIST(SPF)
3.2.3	Source	RCC Ltd Laboratory Animal Services, Füllinsdorf, Switzerland
3.2.4	Sex	Male and female

Section A6.1.3 Acute inhalation toxicity in rats

Annex Point IIA6.1.3

3.2.5	Age at study initiation	Males: 8–10 weeks Females: 10–12 weeks
3.2.6	Weight at study initiation	Males (mean): 264.0–278.4 g Females (mean): 201.5–201.6 g
3.2.7	Number of animals per group	5 males and 5 females
3.2.8	Control animals	No
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Concentrations	*Nominal concentrations* Group 1: 13.9 mg/l air Group 2: 35.9 mg/l air *Analytical concentrations (gravimetric determination)* Group 1 (mean concentration): 1.07 mg/l air (SD: 0.21) Group 2 (mean concentration): 2.47 mg/l air (SD: 0.49)
3.3.2	Particle size	Mass median diameter of the aerosol particles [µm] (geometric standard deviation [µm]): Group 1: 2.7 µm (2.7) Group 2 (sample 1): 2.8 µm (2.8)
3.3.3	Type or preparation of particles	The test atmosphere was generated by means of a dosing-wheel dust generator.
3.3.4	Type of exposure	Head-nose inhalation system
3.3.5	Vehicle	Aerosil® R972 (to improve dust formation)
3.3.6	Concentration in vehicle	2% (w/w)
3.3.7	Duration of exposure	4 hours
3.3.8	Observation period	14 days
3.3.9	Controls	No
3.4	**Examinations**	Clinical examinations Body weights Gross pathology
3.4.1	Clinical signs	Twice a day on workdays and once daily on weekends and public holidays. Detailed clinical observations were recorded for each animal separately several times during exposure and at least once on each workday of the observation period. Additionally, on one Saturday detailed clinical observation was carried out in both test groups.
3.4.2	Body weights	Body weight was determined just prior to exposure, weekly thereafter and at the end of the observation period and additionally in animals that died from study initiation onward.

Section A6.1.3 **Acute inhalation toxicity in rats**
Annex Point IIA6.1.3

3.5	**Method of determination of LC_{50}**	LC_{50} by probit analysis following Finney (1971).
3.6	**Further remarks**	None

4 RESULTS

4.1	**Clinical signs**	No mortality occurred following exposure to the test material at 1.07 mg/l. At 2.47 mg/l, one out of five male and four out of five female animals died. Details are presented in Table A6.1.3- 1. Clinical signs of toxicity in animals exposed to 1.07 mg/l comprised visually accelerated respiration, eyelid closure, apathy, squatting posture, tremor, ataxie, startle reflex and smeared fur. Clinical signs of toxicity in animals exposed to 2.47 mg/l comprised some additional unspecific symptoms like gasping, discharged nose and salivation, indicative for respiratory distress, local irritant action and systemic toxicity. Additionally, contaminated and wet fur around the snout was noted in all three female animals that had died one day after exposure. Findings were observed from hour 0 of exposure until including study day 7. Details are presented in Table A6.1.3- 4.
4.2	**Pathology**	1.07 mg/l: No gross pathological findings 2.47 mg/l: dark red discolouration of all lung lobes in the two females having died one day after exposure; no gross pathological abnormalities in one male and one female having died one hour after exposure, and in those animals that were necropsied at termination.
4.3	**Other**	In the low-dose group the mean body weight of the male animals increased only minimally during the first week post-exposure, but then increased during the second week. The mean body weight of the female animals did not increase adequately throughout the whole study period. This effect is observed sometimes in the rat strain used, because in the required age range the female animals have already reached the phase of slow growth. The mean body weight of the high dosed male animals decreased during the first week post-exposure, but increased during the second week. The only surviving female animal showed only minimal weight increase throughout the whole study period.
4.4	**LC_{50}**	Combined: 2.50 mg/l air Males: 2.79 mg/l air Females: 2.29 mg/l air

Section A6.1.3 **Acute inhalation toxicity in rats**

Annex Point IIA6.1.3

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute inhalation toxicity of Alphacypermethrin was tested in Wistar rats according to OECD 403 (1981), EC B.2 (92/69/EC) and OPPTS 870.1300 (1998). Groups of 5 male and 5 female rats were exposed to Alphacypermethrin with an average solid dust concentration of 1.07 or 2.47 mg/l air for 4 hours.
5.2	**Results and discussion**	One out of five male and four out of five female animals died following exposure to the test material at 2.47 mg/l. Animals exposed to Alphacypermethrin concentrations of 1.07 mg/l and 2.47 mg/l air showed signs of toxicity. The combined LC_{50} was determined to be 2.50 mg/l (males: 2.79 mg/l; females: 2.29 mg/l). Thus, according to the requirements specified by Directive 67/548/EC and subsequent regulations, Alphacypermethrin requires classification with the hazard symbol "Xn" and with R20 "harmful by inhalation" (LD_{50}, inhalation, rat, for aerosols or particulates $1 < LC_{50} \leq 5$ mg/l/4h).
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Applicant's version adopted
Results and discussion	Applicant's version adopted
Conclusion	LC_{50} = 2.29 mg/l
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A6.1.3- 3: Mortality

Dose [mg/l]	Cumulated mortality		Time interval of deaths
	male	female	
1.07	0 / 5	0 / 5	–
2.47	1 / 5	4 / 5	d0 – d1

Table A6.1.3- 4: Maximum incidence and duration of clinical findings.

Symptom	**1.07 mg/l 5 males**	**2.47 mg/l 5 males**	**1.07 mg/l 5 females**	**2.47 mg/l 5 females**
Respiration, visually accelerated	5 (h0 – d7)	5 (h0 – d7)	5 (h0 – d7)	5 (h0 – d7)
Gasping	0	0	0	1 (d0)
Nose, discharge	0	0	0	1 (d0)
Eyelid closure	4 (d0)	0	5 (d0)	0
Salivation	0	0	0	3 (d0)
Apathy	4 (d0 – d7)	2 (d0 – d5)	3 (d0 – d7)	4 (d0 – d5)
Unconsciousness	0	0	0	3 (d0)
Squatting posture	5 (d0 – d7)	3 (d1 – d5)	4 (d0 – d7)	1 (d1 – d5)
Tremor	2 (d0 – d2)	0	2 (d0 – d2)	0
Ataxie	5 (d1 – d3)	4 (d0 – d5)	5 (d1 – d3)	1 (d1)
Startle reflex	5 (d1 – d3)	0	5 (d1 – d3)	0
Convulsions	0	0	0	1 (d0)
Piloerection	0	4 (d0 – d7)	0	4 (d0 – d1)
Fur, smeared	5 (d0 – d2)	4 (d0 – d1)	5 (d0 – d2)	4 (d0 – d7)
Reduced general state	0	4 (d0)	0	4 (d0)

h = hour

d = day

d0 = post-exposure on exposure day

Section A6.1.3 **Acute inhalation toxicity in rats**
Annex Point IIA6.1.3

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.3/03:** [redacted] (1993) Alphacypermethrin: Acute inhalation toxicity in rats, 4-hour exposure. [redacted], Report no. SLL 266/930770, December 14, 1993 (unpublished), BASF RDI No.: AL-413-001.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes EC B.2 (84/449/EC) OECD guideline 403 EPA FIFRA 81-3
2.2	**GLP**	Yes
2.3	**Deviations**	None

3 MATERIALS AND METHODS

3.1	**Test material**	As given in Section A2.
3.1.1	Lot/Batch number	02156
3.1.2	Specification	As given in Section A2.
3.1.3	Purity	956 g/kg
3.1.4	Description	White powder.
3.1.5	Stability	Stated expiry date: 1 July 1994
3.2	**Test animals**	
3.2.1	Species	Rat
3.2.2	Strain	Sprague-Dawley
3.2.3	Source	Charles River UK Ltd., Kent, UK
3.2.4	Sex	Male and female
3.2.5	Age at study initiation	6–8 weeks

Section A6.1.3 Acute inhalation toxicity in rats

Annex Point IIA6.1.3

3.2.6	Weight at study initiation	Males (mean): 202–217g Females (mean): 200–203g
3.2.7	Number of animals per group	5 males and 5 females
3.2.8	Control animals	Yes (5 males and 5 females)
3.3	**Administration/ Exposure**	Inhalation
3.3.1	Concentrations	Average concentration (determined gravimetrically) Group 1: 0 mg/l air Group 2: 0.98 mg/l air (SD: 0.13), Group 3: 1.59 mg/l air (SD: 0.44), maximum attainable concentration
3.3.2	Particle size	Mass median diameter of the aerosol particles [µm] (geometric standard deviation [µm]): Group 2: 6.1 µm (2.29) Group 3: 9.0 µm (2.84) Despite the apparently elevated MMAD for the 1.59 mg/l group, the clinical observations suggest that there was significant exposure of the group to the test material. % respirable (6 µm): Group 2: 49.3 Group 3: 34.8
3.3.3	Type or preparation of particles	The test atmosphere was generated by means of a Wright dust generator.
3.3.4	Type of exposure	Snout-only
3.3.5	Vehicle	None
3.3.6	Concentration in vehicle	Not applicable
3.3.7	Duration of exposure	4 hours
3.3.8	Observation period	14 days
3.3.9	Controls	Clean air only
3.4	**Examinations**	Clinical examinations Body weights Food consumption Water consumption Gross pathology Lung/ body weight ratio Microscopic pathology
3.4.1	Clinical signs	Continuously during the exposure period (0.25, 0.5, 1.0, 2.0, 3.0 and 4.0 hours) and at least twice daily throughout the observation period.

Section A6.1.3 **Acute inhalation toxicity in rats**
Annex Point IIA6.1.3

3.4.2	Body weights	Daily until the end of the observation period.
3.5	**Method of determination of LC_{50}**	None (due to low mortality)
3.6	**Further remarks**	None

4 RESULTS

4.1	**Clinical signs**	One of five female animals died following exposure to the test material at 0.98 mg/l and was found to have a slightly higher lung to body weight ratio. There were no other unscheduled deaths at either treatment level. Signs of toxicity included exaggerated respiratory movement, staggering, fascicular tremors, writhing, ataxia, hunched posture, poorly groomed appearance and urogenital staining. These effects were more pronounced in the 1.59 mg/l exposure group. Complete recovery was observed by day 6. Results are presented in Table A6.1.3- 5and Table A6.1.3- 6.
4.2	**Pathology**	Two rats (male and female) in the 1.59 mg/l group were found to have dark subpleural foci on the lungs. No abnormalities were found in other animals that survived exposure to Alphacypermethrin. The decedent rat showed moderately congested lungs and a distended gas-filled stomach. Also a slightly higher lung weight to body weight ratio was found as a result of exposure. The lung to bodyweight ratio for the surviving rats was considered to be within normal limits. Microscopic pathology revealed no treatment-related changes.
4.3	**Other**	Treated animals showed reduced body weight gain for the first two days post exposure and exhibited reduced water and food consumption. Recovery was complete in all surviving animals by day 6.
4.4	**LC_{50}**	> 1.59 mg/l air (maximum attainable concentration)

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute inhalation toxicity of Alphacypermethrin was tested in Sprague-Dawley rats according to EC method B.2 (84/449/EC), OECD guideline 403 and EPA FIFRA 81-3. Groups of 5 male and 5 female rats were exposed to Alphacypermethrin with average solid dust concentrations of 0.98 and 1.59 mg/l air for 4 hours under snout-only conditions.
5.2	**Results and discussion**	One of five females died following exposure to the test material at 0.98 mg/l. Animals receiving 0.98 mg/l and 1.59 mg/l air showed signs of toxicity. These effects were more pronounced in the 1.59 mg/l exposure group. The LC_{50} was determined to be greater than 1.59 mg/l air (maximum attainable concentration) for both males and females.

Section A6.1.3 Acute inhalation toxicity in rats

Annex Point IIA6.1.3

5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Ad 3.2.1. it should have been mentioned that rats were albinos
Results and discussion	Applicant's version adopted
Conclusion	LC_{50} > 1.59 mg/l air (maximum attainable concentration)
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A6.1.3- 5: Acute inhalation toxicity in male rats.

Dose [mg/l]	Number of dead/ number investigated	Time of death	Observations (clinical signs and gross pathology)
0 (control)	0/5	–	None
0.98	0/5	–	Exaggerated respiratory movement, staggering, poorly groomed
1.59	0/5	–	Occasional writhing, fascicular tremors, staggering, hunched posture, exaggerated respiratory movements, ataxia, poorly groomed

Table A6.1.3- 6: Acute inhalation toxicity in female rats.

Dose [mg/l]	Number of dead/ number investigated	Time of death	Observations (clinical signs and gross pathology)
0 (control)	0/5	–	None
0.98	1/5	Day 1	Fascicular tremors, writhing, exaggerated respiratory movement, poorly groomed, hair loss on head
1.59	0/5	–	Staggering, fascicular tremors, hunched posture, poorly groomed, exaggerated respiratory movements, ataxia staining around urogenital region

Section A6.1.4 Acute dermal irritation in rabbits

Annex Point IIA6.1.4

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.4/01:** [redacted] (2005): BAS 310 I (alpha-Cypermethrin) – Acute dermal irritation / corrosion in rabbits. [redacted]; Report no. 18H0562/042238, May 19, 2005 (unpublished), BASF Doc-ID: 2005/1011606.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 404 (2002) EC method B.4 (2004) OPPTS 870.2500 (1998) MAFF (Japan, 2000)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000165
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Solid white powder
3.1.4	Purity	98.8%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.2	**Test animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand White A 1077 INRA (SPF)
3.2.3	Source	Centre Lago S.A., Vonnas, France

Section A6.1.4 Acute dermal irritation in rabbits

Annex Point IIA6.1.4

3.2.4	Sex	Male and female
3.2.5	Age	8–9 months
3.2.6	Weight at study initiation (day 0)	3.73–4.14 kg
3.2.7	Number of animals	3
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Dermal
3.3.1	Area covered	2.5 cm x 2.5 cm (approx. 6 cm^2)
3.3.2	Vehicle	Doubly-distilled water (for moistening the solid test substance)
3.3.3	Concentration in vehicle	Not applicable.
3.3.4	Preparation of test substance	The solid test substance was minimally moistened with a suitable amount of doubly-distilled water to guarantee skin contact.
3.3.5	Occlusion	Semi-occlusive
3.3.6	Total volume applied	500 mg
3.3.7	Duration of exposure	4 hours
3.3.8	Removal of test substance	With Lutrol® (Polyethylenglycol) and Lutrol® / water (1:1)
3.3.9	Post-exposure period	Up to 14 days
3.3.10	Controls	None
3.4	**Examinations**	
3.4.1	Mortality	Check for dead or moribund animals twice each workday and once daily on Saturdays, Sundays and on public holidays.
3.4.2	Dermal examination	Yes Erythema, eschar and oedema
3.4.3	Scoring system of erythema and eschar formation	According to guideline.
3.4.4	Scoring system of oedema formation	According to guideline.
3.4.5	Examination time points	1, 24, 48, 72 hours, day 7 and day 14 after patch removal
3.4.6	Evaluation	Calculation of mean scores for readings at 24, 48 and 72 hours
3.4.7	Other examinations	Body weight of all animals was determinate just before application of the test substance and after the last reading.
3.5	**Further remarks**	None

Section A6.1.4 **Acute dermal irritation in rabbits**
Annex Point IIA6.1.4

4 RESULTS

4.1	**Average score**	
4.1.1	Erythema/Eschar	1.6 (24–72 h mean) Individual mean scores: 2.0, 2.3, 0.3
4.1.2	Oedema	0.2 (24–72 h mean) Individual mean scores: 0.0, 0.7, 0.0
4.2	**Reversibility**	14 days
4.3	**Other examinations**	Body weight of the animals increased during the post exposure period.
4.4	**Overall results**	Results are presented in Table A6.1.4- 1. Slight erythema were observed in all animals immediately after removal of the patch and persisted in one animal up to 24 hours. Moderate erythema were noted in two animals from 1 hour up to 48 hours and in one animal up to 72 hours. Moderate erythema increased to marked in one animal after 72 hours and decreased to moderate again on day 7. In this animal moderate oedema was also observed after 72 hours. Additionally scaling or severe scaling was noted in two animals on day 7. The cutaneous reactions were reversible in one animal within 48 hours, in another animal within 7 days and in the third animal within 14 days after removal of the patch.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute dermal irritation / corrosion potential of Alphacypermethrin was tested in New Zealand White rabbits, according to OECD 404 (2002), EC method B.4 (2004), OPPTS 870.2500 (1998) and MAFF (Japan, 2000). 500 mg of Alphacypermethrin were applied to the shaved intact skin of three rabbits for a period of 4 hours (semi-occlusive).
5.2	**Results and discussion**	Slight to marked erythema was observed in the animals during the course of the study. Moderate oedema was noted in one animal after 72 hours, only. Additionally, scaling or severe scaling was noted in two animals on day 7. The cutaneous reactions were reversible in all animals within 14 days after removal of the patch. The average score for irritation was calculated to be 1.6 (individual mean scores: 2.0, 2.3, 0.3) for erythema and 0.2 (individual mean scores: 0.0, 0.7, 0.0) for oedema. Considering the described cutaneous reactions as well as the calculated individual value of 2 and more for erythema/eschar in two of three rabbits, Alphacypermethrin shows a skin irritation potential under the test conditions chosen. Thus, according to the requirements specified by Directive 67/548/EC and subsequent regulations, Alphacypermethrin requires classification with the symbol "Xi" and with R38 "irritating to skin".

Section A6.1.4 Acute dermal irritation in rabbits

Annex Point IIA6.1.4

5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Ad 3.3.10 it should have been mentioned that negative control has been performed on untreated skin sites of the animal tested Applicant's version adopted
Results and discussion	
Conclusion	Ad 5.2: The individual mean value (24h-72h) for each of the 3 rabbits tested is widely different. So it is preferable to express the grade for erythema as [0.3, 2.3], and not as the mean value on the 3 animals. Ad 5.3 it should have been mentioned that Alphacypermethrin shows a skin irritation potential under the test conditions chosen. According to the requirements specified by Directive 67/548/EC and subsequent regulations, Alphacypermethrin requires classification with the symbol "Xi" and with R38 "irritating to skin"
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM APPLICANT
Date	7 May 2009
Materials and methods	
Results and discussion	
Conclusion	Ad 5.3: Please note that according to the standard formats provided by the TNsG on dossier preparation headline 5.3 is associated with a "non-entry field". Furthermore, since the classification conclusion is presented in chapter 5.2, repetition of this statement one cell further below would not be very useful. In view of this the CA's remark may be reconsidered.
Reliability	
Acceptability	
Remarks	
	COMMENTS FROM RAPPORTEUR MEMBER STATE
Date	May 2009
Conclusion	Ad 5.2: The individual mean value (24h-72h) for each of the 3 rabbits tested is widely different. So it is preferable to express the grade for erythema as [0.3, 2.3], and not as the mean value on the 3 animals.
Remarks	Comments applicant accepted

Table A6.1.4- 1: Acute dermal irritation in rabbits.

Parameter	Time	Erythema / Eschar	Oedema
Average score (3 animals)	1 h	1.7	0
	24 h	1.7	0
	48 h	1.3	0
	72 h	1.7	0.7
Other time (2 animals)	7 d	1.0	0
Average score	24, 48, 72 h	1.6	0.2
Reversibility*		c	c
Effects reversible after		14 d (48 h; 7 d; 14 d)	n.a.

*) c: completely reversible; nc: not completely reversible; n: not reversible
n.a.: not applicable

Section A6.1.4 Acute dermal irritation in rabbits

Annex Point IIA6.1.4

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.4/02:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute dermal irritation / corrosion in rabbits. [redacted], Report no. 18H0563/042241, May 19, 2005 (unpublished), BASF Doc-ID: 2005/1011570.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 404 (2002) EC method B.4 (2004) OPPTS 870.2500 (1998) MAFF (Japan, 2000)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000166
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Solid white powder
3.1.4	Purity	99.3%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.2	**Test animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand White A 1077 INRA (SPF)
3.2.3	Source	Centre Lago S.A., Vonnas, France

Section A6.1.4 Acute dermal irritation in rabbits

Annex Point IIA6.1.4

3.2.4	Sex	Male and female
3.2.5	Age	About 6 months
3.2.6	Weight at study initiation (day 0)	3.60–3.80 kg
3.2.7	Number of animals	3
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Dermal
3.3.1	Area covered	2.5 cm x 2.5 cm (approx. 6 cm^2)
3.3.2	Vehicle	Doubly-distilled water (for moistening the solid test substance)
3.3.3	Concentration in vehicle	Not applicable.
3.3.4	Preparation of test substance	The solid test substance was minimally moistened with a suitable amount of doubly-distilled water to guarantee skin contact.
3.3.5	Occlusion	Semi-occlusive
3.3.6	Total volume applied	500 mg
3.3.7	Duration of exposure	4 hours
3.3.8	Removal of test substance	With Lutrol® (Polyethylenglycol) and Lutrol® / water (1:1)
3.3.9	Post-exposure period	Up to 14 days
3.3.10	Controls	None
3.4	**Examinations**	
3.4.1	Mortality	Check for dead or moribund animals twice each workday and once daily on Saturdays, Sundays and on public holidays.
3.4.2	Dermal examination	Yes Erythema, eschar and oedema
3.4.3	Scoring system of erythema and eschar formation	According to guideline.
3.4.4	Scoring system of oedema formation	According to guideline.
3.4.5	Examination time points	1, 24, 48, 72 hours, day 7 and day 14 after patch removal
3.4.6	Evaluation	Calculation of mean scores for readings at 24, 48 and 72 hours
3.4.7	Other examinations	Body weight of all animals was determinate just before application of the test substance and after the last reading.
3.5	**Further remarks**	None

Section A6.1.4 **Acute dermal irritation in rabbits**
Annex Point IIA6.1.4

4 RESULTS

4.1	**Average score**	
4.1.1	Erythema/Eschar	1.1 (24–72 h mean) Individual mean scores: 1.0, 0.3, 2.0
4.1.2	Oedema	0.0 (24–72 h mean) Individual mean scores:0, 0, 0
4.2	**Reversibility**	14 days
4.3	**Other examinations**	Body weight of the animals increased during the post exposure period.
4.4	**Overall results**	Results are presented in Table A6.1.4- 2. Slight erythema were observed in all animals immediately after removal of the patch, which increased to moderate in all animals within 1 hour. Moderate erythema persisted in one animal up to day 7 and decreased to slight in two animals at the 24 hour reading. Slight erythema persisted in one of these animals until 72 hours. In one animal severe scaling was noticed on day 7. The cutaneous reactions were reversible in one animal within 48 hours, in another animal within 7 days and in the third animal within 14 days after removal of the patch.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute dermal irritation / corrosion potential of Alphacypermethrin was tested in New Zealand White rabbits, according to OECD 404 (2002), EC method B.4 (2004), OPPTS 870.2500 (1998) and MAFF (Japan, 2000). 500 mg of Alphacypermethrin were applied to the shaved intact skin of three rabbits for a period of 4 hours (semi-occlusive).
5.2	**Results and discussion**	Slight or moderate erythema was observed in all animals during the course of the study. In one animal severe scaling was noticed on day 7. The cutaneous reactions were reversible in all animals within 14 days after removal of the patch at latest. The average score for irritation was calculated to be 1.1 for erythema and 0 for oedema. Considering the described cutaneous reactions as well as the average score for irritation, Alphacypermethrin shows a slight skin irritation potential under the test conditions chosen.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Ad 3.3.10 it should have been mentioned that negative control has been performed on untreated skin sites of the animal tested
Results and discussion	Applicant's version adopted
Conclusion	Ad 5.2: The individual mean value (24h-72h) for each of the 3 rabbits tested is widely different. So it is preferable to express the grade for erythema as [0.3, 2.0], and not as the mean value on the 3 animals. Ad 5.3 it should have been mentioned that Alphacypermethrin shows a skin irritation potential under the test conditions chosen. According to the requirements specified by Directive 67/548/EC and subsequent regulations, Alphacypermethrin requires classification with the symbol "Xi" and with R38 "irritating to skin"
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM APPLICANT
Date	7 May 2009
Materials and methods	
Results and discussion	
Conclusion	Ad 5.3: Please note that according to the standard formats provided by the TNsG on dossier preparation headline 5.3 is associated with a "non-entry field". Furthermore, since the classification conclusion is presented in chapter 5.2, repetition of this statement one cell further below would not be very useful. In view of this the CA's remark may be reconsidered.
	COMMENTS FROM RAPPORTEUR MEMBER STATE
Date	May 2009
Conclusion	Ad 5.2: The individual mean value (24h-72h) for each of the 3 rabbits tested is widely different. So it is preferable to express the grade for erythema as [0.3, 2.0], and not as the mean value on the 3 animals
Remarks	Remarks of applicant accepted

Table A6.1.4- 2: Acute dermal irritation in rabbits.

Parameter	Time	Erythema / Eschar	Oedema
Average score (3 animals)	1 h	2.0	0
	24 h	1.3	0
	48 h	1.0	0
	72 h	1.0	0
Other time (2 animals)	7 d	1.0	0
Average score	24, 48, 72 h	1.1	0
Reversibility*		c	c
Effects reversible after		14 d (48 h; 7 d; 14 d)	n.a.

*) c: completely reversible; nc: not completely reversible; n: not reversible
n.a.: not applicable

Section A6.1.4 Acute dermal irritation in rabbits

Annex Point IIA6.1.4

Official use only

1 REFERENCE

1.1	**Reference**	**Cross-reference to A6.1.1/01:** [redacted] (1993) FASTAC technical: Acute oral and dermal toxicity in rat, skin and eye irritancy in rabbit and skin sensitisation potential in Guinea pig. [redacted], Report no. SBTR.92.033, April 01, 1993 (unpublished), BASF RDI No.: AL-410-003
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes EC method B.4 (84/449/EC)
2.2	**GLP**	Yes
2.3	**Deviations**	Yes The relative humidity in the animal room exceeded 70% on more than two consecutive occasions on only one day and exceeded 74% on one occasion. This is considered not to have adversely influenced the outcome of the study.

3 MATERIALS AND METHODS

3.1	**Test material**	As given in Section A2.
3.1.1	Lot/Batch number	02156
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Off white powder
3.1.4	Purity	95.6%
3.1.5	Stability	Stable for the duration of the study.
3.2	**Test animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand White
3.2.3	Source	Froxfield Farms U.K. Ltd.
3.2.4	Sex	Male and female

Section A6.1.4 Acute dermal irritation in rabbits

Annex Point IIA6.1.4

3.2.5	Age	3–5 months
3.2.6	Weight at study initiation	2.50–3.82 kg
3.2.7	Number of animals per group	6
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	Dermal
3.3.1	Area covered	The shaved and moistened intact dorsal skin (6 cm^2).
3.3.2	Vehicle	None
3.3.3	Concentration in vehicle	Not applicable.
3.3.4	Preparation of test substance	Undiluted test material.
3.3.5	Occlusion	Semi-occlusive
3.3.6	Total volume applied	500 mg
3.3.7	Duration of exposure	4 hours
3.3.8	Removal of test substance	With tap water.
3.3.9	Post-exposure period	72 hours
3.3.10	Controls	None
3.4	**Examinations**	
3.4.1	Clinical signs	No
3.4.2	Dermal examination	Yes Erythema and oedema.
3.4.3	Scoring system of erythema and eschar formation	According to guideline.
3.4.4	Scoring system of oedema formation	According to guideline.
3.4.5	Examination time points	1, 24, 48, 72 hours and 7 days after patch removal.
3.4.6	Evaluation	Calculation of mean scores for readings at 24, 48 and 72 hours
3.4.7	Other examinations	Not stated
3.5	**Further remarks**	None

Section A6.1.4 **Acute dermal irritation in rabbits**
Annex Point IIA6.1.4

4 RESULTS

4.1	**Average score**	
4.1.1	Erythema/Eschar	0.2 (individual mean scores: 0.0, 0.3, 0.3)
4.1.2	Oedema	0.0 (individual mean scores:0, 0, 0)
4.2	**Reversibility**	After 7 days
4.3	**Other examinations**	Not stated
4.4	**Overall results**	Results are presented in Table A6.1.4- 3. 24 hours after removal of the test substance all of the test animals showed no skin irritation. 48 and 72 hours after removal of the test substance two animals showed a very slight erythema at the dermal test-sites. These reactions resolved within 7 days after treatment.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute dermal irritation of Alphacypermethrin was tested in New Zealand White rabbits, according to EC method B.4 (84/449/EC). 500 mg of Alphacypermethrin was applied to the moistened shaved intact skin of six rabbits for a period of 4 hours (semi-occlusive). The relative humidity in the animal room occasionally exceeded 70%, which is considered not to have adversely influenced the outcome of the study.
5.2	**Results and discussion**	No skin reaction were observed 24 hours after removal of the test substance, but two animals showed a very slight erythema 48 and 72 hours after patch removal. There were no other irritation reactions or other dermal changes. Alphacypermethrin was deemed to be slightly irritating under these test conditions.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Ad 3.4.2. it should have been mentioned "and other dermal changes"
Results and discussion	Applicant's version adopted
Conclusion	Applicant's version adopted
Reliability	1
Acceptability	acceptable
Remarks	none
	COMMENTS FROM ...
Date	
Materials and methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A6.1.4- 3: Acute dermal irritation in rabbits.

Score (average animals investigated)	Time	Erythema / Eschar	Oedema
Average score (6 animals)	1 h	0	0
	24 h	0	0
	48 h	0.3	0
	72 h	0.3	0
	7 d	0	0
Average score	24, 48, 72	0.2	0
Reversibility*		c	c
Average time for reversibility		n.s.	n.s.

*) c: completely reversible; nc: not completely reversible; n: not reversible
n.s.: not stated

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

Official use only

1 REFERENCE

1.1	**Reference**	**Cross-reference to A6.1.1/01:** [redacted] (1993) FASTAC technical: Acute oral and dermal toxicity in rat, skin and eye irritancy in rabbit and skin sensitisation potential in Guinea pig. [redacted], Report no. SBTR.92.033, April 01, 1993, BASF RDI No.: AL-410-003 (unpublished).
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes EC method B.5 (84/449/EEC)
2.2	**GLP**	Yes
2.3	**Deviations**	Yes The relative humidity in the animal room exceeded 70% on more than two consecutive occasions on only one day and exceeded 74% on one occasion. This is considered not to have adversely influenced the outcome of the study.

3 MATERIALS AND METHODS

3.1	**Test material**	As given in Section A2.
3.1.1	Lot/Batch number	02156
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Off-white powder
3.1.4	Purity	95.6%
3.1.5	Stability	Stable for the duration of the study.
3.2	**Test animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand White
3.2.3	Source	Froxfield Farms U.K. Ltd.
3.2.4	Sex	Male and female

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

3.2.5	Age	3–5 months
3.2.6	Weight at study initiation	2.50–3.82 kg
3.2.7	Number of animals per group	6
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	
3.3.1	Preparation of test substance	The test substance was used as delivered.
3.3.2	Amount of active substance instilled	45 mg (equivalent to 0.1 mL) Alphacypermethrin per eye.
3.3.3	Exposure period	Not stated.
3.3.4	Removal of test substance	The eyes were not irrigated.
3.3.5	Post-exposure period	7 days
3.4	**Examinations**	
3.4.1	Ophthalmoscopic examination	Not stated
3.4.2	Scoring system	According to guideline, except of conjunctiva discharge which was graded in the report as "a" – slight ocular discharge and "b" – ocular discharge. A score of 1 was allocated to "a" and "b".
3.4.3	Examination time points	1, 4, 24, 48, 72 hours and 7days after instillation.
3.4.4	Evaluation	Calculation of mean scores for readings at 24, 48 and 72 hours
3.4.5	Other examinations	Not stated.
3.5	**Further remarks**	None

4 RESULTS

4.1	**Clinical signs**	Not stated.
4.2	**Average score**	Results are presented in Table A6.1.4- 4.
4.2.1	Corneal opacity	0 (individual mean scores: 0, 0, 0)
4.2.2	Iris	0 (individual mean scores: 0, 0, 0)
4.2.3	Conjunctiva	
	Redness	0.1 (individual mean scores: 0.2, 0.2, 0)
	Chemosis	0.2 (individual mean scores: 0.3, 0.2, 0)

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

4.3	**Reversibility**	Yes Injection of the conjunctival blood vasculature, chemosis and ocular discharge resolved within 72 hours.
4.4	**Overall results**	All animals developed injection of the conjunctival blood vasculature and an ocular discharge within one hour of treatment. At 24 hours, a single animal showed injection of the conjunctival blood vasculature, chemosis sufficient to cause partial eversion of the eyelids and a slight ocular discharge. These proved to be the most intense reactions to treatment and resolved within 72 hours. The cornea and iris remained overtly unaffected by the test material.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute eye irritation of Alphacypermethrin was tested in New Zealand White rabbits, according to EC method B.5 (84/449/EEC). 45 mg of the test substance were placed into the conjunctival sac of one eye each of six rabbits, respectively. The relative humidity in the animal room occasionally exceeded 70%, which is considered not to have adversely influenced the outcome of the study.
5.2	**Results and discussion**	Within 24 hours after treatment, one animal showed injection of the conjunctival blood vasculature, chemosis sufficient to cause partial eversion of the eyelids and a slight ocular discharge. These proved to be the most intense reactions to treatment. The cornea and iris remained overtly unaffected by the test material.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities	
Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	

	EVALUATION BY RAPPORTEUR MEMBER STATE (*)
Date	March 2009
Materials and methods	Ad 3.2.8. it should have been mentioned that the untreated eye serves as the control. Ad 4.2.3. Conjunctiva (average score on 24, 48, 78h) • Redness 0.1 (individual mean scores: 0, 0.66, 0, 0, 0, 0) • Chemosis 0.2 (individual mean scores: 0, 1, 0, 0, 0, 0)
Results and discussion	Ad 5.2. it should have been mentioned that within 4 hour after treatment (at readings at 1 and 4 hours after treatment), all animals show redness conjunctiva (grade 1).
Conclusion	Slight conjunctival redness exists in all animals (readings at one hour and 4 hours after application). Alphacypermethrin shows a slightly eye irritation potential, and therefore requires classification with R36 "irritating to eye".
Reliability	1
Acceptability	acceptable
Remarks	none

	COMMENTS FROM APPLICANT
Date	7 May 2009
Materials and methods	
Results and discussion	

Conclusion	Disagree with R36 proposal. C&L criteria for eye irritation are specified in Annex VI of Directive 2001/59/EC (28th ATP to Dangerous Substance Directive 67/548/EEC). The classification criteria are very clear: R36 (irritating to eyes) applies for substances and preparations which … cause significant ocular lesions…. Ocular lesions are significant if the mean scores of the eye irritation test (performed with 6 rabbits)… have any of the following values: *– cornea opacity equal to or greater than 2 but less than 3* *– iris lesion equal to or greater than 1 but not greater than 1.5* *– redness of the conjunctivae equal to or greater than 2.5* *– oedema of the conjunctivae (chemosis) equal to or greater than 2* There is also need for classification when using the GHS classification criteria as given in Regulation No 1272/2008. The criteria for classification as "irritating to eyes (category 2)" are as follows: "*at least in 2 of 3 tested animals, a positive response of:* *– corneal opacity ≥ 1 and/or* *– iritis ≥ 1, and/or* *– conjunctival redness ≥ 2 and/or* *– conjunctival oedema (chemosis) ≥ 2* *calculated as the mean scores following grading at 24, 48 and 72 hours after installation of the test material, and which fully reverses within an observation period of 21 days*" These criteria are clearly not fulfilled according to the study results. Therefore, there is no scientific and legal basis for considering Alphacypermethrin as an eye irritant. The current legal classification for alpha-cypermethrin as given in Dir. 2008/58/EC (30th ATP to Dir 67/548/EEC) is still valid. COMMENTS FROM RAPPORTEUR MEMBER STATE
Date	May 2009
Conclusion	Applicant's version accepted
Remarks	Remarks from applicant accepted

Table A6.1.4- 4: Acute eye irritation in rabbits of the main study group.

	Cornea	Iris	Conjunctiva	
	Opacity		Redness	Chemosis
Score (average of animals investigated)	0 to 4	0 to 2	0 to 3	0 to 4
1 h	0	0	1.0	0
4 h	0	0	1.0	0.2
24 h	0	0	0.2	0.3
48 h	0	0	0.2	0.2
72 h	0	0	0	0
7 d	0	0	0	0
Average 24, 48, 72 h	0	0	0.1	0.2
Maximum average score (including area affected, maximum: 110)	0	0	1.3	
Reversibility*	n.a.	n.a.	c	c
Average time for reversion	n.a.	n.a.	72 hours	72 hours

n.a.: not applicable

*) c: completely reversible

Calculation of maximum average score according to "Draize Scale for Scoring Ocular Irritation"

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.4/03:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute eye irritation in rabbits. [redacted], Report no. 11H0563/042242, May 19, 2005 (unpublished), BASF Doc-ID: 2005/1011571.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 405 EC method B.5 (2004) OPPTS 870.2400 (1998) MAFF (Japan, 2000)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000166
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Solid, white powder
3.1.4	Purity	99.3%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.2	**Test animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand White A 1077 INRA (SPF)
3.2.3	Source	Centre Lago S.A., Vonnas, France

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

3.2.4	Sex	Male and female
3.2.5	Age	About 3 months
3.2.6	Weight at study initiation	2.41–2.77 kg
3.2.7	Number of animals	3
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	
3.3.1	Preparation of test substance	The test substance was used as delivered.
3.3.2	Amount of active substance instilled	Approx. 40 mg (equivalent to 0.1 mL) Alphacypermethrin
3.3.3	Exposure period	1 hour
3.3.4	Removal of test substance	With 3 to 6 mL of hand warm tap water
3.3.5	Post-exposure period	28 days
3.4	**Examinations**	
3.4.1	Ophthalmoscopic examination	No
3.4.2	Scoring system	According to guideline
3.4.3	Examination time points	1, 24, 48, 72 hours after instillation
3.4.4	Evaluation	Calculation of mean scores for readings at 24, 48 and 72 hours
3.4.5	Other examinations	
	Area of cornea involved	Scoring table 1 = > 0 ≤ ¼ 2 = > ¼ < ½ 3 = > ½ < ¾ 4 = > ¾
	Discharge	Scoring table 0 = No discharge 1 = Any amount different from normal 2 = Discharge with moistening of the lids and hairs just adjacent to lids 3 = Discharge with moistening of the lids and hairs, and considerable area around the eyes
	Body weight	Just before application of the test substance and after the last reading.
	Mortality	Check for dead or moribund animals twice each workday and once daily on Saturdays, Sundays and on public holidays.
3.5	**Further remarks**	None

Section A6.1.4 **Acute eye irritation in rabbits**
Annex Point IIA6.1.4

4 RESULTS

4.1	**Clinical signs**	Not stated.
4.2	**Average score**	Results are presented in Table A6.1.4- 5.
4.2.1	Corneal opacity	0 (individual mean scores: 0, 0, 0)
4.2.2	Iris	0 (individual mean scores: 0, 0, 0)
4.2.3	Conjunctiva	
	Redness	1.0 (individual mean scores: (1.0, 1.0, 1.0)
	Chemosis	0.1 (individual mean scores: (0.3, 0, 0)
4.3	**Reversibility**	Yes The ocular reactions were reversible in all animals within 72 hours after application.
4.4	**Overall results**	Moderate conjunctival redness, observed in all animals 1 and 24 hours after application, decreased to slight in all animals at the 48 hour-reading and resolved within 72 hours. Moderate conjunctival chemosis was noted in all animals at the 1 hour-reading. Slight conjunctival chemosis was observed in one animal after 24 hours. Slight discharge was seen in all animals after 1 hour and in one animal after 24 hours. No other ocular reactions were observed during the study.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute eye irritation of Alphacypermethrin was tested in New Zealand White rabbits, according to OECD 405, EC method B.5 (2004), OPPTS 870.2400 (1998) and MAFF (Japan, 2000). A single ocular application of 0.1 mL (approx. 40 mg) of the test substance placed into the conjunctival sac of one eye each of three rabbits, respectively.
5.2	**Results and discussion**	Slight to moderate conjunctival redness, slight to moderate conjunctival chemosis and slight discharge were observed in the animals during the observation period. The ocular reactions were reversible in all animals within 72 hours after application. The average score (24 to 72 hours) for irritation was calculated to be 0 for corneal opacity and for iris, 1.0 for conjunctival redness and 0.1 for chemosis. Alphacypermethrin does not show an eye irritation potential under the test conditions chosen. Thus, according to the requirements specified by Directive 67/548/EC and subsequent regulations, Alphacypermethrin requires no classification.

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities		
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)	
Date	March 2009	
Materials and methods	Ad 3.2.8. it should have been mentioned that the untreated eye serves as the control.	
Results and discussion	Applicant's version adopted	
Conclusion	Moderate to slight conjunctival redness and conjunctival chemosis exist (readings at one hour until one day after application). Alphacypermethrin shows a slightly eye irritation potential, and therefore requires classification with R36 "irritating to eye".	
Reliability	1	
Acceptability	acceptable	
Remarks	none	
	COMMENTS FROM APPLICANT	
Date	7 May 2009	
Materials and methods		
Results and discussion		

Conclusion	Disagree with R36 proposal. C&L criteria for eye irritation are specified in Annex VI of Directive 2001/59/EC (28th ATP to Dangerous Substance Directive 67/548/EEC). The classification criteria are very clear: R36 (irritating to eyes) applies for substances and preparations which … cause significant ocular lesions…. Ocular lesions are significant if the mean scores of the eye irritation test (performed with 6 rabbits)… have any of the following values: – *cornea opacity equal to or greater than 2 but less than 3* – *iris lesion equal to or greater than 1 but not greater than 1.5* – *redness of the conjunctivae equal to or greater than 2.5* – *oedema of the conjunctivae (chemosis) equal to or greater than 2* There is also need for classification when using the GHS classification criteria as given in Regulation No 1272/2008. The criteria for classification as "irritating to eyes (category 2)" are as follows: "*at least in 2 of 3 tested animals, a positive response of:* – *corneal opacity ≥ 1 and/or* – *iritis ≥ 1, and/or* – *conjunctival redness ≥ 2 and/or* – *conjunctival oedema (chemosis) ≥ 2* *calculated as the mean scores following grading at 24, 48 and 72 hours after installation of the test material, and which fully reverses within an observation period of 21 days*" These criteria are clearly not fulfilled according to the study results. Therefore, there is no scientific and legal basis for considering Alphacypermethrin as an eye irritant. The current legal classification for alpha-cypermethrin as given in Dir. 2008/58/EC (30th ATP to Dir 67/548/EEC) is still valid. COMMENTS FROM RAPPORTEUR MEMBER STATE
Date	May 2009
Conclusion	Applicant's version accepted
Remarks	Remarks on conclusion accepted

Table A6.1.4- 5: Acute eye irritation in rabbits.

	Cornea	Iris	Conjunctiva		
	Opacity		Redness	Chemosis	Discharge
Score (average of animals investigated)	0 to 4	0 to 2	0 to 3	0 to 4	0 to 3
1 h	0	0	2	2	1
24 h	0	0	2	0.3	0.3
48 h	0	0	1	0	0
72 h	0	0	0	0	0
Average 24, 48, 72 h	0	0	1.0	0.1	0.1
Maximum average score (including area affected, maximum: 110)	0	0		5.3	
Reversibility*	n.a.	n.a.	c	c	c
Average time for reversion	n.a.	n.a.	72 h	48 h	48 h

n.a.: not applicable

c: completely reversible

Calculation of maximum average score according to "Draize Scale for Scoring Ocular Irritation"

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.4/04:** [redacted] (2005) BAS 310 I (alpha-Cypermethrin) – Acute eye irritation in rabbits. [redacted], Report no. 11H0562/042239, May 19, 2005 (unpublished), BASF Doc-ID: 2005/1011607.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 405 EC method B.5 (2004) OPPTS 870.2400 (1998) MAFF (Japan, 2000)
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000166
3.1.2	Specification	As given in Section A2.
3.1.3	Description	Solid, white powder
3.1.4	Purity	98.8%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.2	**Test animals**	
3.2.1	Species	Rabbit
3.2.2	Strain	New Zealand White A 1077 INRA (SPF)
3.2.3	Source	Centre Lago S.A., Vonnas, France

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

3.2.4	Sex	Male and female
3.2.5	Age	About 3 months
3.2.6	Weight at study initiation	2.60–2.77 kg
3.2.7	Number of animals	3
3.2.8	Control animals	None
3.3	**Administration/ Exposure**	
3.3.1	Preparation of test substance	The test substance was used as delivered.
3.3.2	Amount of active substance instilled	Approx. 40 mg (equivalent to 0.1 mL) Alphacypermethrin
3.3.3	Exposure period	1 hour
3.3.4	Removal of test substance	With 3 to 6 mL of hand warm tap water
3.3.5	Post-exposure period	28 days
3.4	**Examinations**	
3.4.1	Ophthalmoscopic examination	No
3.4.2	Scoring system	According to guideline
3.4.3	Examination time points	1, 24, 48, 72 hours after instillation
3.4.4	Evaluation	Calculation of mean scores for readings at 24, 48 and 72 hours.
3.4.5	Other examinations	
	Area of cornea involved	Scoring table 1 = > 0 ≤ ¼ 2 = > ¼ < ½ 3 = > ½ < ¾ 4 = > ¾
	Discharge	Scoring table 0 = No discharge 1 = Any amount different from normal 2 = Discharge with moistening of the lids and hairs just adjacent to lids 3 = Discharge with moistening of the lids and hairs, and considerable area around the eyes
	Body weight	Just before application of the test substance and after the last reading.
	Mortality	Check for dead or moribund animals twice each workday and once daily on Saturdays, Sundays and on public holidays.
3.5	**Further remarks**	None

Section A6.1.4 **Acute eye irritation in rabbits**
Annex Point IIA6.1.4

4 RESULTS

4.1	**Clinical signs**	Not stated.
4.2	**Average score**	Results are presented in Table A6.1.4- 6.
4.2.1	Corneal opacity	0 (individual mean scores: 0, 0, 0)
4.2.2	Iris	0 (individual mean scores: 0, 0, 0)
4.2.3	Conjunctiva	
	Redness	0.6 (individual mean scores: (1.0, 0.3, 0.3)
	Chemosis	0.1 (individual mean scores: (0.3, 0, 0)
4.3	**Reversibility**	Yes The ocular reactions were reversible in all animals within 72 hours after application.
4.4	**Overall results**	Moderate conjunctival redness was observed in all animals 1 hour after application and persisted in one animal up to 24 hours. Moderate conjunctival redness decreased to slight in two animals after 24 hours and in one animal at the 48 hour-reading and resolved within 72 hours. Slight or moderate conjunctival chemosis was noted in all animals 1 hour after application. Moderate conjunctival chemosis decreased to slight in one animal after 24 hours. Slight discharge was observed in all animals after 1 hour and persisted in one animal up to 24 hours. No other ocular reactions were observed during the study.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The acute eye irritation of Alphacypermethrin was tested in New Zealand White rabbits, according to OECD 405, EC method B.5 (2004), OPPTS 870.2400 (1998) and MAFF (Japan, 2000). A single ocular application of 0.1 mL (approx. 40 mg) of the test substance placed into the conjunctival sac of one eye each of three rabbits, respectively.
5.2	**Results and discussion**	Slight or moderate conjunctival redness, slight or moderate conjunctival chemosis and slight discharge were observed in the animals during the course of the study. The ocular reactions were reversible in all animals within 72 hours after application. The average score (24 to 72 hours) for irritation was calculated to be 0 for corneal opacity and for iris, 0.6 for conjunctival redness and 0.1 for chemosis. Alphacypermethrin does not show an eye irritation potential under the test conditions chosen. Thus, according to the requirements specified by Directive 67/548/EC and subsequent regulations, Alphacypermethrin requires no classification.

Section A6.1.4 Acute eye irritation in rabbits

Annex Point IIA6.1.4

5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities		
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)	
Date	March 2009	
Materials and methods	Ad 3.2.8. it should have been mentioned that the untreated eye serves as the control.	
Results and discussion	Applicant's version adopted	
Conclusion	Moderate to slight conjunctival redness and conjunctival chemosis exist (readings at one hour until one day after application). Alphacypermethrin shows a slightly eye irritation potential, and therefore requires classification with R36 "irritating to eye".	
Reliability	1	
Acceptability	acceptable	
Remarks	In Table A6.1.4- 6, Average 24, 48, 72 h for conjunctiva redness is equal to 0.6.	
	COMMENTS FROM APPLICANT	
Date	7 May 2009	
Materials and methods		
Results and discussion		

Conclusion	Disagree with R36 proposal. C&L criteria for eye irritation are specified in Annex VI of Directive 2001/59/EC (28th ATP to Dangerous Substance Directive 67/548/EEC). The classification criteria are very clear: R36 (irritating to eyes) applies for substances and preparations which … cause significant ocular lesions…. Ocular lesions are significant if the mean scores of the eye irritation test (performed with 6 rabbits)… have any of the following values: *– cornea opacity equal to or greater than 2 but less than 3* *– iris lesion equal to or greater than 1 but not greater than 1.5* *– redness of the conjunctivae equal to or greater than 2.5* *– oedema of the conjunctivae (chemosis) equal to or greater than 2* There is also need for classification when using the GHS classification criteria as given in Regulation No 1272/2008. The criteria for classification as "irritating to eyes (category 2)" are as follows: "*at least in 2 of 3 tested animals, a positive response of:* *– corneal opacity ≥ 1 and/or* *– iritis ≥ 1, and/or* *– conjunctival redness ≥ 2 and/or* *– conjunctival oedema (chemosis) ≥ 2* *calculated as the mean scores following grading at 24, 48 and 72 hours after installation of the test material, and which fully reverses within an observation period of 21 days*" These criteria are clearly not fulfilled according to the study results. Therefore, there is no scientific and legal basis for considering Alphacypermethrin as an eye irritant. The current legal classification for alpha-cypermethrin as given in Dir. 2008/58/EC (30th ATP to Dir 67/548/EEC) is still valid.
Reliability	
Acceptability	
Remarks	This depends on the aggregation level of the data used for the calculation, thus on the rounding error. With reference to the figures in Table A6.1.4-6 of this summary, the mean score is 0.53, rounded 0.5. When individual data are averaged (see study report), the mean score is 0.555, rounded 0.6, as correctly stated by the RMS. However, since both values fall below the classification criterion, the exact value is of limited relevance. COMMENTS OF RAPPORTEUR MEMBER STATE
Date	May 2009
Conclusion	Conclusion of applicant accepted
Remarks	Remarks on conclusion accepted

Table A6.1.4- 7: Acute eye irritation in rabbits.

	Cornea	Iris	Conjunctiva		
	Opacity		Redness	Chemosis	Discharge
Score (average of animals investigated)	0 to 4	0 to 2	0 to 3	0 to 4	0 to 3
1 h	0	0	2	1.7	1
24 h	0	0	1.3	0.3	0.3
48 h	0	0	0.3	0	0
72 h	0	0	0	0	0
Average 24, 48, 72 h	0	0	0.5	0.1	0.1
Maximum average score (including area affected, maximum: 110)	0	0		4	
Reversibility*	n.a.	n.a.	c	c	c
Average time for reversion	n.a.	n.a.	72 h	48 h	48 h

n.a.: not applicable

c: completely reversible

Calculation of maximum average score according to "Draize Scale for Scoring Ocular Irritation"

Section A6.1.5 **Skin sensitisation**
Annex Point IIA6.1.5 **(Guinea pig maximisation test)**

Official use only

1 REFERENCE

1.1	**Reference**	**A6.1.5/01:** [redacted] (2005): BAS 310 I (alpha-Cypermethrin) – Maximization Test in Guinea pigs. [redacted]; Report no. 30H0562/042240, June 27, 2005 (unpublished), BASF Doc-ID: 2005/1011608.
1.2	**Data protection**	Yes
1.2.1	Data owner	BASF
1.2.2	Companies with letter of access	No
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD 406 (1992) EC method B.6 (1996) OPPTS 870.2600 (2003) MAFF (Japan, 2000)
2.2	**GLP**	Yes
2.3	**Deviations**	None stated.

3 MATERIALS AND METHODS

3.1	**Test material**	BAS 310 I (alpha-Cypermethrin)
3.1.1	Lot/Batch number	COD-000165
3.1.2	Specification	As given in Section A2.
3.1.3	Purity	Solid white powder
3.1.4	Description	98.8%
3.1.5	Stability	The stability under storage conditions over the study period was guaranteed.
3.1.6	Preparation of test substance for application	For induction and for challenge: homogenised in 1% cleaned sodium carboxymethylcellulose (CMC)
3.1.7	Pre-test performed on irritant effects	Yes

Section A6.1.5 **Skin sensitisation**
Annex Point IIA6.1.5 **(Guinea pig maximisation test)**

3.2	**Test animals**	
3.2.1	Species	Guinea pigs
3.2.2	Strain	HsdPoc: DH
3.2.3	Source	Harlan Winkelmann, Borchen, Germany
3.2.4	Sex	Female
3.2.5	Age/weight at study initiation	Age: 6–8 weeks Body weight: 424–507g (upon receipt)
3.2.6	Number of animals per group	10
3.2.7	Control animals	5
3.2.8	Further remarks	For the intradermal pretest animals of the strain/quality "Dunkin Hartley, Crl:HA" of the supplier Charles River Deutschland GmbH were used.
3.3	**Administration/ Exposure**	Adjuvant
3.3.1	Induction schedule	Day 0: intradermal induction Day 7: epicutaneous induction Day 21: challenge
3.3.2	Way of induction	First: intradermal Second: topical
3.3.3	Occlusion	Occlusive (for 48 h)
3.3.4	Concentrations used for induction	Intradermal: 5% test substance in 1% CMC; Epicutaneous: 50% test substance in 1% CMC
3.3.5	Concentration Freund's Complete Adjuvant (FCA)	Freund's Complete Adjuvant (FCA) emulsified with 0.9% aqueous NaCl solution in a ratio of 1:1.
3.3.6	Challenge schedule	Day 21: Three weeks after intradermal induction
3.3.7	Concentrations used for challenge	50% test substance in 1% CMC
3.3.8	Re-challenge	No; since no borderline results were observed, a 2nd challenge was not performed.
3.3.9	Scoring schedule	24h and 48h after challenge
3.3.10	Removal of the test substance	Challenge sites were washed with water after the 24 h exposure period.
3.3.11	Positive control substance	Not tested in this study. However, a separate study with Alpha-Hexylcinnamaldehyde is performed twice a year in the laboratory and is included as an appendix.
3.4	**Examinations**	
3.4.1	Pilot study	Yes
3.5	**Further remarks**	None

Section A6.1.5 **Skin sensitisation**
Annex Point IIA6.1.5 **(Guinea pig maximisation test)**

4 RESULTS

4.1	**Results of pilot studies**	After the intradermal induction intense erythema and swelling were observed at the injection sites at which only Freund's complete adjuvant / 0.9% NaCl solution (1:1) was applied. Intradermal injections of a 5% test substance preparation in 1% CMC-solution in doubly distilled water caused moderate and confluent erythema and swelling. At the injection sites of a 5% test substance preparation in Freund's complete adjuvant / 0.9% aqueous NaCl-solution (1:1) intense erythema and swelling were seen. No skin findings were observed in the animals treated with 50% and 25% test substance preparations 24 and 48 hours after removal of the patch.
4.2	**Results of test**	
4.2.1	24h after challenge	No positive response.
4.2.2	48h after challenge	No positive response.
4.2.3	Other findings	After the intradermal induction intense erythema and swelling were observed at the injection sites at which only Freund's complete adjuvant / 0.9% NaCl solution (1:1) was applied. Intradermal injections of a 5% test substance preparation in 1% CMC-solution in doubly distilled water caused moderate and confluent erythema and swelling. At the injection sites of a 5% test substance preparation in Freund's complete adjuvant / 0.9% aqueous NaCl-solution (1:1) intense erythema and swelling were seen in all test group animals. The control group animals, injected with 1% CMC-solution in doubly distilled water did not show any skin reactions. A 50% formulation of 1% CMC-solution with FCA/NaCl caused intense erythema and swelling in all control group animals. The epicutaneous induction with a 50% test substance preparation in 1% CMC-solution in doubly distilled water led to incrustation, partially open (caused by the intradermal induction) and moderate and confluent erythema in all test group animals.
4.3	**Overall result**	None of the 10 test animals showed positive responses at 24 or 48 hours after removal of the challenge patches. Thus, the test material was considered to be non-sensitising to the skin of Guinea pigs.

Section A6.1.5 **Skin sensitisation**
Annex Point IIA6.1.5 **(Guinea pig maximisation test)**

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	The skin sensitizing potential of Alphacypermethrin was tested using the Guinea pig maximisation test according to OECD 406 (1992), EC method B.6 (1996), OPPTS 870.2600 (2003) and MAFF (Japan, 2000) without any deviation.
5.2	**Results and discussion**	None of the surviving animals showed positive responses at 24 or 48 hours after removal of the challenge patches. Therefore, no classification for Alphacypermethrin is required according to the requirements specified by Directive 67/548/EC and subsequent regulations.
5.3	**Conclusion**	
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities		
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE (*)	
Date	March 2009	
Materials and methods	Applicant's version adopted	
Results and discussion	Applicant's version adopted	
Conclusion	5.3. alpha-cypermethrin does not have a sensitising effect on the skin of the guinea pig in the Maximisation Test under test conditions chosen.	
Reliability	1	
Acceptability	acceptable	
Remarks	none	
	COMMENTS FROM APPLICANT	
Date	30 April 2009	
Materials and methods		
Results and discussion		
Conclusion	5.3.: Thank for this remark, but this is only a repetition of the information provided under 5.2.	
Reliability		
Acceptability		
Remarks		
	COMMENTS FROM RAPPORTEUR MEMBER STATE	
Date	May 2009	
Conclusion	Comments of applicant accepted	

Table A6.1.5- 1: Detailed information including induction/challenge/scoring schedule for skin sensitisation test.

	GPMT		Observations/Remarks
	Day	**Application**	
Induction 1	0	Intradermal	Moderate and confluent to intense erythema and swelling at the injection sites of the test substance preparation in all test group animals
Induction 2	7	Topical	Incrustation, partially open (caused by the intradermal induction) could be observed in addition to moderate and confluent erythema and swelling in all test group animals
Challenge	21	Topical	Not stated
Scoring 1	23	–	No positive response
Scoring 2	24	–	No positive response