Section 6.1.4 Acute Eye Irritation

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

Official use only

1 REFERENCE

1.1	**Reference**	[redacted], 1982, KUE 13 032C (Dichlofluanid) – Studies to determine a primary irritant effect on the skin and mucous membranes, [redacted], Report No. [redacted], 1982-07-07 (unpublished)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 Health, Education, and Welfare, Federal Register 37, 83 of April 24, 1972, p. 8534 – 35. Furthermore the methods used in this study are comparable with the OECD-Guideline 405.
2.2	**GLP**	No GLP was not compulsory at the time the study was performed.
2.3	**Deviations**	Yes Deviations from the OECD-guideline 405: - The purity and stability of the test substance were not reported, - Examination of the eyes before commencement of the study was not performed, - The grading time at 48 hours post-application is missing

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	—

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3.2	**Test Animals**	
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	The untreated eye of the test animals served as control.
3.3	**Administration/ Exposure**	
3.3.1	Preparation of test substance	Test substance was used as delivered.
3.3.2	Amount of active substance instilled	0.1 g
3.3.3	Exposure period	24 h
3.3.4	Postexposure period	14 days
3.4	**Examinations**	
3.4.1	Ophthalmoscopic examination	Yes
3.4.1.1	Scoring system	Grades of ocular lesions: Cornea 0 – 4 (0 = no finding, 1 = slight, disperse, diffuse opacification, 2 = extensive, diffuse opacification, iris blurred, 3 = mother-of-pearl-like opacification, iris and pupil hardly recognisable, 4 = complete opacification, ulceration) Iris 0 – 2 (0 = no finding, 1 = swelling, reddening, positive light reaction, 2 = severe reddening and swelling, no light reaction) Conjunctival Redness 0 – 3 (0 = reddening, vessels normal, 1 = vessels abnormally filled, 2 = diffuse reddening, 3 = diffuse deep reddening) Swelling 0 – 4 (0 = no swelling, 1 = slight swelling, 2 =severe swelling, lids everted, 3 = lids cover one half of eye, 4 = lids cover more than half eye, necroses and ulcers on the conjunctivas)
3.4.1.2	Examination time points	1 h, 24 h, 72 h, 7 d, 14 d
3.4.2	Other investigations	—
3.5	**Further remarks**	—

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4 RESULTS AND DISCUSSION

4.1	**Clinical signs**	—
4.2	**Average score**	Remark: the study bears no average scores. The following values were calculated only for this study summary using the documented individual scoring values.
4.2.1	Cornea	Individual results:
		animal 1/animal 2/animal 3/animal 4/animal 5/animal 6
		24 h: 0/0/0/0/1/0
		48 h: —
		72 h: 0/0/0/0/1/0
		Average score 24 h + 72 h: 0/0/0/0/1/0
		Mean grade: 0.17
4.2.2	Iris	Individual results:
		animal 1/animal 2/animal 3/animal 4/animal 5/animal 6
		24 h: 0/1/0/0/1/1
		48 h: —
		72 h: 0/0/0/0/0/1
		Average score 24 h + 72 h: 0/0.5/0/0/0.5/1
		Mean grade: 0.3
4.2.3	Conjunctiva	
4.2.3.1	Redness	Individual results:
		animal 1/animal 2/animal 3/animal 4/animal 5/animal 6
		24 h: 3/3/3/3/3/3
		48 h: —
		72 h: 1/3/2/3/3/2
		Average score 24 h + 72 h: 2/3/2.5/3/3/2.5
		Mean grade: 2.7
4.2.3.2	Chemosis	Individual results:
		animal 1/animal 2/animal 3/animal 4/animal 5/animal 6
		24 h: 1/3/1/2/3/3
		48 h: —
		72 h: 0/0/0/0/1/0
		Average score 24 h + 72 h: 0/2/1/1/1/1
		Mean grade: 1.0

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4.3	**Reversibility**	Yes Redness and chemosis of the conjunctiva; swelling, reddening and positive light reaction of the iris; slight, disperse and diffuse opacification of the cornea. All effects were reversible within the post-treatment observation time (14 d).	
4.4	**Other**	—	
4.5	**Overall result**	The test substance had a moderately irritant effect on the mucosa.	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The method used in this study is in accordance with the guideline of the US Department of Health, Education, and Welfare, Federal Register 37, 83 of April 24, 1972, p. 8534 - 35. The methods used in this study were also comparable with the OECD-guideline 405, although slight deviations occurred, which are described in 2.3 (this section). 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 test substance had a moderately irritant effect on the mucosa. Mild reversible swelling of the iris was seen in individual cases. A temporary opacification of the cornea was seen in one rabbit. All changes were reversible within the post-treatment observation time.	
5.3	**Conclusion**	The test substance could be classified as moderately irritant to the mucosa.	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 5.2.2 1/2]
Results and discussion	As described above
Conclusion	The score obtained in this study for conjunctival redness meets the EU criteria for classification as an eye irritant
Reliability	2
Acceptability	Acceptable
Remarks	The UK CA agrees with the applicants' assessment, but has amended the conclusion to make it clear that the substance should be considered as an eye irritant.
	COMMENTS FROM ...
Date	
Materials and Methods	
Results and discussion	
Conclusion	
Reliability	
Acceptability	
Remarks	

Table A6_1_4E-1. Results of eye irritation study

	Cornea	**Iris**	**Conjunctiva**	
			redness	chemosis
Score (animal 1/animal 2/animal 3/animal 4/animal 5/animal 6)	0 to 4[#]	0 to 2[#]	0 to 3[#]	0 to4[#]
60 min	0/0/0/0/0/0	0/0/0/0/0/0	0/0/0/0/0/0	0/0/0/0/0/0
24 h	0/0/0/0/1/0	0/1/0/0/1/1	3/3/3/3/3/3	1/3/1/2/3/3
48 h	—	—	—	—
72 h	0/0/0/0/1/0	0/0/0/0/0/1	1/3/2/3/3/2	0/0/0/0/1/0
Average 24h, 72h[&]	0/0/0/0/1/0	0/0.5/0/0/0.5/1	2/3/2.5/3/3/ 2.5	0/2/1/1/1/1
Mean grade[&] (average score 24h + 72h of all animals)	0.17	0.3	2.7	1.0
Maximum average score (including area affected, max 110)	Not determined.			
Reversibility[*]	—	c	c	c
Average time for reversion	—	72 h	14 d	7 d
* c : completely reversible n c : not completely reversible n : not reversible				

[&] Remark: the study bears no average scores. The following values were calculated only for this study summary using the documented individual scoring values.

[#] Grades of ocular lesions:

Cornea 0 – 4:

(0 = no finding, 1 = slight, disperse, diffuse opacification, 2 = extensive, diffuse opacification, iris blurred, 3 = mother-of-pearl-like opacification, iris and pupil hardly recognisable, 4 = complete opacification, ulceration)

Iris 0 – 2:

(0 = no finding, 1 = swelling, reddening, positive light reaction, 2 = severe reddening and swelling, no light reaction)

Conjunctivas:

Redness 0 – 3:

(0 = reddening, vessels normal, 1 = vessels abnormally filled, 2 = diffuse reddening, 3 = diffuse deep reddening)

Swelling 0 – 4:

(0 = no swelling, 1 = slight swelling, 2 = severe swelling, lids everted, 3 = lids cover one half of eye, 4 = lids cover more than half eye, necroses and ulcers on the conjunctivas)