Section 6.1.5(2) Annex Point IIA 6.1.5	Skin sensitisation	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	Not Sensitising	
5.3.1 Reliability	[redacted]	X
5.3.2 Deficiencies	[redacted]	
	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]	
Guideline and Quality Assurance	[redacted]	
Materials and Methods	[redacted]	
Results and discussion	[redacted]	
Conclusion	[redacted]	

Section 6.1.5(2) **Annex Point IIA 6.1.5**	**Skin sensitisation**
Reliability	[redacted]
Acceptability	[redacted]
Remarks	
	COMMENTS FROM OTHER MEMBER STATE
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 6.1.5(3) **Annex Point IIA 6.1.5**	**Skin sensitisation**	
	1. REFERENCE	Official use only
1.1 Reference	Durando, J. (2005). Barquat MB-80: Dermal Sensitization Study in Guinea Pigs (Buehler Method). Study No. 17426. Product Safety Laboratories, Dayton, NJ, USA. (Unpublished) [Ref. No. A112 (LON 4002)]	
1.2 Data protection	Yes	
1.2.1 Data owner	ADBAC Issues Steering Committee	
1.2.2 Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA.	
	2. GUIDELINES AND QUALITY ASSURANCE	
2.1 Guideline study	U.S. EPA Health Effects Test Guidelines, OPPTS 870.2600 (2003) OECD Guideline for the Testing of Chemicals, Procedure 406 (1992)	
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.), alkyl(C_{12}-C_{16})dimethylbenzylammonium chloride (ADBAC; CAS RN 68424-85-1), in aqueous/ethanol solution.	
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	X
3.1.5 Stability	The a.s., ADBAC, 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 five years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	X
3.2 Test Animals		
3.2.1 Species	Guinea pig	
3.2.2 Strain	Hartley albino	
3.2.3 Source	[redacted]	

Section 6.1.5(3) Annex Point IIA 6.1.5	Skin sensitisation	
3.2.4 Sex	Males and females	
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 Preliminary Irritation Testing for HNIC		
3.3.1 Preparation of Animals	[redacted]	
3.3.2 Test Article Concentration	[redacted]	
3.3.3 Vehicle	[redacted]	
3.3.4 Dose Volume	[redacted]	
3.3.5 Route of Administration	Occlusive dermal exposure using a 25 mm Hill Top Chamber	
3.3.6 Exposure Duration	6 hours	
3.3.7 Dermal Evaluations	[redacted]	
3.4 Main Sensitisation Test		
3.4.1 Preparation of Animals	[redacted]	
3.4.2 Induction Phase		
3.4.2.1 Test Article Concentration	[redacted]	
3.4.2.2 Vehicle	[redacted]	
3.4.2.3 Dose Volume	[redacted]	
3.4.2.4 Route of Administration	Occlusive dermal exposure using a 25 mm Hill Top Chamber	
3.4.2.5 Dosing Schedule	[redacted]	
3.4.2.6 Exposure Duration	6 hours	
3.4.2.7 Dermal Evaluations	[redacted]	

Section 6.1.5(3) **Annex Point IIA 6.1.5**	**Skin sensitisation**	
3.4.3 Challenge Phase		
3.4.3.1 Test Article Concentration (HNIC)	[redacted]	
3.4.3.2 Vehicle	[redacted]	
3.4.3.3 Dose Volume	[redacted]	
3.4.3.4 Route of Administration	Occlusive dermal exposure using a 25 mm Hill Top Chamber	
3.4.3.5 Dosing Procedures: Test Animals	[redacted]	
3.4.3.6 Dosing Procedures: Naive Control Animals	[redacted]	
3.4.3.7 Exposure Duration	6 hours	
3.4.3.8 Dermal Evaluations	[redacted]	
3.4.4 Body Weights	[redacted]	
3.5 Evaluations		
3.5.1 Incidence Index	[redacted]	
3.5.2 Severity Index	[redacted]	
3.5.3 Further Remarks	[redacted]	
3.6 Positive Control		
3.6.1 Historical Positive Control Validation Study	[redacted]	
	4. RESULTS	
4.1 Results		
4.1.1 Induction Phase: Test Animals	Very faint to faint erythema (05-1.0) was noted for all sites during the induction phase.	
4.1.2 Challenge Phase		

Section 6.1.5(3) Annex Point IIA 6.1.5	Skin sensitisation	
4.1.2.1 Test Animals	None of the test animals exhibited a positive sensitisation response (score greater than 0.5) at 24 or 48 hours after challenge. Very faint erythema (0.5) was noted for nine of 20 test animals at 24 hours after challenge. Similar irritation persisted at two sites through 48 hours.	
4.1.2.2 Naive Control Animals	[redacted]	
4.1.3 Historical Positive Control Study	[redacted]	
4.1.4 Incidence Index	See Table 6.1.5(3)-2.	
4.1.5 Severity Index	See Table 6.1.5(3)-2.	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	Based on these findings and under the conditions of this study, ADBAC is not considered to be a contact sensitiser.	
5.3.1 Reliability	[redacted].	
5.3.2 Deficiencies	[redacted]	

Section 6.1.5(3) Annex Point IIA 6.1.5	Skin sensitisation
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
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 6.1.5(3)-1

Scoring System

0	No reaction
0.5	Very faint erythema, usually non-confluent*
1	Faint erythema, usually confluent
2	Moderate erythema
3	Severe erythema with or without edema

*Very faint erythema is not considered a positive reaction.

Table 6.1.5(3)-2

	Sensitisation Response Indices			
	Incidence of Positive Response[1]		Severity [2]	
	Hours		Hours	
	24	48	24	48
Test Animals	0/20	0/20	0.23	0.05
Naïve Control Animals	0/10	0/10	0.25	0.10

[1] Animals with scores greater than 0.5.
[2] Sum of the erythema scores divided by the number of animals evaluated.

Section 6.2(1) **Annex Point IIA 6.2**	**Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study**	
	1. REFERENCE	Official use only
1.1 Reference	Selim, S. (1987) Absorption, distribution, metabolism and excretion studies of Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC) in the rat. Biological Test Center, Irvine, CA, USA. BTC Study No. P01359 (unpublished) [Ref Nos A50 and A50a (LON 1872)]	
1.2 Data protection	Yes	
1.2.1 Data owner	ADBAC Joint Venture	
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 Guideline 85-1 1987	
2.2 GLP (only where required)	Yes	
2.3 Deviations	No	
	3. MATERIALS AND METHODS	
3.1 Test material	Alkyldimethylbenzylammonium Chloride	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in section II of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. Non-radiolabelled active substance (a.s.), alkyl(C_{12}-C_{16})dimethylbenzylammonium chloride (ADBAC; CAS RN 68424-85-1), in aqueous/ethanol solution.	
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	X
3.1.5 Stability	The a.s., ADBAC, 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 five years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	

Section 6.2(1) Annex Point IIA 6.2		Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study	
3.2 Test Procedure		*In vivo*	
3.2.1	Method of analysis	[redacted]	
3.3 Test Animals			
3.3.1	Species	Rat	
3.3.2	Strain	Sprague Dawley	
3.3.3	Source	[redacted]	
3.3.4	Sex	Male and female	
3.3.5	Age/weight at study initiation	[redacted]	
3.3.6	Number of animals per group	[redacted]	X
3.3.7	Control animals	[redacted]	
3.4 Administration/ exposure			
3.4.1	Dose route	Experiment 1: Oral gavage – single low dose Experiment 2: Dietary – repeated low dose Experiment 3: Oral gavage – single high dose Experiment 4: Intravenous	X
3.4.2	Post exposure period	[redacted]	X
3.4.3	Concentration	[redacted]	X
3.4.4	Vehicle	[redacted]	X
3.4.5	Concentration in vehicle	[redacted]	X
3.4.6	Controls	[redacted]	
		4. RESULTS	

Section 6.2(1) Annex Point IIA 6.2		Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study	
4.1	**Results**		
4.1.1	% Recovery	Experiment 1: Males: 5.77% urine; 98.61% faeces Female: 6.88% urine; 91.20% faeces Total Recovery: 104.54 ± 5.29% - males; 98.11 ± 3.25% females Experiment 2: Males: 4.76% urine; 95.12% faeces Female: 5.80% urine; 97.22% faeces Total Recovery: 100.19 ± 4.94% - males; 103.1 ± 5.18% females Experiment 3: Males: 7.75 % urine; 90.03% faeces Female: 6.95% urine; 87.48% faeces Total Recovery: 98.36 ± 2.42% - males; 94.58 ± 7.57% females Experiment 4: Males: 30.63% urine; 44.44% faeces Female: 20.58% urine; 55.09% faeces Total Recovery: 108.43 ± 5.56% - males; 111.45 ± 3.96% females Less than 1% in tissues in all oral dosing experiments. Approximately 30-35% of the administered dose in tissues following i.v. dosing.	
4.1.2	Metabolites	Over 50% of the faecal radioactivity was unchanged Alkyldimethylbenzylammonium Chloride. 4 major metabolites were identified. The only metabolism which occurred involved oxidation of the two decyl side chains to hydroxy and hydroxyketo derivatives. All were more polar and presumed less toxic than the parent compound. It is predicted that there is no major metabolite greater than 10% of the dosed radioactivity.	X
4.2	**Remarks**	Residual ^{14}C in tissues was negligible after administration of ^{14}C Alkyldimethylbenzylammonium Chloride by gavage. A high level of residual ^{14}C radioactivity (30-35% of total dose) was present in the tissues following intravenous administration. Most, if not all, the metabolism appears to be in the gut by intestinal microflora. No significant difference in metabolism between male and female rats or among the dosing regimens was observed.	X
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods		[redacted]	

Section 6.2(1) Annex Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study	
	[redacted]	
5.2 Results and discussion	[redacted]	X
5.3 Conclusion	The majority of orally administered Alkyldimethylbenzylammonium Chloride is excreted via the faeces. Residual ^{14}C in tissues was negligible after administration of ^{14}C-Alkyldimethylbenzylammonium Chloride by gavage. In the intravenous experiment, Alkyldimethylbenzylammonium Chloride was found in faeces and in urine, suggesting that both the kidney and liver are capable of excreting Alkyldimethylbenzylammonium Chloride. The majority of orally administered Alkyldimethylbenzylammonium Chloride appears to be metabolised in the gut of rats, apparently by microflora. No significant difference in metabolism between male and female rats or among the dosing regimens was observed. Repeated dosing did not alter the uptake, distribution or metabolism of Alkyldimethylbenzylammonium Chloride.	X
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	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]	

Section 6.2(1) **Annex Point IIA 6.2**	**Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study**
Materials and Methods	[redacted]

Section 6.2(1) Annex Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study
Results and discussion	[redacted]

Section 6.2(1) **Annex Point IIA 6.2**	**Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study**
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	Acceptable
Remarks	[redacted]
COMMENTS FROM OTHER MEMBER STATE	

Section 6.2(1) **Annex Point IIA 6.2**	**Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study**
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 6.2(2) Annex Point IIA 6.2		Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study	
		1 REFERENCE	Official use only
1.1	**Reference**	Roper, C. and Toner, F. (2006). The In Vitro Percutaneous Absorption of Radiolabelled Alkyl(C12-C16)dimethylbenzylammonium Chloride (ADBAC; CAS RN 68424-85-1) in Two Test Preparations Through Human Skin. Report No. 25982. Charles River Laboratories Tranent, Edinburgh, UK. (Unpublished) Ref No. 101809 (LON xxxx)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	ADBAC Issues Steering Committee	
1.2.2	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes OECD Guideline for Testing of Chemicals, Guideline 428. Skin Absorption: *In Vitro* Method (2004); and OECD Environmental Health and Safety Publications Series on Testing and Assessment No. 28. Guidance Document for the Conduct of Skin Absorption Studies (2004).	
2.2	**GLP (only where required)**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	[redacted]	
3.1.1	Lot/Batch number	[redacted]	
3.1.2	Specification	As given in section II of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. Active substance (a.s.), alkyl(C_{12}-C_{16})dimethylbenzylammonium chloride (ADBAC), in aqueous/alcohol solution.	
3.1.3	Description	[redacted]	
3.1.4	Purity	[redacted]	X

Section 6.2(2) Annex Point IIA 6.2		Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study	
3.1.5	Stability	The non-radiolabelled a.s., ADBAC, 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 five years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.1.6	Method of analysis	[redacted]	
3.2	**Test procedure**		
3.2.1	Test system	Human skin membranes, *in vitro*	
3.2.2	Method of application	Automated flow-through diffusion cell system	
3.2.3	Application media	[redacted]r	
3.2.4	Concentrations	[redacted]	
3.2.5	Receptor fluid	[redacted]	
3.2.6	Remarks	[redacted]	
		4 RESULTS	

Section 6.2(2) Annex Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study	
4.1 Application rate	[redacted]	
4.1.1 Target dose levels	[redacted]	
4.2 Mean % recovery after 24 hours	See Table 6.2(2)-1	
4.4 Remarks	At the low dose (0.030%), 0.05% (<0.01 µg equiv./cm^2) ^{14}C-ADBAC was absorbed into the skin over 24 hours. 96.80% was not absorbed. At the high dose (0.300%), 0.03% (0.01 µg equiv./cm^2) ^{14}C-ADBAC was absorbed into the skin over 24 hours. 94.68% was not absorbed.	X
	5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	

Section 6.2(2) Annex Point IIA 6.2		**Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study**	
		[redacted]	
5.3	**Conclusion**	Following topical application of [^{14}C]-ADBAC in low (0.03%, w/w) and high (0.3%, w/w) concentration test preparations to human skin in vitro, the mean absorbed dose and mean dermal delivery of [^{14}C]-ADBAC were 0.05% (<0.01 µg equiv./cm^2) and 2.22% (0.07 µg equiv./cm^2) of the applied dose for the low concentration test preparation, respectively, and 0.03% (0.01 µg equiv./cm^2) and 2.16% (0.67 µg equiv./cm^2) of the applied dose for the high concentration test preparation, respectively. The stratum corneum acted as a barrier to absorption, with the mean total unabsorbed doses (recovered in skin wash, tissue swabs, pipette tips, cell wash, stratum corneum and unexposed skin) of 96.80 and 94.68% of the applied dose of [^{14}C]-ADBAC for the low and high concentration test preparations, respectively. The maximum fluxes for the low and high doses were 0.12 ng equiv./cm^2/h and 0.74 ng equiv./cm^2/h, respectively, at 2 hours.	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]	

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]
Reliability	[redacted]
Acceptability	Acceptable
Remarks	[redacted]
	COMMENTS FROM OTHER MEMBER STATE

Section 6.2(2) Annex Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study
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 6.2(2)-1. Summary of recoveries after 24 hours

Test Preparation	Low Concentration	High Concentration
Target ADBAC Concentration (%, w/w)	0.030	0.300
ADBAC Concentration by Radioactivity (%, w/w)	0.031	0.306
Test Preparation Application Rate (mg/cm^2) [a]	10.01	10.09
ADBAC Application Rate (µg equiv./cm^2)	3.12	30.87
Dislodgeable Dose (% Applied Dose)	60.53	77.87
Unabsorbed Dose (% Applied Dose)	96.80	94.68
Absorbed Dose (% Applied Dose)	0.05	0.03
Dermal Delivery (% Applied Dose)	2.22	2.16
Mass Balance (% Applied Dose)	99.03	96.84
Dislodgeable Dose (µg equiv./cm^2)	1.89	24.05
Unabsorbed Dose (µg equiv./cm^2)	3.02	29.24
Absorbed Dose (µg equiv./cm^2)	<0.01	0.01
Dermal Delivery (µg equiv./cm^2)	0.07	0.67
Mass Balance (µg equiv./cm^2)	3.09	29.91

[a] Milligrams of test preparation per centimetre of skin

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 [ ] 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 6.3.1 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*	

Section 6.3.3 Annex Point IIA.6.3.3	Short term repeated dose toxicity (inhalation)
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 6.4 – 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. and Weaver E.V. (1988) Ninety-day dietary toxicity study with Alkyl dimethyl benzyl ammonium Chloride (ADBAC) in rats. Bushy Run Research Center, Export, PA, U.S.A. Report No: 51-503 (Unpublished). [Ref No: A17 (LON 1885)]	
1.2 Data protection	Yes	
1.2.1 Data owner	ADBAC Joint Venture	
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 No. 408 1988	
2.2 GLP (only where required)	Yes	
2.3 Deviations	No	
	3. MATERIALS AND METHODS	
3.1 Test material	Alkyldimethylbenzylammonium Chloride	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in section II of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted]	X
3.1.3 Description	[redacted]	

Section 6.4.1(1) **Annex Point IIA 6.4.1**	**Sub-chronic oral toxicity test**	
3.1.4 Purity	[redacted]	
3.1.5 Stability	The a.s., ADBAC, 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 five years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2 Test animals		
3.2.1 Species	Rat	
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 mixed in diet	
3.3.2 Duration of test/exposure	95 and 96 days for males and females, respectively.	
3.3.3 Frequency of exposure	7 days/week	
3.3.4 Post exposure period	[redacted]	
3.3.5 Concentration	[redacted]	X
3.3.6 Vehicle	[redacted]	
3.3.7 Concentration in vehicle	[redacted]	

Section 6.4.1(1) Annex Point IIA 6.4.1	Sub-chronic oral toxicity test	
3.3.8 Actual dose received	[redacted]	
3.3.9 Controls	[redacted]	
3.4 Examinations		
3.4.1 Observations		X
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]	

Section 6.4.1(1) Annex Point IIA 6.4.1		Sub-chronic oral toxicity test	
		[redacted]	
		4. RESULTS	
4.1	**Examinations**		
4.1.1	Clinical signs	Treatment-related clinical findings were restricted to animals from the 4000 and 8000 ppm groups. The observations were of two types, general cachexia and loose faeces. Findings for the surviving animals were similar to those that died.	
4.1.2	Mortality	All animals in the 8000 ppm group died. For the 4000 ppm group 12/15 males and 11/15 females died or were sacrificed in a moribund condition.	
4.1.3	Bodyweight	Decrease in body weight was observed for the 4000 and 8000 ppm dose group surviving the first week of the study. A slight decrease was also noticed in the males of the 1000 ppm dose group.	X
4.1.4	Food consumption	Decrease in food consumption was observed for the 4000 and 8000 ppm dose group surviving the first week of the study. A slight decrease in the food consumption was also noticed in the males of the 1000 ppm dose group.	
4.1.5	Water consumption	Not applicable	
4.1.6	Ophthalmoscopic examination	No treatment related findings at any treatment level.	
4.1.7	Haematology	No treatment related changes were observed for males or females from any treatment group (4000 ppm or lower).	
4.1.8	Clinical Chemistry	No treatment related effects up to 1000 ppm. Significant increases in ALT and phosphorus were observed for 3 surviving males of the 4000 ppm group.	
4.1.9	Urinalysis	Not applicable	
4.2	**Sacrifice and Pathology**		
4.2.1	Organ weights	No treatment related effects up to 1000 ppm	
4.2.2	Gross and Histopathology	No treatment related effects up to 1000 ppm . Gross lesions related to the treatment were restricted to the animals that died in the 8000 and 4000 ppm group and to a lesser degree in the animals that survived the 4000 ppm group. The findings were principally ileus consisting of distended fluid – and gas-filled viscera. Histopathologic effects related to the gastro-intestinal changes were observed for animals in the 4000 and 8000 ppm dose group.	
4.2.3	Other examinations	None	
4.2.4	Statistical analysis	As stated above.	

Section 6.4.1(1) **Annex Point IIA 6.4.1**	**Sub-chronic oral toxicity test**	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	NOEL: 500 ppm (31 mg/kg/day for males; 38 mg/kg/day for females)	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
Evaluation by Competent Authorities		
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	

Section 6.4.1(1) **Annex Point IIA 6.4.1**	**Sub-chronic oral toxicity test**
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	Acceptable
Remarks	
	COMMENTS FROM OTHER MEMBER STATE
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*

Section 6.4.1(1) Annex Point IIA 6.4.1	Sub-chronic oral toxicity test
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	Goldenthal, E.I. (1994) Evaluation of ADBAC in a eight–week dietary toxicity study in dogs. International Research and Development Corporation, Mattawan, MI USA. Report No: 638-003 (Unpublished) [Ref No: 19 (LON 3442a)]	
1.2 Data protection	Yes	
1.2.1 Data owner	ADBAC Joint Venture	
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	No – this is an 8-week study for which no specific guideline applies. 1994)	
2.2 GLP (only where required)	Yes	
2.3 Deviations	Not a guideline study	
	3. MATERIALS AND METHODS	
3.1 Test material	Alkyldimethylbenzylammonium Chloride	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in section II of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted] Active substance (a.s.), alkyl(C_{12}-C_{16})dimethylbenzylammonium chloride (ADBAC; CAS RN 68424-85-1), in aqueous/ethanol solution.	X
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	
3.1.5 Stability	The a.s., ADBAC, 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 five 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	
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	Dietary	
3.3.2	Duration of test/ exposure	8 weeks	
3.3.3	Frequency of exposure	Daily	
3.3.4	Post exposure period	[redacted]	
3.3.5	Concentration	[redacted]	X
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	[redacted]	
3.4.2	Clinical signs	[redacted]	
3.4.3	Mortality	[redacted]	

Section 6.4.1(2) **Annex Point IIA 6.4.1**	**Subchronic oral toxicity study.**	
3.4.4 Bodyweight	[redacted]	X
3.4.5 Food consumption	[redacted]	X
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]	X
3.5.2 Gross and histopathology	[redacted]	X
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	None.	
4.1.3 Mortality	None	
4.1.4 Bodyweight	Reduction in body weight gains was noted in all treated animals receiving 1200 and 1600 ppm.	
4.1.5 Food consumption	No treatment-related differences from control observed.	
4.1.6 Water consumption	Not applicable.	

Section 6.4.1(2) Annex Point IIA 6.4.1	Subchronic oral toxicity study.	
4.1.7 Ophthalmoscopic examination	Not applicable.	
4.1.8 Haematology	No treatment-related differences from control observed	
4.1.9 Clinical Chemistry	Decreased total cholesterol was noted in all treated animals receiving 1200 and 1600 ppm.	X
4.1.10 Urinalysis	Not applicable.	
4.2 Sacrifice and Pathology		
4.2.1 Organ weights	No treatment related differences from control.	
4.2.2 Gross and Histopathology	No treatment related differences from control.	
4.2.3 Other examinations	None.	
4.2.4 Statistical analysis	Not applicable.	
4.3 LO(A)EL	1200 ppm (approximately 48 mg/kg/day)	
4.4 NO(A)EL	800 ppm (approximately 31 mg/kg/day)	
	5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1 Materials and methods	[redacted]	
5.2 Results and discussion	[redacted]	
5.3 Conclusion	NOEL = 800 ppm (27.4 mg/kg/day for males; 34.3 mg/kg/day for females	

Section 6.4.1(2) **Annex Point IIA 6.4.1**	**Subchronic oral toxicity study.**	
	LOAEL = 1200 ppm (45.5 mg/kg/day for males; 50.7 mg/kg/day for females	
5.3.1 Reliability	[redacted]	
5.3.2 Deficiencies	[redacted]	
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	

Section 6.4.1(2) **Annex Point IIA 6.4.1**	**Subchronic oral toxicity study.**
Materials and Methods	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	Acceptable
Remarks	

Section 6.4.1(2) **Annex Point IIA 6.4.1**	**Subchronic oral toxicity study.**
	COMMENTS FROM OTHER MEMBER STATE
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. and Weaver E.V. (1988) Ninety-day dietary dose range-finding study with alkyl dimethyl benzyl ammonium Chloride (ADBAC) in mice. Bushy Run Research Center, Export, PA, U.S.A. Report No: 51-504 (Unpublished). [Ref No: A16 (LON 1883)]	
1.2 Data protection	Yes	
1.2.1 Data owner	ADBAC Joint Venture	
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 82-1 OECD Guideline No. 408 1987	
2.2 GLP (only where required)	Yes	
2.3 Deviations	A limited number of endpoints were examined because this study was designed for selecting doses for a chronic oncogenicity study.	
	3. MATERIALS AND METHODS	
3.1 Test material	Alkyldimethylbenzylammonium Chloride	X
3.1.1 Lot/Batch number	[redacted]	
3.1.2 Specification	As given in section II of Annex IIA of Directive 98/8/EC, especially Sections 2.6-2.8 therein. [redacted]	X
3.1.3 Description	[redacted]	
3.1.4 Purity	[redacted]	

Section 6.4.1(3) Annex Point IIA 6.4.1		Subchronic oral toxicity test	
3.1.5	Stability	The a.s., ADBAC, 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 five years under standard laboratory conditions (see Section 2.6.1 of Annex IIA).	
3.2	**Test animals**		
3.2.1	Species	Mice	
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	93 Days (males) and 94 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]	

Section 6.4.1(3) Annex Point IIA 6.4.1	Subchronic oral toxicity test	
	[redacted]	
3.3.9 Controls	[redacted]	
3.4 Examinations		
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	[redacted]	
3.5.4 Statistical analysis	[redacted]	
	4. RESULTS	
4.1 Examinations		