Section A6.1.3 Acute Toxicity

Annex Point IIA6.1 6.1.3 Acute inhalation toxicity to the rat (LC_{50} Test)

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted], 1988, KUE 13032C 90 VM 1146 B- Study for acute inhalation toxicity to the rat according to OECD guideline no. 403, [redacted], Report No. [redacted], 1988-03-07 (unpublished)	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 No. 403 - EC Guideline B.2 and the EPA (FIFRA) Guideline § 81-3.	
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 with slight intrinsic odour.	
3.1.2.2	Purity	[redacted]	
3.1.2.3	Stability	The stability was assured over the period of the study (Analysis: July 15, 1986).	
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: 7-12 weeks Weight: 160-220 g	
3.2.6	Number of animals per group	5 per sex per dose	
3.2.7	Control animals	Yes (air control)	

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3.3	**Administration/ Exposure**	Inhalation
3.3.1	Postexposure period	14 days
3.3.2	Concentrations	For technical reasons, it is impossible to specify exact nominal concentrations. Analytical concentrations: 0, 94.7, 506.7, 1526.7, 2580 [mg/m³]
3.3.3	Particle size	MMAD (mass median aerodynamic diameter) ± GSD (geometric standard deviation) for the dust : 94.7 mg/m³ air: MMAD = 4.8 µm (± 1.79µm) 506.7 mg/m³ air: MMAD = 5.47 µm (± 1.74µm) 1526.7 mg/m³ air: MMAD = 5.78 µm (± 1.8µm) 2580 mg/m³ air: MMAD = 6.0 µm (± 1.59µm)
3.3.4	Type or preparation of particles	The dust-containing atmosphere was generated by using a "[redacted] dust generator" or with an RBG 1000 brush-type dust generator.
3.3.5	Type of exposure	Nose/head only
3.3.6	Vehicle	—
3.3.7	Concentration in vehicle	—
3.3.8	Duration of exposure	4 h
3.3.9	Controls	Controls were exposed to air under the same conditions as the treatment groups.
3.4	**Examinations**	Clinical observations, necropsy, body weight.
3.5	**Method of determination of LC_{50}**	LC_{50} calculation is performed according to the method of A. P. Rosiello, J. M. Essigmann and G. N. Wogan, as modified by Pauluhn. This procedure is based on the "maximum likelihood" method of C.I. Bliss.
		4 RESULTS AND DISCUSSION
4.1	**Clinical signs**	After treatment with 0.095, 0.5, 1.5 and 2.58 mg/l air, males and females showed signs of dyspnoea, laboured breathing, respiratory noises, reduced motility, serosanguineous nasal discharge, languor and blood-encrusted eyes, periorbital hair loss and corneal opacity (only after dosing with 1.5 mg/l air), rough fur, and blood encrusted nose margins (only observed in the 2.58 mg/l dose-group).
4.2	**Pathology**	Gross pathological examinations of the 0.095 mg/l and the 0.5 mg/l group rats sacrificed at the end of the observation period gave no indications of macroscopically apparent organ damage. The frequent presence of distended lungs was not considered to be toxicologically significant since a clear concentration dependency could not be established. The following significant findings were determined in the rats which died during the observation time (treatment groups from

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		0.5 to 2.58 mg/l): markedly distended lung with partially hepatoid appearance; serous fluid in thorax and lungs; liver, spleen, and kidney pale; contents of gastrointestinal tract yellowish-mucid, also bloody isolated cases; glandular stomach inflamed; bloody-encrusted eyes, and corneal opacity.	
4.3	**Other**	A toxicologically significant, substance-induced effect on the body weights during the observation period was determined starting with the 1.5 mg/l treatment group.	X
4.4	**LC_{50}**	LC_{50} approximately 1.2 mg/l air for males + females.	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The method used to perform the study complied with the OECD-Guideline No. 403 and with the EC Guideline B.2 and the EPA (FIFRA) Guideline § 81-3. A study for acute inhalation toxicity in the rat was conducted with the test substance dichlofluanid. 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 substance.	
5.2	**Results and discussion**	The observed clinical signs (starting with the 0.5 mg/l treatment group) as well as the pathological findings were considered to be related to the pronounced respiratory tract irritation potential of the test substance. The no-observed-effect-level was 0.095 mg/l air.	
5.3	**Conclusion**	The study results demonstrate that an elevated acute hazard potential for humans exists when the product (powder) is handled due to its mucous membrane irritation potential. LC_{50} approximately 1.200 mg/l air for males + females.	
5.3.1	Reliability	1	
5.3.2	Deficiencies	No	

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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 5.1.2 1/3]
Results and discussion	Deaths occurred at concentrations of 0.5 mg/l and above, from day 0-day-3 post exposure.
Conclusion	As described above
Reliability	1
Acceptability	Acceptable
Remarks	The UK CA broadly agrees with the applicants' summary and conclusions. The UK CA has added some additional information on the mortalities observed in the study.
	COMMENTS FROM ...
Date	
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A6_1-1.3 Table for acute inhalation toxicity

Dose [mg/m³ air]	Toxicological results*	Duration of clinical signs	Time of death	Mortality (%)	Particles ≤ 5 µm (%)
males					
0	0/0/5	—	—	—	—
94.7	0/0/5	—	—	—	53
506.7	0/5/5	4h – 13d	—	—	44
1526.7	1/5/5	4h – 10d	1d	20	41
2580.0	5/5/5	4h – 3d	0d – 3d	100	35
LC_{50} value approximately 1200 mg/m³ air					

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females					
0	0/0/5	—	—	—	—
94.7	0/0/5	—	—	—	53
506.7	2/5/5	4h – 4d	1d – 2d	40	44
1526.7	2/5/5	4h – 14d	0d – 3d	40	41
2580.0	5/5/5	4h – 3d	0d – 3d	100	45
LC_{50} value approximately 1200 mg/m^3 air					

*first number = number of dead animals

second number = number of animals with signs

third number = number of animals used