Section 6.2(2) Annex Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	[redacted]

Section 6.2(2) Annex Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study
Results and discussion	[redacted]
Conclusion	[redacted]

Section 6.2(2) Annex Point IIA 6.2	**Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study**
Reliability	[redacted]
Acceptability	Acceptable
Remarks	[redacted]
	COMMENTS FROM
Date	*Give date of the comments submitted*
Materials and Methods	*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*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

Section 6.3 – Short-term repeated dose toxicity (28 days)
Annex Point IIA 6.3 – headline only

Section 6.3.1 **Annex Point IIA.6.3.1**	**Short term repeated dose toxicity (oral)**	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible** [ ] **Scientifically unjustified** [X]	
Limited exposure [ ]	**Other justification** [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	Applicant's justification is acceptable.	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	

Section 6.3.1 Annex Point IIA.6.3.1	Short term repeated dose toxicity (oral)
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 6.3.2 Annex Point IIA.6.3.2	Short term repeated dose toxicity (dermal)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] Limited exposure [ ]	Technically not feasible [ ] Scientifically unjustified [X] Other justification [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	Applicant's justification is acceptable.	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Remarks		

Section 6.3.3 Annex Point IIA.6.3.3	Short term repeated dose toxicity (inhalation)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] Limited exposure [ ]	Technically not feasible [ ] Scientifically unjustified [X] Other justification [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	Applicant's justification is acceptable.	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	

Section 6.3.3 Annex Point IIA.6.3.3	Short term repeated dose toxicity (inhalation)
Remarks	

Section 6.4 – Subchronic toxicity
Annex Point IIA 6.4 – headline only

Section 6.4.1(1) **Annex Point IIA 6.4.1**	**Sub-chronic oral toxicity test**	
	1. REFERENCE	Official use only
1.1 Reference	Van Miller, J. P. (1988). Ninety-day dietary subchronic oral toxicity study with Didecyldimethylammonium Chloride in rats. Report No. 51-506. Union Carbide, Bushy Run Research Center, Export, PA, U.S.A. (Unpublished) Ref No. D27 (LON 1257)	
1.2 Data protection	Yes	
1.2.1 Data owner	The Dialkyl Project	
1.2.2 Criteria for data protection	Data submitted to the MS before 14 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 U.S. EPA FIFRA Guideline 82-1; OECD Guideline 408. 1987	
2.2 GLP (only where required)	Yes	
2.3 Deviations	No	
	3. MATERIALS AND METHODS	
3.1 Test material	[redacted]	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution.	
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	
3.1.5 Stability	The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of	

Section 6.4.1(1) Annex Point IIA 6.4.1		Sub-chronic oral toxicity test	
		Annex IIA).	
3.2	**Test animals**		
3.2.1	Species	Rat	
3.2.2	Strain	Sprague-Dawley	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	[redacted]	
3.2.6	Number of animals per group	[redacted]	
3.2.7	Control Animals	[redacted]	
3.3	**Administration/ Exposure**		
3.3.1	Dose route	Oral by diet	
3.3.2	Duration of test/ exposure	90-91 days	X
3.3.3	Frequency of exposure	7 days/week	
3.3.4	Post exposure period	[redacted]	
3.3.5	Concentration	[redacted]	
3.3.6	Vehicle	[redacted]	
3.3.7	Concentration in vehicle	[redacted]	
3.3.8	Actual dose received	[redacted]	
3.3.9	Controls	[redacted]	
3.4	**Examinations**		

Section 6.4.1(1) Annex Point IIA 6.4.1		Sub-chronic oral toxicity test	
3.4.1	Observations		
3.4.2	Clinical signs	[redacted]	
3.4.3	Mortality	[redacted]	
3.4.4	Bodyweight	[redacted]	
3.4.5	Food consumption	[redacted]	
3.4.6	Water consumption	[redacted]	
3.4.7	Ophthalmoscopic examination	[redacted]	
3.4.8	Haematology	[redacted]	
3.4.9	Clinical Chemistry	[redacted]	
3.4.10	Urinalysis	[redacted]	
3.5	**Sacrifice and Pathology**		
3.5.1	Organ weights	[redacted]	
3.5.2	Gross and histopathology	[redacted]	
3.5.3	Other examinations		
3.5.4	Statistical analysis	[redacted]	
		4. RESULTS	
4.1	**Examinations**		
4.1.1	Observations		
4.1.2	Clinical signs	Treatment-related signs were observed in the high dose group only and consisted of signs consistent with general cachexia (emaciation, pallor, etc.)	

Section 6.4.1(1) Annex Point IIA 6.4.1		Sub-chronic oral toxicity test	
4.1.3	Mortality	12/15 male and 13/15 female rats died at 3000 ppm in the diet.	
4.1.4	Bodyweight	No treatment-related effects on body weight were observed at 1000 ppm or lower. Body weights were significantly lower for survivors at 3000 ppm.	
4.1.5	Food consumption	No treatment-related effects on food consumption were observed at 1000 ppm or lower. Food consumption was significantly lower for survivors at 3000 ppm.	
4.1.6	Water consumption		
4.1.7	Ophthalmoscopic examination	No treatment-related findings were observed at any treatment level.	
4.1.8	Haematology	No treatment-related findings were observed at any treatment level except for in the survivors from the 3000 ppm group. Alterations in blood parameters for this group were considered of little toxicological significance because of the high mortality in the group.	X
4.1.9	Clinical Chemistry	No treatment-related findings were observed at any treatment level except for in the survivors from the 3000 ppm group. Alterations in blood parameters for this group were considered of little toxicological significance because of the high mortality in the group.	X
4.1.10	Urinalysis	N/A	
4.2	**Sacrifice and Pathology**		
4.2.1	Organ weights	No treatment-related findings were observed at any treatment level except for in the survivors from the 3000 ppm group. Alterations in organ weights for this group were considered of little toxicological significance because of the high mortality in the group.	X
4.2.2	Gross and Histopathology	Treatment-related findings were limited to animals that died or were sacrificed in a moribund condition from the 3000 ppm group. The principle finding was intestinal ileus consisting of distended fluid and gas-filled viscera affecting the cecum and colon. Histologic findings were consistent with the moribund condition of the animals.	
4.2.3	Other examinations		
4.2.4	Statistical analysis	As stated above	
4.3	**LO(A)EL**		
4.4	**NO(A)EL**	NOAEL = 61 mg/kg/d for males, 74 mg/kg/d for females	
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	[redacted]	

Section 6.4.1(1) Annex Point IIA 6.4.1	Sub-chronic oral toxicity test	
	[redacted]	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	NOAEL = 1000 ppm (61 mg/kg/d for males, 74 mg/kg/d for females)	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	

Section 6.4.1(1) Annex Point IIA 6.4.1	**Sub-chronic oral toxicity test**
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	Acceptable
Remarks	
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)
Date	*Give date of the comments submitted*
Materials and Methods	*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*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

Section 6.4.1(2) Annex Point IIA 6.4.1	Subchronic oral toxicity study.	
	1. REFERENCE	Official use only
1.1 Reference	Osheroff, M.R. (1990). Subchronic oral toxicity study of Didecyldimethylammonium Chloride in dogs. Study No. 2545-100. Hazelton Laboratories America, Inc., 9200 Leesburg Turnpike, Vienna, VA 22182, USA. (Unpublished) Ref No. D16 (LON 1256)	
1.2 Data protection	Yes	
1.2.1 Data owner	The Dialkyl Project	
1.2.2 Criteria for data protection	Data submitted to the MS before 14 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	Not applicable 1990	
2.2 GLP (only where required)	Yes	
2.3 Deviations	Not applicable	
	3. MATERIALS AND METHODS	
3.1 Test material	[redacted]	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution.	
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	
3.1.5 Stability	The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test animals		

Section 6.4.1(2) Annex Point IIA 6.4.1		Subchronic oral toxicity study.	
3.2.1	Species	Dog	
3.2.2	Strain	Beagle, purebred	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	[redacted]	
3.2.6	Number of animals per group	[redacted]	
3.2.7	Control Animals	[redacted]	
3.3	**Administration/ Exposure**		
3.3.1	Dose route	Oral gavage	
3.3.2	Duration of test/ exposure	8 weeks	
3.3.3	Frequency of exposure	First two weeks: once daily. After two weeks: total daily dose administered in two equally divided doses, one in the morning and one in the afternoon.	
3.3.4	Post exposure period	[redacted]	
3.3.5	Concentration	[redacted]	
3.3.6	Vehicle	[redacted]	
3.3.7	Concentration in vehicle	[redacted]	
3.3.8	Actual dose received	[redacted]	
3.3.9	Controls	[redacted]	
3.4	**Examinations**		
3.4.1	Observations	[redacted]	
3.4.2	Clinical signs	[redacted]	

Section 6.4.1(2) Annex Point IIA 6.4.1		Subchronic oral toxicity study.	
3.4.3	Mortality	[redacted]	
3.4.4	Bodyweight	[redacted]	
3.4.5	Food consumption	[redacted]	
3.4.6	Water consumption	[redacted]	
3.4.7	Ophthalmoscopic examination	[redacted]	
3.4.8	Haematology	[redacted]	
3.4.9	Clinical Chemistry	[redacted]	
3.4.10	Urinalysis	[redacted]	
3.5	**Sacrifice and Pathology**		
3.5.1	Organ weights	[redacted]	
3.5.2	Gross and histopathology	[redacted]	
3.5.3	Other examinations		
3.5.4	Statistical analysis	[redacted]	
		4. RESULTS	
4.1	**Examinations**		
4.1.1	Observations		
4.1.2	Clinical signs	7.5 mg/kg/d: soft mucoid faeces 15 mg/kg/d: emesis, soft faeces, and soft mucoid faeces 30 and 60 mg/kg/d: emesis, salivation, few or no faeces, soft faeces, soft mucoid faeces, lacrimation and thin appearance. Incidence of symptoms declined during the divided dosing regimen. 7.5 to 60 mg/kg/d: increased emesis, salivation, soft faeces and soft mucoid faeces with increased dose but less severity of clinical signs than the animals that were started at 60 mg/kg/d.	
4.1.3	Mortality	One male in the high dose group died during week 4; one moribund female in the highest dose group was sacrificed during week 4.	
4.1.4	Bodyweight	Body weights were depressed in all treatment groups relative to the	X

Section 6.4.1(2) Annex Point IIA 6.4.1	Subchronic oral toxicity study.	
	control beginning in week 2. There was a clear dose-response that ranged from slight at 7.5 mg/kg/d to marked at 60 mg/kg/d. A slight depression in body weight gain was observed in dogs switched from 7.5-60 mg/kg/d.	
4.1.5 Food consumption	Food consumption was depressed in all treatment groups relative to the control, beginning in week 2. There was a clear dose-response that ranged from slight at 7.5 mg/kg/d to marked at 60 mg/kg/d. Food consumption returned to control levels after switching to twice daily dosing regimen. A slight depression in body weight gain and food consumption was observed in dogs switched from 7.5-60 mg/kg/d.	
4.1.6 Water consumption		
4.1.7 Ophthalmoscopic examination		
4.1.8 Haematology	At the highest dose, erythrocyte count, haemoglobin, hematocrit, mean cell volume and mean cell haemoglobin concentrations decreased.	
4.1.9 Clinical Chemistry	Decreased total cholesterol was noted in all treated animals.	
4.1.10 Urinalysis		
4.2 Sacrifice and Pathology		
4.2.1 Organ weights	No abnormalities observed	
4.2.2 Gross and Histopathology	No clear treatment-related effects were found from gross pathological or histopathological examinations or in selected organ weights.	
4.2.3 Other examinations		
4.2.4 Statistical analysis	As noted above.	
4.3 LO(A)EL		
4.4 NO(A)EL	NOAEL = 30 mg/kg/d	X
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	

Section 6.4.1(2) Annex Point IIA 6.4.1	Subchronic oral toxicity study.	
	[redacted]	
5.2 Results and discussion	[redacted]	X
5.3 Conclusion	NOAEL = 30 mg/kg/d	X
5.3.1 Reliability	[redacted]	X
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	

Section 6.4.1(2) **Annex Point IIA 6.4.1**	**Subchronic oral toxicity study.**
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	Acceptable
Remarks	[redacted]
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)
Date	*Give date of the comments submitted*
Materials and Methods	*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*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

Section 6.4.1(3) Annex Point IIA 6.4.1	Subchronic oral toxicity test	
	1. REFERENCE	Official use only
1.1 Reference	Van Miller, J. P. (1988). Subchronic dietary dose range finding study with Didecyldimethylammonium Chloride in mice. Report No. 51-507. Union Carbide, Bushy Run Research Center, Export, PA, U.S.A. (Unpublished). Ref No: D19 (LON 1775)	
1.2 Data protection	Yes	
1.2.1 Data owner	The Dialkyl Project	
1.2.2 Criteria for data protection	Data submitted to the MS before 14 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 FIFRA 82-1 1988	
2.2 GLP (only where required)	Yes	
2.3 Deviations	A limited number of endpoints were examined because this study was designed primarily for selecting doses for a chronic Oncogenicity study.	
	3. MATERIALS AND METHODS	
3.1 Test material	[redacted]	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution.	
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	
3.1.5 Stability	The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test animals		

Section 6.4.1(3) Annex Point IIA 6.4.1		Subchronic oral toxicity test	
3.2.1	Species	Mouse	
3.2.2	Strain	CD-1®	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	[redacted]	
3.2.6	Number of animals per group	[redacted]	
3.2.7	Control Animals	[redacted]	
3.3	**Administration/ Exposure**		
3.3.1	Dose route	Oral by diet	
3.3.2	Duration of test/ exposure	89 days (males) and 90 days (females)	
3.3.3	Frequency of exposure	7 days/week.	
3.3.4	Post exposure period	[redacted]	
3.3.5	Concentration	[redacted]	
3.3.6	Vehicle	[redacted]	
3.3.7	Concentration in vehicle	[redacted]	
3.3.8	Actual dose received	[redacted]	
3.3.9	Controls	[redacted]	
3.4	**Examinations**		
3.4.1	Observations		

Section 6.4.1(3) Annex Point IIA 6.4.1	Subchronic oral toxicity test	
3.4.2 Clinical signs	[redacted]	
3.4.3 Mortality	[redacted]	
3.4.4 Bodyweight	[redacted]	
3.4.5 Food consumption	[redacted]	
3.4.6 Water consumption	[redacted]	
3.4.7 Ophthalmoscopic examination	[redacted]	
3.4.8 Haematology	[redacted]	
3.4.9 Clinical Chemistry	[redacted]	
3.4.10 Urinalysis	[redacted]	
3.5 Sacrifice and Pathology		
3.5.1 Organ weights	[redacted]	
3.5.2 Gross and histopathology	[redacted]	
3.5.3 Other examinations		
3.5.4 Statistical analysis	[redacted]	
	4. RESULTS	
4.1 Examinations		
4.1.1 Observations		
4.1.2 Clinical signs	General cachexia (e.g. emaciation and hunched posture) was observed in the 3000 ppm group.	
4.1.3 Mortality	All but one male animal from the 3000 ppm group died or were sacrificed in moribund condition in the first six days of treatment; the remaining animals survived to study termination.	

Section 6.4.1(3) Annex Point IIA 6.4.1	Subchronic oral toxicity test	
4.1.4 Bodyweight	Male and female mice treated with 1000 ppm had depressed body weights and weight gains.	
4.1.5 Food consumption	No effects at 1000 ppm or lower. Food consumption could not be measured at 3000 ppm because of the early mortality.	
4.1.6 Water consumption		
4.1.7 Ophthalmoscopic examination		
4.1.8 Haematology		
4.1.9 Clinical Chemistry		
4.1.10 Urinalysis		
4.2 Sacrifice and Pathology		
4.2.1 Organ weights	No treatment-related effects	
4.2.2 Gross and Histopathology	No treatment-related observations	X
4.2.3 Other examinations		
4.2.4 Statistical analysis	As noted above	
4.3 LO(A)EL	LOAEL = 1000 ppm equivalent to 183 and 224 mg/kg/d for males and females, respectively.	
4.4 NO(A)EL	NOAEL = 600 ppm equivalent to 107 and 134 mg/kg/d for males and females, respectively.	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	

Section 6.4.1(3) **Annex Point IIA 6.4.1**	**Subchronic oral toxicity test**	
5.3 Conclusion	NOAEL = 600 ppm LOAEL = 1000 ppm	X
5.3.1 Reliability	[redacted]	X
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	Acceptable	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)	
Date	*Give date of the comments submitted*	
Materials and Methods	*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*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	

Section 6.4.1(3) Annex Point IIA 6.4.1	**Subchronic oral toxicity test**
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

Section 6.4.2(1) Annex Point IIA 6.4.2	Subchronic dermal toxicity test	
	1. REFERENCE	Official use only
1.1 Reference	Gill, M.W. and Van Miller. J.P. (1988). Ninety-day subchronic dermal toxicity study with Didecyldimethylammonium Chloride in rats. Project No: 51-554. Union Carbide, Bushy Run Research Center, R.D. 4, Mellon Road, Export, PA 15632 USA. (Unpublished) Ref No. D14 (LON 1255)	
1.2 Data protection	Yes	
1.2.1 Data owner	The Dialkyl Project	
1.2.2 Criteria for data protection	Data submitted to the MS before 14 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 USEPA OPP 82-3 1988	
2.2 GLP (only where required)	Yes	
2.3 Deviations	No	X
	3. MATERIALS AND METHODS	
3.1 Test material	[redacted]	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution.	
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	
3.1.5 Stability	The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test animals		

Section 6.4.2(1) Annex Point IIA 6.4.2		Subchronic dermal toxicity test	
3.2.1	Species	Rat	
3.2.2	Strain	Sprague Dawley	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	[redacted]	
3.2.6	Number of animals per group	[redacted]	
3.2.7	Control Animals	[redacted]	
3.3	**Administration/ Exposure**		
3.3.1	Dose route	Dermal, occluded	
3.3.2	Duration of test/ exposure	90 days	
3.3.3	Frequency of exposure	5 days/week; 6 hours/day – Monday through Friday	
3.3.4	Post exposure period	[redacted]	
3.3.5	Concentration	[redacted]	
3.3.6	Vehicle	[redacted]	
3.3.7	Concentration in vehicle	[redacted]	
3.3.8	Actual dose received	[redacted]	X
3.3.9	Controls	[redacted]	
3.4	**Examinations**		
3.4.1	Observations		
3.4.2	Clinical signs	[redacted]	

Section 6.4.2(1) Annex Point IIA 6.4.2	Subchronic dermal toxicity test	
3.4.3 Mortality	[redacted]	
3.4.4 Bodyweight	[redacted]	
3.4.5 Food consumption	[redacted]	
3.4.6 Water consumption	[redacted]	
3.4.7 Ophthalmoscopic examination	[redacted]	
3.4.8 Haematology	[redacted]	
3.4.9 Clinical Chemistry	[redacted]	
3.4.10 Urinalysis	[redacted]	
3.5 Sacrifice and Pathology		
3.5.1 Organ weights	[redacted]	
3.5.2 Gross and histopathology	[redacted]	
3.5.3 Other examinations		
3.5.4 Statistical analysis	[redacted]	
	4. RESULTS	
4.1 Examinations		
4.1.1 Observations		
4.1.2 Clinical signs	No treatment-related signs were observed in either sex at any dose throughout the 90-day dosing period. Skin irritation (erythema, oedema) was observed at 6 and 12 mg/kg/d primarily early in the study (Days 5-8).	
4.1.3 Mortality	One female each from the low and high dose groups died during the study. These deaths were not considered related to treatment.	

Section 6.4.2(1) Annex Point IIA 6.4.2		Subchronic dermal toxicity test	
4.1.4	Bodyweight	No treatment-related effects in either sex at any dose.	
4.1.5	Food consumption	No treatment-related effects in either sex at any dose.	
4.1.6	Water consumption		
4.1.7	Ophthalmoscopic examination	No treatment-related effects in either sex at any dose.	
4.1.8	Haematology	No treatment-related effects in either sex at any dose.	
4.1.9	Clinical Chemistry	No treatment-related effects in either sex at any dose.	
4.1.10	Urinalysis		
4.2	**Sacrifice and Pathology**		
4.2.1	Organ weights	No treatment-related effects in either sex at any dose.	
4.2.2	Gross and Histopathology	Treatment-related gross findings indicative of minimal to mild skin irritation were observed at the two highest doses. Microscopically, lesions were observed in the treated skin for some animals from each treatment group. The high dose female group showed the greater incidence of histologic evidence of dermal and/or epidermal inflammation. No other treatment-related observations were recorded.	
4.2.3	Other examinations		
4.2.4	Statistical analysis	As described above	
4.3	**LOAEL**		
4.4	**NOAEL**	NOAEL = 12 mg/kg body weight	X
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	[redacted]	
5.2	**Results and discussion**	[redacted]	X
5.3	**Conclusion**	NOAEL = 12 mg/kg body weight	X
5.3.1	Reliability	[redacted]	
5.3.2	Deficiencies	[redacted]	

Section 6.4.2(1) Annex Point IIA 6.4.2	Subchronic dermal toxicity test
	Evaluation by Competent Authorities
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Guidelines and Quality Assurance	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	Acceptable
Remarks	[redacted]
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)

Section 6.4.2(1) Annex Point IIA 6.4.2	Subchronic dermal toxicity test
Date	*Give date of the comments submitted*
Materials and Methods	*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*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

Section 6.4.3 Annex Point III-A.6.4.3	Subchronic toxicity test (inhalation)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] Limited exposure [ ]	Technically not feasible [ ] Scientifically unjustified [X] Other justification [ ]	
Detailed justification:	[redacted]	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	Applicant's justification is acceptable	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE *(specify)*	
Date	*Give date of comments submitted*	
Evaluation of applicant's justification	*Discuss if deviating from view of rapporteur member state*	

Section 6.4.3 Annex Point III-A.6.4.3	Subchronic toxicity test (inhalation)
Conclusion	*Discuss if deviating from view of rapporteur member state*
Remarks	

Section 6.5(1) Annex Point IIA 6.5	Chronic toxicity in dogs	
	1. REFERENCE	Official use only
1.1 Reference	Schulze, G.E. (1991). Chronic oral toxicity study of Didecyldimethylammonium Chloride in dogs. Study No. 2545-102. Hazelton Washington, Inc., 9200 Leesburg Turnpike, Vienna, VA 22182, USA. HWA. (Unpublished) Ref No. D18 (LON 1778)	
1.2 Data protection	Yes	
1.2.1 Data owner	The Dialkyl Project	
1.2.2 Criteria for data protection	Data submitted to the MS before 14 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 U.S. EPA FIFRA Subdivision F, Section 158.83-1; OECD Guideline 452 1989	
2.2 GLP (only where required)	Yes	
2.3 Deviations	No	
	3. MATERIALS AND METHODS	
3.1 Test material	[redacted]	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution.	
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	
3.1.5 Stability	The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	

Section 6.5(1) Annex Point IIA 6.5		Chronic toxicity in dogs	
3.2	**Test animals**		
3.2.1	Species	Dog	
3.2.2	Strain	Beagle	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	[redacted]	
3.2.6	Number of animals per group	[redacted]	
3.2.7	Control Animals	[redacted]	
3.3	**Administration/ Exposure**		
3.3.1	Dose route	Oral gavage	
3.3.2	Duration of test/exposure	52 weeks	
3.3.3	Frequency of exposure	Two daily doses, 7 days/week.	
3.3.4	Post exposure period	[redacted]	
3.3.5	Concentration	[redacted]	
3.3.6	Vehicle	[redacted]	
3.3.7	Concentration in vehicle	[redacted]	
3.3.8	Actual dose received	[redacted]	
3.3.9	Controls	[redacted]	
3.4	**Examinations**		
3.4.1	Observations	[redacted]	
3.4.2	Clinical signs	[redacted]	

Section 6.5(1) Annex Point IIA 6.5		Chronic toxicity in dogs	
3.4.3	Mortality	[redacted]	
3.4.4	Bodyweight	[redacted]	
3.4.5	Food consumption	[redacted]	
3.4.6	Water consumption	[redacted]	
3.4.7	Ophthalmoscopic examination	[redacted]	
3.4.8	Haematology	[redacted]	
3.4.9	Clinical Chemistry	[redacted]	
3.4.10	Urinalysis	[redacted]	
3.5	**Sacrifice and Pathology**		
3.5.1	Organ weights	[redacted]	
3.5.2	Gross and histopathology	[redacted]	
3.5.3	Other examinations		
3.5.4	Statistical analysis	[redacted]	
		4. RESULTS	
4.1	**Examinations**		
4.1.1	Observations		
4.1.2	Clinical signs	There were generally higher incidences of emesis, salivation, and soft/mucoid/liquid faeces in the two higher dose groups than in the low dose group and control. The incidence of these clinical signs was high at 30 mg/kg/d but decreased to tolerable levels when dosage was lowered to 20 mg/kg/d.	X
4.1.3	Mortality	One animal in the 3 mg/kg/d died on Day 42 due to gavage error. All other animals survived to study termination.	
4.1.4	Bodyweight	At 30 mg/kg/d, mean body weight changes for Weeks 0-4 were significantly decreased for males and females compared to control groups. When the dose level was decreased, the body weight changes	

Section 6.5(1) Annex Point IIA 6.5		Chronic toxicity in dogs	
		generally became comparable to or greater than the control values.	
4.1.5	Food consumption	Mean total food consumption was significantly decreased in Week 1 for the 3 mg/kg/d males and females and in Weeks 1-4 for females only.	
4.1.6	Water consumption		
4.1.7	Ophthalmoscopic examination	No treatment-related effects in either sex at any dose.	
4.1.8	Haematology	Slight, non-significant decreases in erythrocyte count, haemoglobin and haematocrit were observed in high dose males and females at 13, 26 and 52 weeks. No other differences from control were considered to be treatment-related.	
4.1.9	Clinical Chemistry	Total cholesterol was significantly decreased in high dose group females at 13 weeks and reduced, but not significantly, at 26 and 52 weeks. Total protein was significantly decreased in high dose males at Week 52 and albumin was significantly decreased in this group at all intervals. No other differences from control were considered to be treatment-related.	
4.1.10	Urinalysis	No treatment-related effects in either sex at any dose.	
4.2	**Sacrifice and Pathology**		
4.2.1	Organ weights	No treatment-related effects in either sex at any dose.	
4.2.2	Gross and Histopathology	No treatment-related effects in either sex at any dose for gross or histopathology.	
4.2.3	Other examinations		
4.2.4	Statistical analysis	As noted above	
4.3	**LOAEL**	LOAEL=20 mg/kg/d	X
4.4	**NOAEL**	NOAEL=10 mg/kg/d	X
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	[redacted]	
5.2	**Results and discussion**	[redacted]	

Section 6.5(1) Annex Point IIA 6.5	Chronic toxicity in dogs	
5.3 Conclusion	NOAEL = 10 mg/kg/d	X
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	Acceptable	

Section 6.5(1) Annex Point IIA 6.5	Chronic toxicity in dogs
Remarks	[redacted]
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)
Date	*Give date of the comments submitted*
Materials and Methods	*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*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

Section 6.5(2) Annex IIA Point 6.5	Chronic toxicity in rats.	
	1. REFERENCE	Official use only
1.1 Reference	Gill, M.W., J.S. Chun, and C.L. Wagner. (1991). Chronic dietary toxicity/oncogenicity study with Didecyldimethylammonium Chloride in rats. Report No. 53-566. Union Carbide, Bushy Run Research Center, Export, PA, U.S.A. (Unpublished) Ref No. D30 (LON 1755)	
1.2 Data protection	Yes	
1.2.1 Data owner	The Dialkyl Project	
1.2.2 Criteria for data protection	Data submitted to the MS before 14 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 EPA Guideline 83-5; OECD Guideline 453 1988	
2.2 GLP (only where required)	Yes	
2.3 Deviations	No	
	3. MATERIALS AND METHODS	
3.1 Test material	[redacted]	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution.	
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	
3.1.5 Stability	The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test animals		

Section 6.5(2) Annex IIA Point 6.5		Chronic toxicity in rats.	
3.2.1	Species	Rats	
3.2.2	Strain	Sprague-Dawley CD®	
3.2.3	Source	[redacted]	
3.2.4	Sex	Male and female	
3.2.5	Age/weight at study initiation	[redacted]	
3.2.6	Number of animals per group	[redacted]	
3.2.7	Control Animals	[redacted]	
3.3	**Administration/ Exposure**		
3.3.1	Dose route	Oral feed	
3.3.2	Duration of test/exposure	24 Months (104 Weeks)	
3.3.3	Frequency of exposure	7 days/week	
3.3.4	Post exposure period	[redacted]	
3.3.5	Concentration	[redacted]	
3.3.6	Vehicle	[redacted]	
3.3.7	Actual dose received	[redacted]	
3.3.8	Controls	[redacted]	
3.4	**Examinations**		
3.4.1	Observations		
3.4.2	Clinical signs	[redacted]	

Section 6.5(2) Annex IIA Point 6.5		Chronic toxicity in rats.	
3.4.3	Mortality	[redacted]	
3.4.4	Bodyweight	[redacted]	
3.4.5	Food consumption	[redacted]	
3.4.6	Water consumption	[redacted]	
3.4.7	Ophthalmoscopic examination	[redacted]	
3.4.8	Haematology	[redacted]	
3.4.9	Clinical Chemistry	[redacted]	
3.4.10	Urinalysis	[redacted]	
3.5	**Sacrifice and Pathology**		
3.5.1	Organ weights	[redacted]	
3.5.2	Gross and histopathology	[redacted]	
3.5.3	Other examinations	[redacted]	
3.5.4	Statistical analysis	[redacted]	
		4. RESULTS	
4.1	**Examinations**		
4.1.1	Observations		
4.1.2	Clinical signs	No treatment-related findings were observed at any treatment level.	
4.1.3	Mortality	No treatment-related findings were observed at any treatment level.	
4.1.4	Bodyweight	Male and female rats treated with 1500 ppm had statistically significantly depressed body weights and weight gains for the entire study. No other treatment-related changes were observed.	
4.1.5	Food consumption	Male and female rats treated with 1500 ppm had statistically significantly decreased food consumption for the entire study. No other	

Section 6.5(2) Annex IIA Point 6.5	Chronic toxicity in rats.	
	treatment-related changes were observed.	
4.1.6 Water consumption		
4.1.7 Ophthalmoscopic examination	No treatment-related findings were observed at any treatment level.	
4.1.8 Haematology	No treatment-related findings were observed at any treatment level.	
4.1.9 Clinical Chemistry	No treatment-related findings were observed at any treatment level.	
4.1.10 Urinalysis	No treatment-related findings were observed at any treatment level.	
4.2 Sacrifice and Pathology		
4.2.1 Organ weights	No abnormalities observed.	
4.2.2 Gross and Histopathology	No gross necropsy changes were observed. At 1500 ppm, hyperplasia of the bile ducts in females and changes in the mesenteric lymph nodes of males and females related to blood in the sinuses were the only microscopic changes of potential but undetermined toxicological significance.	
4.2.3 Other examinations		
4.2.4 Statistical analysis	As noted above.	
4.3 LOAEL		
4.4 NOAEL	NOAEL = 750 ppm (equivalent to 32 and 41 mg/kg/d for males and females, respectively)	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	NOAEL = 750 ppm (equivalent to 32 and 41 mg/kg/d for males and	

Section 6.5(2) Annex IIA Point 6.5	Chronic toxicity in rats.	
	females, respectively)	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	Acceptable	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)	
Date	*Give date of the comments submitted*	
Materials and Methods	*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*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

Section 6.6 Genotoxicity studies

Annex Point IIA 6.6- headline only

Section 6.6.1(1) **Annex Point IIA 6.6.1**	**In vitro gene mutation study in bacteria**	
	1. REFERENCE	Official use only
1.1 Reference	Thompson, P.W. (2001). LZ1043 (DDAC): Reverse mutation assay "Ames Test" using *Salmonella typhimurium*. Project No. 102/368. Safepharm Laboratories Limited, Derby, UK. (Unpublished) Ref No. D87 (LON 3341)	
1.2 Data protection	Yes *(indicate if data protection is claimed)*	
1.2.1 Data owner	*Give name of company* The Dialkyl Project	
1.2.2 Criteria for data protection	*Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:* 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 Directive 92/69/EEC, B.14 2001 *(If yes, give references to the guidelines (for example test number in Annex V of Dir. 67/548/EEC); if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")*	
2.2 GLP (only where required)	Yes *(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)*	
2.3 Deviations	No *(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")*	
	3. MATERIALS AND METHODS	
	In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.	
3.1 Test material	[redacted]	X
3.1.1 Lot/Batch number	*List lot/batch number where relevant* [redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein.	

Section 6.6.1(1) Annex Point IIA 6.6.1	In vitro gene mutation study in bacteria	
	[redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution. *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	
3.1.3 Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* [redacted]	
3.1.4 Purity	*Give purity in g/kg, g/l, %w/w or % v/v active substance* [redacted]	
3.1.5 Stability	*Describe stability of test material* The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test species		
3.2.1 Cell type	*Salmonella typhimurium*	
3.2.2 Strain	TA1535, TA1537, TA102, TA98 and TA100	
3.3 Metabolic activation		
3.3.1 Metabolic activation system	S9-mix	
3.3.2 Control in presence of metabolic activation	[redacted]	
3.3.2 Control in absence of metabolic activation	[redacted]	
3.4 Test Methods		
3.4.2 Negative control	[redacted]	
3.4.2 Vehicle Control	[redacted]	
3.4.3 Cytotoxicity concentrations	[redacted]	
3.4.4 Genotoxicity	[redacted]	

Section 6.6.1(1) Annex Point IIA 6.6.1	In vitro gene mutation study in bacteria	
concentrations	[redacted]	
3.4.5 Statistical methods	[redacted]	
3.5 Remarks	[redacted]	
	4. RESULTS	
4.1 Cytotoxicity		
4.1.1 With metabolic activation	See table 6.6.1(1)-1	
4.1.2 Without Metabolic activation	See table 6.6.1(1)-1	
4.1.3 Remarks	The test substance was toxic at concentrations of 50 µg/plate and above.	
4.2 Genotoxicity		
4.2.1 With metabolic activation	See table 6.6.1(1)-2	
4.2.2 Without metabolic activation	See table 6.6.1(1)-2	
4.2.3 Remarks	The test substance was considered to be non-mutagenic.	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	*Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines. Comments from 2.1above are relevant in this table.* [redacted]	
5.2 Results and discussion	*Summarise relevant results; discuss dose-response relationship where relevant.* [redacted]	
5.3 Conclusion	*Subsections for NOAEL, LOAEL etc. if appropriate* The test substance was considered to be non-mutagenic.	
5.3.1 Reliability	*Based on the assessment of materials and methods include appropriate reliability indicator 0, 1, 2, 3 or 4* [redacted]	
5.3.2 Deficiencies	[redacted] *(If yes, discuss the impact of deficiencies and implications on results. If*	

Section 6.6.1(1) **Annex Point IIA 6.6.1**	**In vitro gene mutation study in bacteria**	
	relevant, justify acceptability of study.)	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	The study is acceptable	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)	
Date	*Give date of the comments submitted*	
Materials and Methods	*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*	
Results and discussion	*Discuss if deviating from view of rapporteur member state*	
Conclusion	*Discuss if deviating from view of rapporteur member state*	
Reliability	*Discuss if deviating from view of rapporteur member state*	
Acceptability	*Discuss if deviating from view of rapporteur member state*	

Table 6.6.1(1)-1. Cytotoxicity (Number of revertant colonies)

		Test substance concentration (µg/plate)										
With/ Without S9-mix	**Strain**	**0**	**0.15**	**0.5**	**1.5**	**5**	**15**	**50**	**150**	**500**	**1500**	**5000**
Without	TA100	77	69	99	101	83	51	0	0	0	0	0
With	TA100	77	110	103	86	11	19	0	0	0	0	0

Table 6.6.1(1)-2. Genotoxicity (Mean number of revertant colonies)

Strain	**TA100**		**TA1535**		**TA102**		**TA98**		**TA1537**	
Test substance concentration (µg/plate)										
With S9										
+ve control type (concentration (µg/plate))	[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
Test number	1	2	1	2	1	2	1	2	1	2
+ve control	1772	2031	287	269	886	1073	229	274	582	652
-ve control	142	156	13	12	370	328	36	31	20	18
0.15	110	156	11	17	368	329	32	38	15	17
0.5	107	158	13	15	385	369	32	25	12	15
1.5	122	141	12	15	392	358	35	24	14	18
5	113	158	10	14	391	348	29	25	19	15
15	52	68	7	6	339	323	29	17	11	10
50	0	0	0	0	0	0	0	0	0	0
Without S9										
+ve control type (concentration (µg/plate))	[redacted]		[redacted]		[redacted]		[redacted]		[redacted])	
Test number	1	2	1	2	1	2	1	2	1	2
+ve control	464	786	430	1024	961	1085	126	150	716	838
-ve control	137	150	13	14	330	308	13	18	14	16
0.15	126	146	17	12	353	362	15	13	17	16
0.5	132	168	17	14	344	364	17	16	11	18
1.5	120	156	16	16	350	352	14	18	19	19
5	119	146	17	15	337	340	15	17	15	15
15	81	130	17	16	294	322	17	19	7	16
50	0	0	0	0	0	0	0	0	0	0

Section 6.6.2(1) Annex Point IIA 6.6.2	In-vitro Cytogenicity study in mammalian cells	
	1. REFERENCE	Official use only
1.1 Reference	*Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages) If necessary, copy field and enter other reference(s).* Holmstrom, M., Leftwich, D.J. and Leddy. I.A. (1986). PO151: Chromosomal aberrations assay with Chinese hamster ovary cells in vitro. Project No. 735717, Report No. 4236. Inveresk Research International, Musselburgh, Scotland. (Unpublished) Ref No. D31 (LON 1253)	
1.2 Data protection	Yes *(indicate if data protection is claimed)*	
1.2.1 Data owner	*Give name of company* The Dialkyl Project	
1.2.2 Criteria for data protection	*Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:* Data submitted to the MS before 14 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 U.S. EPA FIFRA 84-2(b) 1986 *(If yes, give references to the guidelines (for example test number in Annex V of Dir. 67/548/EEC); if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")*	
2.2 GLP (only where required)	Yes *(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)*	
2.3 Deviations	No *(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")*	
	3. MATERIALS AND METHODS	
	In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.	
3.1 Test material	[redacted]	X
3.1.1 Lot/Batch number	*List lot/batch number where relevant* [redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein.	

Section 6.6.2(1) Annex Point IIA 6.6.2	In-vitro Cytogenicity study in mammalian cells	
	Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution. *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	
3.1.3 Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* [redacted]	
3.1.4 Purity	*Give purity in g/kg, g/l, %w/w or % v/v active substance* [redacted]	
3.1.5 Stability	The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, e.g. at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test species		
3.2.1 Cell type	Chinese hamster ovary cells	
3.2.2 Strain	CHO-K_1B_4	
3.3 Metabolic activation		
3.3.1 Metabolic activation system	S9	
3.3.2 Positive Control in presence of metabolic activation	[redacted]	
3.3.3 Positive Control in absence of metabolic activation	[redacted]	
3.4 Test Methods		
3.4.1 Negative control	[redacted]	
3.4.2 Vehicle Control	[redacted]	
3.4.3 Cytotoxicity Concentrations	[redacted]	
3.4.4 Genotoxicity concentrations	[redacted] [redacted]	
3.4.5 Statistical methods	[redacted]	

Section 6.6.2(1) Annex Point IIA 6.6.2	In-vitro Cytogenicity study in mammalian cells	
3.4.6 Duplicate/Independent assay	[redacted]	
	4. RESULTS	
4.1 Cytotoxicity		
4.1.1 With Metabolic activation	Completely toxic at 28 µg/ml and higher with S9 activation	
4.1.2 Without Metabolic activation	Completely toxic at 2.8 µg/ml and higher without S9 activation	
4.2 Genotoxicity		
4.2.1 With Metabolic activation	Negative	
4.2.1.1 Polyploidy incidence	None observed	
4.2.1.2 Frequency of effects	Acceptable range: 0.01-0.17 with S9 mix	
4.2.2 Without Metabolic activation	Negative	
4.2.1.1 Polyploidy incidence	None observed	
4.2.1.2 Frequency of effects	Acceptable range: 0.01-0.09 without S9 mix	
4.3 Duplicate Assay	No	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	*Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines. Comments from 2.1above are relevant in this table.* [redacted]	
5.2 Results and discussion	*Summarise relevant results; discuss dose-response relationship where relevant.* [redacted]	

Section 6.6.2(1) **Annex Point IIA 6.6.2**	**In-vitro Cytogenicity study in mammalian cells**
	[redacted]
5.3 Conclusion	*Subsections for NOAEL, LOAEL etc. if appropriate* Cytotoxicity observed. No genotoxicity observed.
5.3.1 Reliability	[redacted]
5.3.2 Deficiencies	[redacted] *(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)*
	Evaluation by Competent Authorities
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted
	EVALUATION BY RAPPORTEUR MEMBER STATE
Date	[redacted]
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	The study is acceptable
Remarks	
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)
Date	*Give date of the comments submitted*

Section 6.6.2(1) Annex Point IIA 6.6.2	In-vitro Cytogenicity study in mammalian cells
Materials and Methods	*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*
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

Section 6.6.3(1) Annex Point IIA 6.6.3	In vitro gene mutation assay in mammalian cells	
	1. REFERENCE	Official use only
1.1 Reference	*Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)* *If necessary, copy field and enter other reference(s).* Young, R. R. (1988). Mutagenicity test on Didecyldimethylammonium Chloride (DDAC) in the CHO/HGPRT forward mutation assay. Report No. 10141-0-435. Hazleton Laboratories America, Inc., Kensington, MD, U.S.A. (Unpublished) Ref No. D32 (LON 1254)	
1.2 Data protection	Yes *(indicate if data protection is claimed)*	
1.2.1 Data owner	*Give name of company* The Dialkyl Project	
1.2.2 Criteria for data protection	*Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:* Data submitted to the MS before 14 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 U.S. EPA FIFRA 84-2 1987 *(If yes, give references to the guidelines (for example test number in Annex V of Dir. 67/548/EEC); if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")*	
2.2 GLP (only where required)	Yes *(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)*	
2.3 Deviations	No *(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")*	
	3. MATERIALS AND METHODS	
	In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.	
3.1 Test material	[redacted]	
3.1.1 Lot/Batch number	*List lot/batch number where relevant* [redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein.	

Section 6.6.3(1) Annex Point IIA 6.6.3	In vitro gene mutation assay in mammalian cells	
	[redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution. *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	
3.1.3 Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* [redacted]	
3.1.4 Purity	*Give purity in g/kg, g/l, %w/w or % v/v active substance* [redacted]	
3.1.5 Stability	*Describe stability of test material* The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test species/strain		
3.2.1 Cell type	Chinese hamster ovary cells (CHO)	
3.2.2 Strain	CHO-K1-BH_4	
3.3 Metabolic activation		
3.3.1 Metabolic activation system	S9	
3.3.2 Control in presence of metabolic activation	[redacted]	
3.3.3 Control in absence of metabolic activation	[redacted]	
3.4 Test Methods		
3.4.1 Negative control	[redacted]	
3.4.2 Vehicle Control	[redacted]	
3.4.3 Cytotoxicity concentrations	[redacted]	X
3.4.4 Genotoxicity concentrations	[redacted]	

Section 6.6.3(1) Annex Point IIA 6.6.3	In vitro gene mutation assay in mammalian cells	
3.4.5 Statistical methods	[redacted]	
3.4.6 Duplicate/ Independent assay	[redacted]	
	4. RESULTS	
4.1 Cytotoxicity		
4.1.1 With Metabolic activation	Completely toxic at 20 µg/ml and higher with activation.	
4.1.2 Without Metabolic activation	Completely toxic at 4.0 µg/ml and higher without activation.	
4.2 Genotoxicity		
4.2.1 With Metabolic activation	Negative	
4.2.1.1 Mutant frequency	Acceptable range for background mutant frequencies (0 to 15E-06 with S9 mix)	
4.2.2 Without Metabolic activation	Negative	
4.2.2.1 Mutant Frequency	Acceptable range for background mutant frequencies (0 to 15E-06 without S9 mix)	
4.3 Duplicate/ Independent assay	Negative	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	*Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines. Comments from 2.1above are relevant in this table.* [redacted]	
5.2 Results and discussion	*Summarise relevant results; discuss dose-response relationship where relevant.* [redacted]	

Section 6.6.3(1) **Annex Point IIA 6.6.3**	**In vitro gene mutation assay in mammalian cells**	
	[redacted]	
5.3 Conclusion	*Subsections for NOAEL, LOAEL etc. if appropriate* Cytotoxic at 4.0 µg/ml (-S9) and at 20 µg/ml (+S9). Not genotoxic.	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted] *(If yes, discuss the impact of deficiencies and implications on results. If relevant, justify acceptability of study.)*	
	Evaluation by Competent Authorities	
	Use separate "evaluation boxes" to provide transparency as to the comments and views submitted	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	
Reliability	[redacted]	
Acceptability	The study is acceptable	
Remarks		
	COMMENTS FROM OTHER MEMBER STATE (SPECIFY)	
Date	*Give date of the comments submitted*	
Materials and Methods	*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*	

Section 6.6.3(1) Annex Point IIA 6.6.3	In vitro gene mutation assay in mammalian cells
Results and discussion	*Discuss if deviating from view of rapporteur member state*
Conclusion	*Discuss if deviating from view of rapporteur member state*
Reliability	*Discuss if deviating from view of rapporteur member state*
Acceptability	*Discuss if deviating from view of rapporteur member state*

Section 6.6.4(1) Annex Point IIA 6.6.4	In-vivo mutagenicity study	
	1. REFERENCE	Official use only
1.1 Reference	*Author(s), year, title, laboratory name, laboratory report number, report date (if published, list journal name, volume: pages)* *If necessary, copy field and enter other reference(s).* Allen, J.A., Proudlock, R.J., Brooker, P.C. (1987). Analysis of Metaphase Chromosomes Obtained from Bone Marrow of Rats Treated with P0151 (Bardac 22). Study No. LZA 24/8761. Huntingdon Research Centre, Ltd., Huntingdon, England. (Unpublished) Ref No. D84 (LON 1252)	
1.2 Data protection	Yes *(indicate if data protection is claimed)*	
1.2.1 Data owner	*Give name of company* The Dialkyl Project	
1.2.2 Criteria for data protection	*Choose one of the following criteria (see also TNsG on Product Evaluation) and delete the others:* Data submitted to the MS before 14 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 Test Guideline No. 475 1987 *(If yes, give references to the guidelines (for example test number in Annex V of Dir. 67/548/EEC); if no, give justification, e.g. "no guidelines available" or "methods used comparable to guidelines xy")*	
2.2 GLP (only where required)	Yes *(If no, give justification, e.g. state that GLP was not compulsory at the time the study was performed)*	
2.3 Deviations	No *(If yes, describe deviations from test guidelines or refer to respective field numbers where these are described, e.g. "see 3.x.y")*	
	3. MATERIALS AND METHODS	
	In some fields the values indicated in the EC or OECD test guidelines are given as default values. Adopt, change or delete these default values as appropriate.	
3.1 Test material	[redacted]	
3.1.1 Lot/Batch number	*List lot/batch number where relevant* [redacted]	
3.1.2 Specification	As given in Section 2 of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein.	

Section 6.6.4(1) Annex Point IIA 6.6.4	In-vivo mutagenicity study	
	[redacted] Active substance (a.s.), Didecyldimethylammonium Chloride (DDAC; CAS RN 7173-51-5), in aqueous/alcohol solution. *(describe specification under separate subheadings, such as the following; additional subheadings may be appropriate):*	
3.1.3 Description	*If appropriate, give e.g. colour, physical form (e.g. powder, grain size, particle size/distribution)* [redacted]	
3.1.4 Purity	*Give purity in g/kg, g/l, %w/w or % v/v active substance* [redacted]	
3.1.5 Stability	*Describe stability of test material* The a.s., DDAC, is hydrolytically and photolytically stable under the conditions of this study and has been shown to be stable in aqueous, alcohol and alcohol/aqueous solutions for extended periods, *e.g.* at least seven years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test species		
3.2.1 Species	Rat	
3.2.2 Strain	Sprague-Dawley	
3.2.3 Source	[redacted]	
3.2.4 Sex	Male and Female	
3.2.5 Age/weight at study initiation	[redacted]	
3.2.6 Number of animals per group	[redacted]	
3.2.7 Control Animals	[redacted]	
3.3 Administration/ Exposure		
3.3.1 Dose route	Gastric intubation, [redacted]	
3.3.2 Duration of test/exposure	[redacted]	
3.3.3 Concentration	[redacted]	
3.3.4 Vehicle	[redacted]	
3.3.5 Concentration in	[redacted]	

Section 6.6.4(1) Annex Point IIA 6.6.4	In-vivo mutagenicity study	
vehicle		
3.3.6 Controls	[redacted]	
3.4 Test Methods	OECD Test Guideline No. 475	
3.4.1 Pre-sacrifice treatment	[redacted]	
3.4.2 Cell type	Femur bone marrow cells	
	4. RESULTS	
4.1 Animal observations		
4.1.1 Clinical signs	No effects observed	
4.1.2 Mortality	One female dosed with test substance died, but this was not thought to be due to test substance.	
4.2 Cell observations		
4.2.1 Test substance	No increase in the incidence of cells showing aberrant chromosomes	
4.2.2 Positive control	Highly significant increase of metaphase figures showing aberrant chromosomes.	
4.3 Remarks	The test substance did not cause any chromosomal damage.	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	*Give concise description of method; give test guidelines no. and discuss relevant deviations from test guidelines. Comments from 2.1above are relevant in this table.* [redacted]	
5.2 Results and discussion	*Summarise relevant results; discuss dose-response relationship where relevant.* [redacted]	
5.3 Conclusion	*Subsections for NOAEL, LOAEL etc. if appropriate* Didecyldimethylammonium Chloride did not cause any chromosomal damage.	
5.3.1 Reliability	[redacted]	