Section A6.1.1 Acute Toxicity

Annex Point IIA6.1 6.1.1 Acute oral toxicity in rats (LD_{50} test)

Official use only

1 REFERENCE

1.1	**Reference**	[redacted], 1990, KUE 13032 C 90 VM 00670/1146 B - Study for acute oral toxicity in rats, [redacted], Report [redacted], 1990-07-19 (unpublished)
1.2	**Data protection**	Yes
1.2.1	Data owner	Bayer CropScience AG
1.2.2	Companies with letter of access	Bayer Chemicals AG
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/IA.

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes OECD-Guideline 401, EPA-Guideline Subdivision F, Series 81-1
2.2	**GLP**	Yes
2.3	**Deviations**	No

3 MATERIALS AND METHODS

3.1	**Test material**	As given in section 2 of dossier.
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	As given in section 2 of dossier.
3.1.2.1	Description	White powder
3.1.2.2	Purity	[redacted]
3.1.2.3	Stability	No analytical confirmation of the stability of the test substance was performed.
3.2	**Test Animals**	
3.2.1	Species	Rat
3.2.2	Strain	Wistar (Bor: WISW)
3.2.3	Source	[redacted]
3.2.4	Sex	Males and females (1:1)
3.2.5	Age/weight at study initiation	Age: 7-10 weeks Weight: 167-181 g
3.2.6	Number of animals per group	5 per sex per group
3.2.7	Control animals	No

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3.3	**Administration/ Exposure**	Oral
3.3.1	Postexposure period	14 days
		Oral
3.3.2	Type	Gavage
3.3.3	Concentration	1000, 2500, or 5000 mg/kg
3.3.4	Vehicle	The test substance was formulated in demineralized water using Cremophor EL 2 % v/v.
3.3.5	Concentration in vehicle	100 mg/ml; 250 mg/ml; 500 mg/ml
3.3.6	Total volume applied	10 ml/kg bw
3.3.7	Control	—
3.4	**Examinations**	Clinical observations, necropsy, body weights
3.5	**Method of determination of LD_{50}**	Not determined since no mortality occurred.
3.6	**Further remarks**	None
		4 RESULTS AND DISCUSSION
4.1	**Clinical signs**	The 1000 mg/kg males and females showed signs of soft faeces. Apathy and piloerection also occurred in the higher doses. Additionally, laboured breathing, increased urine discharge and a slight increase in water intake were only observed in the 5000 mg /kg dose group. Symptoms occurred within the first 3 hours until day 6 post-application.
4.2	**Pathology**	No effects observed.
4.3	**Other**	A transient influence on body weights was observed during the post-treatment observation period in male and female rats in the 5000 mg/kg dose group as well as in one male and one female in the 2500 mg/kg dose group.
4.4	**LD_{50}**	LD_{50} >5000 mg/kg for males + females. No lethal effect at maximal dose.

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		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	A study for acute oral toxicity in the rat was conducted with the test substance dichlofluanid. The methods used to perform the study complied with the OECD-Guideline 401 and the US-EPA-Guideline, Subdivision F, Series 81-1. The purpose of the study was to enable the product to be classified (labelling), and to assess the potential acute health hazard when handling the test substance.	
5.2	**Results and discussion**	The clinical signs observed (apathy, breathing disorders, piloerection, soft faeces, increased urine discharge, increased water intake) were mainly moderate and lasted maximally until day 6. There were no delayed effects observed. No lethality occurred.	X
5.3	**Conclusion**	As in this study occurred, the test substance dichlofluanid proved to be of low toxicity following acute oral administration	X
5.3.1	Reliability	2	
5.3.2	Deficiencies	Yes No analytical confirmation of the homogeneity, stability or concentration of the test substance in the administered formulations was performed. The validity and assessment of the results are not limited as a result of these deficiencies.	

Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	20/09/04
Materials and Methods	As described above - IUCLID 5.1.1
Results and discussion	Clinical signs of toxicity were observed in all treated animals comprising; soft faeces at all doses, apathy and piloerection at 2500 mg/kg and above, with laboured breathing, increased urine discharge and a slight increase in water intake observed at 5000 mg/kg only. These signs occurred within 3 hours post–dose and resolved by day 6 post-dose. No deaths were observed.
Conclusion	It was not possible to identify an acute oral NOAEL as clinical signs of toxicity were observed at all dose levels.
Reliability	2
Acceptability	Acceptable
Remarks	The UK agrees with the conclusions presented, but has presented further dose-response information, and added further information to the conclusion.
	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 bw]	Toxicological results*	Duration of clinical signs	Time of death	Mortality (%)
males				
1000	0/2/5	2h45' – 2d	—	—
2500	0/2/5	3h45' – 3d	—	—
5000	0/2/5	2h15' – 6d	—	—
LD_{50} value> 5000 mg/kg bw				
females				
1000	0/2/5	6h00' – 1d	—	—
2500	0/2/5	3h45' – 3d	—	—
5000	0/2/5	2h15' – 6d	—	—
LD_{50} value> 5000 mg/kg bw				

* first number = number of dead animals

second number = number of animals with signs

third number = number of animals used