Section A6.12.6 Medical Data – sensitization/allergenicity observations – reference A6.12.6/03

Annex Point IIA6.9.6

			Official use only
		1 REFERENCE	
1.1	**Reference**	Reference type: Study report Year: 1991 Report date: 24 June 1991 [redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Rohm and Haas Company	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE **Not applicable**	
		3 MATERIALS AND METHODS	
3.1	**Substance**	RH-287 Technical	X
3.2	**Persons exposed**		
3.2.1	Sex	Male and female	
3.2.2	Age	Adults	
3.3	**Exposure**	Dermal	
3.3.1	Frequency of exposure	21-day cumulative irritation study	
3.3.2	Exposure concentration/dose	21-day cumulative irritation in humans: 100, 500, or 1000 ppm DCOIT in corn oil; 10-11 subjects per dose level.	X
3.3.3	Other information	Not applicable	
3.4	**Examinations**	Dermal examination of treated areas	
3.5	**Remarks**	None	

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 Annex Point IIA6.9.6	Medical Data – sensitization/allergenicity observations – reference A6.12.6/03

4 RESULTS

4.1 Clinical Signs

21-day cumulative irritation: non-irritating and no cumulative effects with corn oil vehicle at concentrations up to and including 1000 ppm DCOIT.

Sensitization : no sensitization effects in corn oil up to and including 1000 ppm.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

21-day cumulative irritation occlusive human patch tests were conducted at either 100, 500 or 1000 ppm DCOIT using corn oil as the vehicle. After a 7-12 day rest period, the subjects received a 48-hour occluded challenge patch (with the exception of the 100 ppm DCOIT induction group) at a naïve site at the same concentration of DCOIT in corn oil that they received during induction.

5.2 Results and discussion

Eleven subjects completed 100 ppm DCOIT, 10 subjects completed 500 ppm DCOIT and 10 subjects completed 1000 ppm DCOIT 21-day cumulative irritation studies. One individual induced with 100 ppm DCOIT exhibited a transient (non-cumulative) level 1 (mild) response at the 20th reading. There were no reactions observed in subjects induced with 500 or 1000 ppm DCOIT.

5.3 Conclusion

Under the conditions of the occlusive 21-day cumulative irritation study, concentrations as high as 1000 ppm DCOIT in corn oil were found to be essentially non-irritating, without cumulative irritation effects and with no evidence of allergic contact dermatitis.

Evaluation by Competent Authorities

Evaluation by Rapporteur Member State

Date

26 September 2006

Materials and Methods

Agree with applicant´s summary and conclusion.

Comment (3.1):

Personal communication with Rohm and Haas, January 2008:

Kathon™ 930, Lot 5094, (30% DCOIT in xylene) diluted in corn oil

DCOIT test concentrations: 100 ppm, 250 ppm, 500 ppm, 1000 ppm in corn oil

Comment (3.3.2): The quantity of test substance (0.2 ml) applied should have been stated.

Results and discussion

Agree with applicant´s version

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 **Annex Point IIA6.9.6**	**Medical Data – sensitization/allergenicity observations – reference A6.12.6/03**
Conclusion	Agree with applicant's version
Remarks	

Section A6.12.6 Medical Data – sensitization/allergenicity observations – reference A6.12.6/04

Annex Point IIA6.9.6

			Official use only
		1 REFERENCE	
1.1	**Reference**	Reference type: Study report Year: 1991 Report date: 24 May 1991 [redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Rohm and Haas Company	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE **Not applicable**	
		3 MATERIALS AND METHODS	
3.1	**Substance**	RH-287 (30% a.s. in xylene)	X
3.2	**Persons exposed**		
3.2.1	Sex	Male and female	
3.2.2	Age	Adults	
3.3	**Exposure**	Dermal	
3.3.1	Frequency of exposure	21-day cumulative irritation study	
3.3.2	Exposure concentration/dose	21-day cumulative irritation in humans: 100, 250, 500, 1000 ppm DCOIT in corn oil; 10 subjects per dose level. -Induction phase : 100, 250, 500, 1000 ppm DCOIT in corn oil over a 21-day period -Challenge phase : 2 consecutive 48 hours patches at 250, 500, 1000 ppm DCOIT in corn oil	X
3.3.3	Other information	Not applicable	

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 Annex Point IIA6.9.6	Medical Data – sensitization/allergenicity observations – reference A6.12.6/04
3.4 Examinations	Dermal examination of treated areas
3.5 Remarks	None
	4 RESULTS
4.1 Clinical Signs	21-day cumulative irritation: non-irritating and no cumulative effects with corn oil at concentrations up to and including 1000 ppm DCOIT. Sensitization : no sensitization effects in corn oil up to and including 1000 ppm.
	5 APPLICANT'S SUMMARY AND CONCLUSION
5.1 Materials and methods	Occlusive human patch tests were conducted using corn oil as the vehicle. 0.2 ml of the RH-287 test concentration was applied to a Readi-Band bandage using a micropipette. The bandage was removed and changed 24 hours later.
5.2 Results and discussion	Evaluations for signs of irritation during the induction phase of the study were made within 15 minutes of the removal of the patch. The 15 induction evaluations were negative for signs of irritation at all test substance concentrations.
5.3 Conclusion	DCOIT (30% a.s. in xylene) was neither irritating or sensitizing to the skin in corn oil at concentrations up to and including 1000 ppm DCOIT

Evaluation by Competent Authorities

Evaluation by Rapporteur Member State

Date	26 September 2006
Materials and Methods	Agree with applicant's summary and conclusion
	Comment (3.1): Personal communication with Rohm and Haas, January 2008: Kathon™ 930, Lot 5094, (30% DCOIT in xylene) diluted in corn oil DCOIT test concentrations: 100 ppm, 250 ppm, 500 ppm, 1000 ppm in corn oil
Results and discussion	Agree with applicant's summary and conclusion
	Comment (3.3.2): Induction phase: 15 test applications over a period of 3 weeks, changed every 24-72 hours.
Conclusion	Agree with applicant's version
Remarks	

Section A6.12.6 Medical Data – sensitization/allergenicity observations – reference A6.12.6/05

Annex Point IIA6.9.6

			Official use only
		1 REFERENCE	
1.1	**Reference**	Reference type: Study report Year: 1992 Report date: 10 April 1992 [redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Rohm and Haas Company	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE **Not applicable**	
		3 MATERIALS AND METHODS	
3.1	**Substance**	RH-287 Technical	X
3.2	**Persons exposed**		
3.2.1	Sex	Male and female	
3.2.2	Age	Adults	
3.3	**Exposure**	Dermal	
3.3.1	Frequency of exposure	21-day cumulative irritation study	
3.3.2	Exposure concentration/dose	21-day cumulative irritation in humans: 50.5, 112.5, 265.4 ppm DCOIT in ethanol; 10-11 subjects per dose level.	
3.3.3	Other information	Not applicable	
3.4	**Examinations**	Dermal examination of treated areas	
3.5	**Remarks**	None	

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 Annex Point IIA6.9.6	Medical Data – sensitization/allergenicity observations – reference A6.12.6/05	
	4 RESULTS	
4.1 Clinical Signs	Subjects were free of any physical or dermatological conditions prior to entering the study.	
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	Occlusive human patch tests were conducted using ethanol as the vehicle. Patches containing 0.2 ml of the test material were applied daily for 21 consecutive days and visually scored just prior to the next patch application. After a 3-week rest period, only those subjects induced with 265 ppm a.i. received a 48-hr occluded challenge patch at naïve sites with 3 test substance concentrations, 50, 112 and 265 ppm a.i. in absolute ethanol as well as an absolute ethanol control.	X
5.2 Results and discussion	The report concluded that it was difficult to interpret whether or not DCOIT is capable of inducing contact dermatitis at the concentrations tested. Signs suggestive of "angry-skin" syndrome, identical reactivity to the vehicle, and lack of reactivity between the 3 challenge concentrations were documented in the challenge readings.	
5.3 Conclusion	Studies of RH-287 in ethanol at concentrations as high as 250 ppm a.i. DCOIT in absolute ethanol were found to be essentially non-irritating and without cumulative irritant effects.	X

Evaluation by Competent Authorities

Evaluation by Rapporteur Member State

Date

26 September 2006

Materials and Methods

Occlusive human patch tests were conducted using ethanol as the vehicle. Patches containing 0.2 ml of the test material were applied daily for 21 consecutive days and visually scored just prior to the next patch application. After a 3-week rest period, only those subjects induced with 265 ppm a.i. received a 24 -hr occluded challenge patch at naïve sites with 3 test substance concentrations, 50, 112 and 265 ppm a.i. in absolute ethanol as well as an absolute ethanol control.

Comment (3.1):

Personal communication with Rohm and Haas, January 2008:

Kathon™ 930, (30% DCOIT in xylene) diluted in absolute ethanol

DCOIT test concentrations: 50.5 ppm, 112.5 ppm, 265.4 ppm in absolute ethanol

Results and discussion

Agree with applicant's version

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 — Medical Data – sensitization/allergenicity observations – reference A6.12.6/05

Annex Point IIA6.9.6

Conclusion	Studies of RH-287 in ethanol at concentrations as high as 250 ppm a.i. DCOIT in absolute ethanol were found to be without cumulative irritant effects. The challenge patch results were difficult to interpret as dermal reactivity suggestive of allergic was observed.
Remarks	

Section A6.12.6 — Medical Data – sensitization/allergenicity observations – reference A6.12.6/06

Annex Point IIA6.9.6

			Official use only
		1 REFERENCE	
1.1	**Reference**	Reference type: Study report Year: 1992 Report date: 14 December 1992 [redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Rohm and Haas Company	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE	
		Not applicable	
		3 MATERIALS AND METHODS	
3.1	**Substance**	Kathon 930 (30% DCOIT in xylene)	X
3.2	**Persons exposed**		
3.2.1	Sex	Male and female	
3.2.2	Age	Adults	

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 Annex Point IIA6.9.6	Medical Data – sensitization/allergenicity observations – reference A6.12.6/06	
3.3 Exposure	Dermal	
3.3.1 Frequency of exposure	Repeat insult patch test (RIPT)	
3.3.2 Exposure concentration/dose	RIPT: 250 and 350 ppm DCOIT in ethanol in induction phase (9 applicatons); 34 subjects per dose level and 100, 250, 350 ppm DCOIT in ethanol in challenge phase	X
3.3.3 Other information	Not applicable	
3.4 Examinations	Dermal examination of treated areas	
3.5 Remarks	None	
	4 RESULTS	
4.1 Clinical Signs	Barely perceptible (+) to moderate (2-level) non-specific or low-grade, irritant/cumulative irritant patch test responses were observed on 16/34 subjects during the induction and/or challenge phases of the study.	
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	Human repeated insult patch test was conducted using ethanol as the vehicle. Patches were applied 3 times per week for three weeks for a total of 9 applications. Following an approximate two-week rest period, all subjects were challenged at naïve sites with patches containing DCOIT at concentrations of 100, 250 and 350 ppm in ethanol and an ethanol control for a 24 hour application.	
5.2 Results and discussion	Results indicate that a total of 4/34 (12%) of subjects induced with 250 ppm DCOIT and a total of 14/34 (41% subjects) induced with 350 ppm DCOIT exhibited sensitization. The data demonstrates a dose-response with respect to the induction concentration.	
5.3 Conclusion	Studies of DCOIT in ethanol demonstrated that 350 ppm DCOIT is at or near the threshold concentration for irritation and sensitization.	X

Evaluation by Competent Authorities	
Evaluation by Rapporteur Member State	
Date	26 September 2006

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 **Annex Point IIA6.9.6**	**Medical Data – sensitization/allergenicity observations – reference A6.12.6/06**
Materials and Methods	Agree with applicant´s summary and conclusion **Comment (3.1):** Personal communication with Rohm and Haas, January 2008: Kathon™ 930, (30% DCOIT in xylene) diluted in absolute ethanol DCOIT test concentrations: Induction = 250 ppm, 350 ppm in absolute ethanol; Challenge = 100 ppm, 250 ppm, 350 ppm in absolute ethanol **Comment (3.3.2):** The quantity of test substance applied (0.2 ml) should have been stated.
Results and discussion	Agree with applicant's version
Conclusion	Studies of DCOIT in ethanol demonstrated that 250 ppm DCOIT is at or near the threshold concentration for irritation and sensitization.
Remarks	This was followed up in A 6.12.6-07

Section A6.12.6 Medical Data – sensitization/allergenicity observations – reference A6.12.6/07

Annex Point IIA6.9.6

			Official use only
		1 REFERENCE	
1.1	**Reference**	Reference type: Study report Year: 1993 Report date: 14 May 1993 [redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Rohm and Haas Company	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE **Not applicable**	
		3 MATERIALS AND METHODS	
3.1	**Substance**	Kathon 930 (30% DCOIT in xylene)	X
3.2	**Persons exposed**		
3.2.1	Sex	Male and female	
3.2.2	Age	Adults	
3.3	**Exposure**	Dermal	
3.3.1	Frequency of exposure	24-hour Occlusive Patch Test	
3.3.2	Exposure concentration/dose	24-hour Occlusive Patch Test: 0 and 250 ppm DCOIT in ethanol; 8 subjects.	

Document III-A / Sections A6.8 to A6.17

Section A6.12.6
Annex Point IIA6.9.6

Medical Data – sensitization/allergenicity observations – reference A6.12.6/07

3.3.3 Other information: This study was a follow-up study to Report 92RC-086. Eight subjects that responded positively to induction and challenge to 350 ppm DCOIT in ethanol were rechallenged with 0 (ethanol) and 250 ppm DCOIT in ethanol to examine reproducibility of elicitation. The subjects were also challenged with 9 (water) and 100 ppm CMIT/MIT in water and 0 (petrolatum with 0.625% Tween 80) and 250 ppm OIT in petrolatum with 0.625% Tween 80 to investigate cross sensitization potential with other isothiazolones. X

3.4 Examinations: Dermal examination of treated areas

3.5 Remarks: None

4 RESULTS

4.1 Clinical Signs

E = edema
V = vesiculation
P = papular

Subject	Challenge, 250 ppm DCOIT			Rechallenge, 250 ppm DCOIT		
	24 hr	48 hr	72 hr	24 hr	48 hr	96 hr
2	+	+	1	+	0	0
5	+	2e	2e	0	0	0
10	2e	2e	3ev	0	2	3e
19	0	1e	2e	1	3e	3
25	+	2e	2e	+	0	0
29	+	1ep	1ep	0	1	+
31	0	0	0	0	0	0
370	0	1p	2ep	0	0	0

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods: All challenges were done on naïve (previously untreated) sites. Occluded patches were applied for 24 hours and the sites were scored 24, 48 and 96 hr after patch application.

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 **Annex Point IIA6.9.6**	**Medical Data – sensitization/allergenicity observations – reference A6.12.6/07**	
5.2 Results and discussion	5 of the 8 subjects did not respond to rechallenge with DCOIT. The other 3 subjects responded positively to rechallenge with 250 ppm DCOIT. One each responded with a lower, higher, or similar intensity than they did in the initial challenge approximately 6 months earlier. Possible explanations for these results are that a number of the sensitization responses in the previous study may have been irritant responses of that the intensity of the elicitation (sensitization) response in DCOIT sensitized subjects decreases over time. None of the 8 subjects responded positively to challenge with CMIT/MIT or OIT.	X
5.3 Conclusion	Studies of RH-287 Technical in ethanol demonstrated that 350 ppm DCOIT is at or near the threshold concentration for irritation and sensitization.	X

Evaluation by Competent Authorities

Evaluation by Rapporteur Member State

Date 26 September 2006

Materials and Methods Agree with applicant's summary and conclusion

Comment (3.1):

Personal communication with Rohm and Haas, January 2008:

Kathon™ 930, (30% DCOIT in xylene) diluted in absolute ethanol

Test concentration: 0 ppm in ethanol, 250 ppm DCOIT in absolute ethanol, 100 ppm CMIT/MIT in water, 0 ppm petrolatum with 0.625% Tween 80, and 250 ppm OIT in petrolatum with 0.625% Tween 80 for re-challenge to investigate cross-sensitization potential of the isothiazolones.

Comment (3.3.3) 14 out of 34 subjects (41%) induced with 350 ppm DCOIT 6 months earlier exhibited sensitization. 8 of these 14 subjects returned to the clinic for further testing .

Results and discussion 5 of the 8 subjects did not respond to rechallenge with DCOIT. The other 3 subjects responded positively to rechallenge with 250 ppm DCOIT. One each responded with a lower, higher, or similar intensity than they did in the initial challenge approximately 6 months earlier. Possible explanations for these results are that a number of the sensitization responses in the previous study may have been irritant responses or that the intensity of the elicitation (sensitization) response in DCOIT sensitized subjects decreases over time. None of the 8 subjects responded positively to challenge with oher isothiazolones/isothiazolinones (CMIT/MIT) or OIT except for a transient and mild reaction in one subject to OIT (Kathon RH-893).

Conclusion Studies of RH-287 Technical in ethanol demonstrated that 250 ppm DCOIT is at or near the threshold concentration for irritation and sensitization.

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 **Annex Point IIA6.9.6**	**Medical Data – sensitization/allergenicity observations – reference A6.12.6/07**

Remarks

Section A6.12.6 Medical Data – sensitization/allergenicity observations – reference A6.12.6/08

Annex Point IIA6.9.6/01

			Official use only
		1 REFERENCE	
1.1	**Reference**	Reference type: Study report Year: 1994 Report date: 13 May 1994 [redacted]	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Rohm and Haas Company	
1.2.2	Companies with letter of access	[redacted]	
1.2.3	Criteria for data protection	[redacted]	
		2 GUIDELINES AND QUALITY ASSURANCE **Not applicable**	
		3 MATERIALS AND METHODS	
3.1	**Substance**	RH-287 Technical	X
3.2	**Persons exposed**		
3.2.1	Sex	Male and female	
3.2.2	Age	Adults	
3.3	**Exposure**	Dermal	
3.3.1	Frequency of exposure	24-hours and 48 hours Occlusive Patch Tests	
3.3.2	Exposure concentration/dose	24-hours and 48 hours Occlusive Patch Test: 350, 500, 750, 1000 ppm DCOIT in ethanol; 10 subjects.	X
3.3.3	Other information	Not applicable	
3.4	**Examinations**	Dermal examination of treated areas	
3.5	**Remarks**	None	

Document III-A / Sections A6.8 to A6.17

Section A6.12.6 Annex Point IIA6.9.6/01	Medical Data – sensitization/allergenicity observations – reference A6.12.6/08	
	4 RESULTS	
4.1 Clinical Signs	Approximately one-half of the subjects dosed with 350 ppm DCOIT showed responses that ranged between barely perceptible to moderate in degree.	
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	Duplicate occlusive human patch tests were conducted using ethanol as the vehicle. One set of patches was removed after 24 hours and the second set of patches was removed after 48 hours.	
5.2 Results and discussion	There were no distinct differences in irritation between the four concentrations of DCOIT tested. The number and degree of responses observed at the lowest concentration (350 ppm DCOIT) were not markedly different from the responses observed at the highest concentration (1000 ppm DCOIT). Two subjects reacted adversely to all test concentrations of DCOIT and still exhibited reactions 10 to 15 days after patch removal.	
5.3 Conclusion	Studies of RH-287 Technical in ethanol demonstrated that 350 ppm DCOIT is at or near the threshold concentration for irritation and sensitization.	X

Evaluation by Competent Authorities

Evaluation by Rapporteur Member State

Date	26 September 2006
Materials and Methods	Agree with applicant´s summary and conclusion. **Comment (3.1):** Personal communication with Rohm and Haas, January 2008: Kathon™ 930, (30% DCOIT in xylene) diluted in ethanol DCOIT test concentrations: 350 ppm, 500 ppm, 750 ppm, 1000 ppm in ethanol **Comments (3.3.2):** The quantity of test substance applied (0.01 ml on 8mm circular chamber discs) should have been stated.
Results and discussion	Agree with applicant´s version
Conclusion	Studies of RH-287 Technical in ethanol elicited about the same degree of skin irritation in test subjects when applied in various concentrations from 350 to 1000 ppm. Two subjects experienced reactions that appeared to be of allergic nature probably from exposure to the test substance
Remarks	

Section A6.12.6/09 Medical Data – sensitization/allergenicity observations
Annex Point IIA6.12.6/09 Reference A6.12.6/09

			Official use only
		1 REFERENCE	
1.1	**Reference**	A6.12.6/09.Kawai K, Nakagawa M, Sasaki Y, Kawai K: **Occupational contact dermatitis from Kathon™ 930.** Contact Dermatitis 1993 Feb;28(2):117-8.	
		2 GUIDELINES AND QUALITY ASSURANCE (NOT APPLICABLE)	
		3 MATERIALS AND METHODS	
3.1	**Substance**	Kathon™930 biocide (30 % DCOIT in xylene)	
3.2	**Persons exposed**		
3.2.1	Sex	Males and females	
3.2.2	Age/weight	Only indicated for the 8 workers with dermatitis; i.e. 20-63 years old	
3.2.3	Known Diseases	Not specified	
3.2.4	Number of persons	19 workers	
3.2.5	Other information		
3.3	**Exposure**	Dermal	
3.3.1	Reason of exposure	Occupational exposure in a textile finishing factory in Japan	
3.3.2	Frequency of exposure	Repeated exposure	
3.3.3	Overall time period of exposure	A new type of biocide (Kathon™930) was added to the finishing agent about 3 weeks prior to the occurrence of dermatitis.	
3.3.4	Duration of single exposure	Not specified	
3.3.5	Exposure concentration/dose	30% active ingredient (DCOIT) solution in xylene was used as a biocide added to the finishing agent of textiles.	
3.3.6	Other information	The textile finishing unit: Protective gloves used when handling the finishing agent. Short-sleeved shirts worn and no protective equipment on upper arms or forearms. The drying and inspection unit: The finished textiles were dried at room temperature for about 24 hours, and then checked for quality. The finished textiles were handled directly. Because of the length of the textiles, the workers carried them by using their forearms.	

3.4	**Examinations**	Open patch test were performed on 6 patients with the finishing agents, with and without 0.2% biocide. Dermal examination of treated areas was carried out. Closed patch test with Kathon™CG [5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one in the ratio of 3:1] (50 ppm aq.) in the same patients.
3.5	**Treatment**	Not reported
3.6	**Remarks**	None
		4 RESULTS
4.1	**Clinical Signs**	Eight out of 19 workers (2 males and 6 females) developed itchy reddish eruptions on exposed areas of skin 23-38 days after the new biocide was introduced. The 8 workers worked in the textile finishing unit (2 persons) and the drying and inspection unit (6 persons). In addition to dermatitis on the forearm and/or upperarm four of the patients working in the drying and inspection unit also developed erythema on their faces/necks. Airborne contact dermatitis may have occurred in these patients.
4.2	**Results of examinations**	Five out of 6 patients tested with open patch test showed strong positive reactions to the finishing agents with 0.2% biocide, and none showed any reaction to the finishing agents without biocide. The patient who showed no positive reaction to the finishing agents with 0.2% biocide at D2 and D3, did show pigmentation on the same tested skin at D17. She had taken corticosteroids orally 2 days prior to the tests because her dermatitis was severe. As a result she may have shown a false negative reaction. No cross reaction to Kathon CG observed.
4.3	**Effectivity of medical treatment**	Not reported
4.4	**Outcome**	Not reported
4.5	**Other**	
		5 APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	An outbreak of occupational contact dermatitis due to Kathon ™-930 added to the finishing agent was described. Eight out of 19 persons employed in a Japanese textile finishing factory developed oedematous reddish eruptions on their forearms, upper arms, face or neck approximately three weeks after the biocide was introduced. Patch test was carried out on 6 of the patients
5.2	**Results and discussion**	Five out of 6 patients showed strong positive reactions in the open patch test to the finishing agents with 0.2% biocide

Document III-A / Sections A6.8 to A6.17

Section A6.12.6/09	**Medical Data – sensitization/allergenicity observations**
Annex Point IIA6.12.6/09	**Reference A6.12.6/09**

5.3 Conclusion	DCOIT showed a strong sensitizing effect among workers after skin exposure in a textile finishing factory.

Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	22 March 2007
Materials and Methods	The applicant´s version is acceptable
Results and discussion	Agree with applicant´s version
Conclusion	Agree with applicant´s version
Remarks	The concentration of DCOIT in the finishing solution causing the outbreak of occupational contact dermatitis, is not clearly stated in the article.

Section A6.12.7
Annex Point IIA6.9.7

Specific treatment in case of an accident or poisoning: first aid measures, antidotes and medical treatment

Reference A6.12.7

Official use only

1 REFERENCE

1.1 Reference

A6.12.5/01 Wooder M. (2006) 4,5-Dichloro-2-n-octyl-4-isothiazolin-3-one – DCOIT (CAS 64359-81-5), Diagnosis of poisoning including specific signs of poisoning and clinical tests, Treatment in case of accidental exposure or poisoning Rohm and Haas Company memo, Unpublished.

2 GUIDELINES AND QUALITY ASSURANCE (NOT APPLICABLE)

3 MATERIALS AND METHODS

3.1 Substance

The information given below refers to DCOIT/RH-287.

3.2 Persons exposed

Potentially industrial of professional workers handling DCOIT concentrated formulations, in case of accident.

3.3 Exposure

Ingestion, Dermal, Inhalation: In case of accident.

4 RESULTS

4.1 Clinical Signs

See section A6.12.5.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Results and discussion

There is no antidote for the effects of DCOIT. In all cases the patient should be treated symptomatically.

In case of accidental exposure the following actions are recommended:

Inhalation: Move the patient to fresh air. Give artificial respiration if breathing has stopped. If symptoms persist, seek medical attention.

Skin contact: Immediately wash the contaminated skin site with water, under a shower if available. Remove contaminated clothing and seek medical attention.

Eye contact: Rinse the eye(s) immediately with running water for at least 15 minutes. Seek medical attention.

Ingestion: Drink 1 or 2 glasses of water. Immediately consult a physician.

Note to physician: DCOIT is corrosive. It may not be advisable to induce vomiting. Possible mucosal damage may contraindicate the use of gastric lavage. It may be necessary to employ measures against circulatory shock and convulsions.

5.2 Conclusion

The treatment in case of accident or poisoning is the general treatment recommended for corrosive substances.

Evaluation by Competent Authorities	
	Evaluation by Rapporteur Member State
Date	22 March 2007
Materials and Methods	The applicant´s version is acceptable
Results and discussion	Agree with aplicant´s version
Conclusion	Agree with applicant´s version
Remarks	

Section A6.12.8 Prognosis following poisoning
Annex Point IIA6.9.8 **Reference A6.12.8**

Official use only

1 REFERENCE

1.1 Reference

A6.12.5/01 Wooder M. (2006) 4,5-Dichloro-2-n-octyl-4-isothiazolin-3-one – DCOIT (CAS 64359-81-5), Diagnosis of poisoning including specific signs of poisoning and clinical tests, Treatment in case of accidental exposure or poisoning Rohm and Haas Company memo, Unpublished.

2 GUIDELINES AND QUALITY ASSURANCE (NOT APPLICABLE)

3 MATERIALS AND METHODS

3.1 Substance

The information given below refers to DCOIT/RH-287.

3.2 Persons exposed

Potentially industrial of professional workers handling DCOIT concentrated formulations, in case of accident.

3.3 Exposure

Ingestion, Dermal, Inhalation: In case of accident.

4 RESULTS

4.1 Clinical Signs

See section A.12.5

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Results and discussion

5.2 Conclusion

The prognosis following accidental exposure or poisoning will depend upon the extent of the exposure and the speed of obtaining appropriate medical treatment.

Evaluation by Competent Authorities	
	Evaluation by Rapporteur Member State
Date	22 March 2007
Materials and Methods	The applicant´s version is acceptable
Results and discussion	Agree with applicant´s version
Conclusion	Agree with applicant´s version
Remarks	

Section A6.13 Annex Point IIIA6.2	Toxic effects on livestock and pets	
	Justification for non-submission of data	Official use only
Other existing data [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [ ]	
Limited exposure [X]	**Other justification** []	
Detailed justification:	Detailed justification is considered as confidential information.	

Document III-A / Sections A6.8 to A6.17

Section A6.13 **Annex Point IIIA6.2**	**Toxic effects on livestock and pets**
	[redacted]
Undertaking of intended data submission [ ]	No
	Evaluation by Competent Authorities
	Evaluation by Rapporteur Member State
Date	22 October 2007
Evaluation of applicant's justification	Acceptable
Conclusion	Acceptable
Remarks	

Section A6.14 Annex Point IIIA11.2	Other tests related to the exposure of humans	
	Justification for non-submission of data	Official use only
Other existing data [ ] **Limited exposure** [X]	**Technically not feasible** [ ] **Scientifically unjustified** [X] **Other justification** [ ]	
Detailed justification:	Detailed justification is considered as confidential information. [redacted]	
Undertaking of intended data submission [ ]	No	
	Evaluation by Competent Authorities	
	Evaluation by Rapporteur Member State	
Date	22 October 2007	
Evaluation of applicant's justification	Acceptable	
Conclusion	Acceptable	
Remarks		

Section A6.15 Annex Point IIIA6.4	Food and feedingstuffs	
	Justification for non-submission of data	Official use only
Other existing data [ ] **Limited exposure** [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [ ] **Other justification** [X]	
Detailed justification:	The use of DCOIT based wood preservatives on wood which is likely to come into prolonged direct contact with foodstuffs or feedstuffs are not expected. It is therefore justified not to submit data on residue in food and feedstuffs.	
Undertaking of intended data submission [ ]	No	
	Evaluation by Competent Authorities	
	Evaluation by Rapporteur Member State	
Date	22 October 2007	
Evaluation of applicant's justification	Acceptable	
Conclusion	Acceptable	
Remarks		

Section A6.16 Annex Point IIIA6.3.5-IIIA11.2	Any other tests related to the exposure of the active substance to humans, in its proposed biocidal products, that are considered necessary	
	Justification for non-submission of data	Official use only
Other existing data [ ] **Limited exposure** [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [ ] **Other justification** [X]	
Detailed justification:	No further studies are considered necessary.	
Undertaking of intended data submission [ ]	No	
	Evaluation by Competent Authorities	
	Evaluation by Rapporteur Member State	
Date	22 October 2007	
Evaluation of applicant's justification	Acceptable	
Conclusion	Acceptable	
Remarks		

Section A6.17 Annex Point IIIA6.6	Toxicity test on metabolites from treated plants	
	Justification for non-submission of data	Official use only
Other existing data [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [ ]	
Limited exposure [ ]	**Other justification** [X]	
Detailed justification:	DCOIT is not used in products for action against plants. Therefore toxic effects of metabolites from treated plants do not need to be assessed and could be waived.	
Undertaking of intended data submission [ ]	No	
	Evaluation by Competent Authorities	
	Evaluation by Rapporteur Member State	
Date	22 October 2007	
Evaluation of applicant's justification	Acceptable	
Conclusion	Acceptable	
Remarks		

Directive 98/8/EC on the placing of biocidal products on the market

Dossier for the inclusion of an active substance in the Annex 1

4,5-Dichloro-2-octyl-2H-isothiazol-3-one (DCOIT)

Product type 21: Antifouling products

Document III-A (A7)
Study summaries – Active substance
Ecotoxicological profile including environmental fate and behaviour

Part I

Fate and behaviour in the environment

Section A7.1.1: Fate and behaviour in water

Degradation, initial studies

Document III-A / Section A7.1.1

TABLE OF CONTENTS

Document III-A / Section A7.1.1

Section A7.1.1.1.1/01 Hydrolysis as a function of pH and identification of breakdown products

Annex Point IIA7.6.2.1

Official use only

1 REFERENCE

1.1	**Reference**	Reference type: Study report Year: 2001 Report date: 7 May 2001 [redacted]
1.2	**Data protection**	*Yes*
1.2.1	Data owner	Rohm and Haas Company
1.2.2		
1.2.3	Criteria for data protection	[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	Yes. U.S. Environmental Protection Agency, 40 CFR § 158, Subdivision N, Chemistry, Environmental Fate 161-1 and OECD 111.
2.2	**GLP**	Yes
2.3	**Deviations**	To satisfy the US EPA guidelines, the OECD screening test was not performed and instead the definitive test was directly initiated. The degradate standards, N-(n-octyl) malonamic acid, N-(n-octyl) oxamic acid, and N-(n-octyl) acetamide were not GLP characterized at the time. However, standards were used only for qualitative and not quantitative purposes and none of these compounds were subsequently identified as hydrolytic degradation products. Sterile agar plates used for examining solution sterility were not prepared under GLP procedures. The FT-ICR-MS instrument was not GLP validated. However, it was used to confirm the LC-MS/MS data and this instrument was GLP validated.

3 MATERIALS AND METHODS

3.1	**Test material**	^{14}C-DCOIT [redacted]
3.1.1	Lot/Batch number	[redacted]

Document III-A / Section A7.1.1

Section A7.1.1.1.1/01 **Hydrolysis as a function of pH and identification of breakdown products**

Annex Point IIA7.6.2.1

3.1.2	Specification	[redacted]	
3.1.3	Purity	[redacted]	
3.1.4	Further relevant properties	[redacted]	x
3.2	**Reference substance**	[redacted]	
3.2.1	Initial concentration of reference substance	[redacted]	
3.3	**Test solution**	[redacted]	

3.4 Testing procedure

3.4.1	Test system	[redacted]	
3.4.2	Temperature	[redacted]	x
3.4.3	pH	[redacted]	

Document III-A / Section A7.1.1

Section A7.1.1.1.1/01 **Hydrolysis as a function of pH and identification of breakdown products**

Annex Point IIA7.6.2.1

[redacted]

3.4.4 Duration of the test

3.4.5 Number of replicates

3.4.6 Sampling

3.4.7 Analytical methods

Document III-A / Section A7.1.1

Section A7.1.1.1.1/01 Annex Point IIA7.6.2.1	Hydrolysis as a function of pH and identification of breakdown products

[redacted]

3.5 Preliminary test

[redacted]

4 RESULTS

4.1 Concentration and hydrolysis values

[redacted] Recoveries ranged from 96.6% to 108.9% with an average of 100.9 ± 2.3%.

Table A7.1.1.1.1/01-4 contains the replicate average data for the quantitation of parent compound at three pH's and two temperatures. These results show that parent compound is very stable in acidic solutions. The higher the pH and or temperature the more rapid the degradation.

Tables A7.1.1.1.1/01-5, A7.1.1.1.1/01-6, and A7.1.1.1.1/01-7 contain the replicate average percentage of ^{14}C hydrolytic products detected at pH 7/40°C, pH 9/25°C, and pH 9/40°C, respectively. The structure of the degradates is presented in Table A7.1.1.1.1/01-9. In the report the major metabolite is identified as isomers of 2-(n-octyl)carbamoyl-2-chloro-1-oxoethane sulfinic acid. Subsequent analysis using NMR (see Report N° TR-04-017 summarized in next section A7.1.1.1.1/02 below) has identified the compound instead as isomers of 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid. x

4.2 Hydrolysis rate constant (k_h)

The rate constants for degradation of parent compound at pH 4, 7, and 9 as well as 25°C and 40°C is presented in Table A7.1.1.1.1/01-8. The rate constant was calculated from the equation $k = \ln 2/t_{½}$. Correlating with the quantitation data in Table A7.1.1.1.1/01-4, the higher the pH and temperature, the larger the degradation rate constant and the more rapid the degradation.

The correlation coefficient (r^2) for parent degradation kinetics is also presented in Table A7.1.1.1.1/01-8. Except for pH 4 and 25°C the correlation coefficient is good exceeding 0.98 at the faster reaction rates. The low r^2 (and thus low linearity) value observed for pH4/25°C is most likely due to the very limited degradation that occurred.

4.3 Dissipation time

Table A7.1.1.1.1/01-8 also contains the calculated DT_{50} and DT_{90} for degradation of parent at the three pH's and two temperatures examined in this study. The higher the pH and temperature, the shorter the DT_{50} and DT_{90} for DCOIT and thus the more rapid its hydrolytic degradation.

4.4 Concentration – time data

Figure A7.1.1.1.1/01-1 presents a graphical presentation of the hydrolysis of DCOIT for pH 9/40°C, pH 9/25°C, and pH 7/40°C.

Document III-A / Section A7.1.1

Section A7.1.1.1.1/01 Hydrolysis as a function of pH and identification of breakdown products

Annex Point IIA7.6.2.1

4.5 Specification of the transformation products

Table A7.1.1.1.1/01-9 provides the structure and nomenclature of the major (>10%) and a number of the minor (<10%) hydrolytic products. Figure A7.1.1.1.1/01-2 presents a proposed hydrolytic pathway.

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1 Materials and methods

[redacted]

5.2 Results and discussion

Sample	K (hrs^{-1})	DT_{50} (days)	r_2
pH 4/25°C	0.0001	>60	0.575
pH 4/40°C	0.0003	>60	0.926
pH 7/25°C	0.0004	>60	0.864
pH 7/40°C	0.002	18.7	0.987
pH 9/25°C	0.008	3.5	0.989
pH 9/40°C	0.048	0.6	0.997

x

^{14}C-material balance (Table A7.1.1.1.1/01-3) and recovery from HPLC quantitation (Table A7.1.1.1.1/01-2) was very good through the experiment.

5.2.1 k_H See Table above.

5.2.2 DT_{50} See Table above.

5.2.3 r^2 See Table above.

5.3 Conclusion

This study fulfils the requirement for determining the effect of aqueous hydrolysis on the fate of DCOIT in the environment. As discussed further in Document IIIA sections A7.1.2, A7.2.1 and Document IIA the rate of biodegradation is much more rapid than abiotic degradation. Therefore, biodegradation will determine the kinetic fate of DCOIT. Hydrolysis will have minimal, if any influence on the fate of DCOIT and on its risk assessment. The major degradation products are presented in Table A7.1.1.1.1/01-9. The major degradative pathway involves cleavage of the isothiazolone ring (Figure A7.1.1.1.1/01-2). Various classes of these ring cleaved products have been tested and

x

Document III-A / Section A7.1.1

Section A7.1.1.1.1/01 Annex Point IIA7.6.2.1	Hydrolysis as a function of pH and identification of breakdown products

		found to be readily biodegradable (section A7.1.2.3).
5.3.1	Reliability	1, valid without restrictions.
5.3.2	Deficiencies	No significant deficiencies that will affect the results and conclusions

Evaluation by Competent Authorities	
Evaluation by Rapporteur Member State	
Date	5 October 2006, revised 7 January 2009
Materials and Methods	Comment **(3.1.4):** The water solubility of DCOIT at pH 7 is 3.47 mg/l (20°C).
	Comment **(3.4.2):** The temperature of the test system varied more than 2 °C during the test. OECD 111 requires that the temperature is kept constant within a range of ± 0.1 °C. However, the observed temperature variations are not expected to seriously affect the outcome of the study.
Results and discussion	Comment **(4.1):** In tables A7.1.1.1.1/01-5, -6, -7 and -9 the correct metabolite 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid, identified by NMR in study A7.1.1.1.1/02, is stated, instead of 2-(n-octyl)carbamoyl-2-chloro-1-oxoethane sulfinic acid, which is mentioned in the study report to this study summary.
	Comment **(5.2):** The DT50 at pH7 (25°C), which represents best environmental conditions, is 71.4 days
Conclusion	Agree with applicant's version
	Comment **(5.3):** The metabolite 2-chloro-2-(n-octylcarbamoyl)-1-1ethene sulfonic acid is found not to be readily biodegradable.
Reliability	1, valid without restrictions
Acceptability	Acceptable
Remarks	-

Document III-A / Section A7.1.1

Section A7.1.1.1.1/01	Hydrolysis as a function of pH and identification of breakdown products **TABLES AND FIGURES**

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Document III-A / Section A7.1.1

[redacted]

[redacted]	[redacted]						
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Document III-A / Section A7.1.1

Table A7.1.1.1.1/01-4: Percent of Parent Compound Quantitated by HPLC

Day	Parent Compound as a Percent of ^{14}C Applied (average of replicates)					
	pH 4/25°C	pH 4/40°C	pH 7/25°C	pH 7/40°C	pH 9/25°C	pH 9/40°C
0	100	100	100	100	100	100
0.08						93.3
0.17						87.2
0.25						78.6
0.33						70.6
1					83.5	26.0
1.3						19.2
2					69.1	8.3
3	98.2	96.9	93.8	88.9	53.4	0
4					44.0	
7	96.1	93.0	86.2	70.8	22.9	
11					13.5	
15	89.8	84.3	80.2	54.1		
21	92.0	86.0	84.0	46.1		
30	93.5	80.0	71.8	35.1		

Table A7.1.1.1.1/01-5: Percent of Hydrolysis Products of DCOIT at pH 7 and 40°C

Hydrolysis Product[1]	Percent ^{14}C-activity				
	Day 3	Day 7	Day 15	Day 21	Day 30
1					2.33
2			1.39	12.64	11.05
3		2.57	2.38	6.29	15.57
4					3.39
5				0.45	0.9
6				3.70	1.92
7			3.67	11.76	6.92

[1] Product 1 is unknown

Product 2 is 2-chloro-2-(n-octylcarbamoyl)-l-ethene sulfonic acid

Product 3 is 1-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid

Product 4 is 4-chloro-5-hydroxy-2-(n-octyl)-4-isothiazolin-3-one

Product 5 is N-(n-octyl) propiolic acid amide

Product 6 is 4-chloro-2-(n-octyl)-4-isothiazolin-3-one

Product 7 is 4-chloro-5-methoxy-2-(n-octyl)-4-isothiazolin-3-one.

Table A7.1.1.1.1/01-6: Percent of Hydrolysis Products of DCOIT at pH 9 and 25°C

Hydrolysate Product[1]	Percent ^{14}C-activity					
	Day 0	Day 0.21	Day 0.29	Day 4	Day 7	Day 8
1				19.46	21.74	19.60
2		1.48	1.66	40.74	36.41	39.62
3				12.12	16.25	3.41
4						13.35

[1] Product 1 is 2-chloro-2-(n-octycarbamoyl)-1-ethene sulfonic acid

Product 2 is 1-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid

Product 3 is unknown

Product 4 is N-(n-octyl) propiolic acid amide.

Table A7.1.1.1.1/01-7: Percent of Hydrolysis Products of RH-5287 at pH 9 and 40°C

Sample Day	Percent ^{14}C-Activity	
	Product 1	Product 2
0		
0.08	5.00	
0.17	9.61	
0.25	16.03	
0.33	19.81	2.25
1	46.6	8.88
1.3	51.69	8.90
2	56.64	12.12
3	59.06	15.92

[1] Product 1 is a 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid and 1-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid

Product 2 is N-(n-octyl) propiolic acid amide.

Table A7.1.1.1.1/01-8: Kinetics for Parent Compound

Day	Parent Compound as a Percent of ^{14}C Applied					
	pH 4/25°C	pH 4/40°C	pH 7/25°C	pH 7/40°C	pH 9/25°C	pH 9/40°C
k[a] (hrs^{-1})	0.0001	0.0003	0.0004	0.002	0.008	0.048
R^2	0.575	0.926	0.864	0.987	0.989	0.997
DT_{50}[b] (days)	259.8	93	71.4	18.7	3.5	0.6
DT_{90}[c] (days)	>700	>300	>250	62.2	11.6	2.0

[a] Rate constant calculated from k = ln2/half-life.
[b] Half-life (DT_{50}) calculated from regression analysis (bivariate fit) performed by JMP Statistical Software Package (SAS Institute).
[c] Time for 90% reduction calculated from DT_{90} = ln10/k.

Table A7.1.1.1.1-9: Structure of metabolites

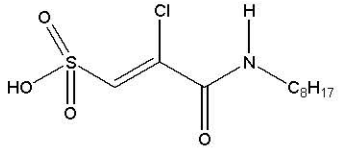
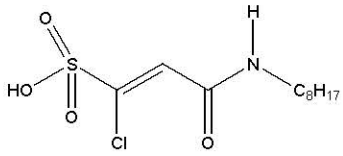
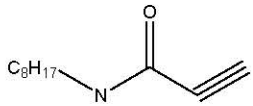
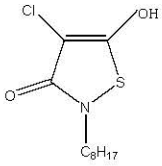
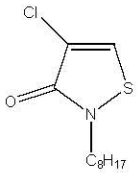
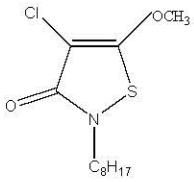
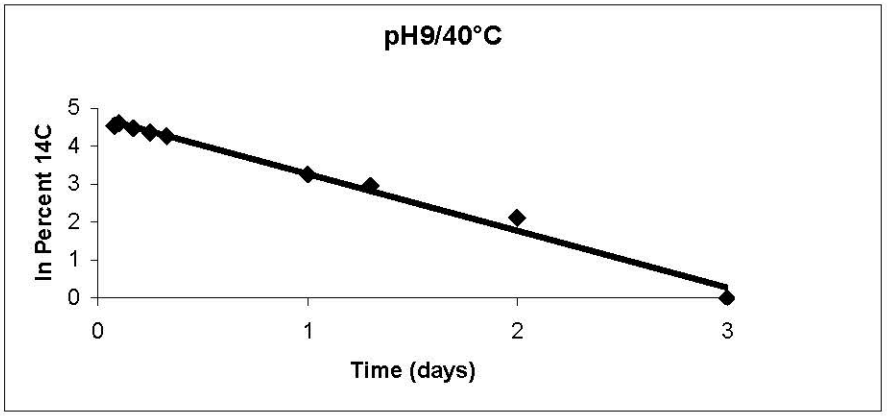
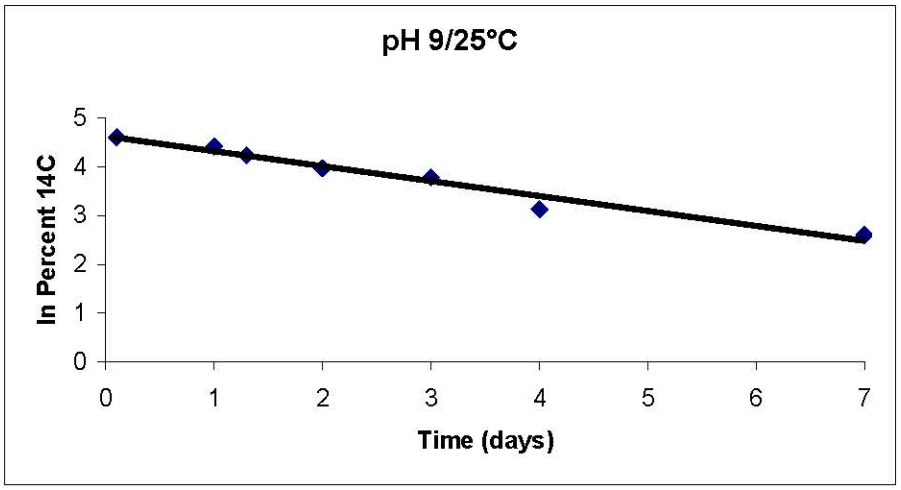
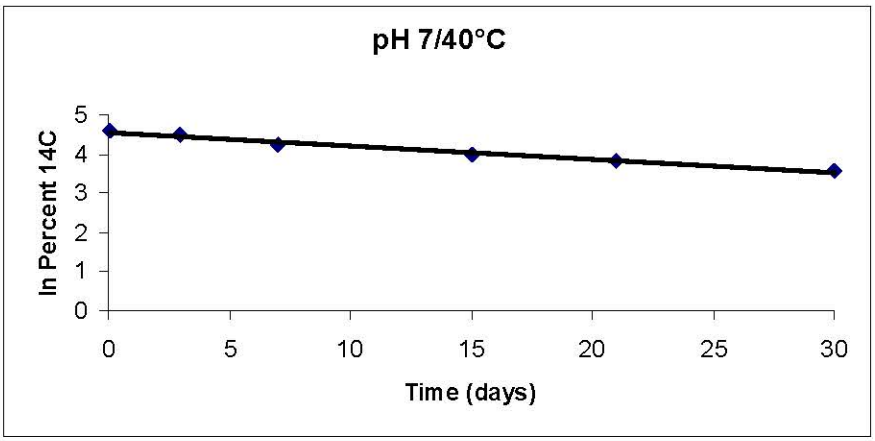
Hydrolysis Prod #		Compound/Structure	pH	Max %
PH 7	pH 9			
2	1	 2-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid Mol. Wt = 297	pH 7 pH 9	>10%
3	2	 1-chloro-2-(n-octylcarbamoyl)-1-ethene sulfonic acid Mol. Wt = 297	pH 7 pH 9	>10%
5	4	 N-(n-octyl) propiolic acid amide, Mol. Wt. = 181	pH 7 pH 9	>10% at pH 9
4		 4-chloro-5-hydroxy-2-(n-octyl)-3(2H) isothiazolone, Mol. Wt. = 263	pH 7	<10%
6		 4-chloro-2-(n-octyl)-3(2H) isothiazolone, Mol Wt = 247	pH 7	<10%
7		 4-chloro-5-methoxy-2-(n-octyl)-3(2H) isothiazolone, Mol. Wt = 277	pH 7	>10%

Figure A7.1.1.1.1/01-1: Natural log (ln) of the Percent ^{14}C DCOIT Versus Time

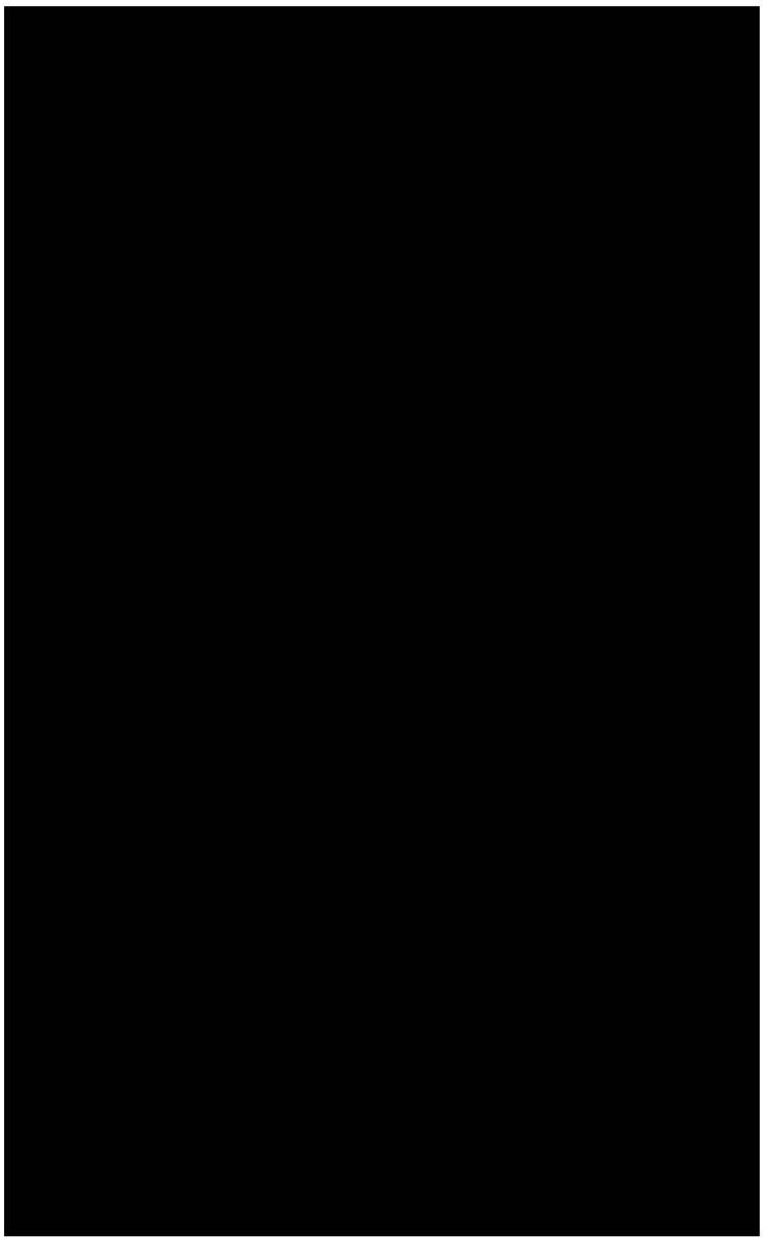






Document III-A / Section A7.1.1

[redacted]



Document III-A / Section A7.1.1

Section A7.1.1.1.1/02	**Hydrolysis as a function of pH and identification of breakdown products - Supplemental study**
Annex Point IIA7.6.2.1	**Structural confirmation of the major hydrolysis product**

Official use only

1 REFERENCE

1.1	**Reference**	Reference type: Study report Year: 2004 Report date: 9 August 2004 [redacted]
1.2	**Data protection**	Yes
1.2.1	Data owner	Rohm and Haas Company
1.2.2		
1.2.3	Criteria for data protection	[redacted]

[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1	**Guideline study**	No applicable guideline followed.
2.2	**GLP**	No
2.3	**Deviations**	This study is a supplemental study to the hydrolysis study summarized in section A7.1.1.1.1/01, providing structural confirmation of the major metabolite. The main study was guideline compliant.

3 MATERIALS AND METHODS

3.1	**Test material**	^{14}C DCOIT [redacted]
3.1.1	Lot/Batch number	[redacted]
3.1.2	Specification	[redacted]
3.1.3	Purity	[redacted]
3.1.4	Further relevant properties	-

Document III-A / Section A7.1.1

Section A7.1.1.1.1/02	**Hydrolysis as a function of pH and identification of breakdown products - Supplemental study**
Annex Point IIA7.6.2.1	**Structural confirmation of the major hydrolysis product**

3.2 Reference substance

[redacted]

3.2.1 Initial concentration of reference substance

[redacted]

3.3 Test solution

[redacted]

3.4 Testing procedure

[redacted]

3.5 Preliminary test

[redacted]

4 RESULTS

[redacted]

Document III-A / Section A7.1.1

Section A7.1.1.1.1/02	**Hydrolysis as a function of pH and identification of breakdown products - Supplemental study**
Annex Point IIA7.6.2.1	**Structural confirmation of the major hydrolysis product**

[redacted]

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Results discussions, and conclusions**	A major metabolite(s) observed in the aqueous hydrolysis and other experiments has been definitively identified by NMR as a sulfonic acid and not a sulfinic acid. The major isomer is C_8H_{17}-NH-C(O)-C(Cl)=CH-SO_3H and the secondary isomer, C_8H_{17}-NH-C(O)-CH=C(Cl)-SO_3H.
5.1.1	Reliability	2, valid with restriction
5.1.2	Deficiencies	Supplemental study to the hydrolysis key study. Non GLP.

Document III-A / Section A7.1.1

Evaluation by Competent Authorities	
Evaluation by Rapporteur Member State	
Date	5 October 2006
Materials and Methods	Agree with applicant's version
Results and discussion	Agree with applicant's version
Conclusion	**Comment (5.2)**: No version supplied by the applicant. It is suggested to adopt the results and discussion as the conclusion. A major metabolite observed in the aqueous hydrolysis of DCOIT has been definitively identified by NMR as a sulfonic acid and not a sulfinic acid. The major isomer is C_8H_{17}-NH-C(O)-C(Cl)=CH-SO_3H and the secondary isomer, C_8H_{17}-NH-C(O)-CH=C(Cl)-SO_3H.
Reliability	2, valid with restrictions
Acceptability	Study was not performed under GLP. Acceptable as supplementary data which provides further structural information on the metabolites of DCOIT hydrolysis.
Remarks	-

Document III-A / Section A7.1.1

Section A7.1.1.1.2 Phototransformation in water including identity of transformation products

Annex Point IIA7.6.2.2

Official use only

1 REFERENCE

1.1 Reference

Reference type: Study report

Year: 1990

Report date: 27 December 1990

[redacted]

Reference type: Study report

Year: 1993

Report date: 15 April 1993

[redacted]

1.2 Data protection Yes

1.2.1 Data owner Rohm and Haas Company

1.2.2

1.2.3 Criteria for data protection

[redacted]

[redacted]

2 GUIDELINES AND QUALITY ASSURANCE

2.1 Guideline study Yes. U.S. Environmental Protection Agency, 40 CFR § 158, Environmental Fate Assessment Guidelines, Subdivision N, Chemistry, Environmental Fate 161-2

2.2 GLP Yes

2.3 Deviations

- The ^{14}C test materials used in this study was synthesized prior to the enactment of U.S. EPA GLP guidelines. However, as part of the study a GLP radiopurity determination was performed.
- No actinometer study employing p-nitroacetophenone-pyridine, which measures the sunlight's intensity incident on the sample, was performed.

3 MATERIALS AND METHODS

Document III-A / Section A7.1.1

Section A7.1.1.1.2 Phototransformation in water including identity of transformation products

Annex Point IIA7.6.2.2

3.1	**Test material**	For both studies referenced above, ^{14}C DCOIT (RH-5287) was employed	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	[redacted]	
3.1.3	Purity	[redacted]	
3.1.4	Radiolabelling	[redacted]	
3.1.5	UV/VIS absorption spectra and absorbance value	[redacted]	
3.1.6	Further relevant properties	[redacted]	x
3.2	**Reference substances**	[redacted]	

Document III-A / Section A7.1.1

Section A7.1.1.1.2 Annex Point IIA7.6.2.2	Phototransformation in water including identity of transformation products

3.3 Test solution

[redacted]

3.4 Testing procedure

3.4.1 Test system

[redacted]

3.4.2 Properties of light source

[redacted]

3.4.3 Determination of irradiance

[redacted]

3.4.4 Temperature

[redacted]

Document III-A / Section A7.1.1

		[redacted]
3.4.5	pH	[redacted]
3.4.6	Duration of the test	[redacted]
3.4.7	Number of replicates	[redacted]
3.4.8	Sampling	[redacted]
3.4.9	Analytical methods	[redacted]