

**Section A7.1.1.1.1 Hydrolysis as a function of pH and identification of
Annex Point IIA7.6.2.1 breakdown products**

			Official use only
1 REFERENCE			
1.1	Reference	R. Wilmes, 1982, Properties of Pesticides in Water, Hydrolytic stability – Euparen, Bayer AG, Report No. MR 86003 (unpublished), 1982-05-21	
1.2	Data protection	Yes	
1.2.1	Data owner	Bayer Crop Science 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 Method “Hydrolysis as a function of pH” (OECD guideline No. 111)	
2.2	GLP	No, GLP was not compulsory at the time the study was performed	
2.3	Deviations	No	
3 MATERIALS AND METHODS			
3.1	Test material	As given in section 2 of dossier (dichlofluanid (= Euparen))	
3.1.1	Lot/Batch number	No lot or batch no. mentioned	X
3.1.2	Specification	As given in section 2 of dossier	
3.1.3	Purity	■	
3.1.4	Further relevant properties	Water solubility: 1.8 mg/l at 293 K; Vapour pressure: 1.1×10^{-7} at 293 K	
3.2	Reference substance	No	X
3.2.1	Initial concentration of reference substance	-	
3.3	Test solution	A solution of 100 mg /l Euparen in acetonitrile was diluted with buffer solution (pH 4: Merck Titrisol, Citrate buffer; pH 7: Riedel de Haen Fixanal, Phosphate buffer and pH 9: Merck Titrisol; each one diluted 1:1 with redistilled water) at a ratio of 1:100, so that solution of 1 mg/l Euparen resulted containing 1% acetonitrile. To get a test solution of dimethylaminosulfanilid (DMSA), between 8 and 10 mg/l DMSA were diluted with buffer solutions of pH 4, 7 and 9 (pH 4 and 9: Merck Titrisol, pH 7: Riedel de Haen Fixanal; each diluted 1:1 with redistilled water)	X
3.4	Testing procedure		
3.4.1	Test system	The buffer solutions were sealed into glass ampoules and stored in a water bath of given temperature (personal communication with study	X

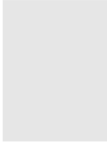
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		author).	
		Buffer solutions of DMSA were incubated for one week at 55 °C or kept in a refrigerator.	
		A Hewlett Packard hp 1084 B HPLC was used to determine the concentrations of dichlofluanid and DMSA.	
3.4.2	Temperature	Experiments were run at different temperatures. pH 7: 20 and 30 °C; pH 4: 30 and 40 °C; pH 9: room temperature Test solutions of DMSA were incubated at 55 °C or kept in a refrigerator.	X
3.4.3	pH	4 / 7 / 9	
3.4.4	Duration of the test	The test durations were different depending on pH and temperature: 48.2 hours at 20 °C and pH 7; 7.9 hours at 30 °C and pH 7; 8 days at 30 °C and pH 4 7 days at 40 °C and pH 4 Test solutions of DMSA were incubated for one week.	X
3.4.5	Number of replicates	One experiment was conducted at each temperature/pH	X
3.4.6	Sampling	The sampling intervals were different depending on pH and temperature: pH 7 (20 °C): sampling at 0, 1.8, 4.3, 6.3, 6.8, 24.3, 25.6, 30.9 and 48.2 hours; pH 7 (30 °C): sampling at 0, 0.6, 2.1, 3.0, 4.2, 5.0, 6.5, 7.3 and 7.9 hours; pH 4 (30 °C): sampling at 0, 1, 4, 5, 6 and 8 days; pH 4 (40 °C): sampling at 0, 3.0, 3.2, 4.0, 4.3, 5.0, 6.0 and 7.0 days	
3.4.7	Analytical methods	The concentrations of dichlofluanid were determined using reversed phase HPLC under the following conditions: Column: Merck LiChrosorb RP 18, 5 µm, 250 mm; Mobile phase: 68% acetonitrile/ 32% water; Flow rate: 1 ml/min.; Detector: UV, 218 nm; Injection volume: 50 µl; For the determination of DMSA the mobile phase was made of 50% acetonitrile/50% water, the flow rate was 1.2 ml/min. and the injection volume was 20 µl. Detection followed by UV at 232 nm. All other conditions were equal to those used for the determination of dichlofluanid.	X
3.5	Preliminary test	No	
		4 RESULTS	
4.1	Concentration and hydrolysis values	see table A7_1_1_1_1-1a and table A7_1_1_1_1-1b	X

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4.2	Hydrolysis rate constant (k_h)	see table A7_1_1_1_1-2	X
4.3	Dissipation time	see table A7_1_1_1_1-2	X
4.4	Concentration – time data	The nominal concentration of test substance was 1 mg/l. Concentration of dichlofluanid expressed as percentage of initial concentrations is given table A7_1_1_1_1-1a and table A7_1_1_1_1-1b. Concentration-time plots are provided in the report.	
4.5	Specification of the transformation products	-	X
5 APPLICANT'S SUMMARY AND CONCLUSION			
5.1	Materials and methods	The hydrolytic stability of Euparen (dichlofluanid) was tested in accordance with the OECD Method "Hydrolysis as a function of pH" at pH 4, 7, and 9 at different temperatures in phosphate and citrate buffer solutions. A solution of 100 mg /l Euparen in acetonitrile was diluted with buffer solutions at a ratio of 1:100, so that solutions of 1 mg/l Euparen are resulted containing 1% acetonitrile. The buffer solutions were sealed into glass ampoules and stored in a water bath of given temperature. In this study also the hydrolytic stability of the decomposition product dimethylaminosulfanilid (DMSA) was tested. Test solutions of DMSA were incubated in buffer solutions of pH 4, 7 and 9 for one week at 55 °C or kept in a refrigerator. The study shows no significant deviations from the OECD method.	
5.2	Results and discussion	The half-lives and hydrolysis rate constants of dichlofluanid for pH 4 and 7 at the different temperatures are given in table A7_1_1_1_1-2. At pH 9, the hydrolytic degradation was so rapid that at room temperature, even when the analysis was conducted immediately, no parent compound could be detected. The half-lives at 22 °C were determined graphically via extrapolation by plotting log k against 1/T (T = absolute temperature). Half-lives of 18.8 hours were resulted at pH 7 ($k = 1.0 \times 10^{-5} \text{ sec}^{-1}$) and 15.3 days at pH 4 ($k = 5.2 \times 10^{-7} \text{ sec}^{-1}$). No degradation of DMSA was detectable in the samples incubated at 55 °C when compared to the refrigerated samples. This result corresponds to a half-life of far more than one year at 22 °C and pH 4, 7 and 9.	X
5.2.1	k_h	see table A7_1_1_1_1-2	
5.2.2	DT ₅₀	see table A7_1_1_1_1-2	
5.2.3	r ²	-	
5.3	Conclusion	Validity criteria can be considered as fulfilled. Hydrolysis of dichlofluanid takes place quickly at environmental relevant pH-values and temperatures.	

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5.3.1	Reliability	2	
5.3.2	Deficiencies	Yes, no lot or batch no. of test substance mentioned	

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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	09/11/04
Materials and Methods	<p>Applicant's version is acceptable with the following comments:</p> <p>3.1.1 No lot or batch number for the Eurapen is mentioned.</p> <p>3.2 No reference substance was used.</p> <p>3.3 Technical details and concentrations for the citrate and phosphate buffers are not given.</p> <p>3.4.1 The use of glass ampoules to incubate the buffer is not mentioned in the study, only in the summary.</p> <p>3.4.2 The actual temperatures of the room and refrigerator are not given. The temperature and pH values appear to be nominal values and not measured during the study.</p> <p>3.4.4 No test duration is given for the dichlofluanid at pH 9.</p> <p>3.4.5 No replicate samples were used.</p> <p>3.4.7 No details are given on the expected retention times for the Dichlofluanid and DMSA (to confirm no coelution), the calibration of the system (to ensure system stability), nor the method for calculating the concentrations of the test substances.</p>
Results and discussion	<p>Applicant's version is acceptable with the following comments:</p> <p>4.1 No raw data/chromatograms provided. The tabulated data given omits the data for the hydrolysis of dichlofluanid at pH 9 and DMSA at pHs 4, 7 and 9, although the conclusions are given in 5.2.</p> <p>4.2 and 4.3 No details given on the extrapolation from % initial concentration to test sample concentration nor how the hydrolysis constants and half-lives have been determined, although the values for dichlofluanid seem reasonable if pseudo first-order decay is assumed.</p> <p>4.5 No evidence is provided on the quantification of transformation products formed from during the hydrolysis of dichlofluanid.</p>
Conclusion	<p>Applicant's version is acceptable with the following comments:</p> <p>5.2 The reason for extrapolation to the half-life of dichlofluanid at 22 °C is unclear. Whilst possible at pH 7 (since the test temperatures were 20 °C and 30 °C), 22 °C is outside the temperature range tested at pH 4.</p> <p>5.2 No data, nor explanation, are given to support the statement that DMSA has a half-life of more than one year at 22 °C and pH 4, 7 and 9.</p>
Reliability	2

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Acceptability	Acceptable Consistency of data for hydrolysis of dichlofluanid at different pH values and temperatures suggest the method and results are reliable, despite a lack of detail in reporting this study.
Remarks	All endpoints and data presented in the summary and tables have been checked against the original summary and are correct.
Date	COMMENTS FROM ... <i>Give date of comments submitted</i>
Materials and Methods	<i>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</i>
Results and discussion	<i>Discuss if deviating from view of rapporteur member state</i>
Conclusion	<i>Discuss if deviating from view of rapporteur member state</i>
Reliability	<i>Discuss if deviating from view of rapporteur member state</i>
Acceptability	<i>Discuss if deviating from view of rapporteur member state</i>
Remarks	

Table A7_1_1_1_1-a: Hydrolysis of dichlofluanid expressed as percentage of initial concentrations (mg/l, nominal initial concentration = 1 mg/l) at pH 4

Parent compound	Sampling times (days)							
	0	1	4	5	6	8	-	-
pH 4 (30 °C)	100	83	62	58	46	47	-	-
Parent compound	Sampling times (days)							
	0	3.0	3.2	4.0	4.3	5.0	6.0	7.0
pH 4 (40 °C)	100	51	47	39	34	29	23	17

Table A7_1_1_1_1-b: Hydrolysis of dichlofluanid expressed as percentage of initial concentrations (mg/l, nominal initial concentration = 1 mg/l) at pH 7

Parent compound	Sampling times (hours)								
	0	1.8	4.4	6.3	6.8	24.3	25.6	30.9	48.2
pH 7 (20 °C)	100	93	85	82	79	52	49	42	25
Parent compound	Sampling times (hours)								
	0	0.6	2.1	3.0	4.2	5.0	6.5	7.3	7.9
pH 7 (30 °C)	100	91	79	69	63	53	44	40	36

Table A7_1_1_1_1-2: Half lives and hydrolysis rate constants of dichlofluanid

Buffer	Temperature [°C]	Half-life, t _{1/2}	Hydrolysis rate Constant, k [sec ⁻¹]
pH 7	20	25.6 h	7.5 x 10 ⁻⁶
pH 7	30	5.4 h	3.6 x 10 ⁻⁵
pH 4	30	6.9 d	1.2 x 10 ⁻⁶
pH 4	40	2.8 d	2.9 x 10 ⁻⁶