Section A6.1.4 Acute Skin Irritation

Annex Point IIA6.1 6.1.4 Acute dermal irritation toxicity in rabbits

Official use only

1 REFERENCE

1.1	**Reference**	[redacted], 1982, KUE 13 032 C (Dichlofluanid) - Studies to determine a primary irritant effect on the skin and mucous membranes, [redacted] 1982-07-07 (unpublished)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 The study was performed in accordance with the guidelines of the US Department of Agriculture, Federal Register, Vol. 38, No. 187, p. 27019, 1973. The methods used in this study are also comparable with the OECD-Guideline 404.
2.2	**GLP**	No GLP was not compulsory at the time the study was performed.
2.3	**Deviations**	Yes Deviations from the OECD-Guideline 404: With an exposure period of 24 hours and occlusive dressing the treatment in the test is even more intense than requested according to current OECD-guideline (exposure 4 hours, semi-occlusive dressing). In addition 6 animals were examined for signs only at 24 and 72 hours after patch removal (OECD-Guideline 404: 3 animals were examined at 60 minutes, 24, 48 and 72 hours after patch removal). The further observations until day 7 post-exposure were not documented. The substance was tested on the intact and scarified skin, whilst the OECD-Guideline 404 recommended the testing only on intact skin. Description, purity, and stability of the test substance were not reported.

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	—
3.1.2.2	Purity	—
3.1.2.3	Stability	—
3.2	**Test Animals**	

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3.2.1	Species	Rabbits
3.2.2	Strain	New Zealand White
3.2.3	Source	[redacted]
3.2.4	Sex	Males and females
3.2.5	Age/weight at study initiation	Age: adult Weight: 3 – 4 kg
3.2.6	Number of animals per group	6
3.2.7	Control animals	Untreated skin areas of the test animals served as control.
3.3	**Administration/ Exposure**	Dermal
3.3.1	Application	
3.3.1.1	Preparation of test substance	0.5 g of the test substance was pasted with water.
3.3.1.2	Test site and Preparation of Test Site	The substance was tested on intact and scarified skin.
3.3.2	Occlusion	Occlusive
3.3.3	Vehicle	—
3.3.4	Concentration in vehicle	—
3.3.5	Total volume applied	0.5 g
3.3.6	Removal of test substance	Water
3.3.7	Duration of exposure	24 h
3.3.8	Post-exposure period	7 days
3.3.9	Controls	Untreated skin areas of the test animals served as control.
3.4	**Examinations**	
3.4.1	Clinical signs	—
3.4.2	Dermal examination	Yes

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3.4.2.1	Scoring system	Reddening 0 – 4 (0 = no reddening, 1 = mild, 2 = minimal to moderate, 3 = moderate to severe reddening, 4 = deep reddening, with partial cauterisation) Swelling 0 – 4 (0 = no swelling, 1 = very slight, 2 = slight; margins well defined, 3 = moderate; margins raised approximately 1 mm, 4 = severe swelling; margins raised > 1 mm, swelling larger than the exposed area)
3.4.2.2	Examination time points	24 h, 72 h
3.4.3	Other examinations	—
3.5	**Further remarks**	None

4 RESULTS AND DISCUSSION

4.1	**Average score**	Remark: the original study bears no average scores. The average scores reported below were calculated following the recommendations of the EU and Norway authorities. In this case: for a 6-animal test a mean score was calculated across the two scoring times (24 and 72 hours) divided by 12 and across all 6 animals for oedema grades and for erythema grades, separately. No information was provided at 48 hours. Two discrete assessments were done for intact and scarified skin.
4.1.1	Erythema	Intact skin: Individual results: animal 1/animal 2/animal 3/animal 4/animal 5/animal 6 24 h: 2/1/1/1/1/1 grade sum: 7 48 h: — 72 h: 2/1/0/1/0/1 grade sum: 5 Average score 24 h + 72 h: 1.0 Scarified skin: Individual results: animal 1/animal 2/animal 3/animal 4/animal 5/animal 6 24 h: 2/2/2/2/1/2 grade sum: 11 48 h: — 72 h: 2/2/1/0/0/1 grade sum: 6 Average score 24 h + 72 h: 1.4

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4.1.2	Oedema	Intact skin: Individual results: animal 1/animal 2/animal 3/animal 4/animal 5/animal 6 24 h: 1/1/1/1/0/1 grade sum: 5 48 h: — 72 h: 0/0/0/0/0/0 grade sum: 0 Average score 24 h + 72 h: 0.4 Scarified skin: Individual results: animal 1/animal 2/animal 3/animal 4/animal 5/animal 6 24 h: 1/1/2/1/0/1 grade sum: 6 48 h: — 72 h: 0/0/0/0/0/0 grade sum: 0 Average score 24 h + 72 h: 0.5	
4.2	**Reversibility**	The mild primary irritation of the skin was not entirely reversible within 72 h. The very slight swelling was reversible within 72 h.	
4.3	**Other examinations**	None	
4.4	**Overall result**	The dermal application of the test substance caused a mild primary irritant effect. The primary skin irritation index is 1.6	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The methods used in this study are in accordance with the guidelines of the US Department of Agriculture, Federal Register, Vol. 38, No. 187, p. 27019, 1973. The methods are also comparable with the OECD-Guideline 404, however some deviations occur, which are described in 2.3 (this section). This study for acute dermal irritation toxicity in rabbits was conducted with the test substance KUE 13 032C (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 test substance.	
5.2	**Results and discussion**	The mild primary irritation of the skin was not entirely reversible within 72 h. The very slight swelling was reversible within 72 h.	
5.3	**Conclusion**	The dermal application of the test substance caused a mild primary irritant effect.	X
5.3.1	Reliability	2	
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	20/09/04
Materials and Methods	As described above. [IUCLID 5.2.1 1/2]
Results and discussion	As described above
Conclusion	The scores obtained in this study did not meet the EU criteria for classification as a skin irritant.
Reliability	2
Acceptability	Acceptable
Remarks	The UK CA agrees with the applicants summary and conclusions, but has suggested an additional comment to make it clear that the substance is not a skin irritant.
	COMMENTS FROM ...
Date	
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A6_1-4S-1. Table for skin irritation study

Score (6 rabbits; exposure for 24 h under occlusive conditions)	**Examination time point**	**Erythema** (reddening)	**Edema** (swelling)
Grade sum (0 to maximum 4)[#]	**Intact skin**		
	24 h	7	5
	72 h	5	0
	Scarified skin		
	24 h	11	6
	72 h	6	0
Average* score intact skin	24h, 72h	1.0	0.4
Average* score scarified skin	24h, 72h	1.4	0.5
Reversibility:		not completely reversible	completely reversible
Average time for reversibility		—	72 h

[#] Reddening (Erythema) 0 – 4

0 = no reddening,

1 = mild,

2 = minimal to moderate,

3 = moderate to severe reddening,

4 = deep reddening, with partial cauterisation

[#] Swelling (Edema) 0 – 4

0 = no swelling,

1 = very slight,

2 = slight; margins well defined,

3 = moderate; margins raised approximately 1 mm,

4 = severe swelling; margins raised > 1 mm, swelling larger than the exposed area)

* Remark: the original study bears no average scores. The above reported average scores were calculated following the recommendations of the EU and Norway authorities. In this case: for a 6-animal test a mean score was calculated across the two scoring times (24 and 72 hours) divided by 12 and across all 6 animals for edema grades and for erythema grades, separately. No information was provided at 48 hours. Two discrete assessments were done for intact and scarified skin.