Section A6.1.1 Acute Oral Toxicity - Rat

Annex Point IIA 6.1

Rat, cypermethrin, oral LD50

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted]; Acute Oral LD50 in the Rat of CGA 55186 Tech. (cypermethrin) – (administration in oily medium); [redacted], report No.: [redacted] 9 April 1984 (unpublished) Dates of work: 13 February 1984 – 2 May 1984	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Chimac-Agriphar s.a.	
1.2.2			
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 authorisation	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No Existing study partially conforming to 92/69/EEC (OECD 401)	
2.2	**GLP**	No GLP was not compulsory at the time the study was performed	
2.3	**Deviations**	Yes Protocol partially conforms to OECD 401 (EC method B1) but with limited enquiries	
		3 MATERIALS AND METHODS	
3.1	**Test material**	CGA 55186 tech (cypermethrin cis:trans/40:60)	
3.1.1	Lot/Batch number	307046	
3.1.2	Specification	Deviating from specification given in section 2 as follows	
3.1.2.1	Description	Liquid	
3.1.2.2	Purity	92.6%	
3.1.2.3	Stability	Guaranteed by original sponsor (Ciba-Geigy Ltd)	X
3.2	**Test Animals**		
3.2.1	Species	Rat	
3.2.2	Strain	Tif:RAIf (SPF), F3-crosses of RII 1/Tiff x RII 2/Tif	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	7-8 weeks, 162-225 g	
3.2.6	Number of animals per group	5 males, 5 females	
3.2.7	Control animals	No	

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3.3	**Administration/ Exposure**	Oral	
3.3.1	Postexposure period	14 days or until all symptoms disappeared	
		Oral	
3.3.2	Type	Gavage	
3.3.3	Concentration	Gavage: 5000, 2500, 1200, 600, 300 mg/kg bw food consumption per day - ad libitum	
3.3.4	Vehicle	Arachis oil Ph.H.VI Siegfried AG	
3.3.5	Concentration in vehicle	As 3.3.3	
3.3.6	Total volume applied	10 ml/kg bw	
3.3.7	Controls	None	
3.4	**Examinations**	Mortality recorded twice daily (once daily on weekends), clinical observations daily, body weight recorded on days 1, 7, 14 and at death. Gross necropsy at death and all survivors at the end of the observation period.	
3.5	**Method of determination of LD_{50}**	Logit method (J. Berkson, J.Am.Stat. Ass. 39. 357-65, 1944): LD50 including the 95% confidence limit	
3.6	**Further remarks**	-	
		4 RESULTS AND DISCUSSION	
4.1	**Clinical signs**	Dyspnoea, exophthalmus, ruffled fur and curved body position observed. Diarrhoea, tremor, tonic clonic convulsion, salivation, sedation and lateral/ventral body positions were also seen. Surviving animals recovered within 10 to 12 days.	X
4.2	**Pathology**	Autopsies showed no gross lesions in the three lowest dose groups (300, 600, and 1200 mg/kg bw groups). In the 2500 mg/kg bw group one female had nasal discharge. In the 5000 mg/kg bw group a reddish and mottled lung was found and one animal had a dilated small intestine.	
4.3	**Other**		
4.4	**LD_{50}**	LD50 in males 1732 (1027-2922) mg/kg bw LD50 in females 2150 (1342-4024) mg/kg bw LD50 in both sexes 1945 (1449-2676) mg/kg bw	

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		5 APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	Acute oral administration in rat with 14 day post-treatment observation based on OECD guideline 401.
5.2	**Results and discussion**	An LD50 of 1945 mg/kg (with 95% confidence limits) was calculated for both sexes.
5.3	**Conclusion**	
5.3.1	Reliability	2
5.3.2	Deficiencies	Yes Limited enquiries, however protocol was based on EC test method B1. Study has been previously evaluated under Directive 91/414/EC.

	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, 2007.
Materials and Methods	The applicant's version is acceptable with the following amendment: 3.1.2.3 Stability: …but data not shown.
Results and discussion	The applicant's version is adopted with the following amendments: Revised version **4.1 Clinical signs**: Dyspnoea, exophthalmus, ruffled fur and curved body position was observed in all test groups. Diarrhoea and tremor were also observed. Tonic clonic convulsion was observed from 600 mg/kg bw onwards. At higher concentrations also salivation, sedation and lateral/ventral body positions were observed. Surviving animals recovered within 10 to 12 days. Animals died during the first 3 days post-exposure.
Conclusion	LD50 in both sexes: 1945 (1449-2676) mg/kg bw LD50 in females: 2150 (1342-4024) mg/kg bw **LD50 in males: 1732 (1027-2922) mg/kg bw** LD50 males = 1732 mg/kg bw will be used for risk characterization purposes.
Reliability	*2*
Acceptability	acceptable (Although the study was performed before GLP and despite the limited enquiries, the protocol was based on EC test method B and is found acceptable.)
Remarks	

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	COMMENTS FROM ...
Date	*Give date of comments submitted*
Materials and Methods	*Discuss additional relevant discrepancies referring to the (sub)heading numbers and to applicant's summary and conclusion.* *Discuss if deviating from view of rapporteur member state*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*
Remarks	

Table A6_1_1. Table for Acute Oral Toxicity

Dose [mg/kg]	*Number of dead / number of investigated*	*Time of death (range)*	*Observations*
300	0/10	-	Dyspnoea, exophthalmus, ruffled fur, curved body position. All animals recovered by day 10.
600	0/10	-	Dyspnoea, exophthalmus, ruffled fur, diarrhoea, curved body position, convulsion. All animals recovered by day 11.
1200	1/10	Day 1 (post-exposure period)	Dyspnoea, exophthalmus, ruffled fur, ventral or curved body position, tremor, convulsion. All surviving animals recovered by day 10.
2500	7/10	Day 1 (post-exposure period)	Sedation, dyspnoea, salivation, ruffled fur, diahrroea, lateral or curved body position, convulsion. Surviving animals recovered by day 12.
5000	10/10	Days 1 to 3 (post-exposure period)	Dyspnoea, exophthalmus, salivation, ruffled fur, ventral, lateral or curved body position, tremor, convulsion.
LD_{50} value	1945 (1449-2676) mg/kg bw		