Section A6.1.2 Acute Dermal Toxicity - Rat

Annex Point IIA 6.1.2

Rat, cypermethrin, dermal LD50 (limit test)

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted]; Acute Dermal LD50 in the Rat of CGA 55186 Tech. (cypermethrin); [redacted] Dates of work: 14 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**	Yes Existing study partially conforming to method B.3. of Directive 92/69/EEC (OECD guideline 402).	
2.2	**GLP**	No GLP was not compulsory at the time the study was performed	
2.3	**Deviations**	Yes Description of necropsy findings are missing. Substance should normally be applied under semi-occluded dressing.	
		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/Tif x RII 2/Tif	
3.2.3	Source	[redacted]	
3.2.4	Sex	Males and females	
3.2.5	Age/weight at study initiation	7-8 weeks, 179-224 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	X
3.3.1	Post exposure period	14 days or until all symptoms disappeared	
		Dermal	
3.3.2	Area covered	10% of body surface	
3.3.3	Occlusion	Dermal gauze lined occlusive dressing	
3.3.4	Vehicle	None	
3.3.5	Concentration in vehicle	2000 mg/kg bw	
3.3.6	Total volume applied	Linear to dose	
3.3.7	Removal of test substance	Water (lukewarm)	
3.3.8	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**	No mortalities in either males or females. Clinical observations included dyspnoea, ruffled fur, curved and ventral body position. A transient diarrhoea was observed. All animals recovered within 10 days. No reaction at site of application.	
4.2	**Pathology**	No gross lesions found at necropsy.	
4.3	**Other**		
4.4	**LD_{50}**	LD50 in both sexes >2000 mg/kg bw	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Dermal occlusive application in rat of 2000 mg/kg cypermethrin for 24 hours with 14 day post-treatment observation (based on OECD guideline 402).	
5.2	**Results and discussion**	No mortalities were observed. An LD50 of >2000 mg/kg (with 95% confidence limits) was determined for both sexes.	
5.3	**Conclusion**		
5.3.1	Reliability	2	

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5.3.2	Deficiencies	Yes Detailed description of necropsy findings are missing and the test substance should be applied under semi-occluded dressing. Considering that no mortalities were observed and all animals recovered within 10 days, this is not thought to influence the acceptability of the study. Study has been previously evaluated and accepted 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 adopted with following amendments: 3.1.2.3 Stability: … but data not shown. 3.3 Administration/exposure: Dermal, one single dose applied onto the skin of the back.
Results and discussion	The applicant's version is adopted with the following amendment: Table A6.1.2_1: Table for acute dermal toxicity.
Conclusion	LD50 of >2000 mg/kg (with 95% confidence limits) determined for both sexes.
Reliability	2
Acceptability	acceptable (Although the study was performed before GLP and despite the limited enquiries, the protocol was based on OECD guideline No. 402 and EC test method B3.)
Remarks	
	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 A6.1.2_1: Table for Acute Dermal Toxicity

Dose [mg/kg]	*Number of dead / number of investigated*	*Time of death (range)*	*Observations*
2000 (limit dose)	0/10	-	Dyspnoea, ruffled fur, ventral and curved body position. Transient diarrhea. All animals recovered by day 10. **No** local reaction on the site of application.
LD_{50} value	> 2000 mg/kg bw		