SECTION 6

TOXICOLOGICAL AND METABOLIC STUDIES

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	Introduction



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6.0.2 Names and synonyms of test material used for the individual studies



		a	
	1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	1	
		0	
		in a liter	
1			

Section 6.1 Acute toxicity

Annex Point IIA 6.1 - headline only

Section 6.1.1 Acute oral toxicity test in the rat

Section Annex	n 6.1.1 (1) : Point IIA 6.1.1	Acute	e oral toxicity test in the rat	
		1.	REFERENCE	Official use only
1.1	Reference	Dosag No. 9 Refer	(1994) Acute Oral Toxicity in Rats – Median Lethal ge Determination Using a 5% Active Ingredient Formulation of Hill Top Biolabs, Inc. Report 3-8185-21 (A) (unpublished). ence No.; LR 3718	
1.2	Data protection			
1.2.1	Data owner			2
1.2.2 protect	Criteria for data ion)		
		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes OECI 1994	D Guideline No. 401; FIFRA (40 CFR)	
2.2 (only v	GLP where required)	Yes		
2.3	Deviations	No		
1.0		3.	MATERIALS AND METHODS	
3.1	Test material	1		
3.1.1	Lot/Batch number			
3.1.2	Specification			
3.1.3	Description	-		-
3.1.4	Purity			-
3.1.5	Stability			
3.2	Test animals	2 D		
3.2.1	Species			
3.2.2	Strain			
3.2.3	Source			
3.2.4	Age/weight at study			

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Section 6.1.1 (1) Annex Point IIA 6.1.1	Acute oral toxicity test in the rat	
Results and discussion		
Conclusion		(
Reliability		
Acceptability		



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Section 6.1.2 Acute dermal toxicity test in rats

Sectio Annez	n 6.1.2 (1) x Point IIA 6.1.2	Acute	e dermal toxicity test in rats	
15		1.	REFERENCE	Official use only
1.1	Reference	RAT. 102/4 Refer	(2004) ACUTE DERMAL TOXICITY (LIMIT TEST) IN THE Safepharm Laboratories Limited. SPL Project No. 61(unpublished). ence No.: LR 3900	
1.2	Data protection			
1.2.1	Data owner	1		
1.2.2 protec	Criteria for data tion			
-		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes Anne: 2004	x V of Directive 67/548/EEC; OECD Guideline No. 402	
2.2 (only	GLP where required)	Yes		
2.3	Deviations	No		
i		3.	MATERIALS AND METHODS	
3.1	Test material	1		
3.1.1	Lot/Batch number	i.		
3.1.2	Specification			
3.1.3	Description			-
3.1.4	Purity			-
3.1.5	Stability			
3.2	Test animals			
3.2.1	Species			
3.2.2	Strain			-
3.2.3	Source			
3.2.4	Sex			
initiati	on			
3.2.6 per 9r	Number of animals			
3.2.7	Control animals			-
3.3	Administration/			
exposi	ure			
3.3.1	Dose route	1	7	-
3.3.2	Duration of			



	2	DDACarbonate	February 2009
Sectio Annez	on 6.1.2 (1) x Point IIA 6.1.2	Acute dermal toxicity test in rats	
5.3	Conclusion	The animals showed no signs of toxicity but were killed i to the severity of the dermal reactions. The acute dermal dose may be considered to be greater than 2000 mg/Kg al insufficient data available to confirm this finding.	n extremis due median lethal lthough there is
5.3.1	Reliability		
5.3.2	Deficiencies		
		Evaluation by Competent Authorities	
		EVALUATION BY RAPPORTEUR MEMBER STAT	ГЕ
Date			
Materi	ials and methods		
Result	s and discussion		
Conch	usion		
Reliab	oility		
Accep	tability		
Remai	ʻks		
		Comments from other member state (specify)	
Date			
Materi	ials and methods		
Result	s and discussion		
Conch	usion		
Reliab	oility		
Accep	tability		

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Section 6.1.3 Acute inhalation toxicity test



Section Annex	n 6.1.4 (1) : Point IIA 6.1.4	Skin irritation study in rabbits	
15		1. REFERENCE	Official use only
1.1	Reference	(1994) Primary Skin Irritation Study in Rabbits using a 50% Active Ingredient Formulation of the second state of the second st	
1.2	Data protection		
1.2.1	Data owner		
1.2.2	Criteria for data		
protect	tion		
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes EPA 81-5 1994	
2.2 requir	GLP (only where ed)	Yes	
2.3	Deviations	Only one animal was employed for testing and that animal was maintained only through the 24 hour reading of the study, at which time it was sacrificed due to the severity of the response.	
):		3. MATERIALS AND METHODS	
3.1	Test material		
3.1.1	Lot/Batch number		
3.1.2	Specification		
3.1.3	Description		
3.1.4	Purity		1
3.1.5	Stability		
3.2	Test animals		
3.2.1	Species		
3.2.2	Strain		
3.2.3	Source		
3.2.4	Sex		
3.2.5 initiati	Age/weight at study on		
3.2.6 per gro	Number of animals		
3.2.7	Control animals		
3.3 exposi	Administration/ are		
3.3.1	Dose route		
3.3.2 period	Post exposure		

Section 6.1.4 Skin and eye irritation



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	S	_	DDACarbonate Fe	bruary 2009
Sectio Annex	n 6.1.4 (2) 2 Point IIA 6.1.4	Skin	irritation study in rats	
		1.	REFERENCE	Official use only
1.1	Reference	With No. 1 Refer	(2006) 21-Day Repeated Dose Dermal Irritation Study in Female Rats. Product Safety Laboratories. Report 9072 (unpublished). ence No.: LR 4019	
1.2	Data protection			
1.2.1	Data owner			
1.2.2	Criteria for data			
protect	tion			
1		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	No The s 2006	tudy was not conducted to a specific guidelines as none available	
2.2 requir	GLP (only where red)	Yes		
2.3	Deviations	No		
	The second second	3.	MATERIALS AND METHODS	-
3.1	Test material			
3.1.1	Lot/Batch number			
3.1.2	Specification			
3.1.3	Description			
3.1.4	Purity			
3.1.5	Stability			-
3.2	Test animals			
3.2.1	Species			
3.2.2	Strain			
3.2.3	Source			
3.2.4	Sex			
3.2.5	Age/weight at study			
initiati	on N. I. C. i. I.			-
3.2.0 ner oro	Number of animals	1	-	
2.2	Administration/			
exposi	ire	-		
3.3.1	Dose route	1	7,	
3.3.2	Post exposure		F	
2 2 2	Concentration			
331	Duration of			-
treatm	ent			
3.3.5	Vehicle	1		
3.3.6	Concentration in			
vehicle	8	-		
3.3.7	Total volume			

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Section Annex	0.1.4 (2) Point IIA 6.1.4	Skin irritation study in rats	
applied			
3.3.8	Control animals		
3.4 Sacrific	Observations, ce and pathology		
3.4.1	Clinical signs		
3.4.2	Mortality		ĺ.
3.4.3	Skin responses		
3.4.4	Scoring system		
3.4.5 points	Examination time		
3.4.6	Bodyweight		
3.4.7	Necropsy		
3.4.7	Histopathology		
3.5	Further remarks		-
		4. RESULTS	
4.1 Sacrific	Observations, ce and pathology		
4.1.1	Clinical signs		-
			1000
412	Montality		_
4.1.2	Mortanty		
4.1.3	Scores		
4.1.4	Bodyweight		
4.1.5	Necropsy		
4.1.6	Histopathology		
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	Materials and		
method	ls		

	DDACarbonate	February 2009
Section 6.1.4 (2) Annex Point IIA 6.1.4	Skin irritation study in rats	
5.2 Results and discussion		
		_
5.3 Conclusion	NOAEC 10 µg/cm ² /day	
5.3.1 Reliability		
5.3.2 Deficiencies		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER	STATE
Date		
Materials and methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		
Demadra		
Remarks	Comments from other member state (merifit	
Date	comments from other member state (specify)	
Materials and methods		
Results and discussion		
Conclusion		

	DDACarbonate	February 2009
Section 6.1.4 (2) Annex Point IIA 6.1.4	Skin irritation study in rats	
Reliability		
Acceptability		

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 Table 6.1.4(2)-1
 Summary of Mean Skin Irritation Scores¹



	DDACarbonate	February 2009
Section 6.1.4 (3) Annex Point IIA 6.1.4	Eye irritation study in rabbits	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
		-
Detailed justification:		
		-
	Evaluation by Competent Authorities	
	EVALUATION DV DABOOTTUD MEMBER CTATE	
Date Evaluation of applicant's justification Conclusion		÷
Remarks		
Date Evaluation of applicant's justification	Comments from other Member State (specify)	
Remarks		

Section 6.1.5 Skin sensitisation

Sectio Annez	n 6.1.5 (1) x Point IIA 6.1.5	Skin sensitisation (guinea pig Buehler test)	
		1. REFERENCE	Official use only
1.1	Reference	No. 93-8123-21 (A) (unpublished). Reference No.: LR 3716	
1.2	Data protection		
1.2.1	Data owner		
1.2.2	Criteria for data		
protec	tion		-
_	-	2. GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes	
		EPA 81-6	
		1994	
2.2	CLB	Vac	1
(only	where required)	ies	
2.3	Deviations	No	
	and the second	3. MATERIALS AND METHODS	
3.1	Test material		
3.1.1	Lot/Batch number		-
3.1.2	Specification		
3.1.3	Description		
3.1.4	Purity		-
3.1.5	Stability		
3.2	Test animals		
3.2.1	Species		
3.2.2	Strain		
3.2.3	Source		
3.2.4	Sex		
3.2.5	Age/weight at study		
initiati	on		
3.2.6	Number of animals		
in trea	ted group		
3.2.7	Control animals		
3.2.8	Positive control		-
animal	ls (number)		
3.3	Administration/		

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	C.	DDACarbonate	February 2009
Section Annex	a 6.1.5 (1) Point IIA 6.1.5	Skin sensitisation (guinea pig Buehler test)	
exposu	re		
3.3.1	Dose route		
3.3.2	Irritation phase		
3.3.2.1 applica	Days of irritation tions		
3.3.2.2 irritatio	Concentration of n applications		
3.3.2.3	Vehicle		
3.3.2.4	Volume applied		
3.3.3	Induction		
3.3.3.1 applica	Days of induction tions		
3.3.3.2 induction	Concentration of on applications		
3.3.3.3	Vehicle		
3.3.3.4	Volume applied		
3.3.4	Challenge phase		
3.3.4.1 and cha	Days of induction llenge applications		
3.3.4.2 challen 3.3.4.3	Concentration of ge applications Vehicle		
3.3,4.4	Volume applied		





Table 6.1.5(1)-1 Number of animals assigned to groups



Table 6.1.5(1)-2 Sample preparation and application





Table 6.1.5(1)-4 Incidence and severity of skin reaction scores following challenge with test material and TSCA

					100 million (1997)
			1.		
		30,124,11			
1.11				- 1 h - 1 h -	
1.11	i se si i ca				11111111
S	4			A A	

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Table 6.1.5(1)-5 UVA and UVB Levels at Various Phases of Testing



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Section 6.2 Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study

Section 6.2 Annex Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, including a dermal absorption study	
	Justification for non-submission of data	Official
		use only
Detailed justification:		
	Evaluation by Competent Authorities	
	Evaluation by Rapporteur Member State	
Date		
Evaluation of applicant's		
Conclusion	200 million 100	
Remarks	the second se	
	Comments from other Member State (specify)	
Date		
iustification		
Conclusion		
Remarks		

	2.	_	DDACarbonate Febr	ruary 2009
Section Annex	1 6.2(1) Point IIA 6.2	Meta derm	bolism studies in mammals. Basic toxicokinetics, including a al absorption study	
1		1.	REFERENCE	Official use only
1.1	Reference	Repo	(2001). The In Vitro Percutaneous Absorption of Through Human Skin. Through Human Skin. rt No. 19128. Inveresk Research. (unpublished)	
12	Data protection	RefN	Io. LON 3329	-
1.2 1	Data protection	-		-
1.2.1	Data owner			-
1.4.4	ion	1		
protect				
		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes OEC metho skin a guide 2001	D guideline for the testing of chemicals. Skin absorption: in vitro od. 1999. (Draft); OECD guidance document for the conduct of absorption studies. 1999. (Draft); COLIPA. Cosmetic ingredients lines for percutaneous absorption/penetration. 1995.	
2.2 require	GLP (only where ed)	Yes		
2.3	Deviations	No		
		3.	MATERIALS AND METHODS	
3.1	Test material			
3.1.1	Lot/Batch number			
3.1.2	Specification			
3121	Non-radiolabelled			-
3.1.3	Description			
3.1.4	Purity			
3.1.5	Stability			1
316	Method of analysis			_
3.2	Test procedure			
3.2.1	Test system			
3.2.2	Method of application			
3.2.3	Application media			
3.2.4	Concentration			
3.2.5	Receptor fluid			
3.2.6	Remarks			
-		1		

	20	DDACarbonate	February 200
Sectio Annex	n 6.2(1) : Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, i dermal absorption study	ncluding a
		4. RESULTS	
.1	Application rate	-2	
4.1.1	Target dose level		
ifter 2	Mean % recovery 4 hours		
1.3	Cumulative flux		
1.4	Remarks		
_			
		5. APPLICANT'S SUMMARY AND CONC	LUSION
5.1 metho	Materials and ds		
5.2	Results and		
discus	sion		
5.3	Conclusion	Less than 0.1% of the ¹⁴ C-DDAC penetrated human skin. absorption was 2.92%.	Total
5.3.1	Reliability		
5.3.2	Deficiencies		
		Evaluation by Competent Authorities	
		EVALUATION BY RAPPORTEUR MEMBER STAT	E
Date			



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Table 6.2(1)-1. Mean % recovery after 24 hours



	\$	_	DDACarbonate F	ebruary 2009	
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		(1989). Absorption, Distribution, Metabolism and Excretion	1	
		Studi Study Ref N	in the Rat. y No. P01421. Biological Test Center, (Unpublished) Nos.: LON 1779		
1.2	Data protection				
1.2.1	Data owner				
1.2.2	Criteria for data				
protect	tion			-	
-		2.	GUIDELINES AND QUALITY ASSURANCE		
2.1	Guideline study	Yes			
		U.S.	EPA Guideline 85-1		
		1989			
		Vac			
2.2 (only)	GLP where required)	Ies			
(only	where required)	No		-	
2.3	Deviations	INU			
		3.	MATERIALS AND METHODS		
3.1	Test material				
3.1.1	Lot/Batch number	1			
312	Specification			-	
3.1.2	specification				
313	Description				
3.1.4	Purity	1		-	
- 100 C		1			
3.1.5	Stability				
		1			
		1			
		1			
3.2	Test Procedure				
3.2.1	Method of analysis				
3.3	Test Animals				
3.3.1	Species				
3.3.2	Strain				
3.3.3	Source				
335	Age/weight at study				
initiati	on				
3.3.6	Number of animals	1			
per gro	oup				
3.3.7	Control animals				
3.4	Administration/				
exposi	D	-			
5.4.1	Dose route				


	DDACarbonate	February 2009
Section 6.2(2) Annex Point IIA 6.2	Metabolism studies in mammals. Basic toxicokinetics, i dermal absorption study	including a
5.3 Conclusion	The majority of orally administered Didecyldimethylamm. Chloride is excreted via the faeces and appears to be metal gut of rats, apparently by microflora. Metabolism in fema greater than in males and lower doses were more extensive metabolised than higher doses in females. No tissue accur the test substance was observed. Repeated dosing did not uptake, distribution or metabolism of Didecyldimethylamm Chloride.	onium bolised in the les was ely mulation of alter the monium
5.3.1 Reliability		
5.3.2 Deficiencies		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STAT	E
Date		
Materials and Methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		
Remarks		
Ý	Comments from other member state (specify)	
Date		
Materials and Methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		

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
)etailed justification:		
		=
	Evaluation by Competent Authorities	
Date Evaluation of applicant's	Evaluation by Rapporteur Member State	
ustification Conclusion		
Remarks	and the state of t	
Date Evaluation of applicant's ustification	Comments from other member state (specify)	
Conclusion Remarks		









DDACarbonate Section 6.4.1(1) Sub-chronic oral toxicity test Annex Point IIA 6.4.1 Sub-chronic oral toxicity test		DDACarbonate	February 2009	
		Sub-chronic oral toxicity test		
		1. REFE	ERENCE	Official use only
1.1	Reference	study with Report No. 51-5 Ref No.: LON 1	(1988). Ninety-day dietary subchronic on in rats. U 506 (unpublished) 1257	ral toxicity Jnion Carbide,
1.2	Data protection			
1.2.1	Data owner			
1.2.2	Criteria for data			
protec	tion			
		2. GUID	ELINES AND QUALITY ASSURA	INCE
2.1	Guideline study	Yes U.S. EPA FIFR 1987	A Guideline 82-1; OECD Guideline 408.	
2.2 (only	GLP where required)	Yes		
2.3	Deviations	No		
1		3. MATE	ERIALS AND METHODS	
3.1	Test material			
3.1.1	Lot/Batch number			/
3.1.2	Specification			
3.1.3	Description			
3.1.4	Purity			
3.1.5	Stability			
3.2	Test animals			
3.2.1	Species			
3.2.2	Strain			
3.2.3	Source			
3.2.4	Sex			
initiati	on			
3.2.6	Number of animals			
3.2.7	Control Animals			
3.3	Administration/			
exposi	ure	· · · · ·		
3.3.1	Dose route		5	
3.3.2	Duration of test/			
expost 3.3.3	ire Frequency of			
expost 334	Post exposure			

	2	DDACarbonate	February 2009
Section Annex	n 6.4.1(1) Point IIA 6.4.1	Sub-chronic oral toxicity test	
period	1. Z	a second s	
3.3.5	Concentration		
336	Vehicle		
3.3.7 vehicle	Concentration in		
3.3.8	Actual dose		
receive	:d		
3.3.9	Controls		
3.4	Examinations		
3.4.1	Observations		
3.4.2	Clinical signs		
3.4.3	Mortality		
3.4.4	Bodyweight		
3.4.5	Food consumption		
3.4.6	Water consumption		
3.4.7	Ophthalmoscopic		
examin	nation		
3.4.8	Haematology		
3.4.9	Clinical Chemistry		
3.4.10	Urinalysis		
3.5 patholo	Sacrifice and	7	
3.5.1	Organ weights		
3.5.2	Gross and		
шятора	unology		
3.5.3	Other examinations		
3.5.4	Statistical analysis		
		4. RESULTS	
4.1	Examinations		
4.1.1	Observations		
4.1.2	Clinical signs		
4.1.3	Mortality		
4.1.4	Bodyweight		





Section 6.4.1(2) Annex Point IIA 6.4.1		DDACarbonate	February 2009
		Subchronic oral toxicity study.	
		1. REFERENCE	Official use only
1.1	Reference	(1990). Subchronic oral toxicity study of in dogs. Study No. 1	2545-100.
		Hazelton Laboratories America, Inc., (unpublished) Ref No. LON 1256	
1.2	Data protection		
1.2.1	Data owner		
1.2.2	Criteria for data		
protec	tion	2 CUIDELINES AND QUALITY ASSUDANCE	C
2.1	Guideline study	Not applicable	
2.2	GLP	Yes	
(only v	where required)	(If no, give justification, e.g. state that GLP was not comp time the study was performed)	nulsory at the
2.3	Deviations	Not applicable	
		3. MATERIALS AND METHODS	
3.1	Test material		
3.1.1	Lot/Batch number		
3.1.2	Specification		
			_
3.1.3	Description		
3.1.4	Purity		
3.1.5	Stability		
			=
3.2	Test animals		
3.2.1	Species		
3.2.2	Strain		
3.2.3	Source		
3.2.4	Sex		
3.2.5	Age/weight at study		
3.2.6	Number of animals		
per gro	oup		
3.2.7	Control Animals		
3.3 exposi	Administration/ re		
3.3.1	Dose route		
3.3.2	Duration of test/		
3 3 3	Frequency of		
exposi	irequency of		

	(2	DDACarbonate	February 2009
Section Annex	a 6.4.1(2) Point IIA 6.4.1	Subchronic oral toxicity study.	
3.3.4	Post exposure		
period	rostenposare		
3.3.5	Concentration		
3.3.6	Vehicle		
3.3.7	Concentration in		
vehicle	A atual dasa		
3.3.0 receive	d Actual dose		
lective			
339	Controls		
3.4	Examinations		
2 4 1	Observations		
3.4.1	Clinical signs		
3.4.2	Mortality		
3.4.4	Bodyweight		
3.4.5	Food consumption		
3.4.6	Water consumption		
3.4.7	Ophthalmoscopic		
examin	ation		
3.4.8	Haematology		
3.4.9	Clinical chemistry		
3.4.10	Urinalysis		
3.5	Sacrifice and		
patholo	gy	7	
3.5.1	Organ weights		
3.5.2	Gross and		
histopa	thology		
3.5.3	Other examinations		
3.5.4	Statistical analysis		
		4. RESULTS	
4.1	Examinations		
4.1.1	Observations		
4.1.2	Clinical signs		
412	Montolity		
4.1.3	Monanty		
4.1.4	Bodyweight		

		DDACarbonate	February 2009
Sectio Annex	n 6.4.1(2) Point IIA 6.4.1	Subchronic oral toxicity study.	
4.1.5	Food consumption		
4.1.6	Water consumption Ophthalmoscopic		
exami 4.1.8	Haematology		
4.1.9 4.1.10 4.2 pathole	Clinical chemistry Urinalysis Sacrifice and ogy		
4.2.1	Organ weights		
4.2.2 histopa	Gross and athology		
4.2.3	Other examinations		
4.2,4	Statistical analysis		
4.3	LO(A)EL		
4.4	NO(A)EL		CT LICION
5.1 metho	Materials and ds		
5.2 discus	Results and sion		
5.3	Conclusion	NOAEL = 30 mg/kg/d	
5.3.1	Reliability		

	DDACarbonate	February 2009
Section 6.4.1(2) Annex Point IIA 6.4.1	Subchronic oral toxicity study.	
5.3.2 Deficiencies		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STAT	ГЕ
Date		
Materials and Methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		
2		5
Remarks		
Data	COMMENTS FROM OTHER MEMBER STATE (sp	pecify)
Date		
Materials and Methods		1
Results and discussion		
Conclusion		
Reliability		
Acceptability		

Section 6.4.1(3) Annex Point IIA 6.4.1		Subchronic oral toxicity test	
		1. REFERENCE	Official use only
1.1	Reference	(1988) Subchronic dietary dose range finding study with	
		Carbide, (unpublished). Ref No: LON 1775	
1.2	Data protection		
1.2.1	Data owner		
1.2.2 protec	Criteria for data tion		
6		2. GUIDELINES AND QUALITY ASSURANCE	-
2.1	Guideline study	Yes	
		FIFRA 82-1	
		1988	
12			-
2.2 (only	GLP 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		
3.1.1	Lot/Batch number		
3.1.2	Specification		
3.1.3	Description		-
3.1.4	Purity		
3.1.5	Stability		ł
3.2	Test animals		
3.2.1	Species		
3.2.2	Strain		
3.2.3	Source		
3.2.4	Sex		
3.2.5 study	Age/weight at initiation		
3.2.6	Number of animals		
3.2.7	Control Animals		
3.3 expos	Administration/ ure		
3.3.1	Dose route		
3.3.2 exposi	Duration of test/ re		
3.3.3 exposi	Frequency of are		







	DDACarbonate Fe		February 200	
Section 6.4.1(4) Annex Point IIA 6.4.1		Subchronic oral toxicity study.		
1°F		1. REF	ERENCE	Official use only
1.1	Reference	quaternary an Drug Researc Ref No. LON	nonium sanitizer Markov (1975) . 90-day feeding study honium sanitizer Markov (1975) . Study No. 222. h Laboratories, Inc., (unpublished) i 1256 A	in dogs with a 4 a. Food and
1.2	Data protection			
1.2.1	Data owner			
1.2.2	Criteria for data			
protec	tion	1 (11)	DELINES AND OUT LITY ASSUDANC	T
	Cuttaline stude	Z. GUI	DELINES AND QUALITY ASSURANC	E
2.1	Guidenne study	Not applicabl	e	
(only v	where required)	No (GLP was not	t compulsory at the time the study was perfe	ormed)
2.3	Deviations	Not applicabl	e	
		3. MAT	TERIALS AND METHODS	
3.1	Test material			
3.1.1	Lot/Batch number			
312	Specification			
	operation			
3.1.3	Description	1		
3.1.4	Purity	1		
3.1.5	Stability			
		- <u>-</u>		
3.2	Test animals			
3.2.1	Species			
3.2.2	Strain			
3.2.3	Source			
3.2.4	Sex			
325	Age/weight at study			
initiati	on		and the state of t	
3.2.6	Number of animals	1		
per gro	Control Animale	_		
3.4.1	Control Annihiais			
3.3 expos	Administration/			
331	Dose route	1		
332	Duration of test/	1		
expost	ire	1		
333	Eramonov of	1 Contraction of the second se		

	2.	DDACarbonate	February 2009
Section Annex	1 6.4.1(4) Point IIA 6.4.1	Subchronic oral toxicity study.	
exposu	re		
3.3.4 period	Post exposure		
3.3.5	Concentration		
3.3.6	Vehicle		
3.3.7 vehicle	Concentration in		
3.3.8 receive	Actual dose d		
3.3.9	Controls		
3.4	Examinations		
3.4.1	Observations		
3.4.2	Clinical signs		
3.4.3	Mortality		
3.4.4	Bodyweight		
3.4.5	Food consumption		
3.4.0	Water consumption		
examin	ation		
3.4.8	Haematology		
349	Clinical chemistry		
3.4.10	Urinalysis		
3.5	Sacrifice and		
patholo	gy		
3.5.1	Organ weights		
3.5.2	Gross and		
histopa	thology		
3.5.3	Other examinations		
3.5.4	Statistical analysis		
		4. RESULTS	
4.1	Examinations		
4.1.1	Observations		
4.1.2	Clinical signs		
4.1.3	Mortality		
4.1.4	Bodyweight		
4.1.5	Food consumption		
4.1.6	Water consumption		
4.1.7	Ophthalmoscopic		
examin	ation		
4.1.8	Haematology		
4.1.9	Clinical chemistry		0
4.1.10	Urinalysis		



	DDACarbonate	February 2009
Section 6.4.1(4) Annex Point IIA 6.4.1	Subchronic oral toxicity study.	
	Evaluation by Competent Authorities	1
Date	EVALUATION BY RAPPORTEUR MEMBER STA	ATE
Materials and Methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		
Remarks		
Remarks	COMMENTS FROM OTHER MEMBER STATE (:6.5
Date	COMMENTS FROM OTHER MEMBER STATE (S	specify)
Materials and Methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		



Section Annex	n 6.4.2(1) Point IIA 6.4.2	Subcl	aronic dermal toxicity test	
		1.	REFERENCE	Officia use onl
1.1	Reference	toxicit Carbio	(1988) Ninety-day subchronic dermal ty study with the second seco	
		Ref N	o.: LON 1255	
1.2	Data protection			
1.2.1	Data owner			
1.2.2 protect	Criteria for data tion	purpo	May 2000 on existing a.s. for the se of its entry into Annex I/IA	
		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes US EI	PA OPP 82-3	
		1988		
2.2 (only v	GLP where required)	Yes		
2.3	Deviations	No	535 - Contractor	
		3.	MATERIALS AND METHODS	5
3.1	Test material			
3.1.1	Lot/Batch number	1		1
3.1.2	Specification			
3.1.3	Description			
3.1.4	Purity	1		
3.1.5	Stability			
3.2	Test animals			
3.2.1	Species			
3.2.2	Strain	1		
3.2.3	Source			
3.2.4	Sex	-		
3.2.5 initiati	Age/weight at study on			
3.2.6 per gro	Number of animals		ĺ.	

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	2.	DDACarbonate	February 2009
Section Annex	a 6.4.2(1) Point IIA 6.4.2	Subchronic dermal toxicity test	
3.3.1	Dose route		
3.3.2	Duration of test/		
exposu	re		
3.3.3	Frequency of		
334	Post exposure		
period	rostenpostate		
3.3.5	Concentration		
3.3.6	Vehicle		
3.3.7	Concentration in		
	vehicle		
3.3.8	Actual dose		
339	Controls		
3.4	Examinations		1 mar 1 m
3.4.1	Observations		1
3.4.2	Clinical signs		
	6		
212	Mantality		
3.4.3	Monanty		
3.4.4	Bodyweight		
3.4.5	Food consumption		
3.4.6	Water consumption		
3.4.7	Ophthalmoscopic		
	examination		
3.4.8	Haematology		
349	Clinical Chemistry		
5.10	chineta chemistry		
3.4.10	Urinalysis		
3.5	Sacrifice and		
a 5 1	gy Organ weights		
3.5.2	Gross and		
histopa	thology		
3.5.3	Other examinations		
3.5.4	Statistical analysis		
	and a second		
-		4 RESULTS	
41	Framinations		1
411	Obcarriations		
4.1.1	Observations		

	2	DDACarbonate	February 2009
Sectio Annex	n 6.4.2(1) Point IIA 6.4.2	Subchronic dermal toxicity test	
4.1.2	Clinical signs		
4.1.3	Mortality		
4.1.4	Bodyweight		
4.1.5	Food consumption		1
4.1.6	Water consumption		
4.1.7	Ophthalmoscopic ation		
4.1.8	Haematology		
4.1.9	Clinical Chemistry		
4.1.10	Urinalysis		
4.2 pathole	Sacrifice and		
4.2.1	Organ weights		
122	Grace and		
4.2.3	Other examinations		
4.2.4	Statistical analysis		
4.3	LOAEL		
4.4	NOAEL		
14 million (1997)		5. APPLICANT'S SUMMARY AND CONCLUS	SION
5.1 metho	Materials and ds		
5.2 discus	Results and sion		
5.2	Conclusion	NOAEL $= 12$ mg/kg hady weight	-
5.5	Conclusion	NOAEL - 12 mg/kg body weight	
5.3.1			
5.3.2	Deficiencies		
		Evaluation by Competent Authorities	
-		EXALL TATION BY BARRONTEVER MEMORY OF	
		EVALUATION BY KAPPORTEUR MEMBER STAT	E



	DDACarbonate	February 2009
Section 6.4.3 Annex Point III-A.6.4.3	Subchronic toxicity test (inhalation)	
	JUSTIFICATION FOR NON-SUBMISSION OF DAT.	A Official use only
Detailed justification:		
		_
	Evaluation by Competent Authorities	
	EVALUATION BY PAPPORTEUP MEMBER ST	ATE
Date		ATE
Evaluation of applicant's		
Conclusion		
Remarks		
	Comments from other Member State (specify)	
Date Evaluation of applicantle		
ustification		
Conclusion		
Remarks	0.1	

February 2009

Section 6.5 Chronic toxicity Annex Point IIA 6.5- headline only



	Z	DDACarbonate Febr	ruary 200
Sectio Annex	n 6.5(1) t Point IIA 6.5	Chronic toxicity in dogs	
1		1. REFERENCE	Official use only
1.1	Reference	Inc., HWA. Study No. 2545-102. (unpublished) Ref No.: LON 1778	
1.2	Data protection		
1.2.1	Data owner		1
1.2.2	Criteria for data		
protect	tion		
		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 (only v	GLP where required)	Yes	
2.3	Deviations	No	
		3. MATERIALS AND METHODS	
3.1	Test material		
3.1.1	Lot/Batch number		
3.1.2	Specification		
3.1.3	Description		-
3.1.4	Purity		
3.1.5	Stability		
3.2	Test animals		6
3.2.1	Species		
3.2.2	Strain		
3.2.3	Source		2
3.2.4	Sex		
3.2.5 initiati	Age/weight at study		
3.2.6	Number of animals		
per gro	oup	273	
3.2.7	Control Animals		
3.3 exposi	Administration/		
3.3.1	Dose route		
332	Duration of test/		
exposi	re		
3.3.3 exposi	Frequency of are		
3.3.4 period	Post exposure		

	Če.	DDACarbonate	February 2009
Section Annex	а 6.5(1) Point ПА 6.5	Chronic toxicity in dogs	
3.3.5	Concentration		
3.3.6	Vehicle		
3.3.7 vehicle	Concentration in		
3.3.8	Actual dose		
receive	d		
3.3.9	Controls		
3.4	Examinations		
3.4.1	Observations		-
3.4.2	Clinical signs		
3.4.3	Mortality		
3.4.4	Bodyweight		
3.4.5	Food consumption		
3.4.6	Water consumption		
3.4.7	Ophthalmoscopic		
examin	ation		
3.4.8	Haematology		
3.4.9	Clinical Chemistry		
3.4.10	Urinalysis		
3.5	Sacrifice and		
patholo	gy		
3.5.1	Organ weights		
3.5.2	Gross and		
histopa	thology		
3.3.3	Other examinations		
5.5.4	Statistical analysis		
		4 RESULTS	
4.1	Examinations		
4.1.1	Observations		
4.1.2	Clinical signs		
	Cimiton orBin		
110	N		
4.1.3	Mortality		
4.1.4	Bodyweight		

	22	DDACarbonate	February 2009
Section Annex	a 6.5(1) Point IIA 6.5	Chronic toxicity in dogs	
4.1.5	Food consumption		
4.1.6	Water consumption		
4.1.7	Ophthalmoscopic		
examin 418	Haematology		
4.1.0	nachatology		-
4.1.9	Clinical Chemistry		F
4.1.10	Urinalysis		
4.2 patholo	Sacrifice and ogy		
4.2.1	Organ weights		
4.2.2 histopa	Gross and thology		
4.2.3	Other examinations		
4.2.4	Statistical analysis		
4.3	LOAEL		
4.4	NOAEL		1105.44
5.1 method	Materials and ls	5. APPLICANT'S SUMMARY AND CONCLUS	
5.2 discuss	Results and ion		
5.3	Conclusion	NOAEL = 10 mg/kg/d	-
5.3.1	Reliability		
5.3.2	Deficiencies		
		Evaluation by Competent Authorities	



	2	DDACarbonate	February 2009
Sectio Annex	n 6.5(2) : IIA Point 6.5	Chronic toxicity in rats.	
		1. REFERENCE	Official use only
1.1	Reference	(1991) Chronic dietary toxicity/oncogenicity study with in rats. Report No. 53-566. Union Carbide. (unpublished) Ref No. LON 1755	
1.2	Data protection		
1.2.1	Data owner		
1.2.2 protec	Criteria for data tion		-
		2. GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes EPA Guideline 83-5; OECD Guideline 453 1988	
2.2 (only y	GLP where required)	Yes	
2.3	Deviations	No	
		3. MATERIALS AND METHODS	
3.1	Test material		
3.1.1	Lot/Batch number		
3.1.2	Specification		
3.1.3	Description		
3.1.4	Purity		
3.1.5	Stability		L
3.2	Test animals		
3.2.1	Species		
3.2.2	Strain		
3.2.3	Source		
3.2.4	Sex		
3.2.5 initiati	Age/weight at study on		
3.2.6	Number of animals		
per gro	Control Animals		
33	Administration/		

	20	DDACarbonate	February 2009
Section Annex	n 6.5(2) IIA Point 6.5	Chronic toxicity in rats.	
exposu	ire	Antonio and antonio anto	
3.3.1	Dose route		
3.3.2 test/exp	Duration of posure		
3.3.3	Frequency of		
exposu	re		
3.3.4	Post exposure		
2 2 5	Concentration		
5.5.5	Concentration		
336	Vehicle		
3.3.7	Actual dose		
receive	d		
3.3.8	Controls		
3.4	Examinations		
3.4.1	Observations		
3.4.2	Clinical signs		
3.4.3	Mortality		
3.4.4	Bodyweight		
3.4.5	Food consumption		
3.4.6	Water consumption	· · · · · · · · · · · · · · · · · · ·	
5.4./	ophinaimoscopic		-
3.4.8	Haematology		
3.4.9	Clinical Chemistry		
3.4.10	Urinalysis		
3.5 pathole	Sacrifice and ogy	1	
3.5.1	Organ weights		
3.5.2	Gross and		
histopa	thology		
3.5.3	Other examinations		
3.5.4	Statistical analysis		
		A DESULTS	
4.1	Examinations	T. RESULTS	
4.1.1	Observations		
412	Clinical sions		

Section Annex	п 6.5(2) ПА Point 6.5	Chronic toxicity in rats.
4.1.3	Mortality	
4.1,4	Bodyweight	
4.1.5	Food consumption	
4.1.6	Water consumption	
4.1.7	Ophthalmoscopic	
	Haematology	
410	Clinical Chemistry	
4110	Urinalveis	
4.2 pathole	Sacrifice and	
4.2.1	Organ weights	
4.2.2 histopa	Gross and thology	
4.2.3	Other examinations	
4.2.4	Statistical analysis	
4.3	LOAEL	
4.4	NOAEL	
		5. APPLICANT'S SUMMARY AND CONCLUSION
5.1 method	Materials and ds	
5.2 discuss	Results and sion	
5.3	Conclusion	NOAEL = 750 ppm (equivalent to 32 and 41 mg/kg/d for males and
5.3.1	Reliability	females, respectively)
5.3.2	Deficiencies	
		Evaluation by Competent Authorities
	DDACarbonate	February 2009
---------------------------------------	--	---------------
Section 6.5(2) Annex IIA Point 6.5	Chronic toxicity in rats.	
		ý.
	EVALUATION BY RAPPORTEUR MEMBER	STATE
Date		
Materials and Methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		
Remarks		
	Comments from other member state (specify)	
Date		
Materials and Methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		

Section 6.6 Genotoxicity studies Annex Point IIA 6.6- headline only

Sectio Annex	n 6.6.1(1) : Point IIA 6.6.1	In vitro gene mutation study in bacteria	
		1. REFERENCE	Official use only
1.1	Reference	(2004) REVERSE MUTATION ASSAY "AMES TEST" USING SALMONELLA TYPHIMURIUM. Safepharm Laboratories Limited. Report/Project No. 102/464 (unpublished). Reference No.: LR 3889	
1.2	Data protection		
1.2.1	Data owner		
1.2.2 protec	Criteria for data tion		
(2. GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes OECD Guideline No. 471; Directive 2000/32/EC Method B13/14 2004	
2.2 (only)	GLP where required)	Yes	
2.3	Deviations	No	
1		3. MATERIALS AND METHODS	
3.1	Test material		
3.1.1	Lot/Batch number		
3.1.2	Specification		
3.1.3	Description		-
3.1.4	Purity		
3.1.5	Stability		
3.2	Test species		-
3.2.1	Cell type		
3.2.2	Strain		
3.3 activa	Metabolic tion		-
Metab	olic activation system		
Positiv of met	e control in presence abolic activation		
3.3.2 absence activat	Positive control in e of metabolic ion		
3.4	Test methods	T	



	DDACarbonate	February 2009
Section 6.6.1(1) Annex Point IIA 6.6.1	In vitro gene mutation study in bacteria	
Reliability		
Acceptability		
Remarks		
	Comments from other member state (specify)	
Date		
Materials and methods		
Results and discussion		1.00
Conclusion		
Reliability		
Acceptability		

	2	_	DDACarbonate Febr	ruary 2009
Section 6.6.2(1) Annex ПА 6.6.2		<i>In vitro</i> cytogenetics study in mammalian cells (human lymphocytes)		
1		1.	REFERENCE	Official use only
1.1	Reference	CHR LYM No. 1 Refer	(2004) OMOSOME ABERRATION TEST IN HUMAN PHOCYTES <i>IN VITRO</i> . Safepharm Laboratories Limited. Report 02/463 (unpublished). rence No.: LR 3927	
1.2	Data protection			
1.2.1	Data owner			
1.2.2 protec	Criteria for data tion			
1.00		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes OECI 2004	D Guideline No. 473; Directive 2000/32/EC Method B10	
2.2 (only y	GLP where required)	Yes		
2.3	Deviations	No		
1		3.	MATERIALS AND METHODS	
3.1	Test material			
3.1.1	Lot/Batch number			1
3.1.2	Specification			
3.1.3	Description			
3.1.4	Purity			
5.1.5	Statinty			
3.2	Test species			
3.2.1	Cell type			
3.2.2	Strain			
3.3	Metabolic			
3.3.1 activat	Metabolic ion			
3.3.2 presen activat	Positive control in ce of metabolic ion			
3.3.3 absence activat	Positive control in e of metabolic ion			
3.4	Test methods			
3.4.1	Vehicle control	2		
3.4.2	Concentrations for			

	DDACarbonate	February 200
Section 6.6.2(1) Annex IIA 6.6.2	<i>In vitro</i> cytogenetics study in mammalian cells (human lymphocytes)	
cytotoxicity testing		
3.4.3 Concentrations for genotoxicity testing		
3.4.4 Duplicate/ independent assay		
3.4.5 Statistical methods		
8. at 1	4. RESULTS	
4.1 Cytotoxicity 4.1.1 With metabolic		-
4.1.2 Without metabolic activation		-
4.2 Genotoxicity 4.2.1 With metabolic activation		
	5. APPLICANT'S SUMMARY AND CONCLUSION	
methods		
5.2 Results and discussion		=
5.3 Conclusion	The test material was considered to be non-clastogenic to huma lymphocytes in vitro.	m
5.3.1 Reliability		
5.3.2 Deficiencies		
	Evaluation by Competent Authorities	
Date	EVALUATION BY RAPPORTEUR MEMBER STATE	
Materials and methods		
internets and memous		



	2		DDACarbonate	February 2009
Sectio Annez	n 6.6.3 (1) : Point IIA 6.6.3	In viti (mou	ro mammalian cell forward mutation assay se lymphoma TK+/- gene mutation)	1 I I I
		1.	REFERENCE	Official use only
1.1	Reference	Labor Refer	(2005) L5178Y TK+/- MOUSE LYMPHOMA ASSAY. Safepharm ratories Limited. Report No. 102/484 (unpublished). ence No.: LR 3898	
1.2	Data protection			
1.2.1	Data owner	4		
1.2.2	Criteria for data			
protec	tion	1		-
(2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes OECI 2005	O Guideline No. 476; Directive 2000/32/EC Method B17	
2.2	GLP	Yes		
1 2 2	Deviations	No		-
2.3	Deviations	1	MATERIALS AND METHODS	-
3.1	Test material	5.	MATERIALS AND METHODS	
311	Lot/Batch number			-
3.1.2	Specification			
	111 1 17 - Mark Barrison			
3.1.3	Description			
3.1.4	Purity			
3.1.5	Stability			
3.2	Test species/strain	1		1
3.2.1	Cell type			
3.2.2	Strain	1		
3.3 activa	Metabolic tion			
3.3.1	Inducing agent			
3.3.2 presen activat	Positive control in ce of metabolic ion			
3.3.3 absence activat	Positive control in e of metabolic ion			
3.4	Test methods			
3.4.1	Vehicle control			
3.4.2 concer	Cytotoxicity test ntrations			
3.4.3	Genotoxicity test			



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	DDACarbonate	February 2009
Section 6.6.3 (1) Annex Point IIA 6.6.3	<i>In vitro</i> mammalian cell forward mutation assay (mouse lymphoma TK+/- gene mutation)	
Acceptability		
Remarks	Comments from other member state (coecify)	
Date	comments from other memoer state (specify)	1
Materials and methods		
Results and discussion		
Conclusion		
Reliability		
Acceptability		

	DDACarbonate	February 2009
Section 6.6.4 Annex IIA 6.6.4	<i>In vivo</i> cytogenetics assay in mammalian cells (rat bone marrow micronucleus test)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
		-
Detailed justification:		
		-
	Evaluation by Competent Authorities	-
	EVALUATION BY RAPPORTEUR MEMBER STATE	_
Date Evaluation of applicant's justification		
Conclusion		
Remarks		
Date Evaluation of applicant's instification	Comments from other Member State (specify)	
Conclusion		



	DDACarbonate	February 2009
Section 6.6.6 Annex IIA 6.6.6	Germ cell effects	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Detailed justification:		_
		=
	Evaluation by Competent Authorities	_
Date Evaluation of applicant's justification Conclusion	Evaluation by Rapporteur Member State	
Remarks		
Date Evaluation of applicant's justification	Comments from other Member State (specify)	
Remarks Date Evaluation of applicant's justification Conclusion	Comments from other Member State (specify)	



	DDACarbonate	February 2009
Section 6.6.7 Annex IIA 6.6.7	Further genetic toxicity tests on metabolites of concern	
Date	Comments from other Member State (specify)	
Evaluation of applicant's justification Conclusion		



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	2		DDACarbonate	February 2009
Sectio Annez	n 6.7(1) x Point IIA 6.7	Carc	inogenicity study in mice	1.00
1		1.	REFERENCE	Official use only
1.1	Reference	Unio Ref N	n Carbide, Report No: 53-528, (unpublished) No.: LON 1776	ice.
1.2	Data protection			
1.2.1	Data owner			
1.2.2	Criteria for data			
protec	tion			
2.1	Guideline study	Z. Yes USE	GUIDELINES AND QUALITY ASSURANCE PA OPP 83-2	
2.2 (only	GLP where required)	Yes		
2.3	Deviations	No		
1		3.	MATERIALS AND METHODS	
3.1	Test material			
3.1.1	Lot/Batch number			
3.1.2	Specification			
3.1.3	Description			
3.1.4	Purity			
3.1.5	Stability			
3.2	Test animals	-		
3.2.1	Species			1
3.2.2	Strain			
3.2.3	Source			
3.2.4 3.2.5 initiati	Sex Age/weight at study on			
3.2.6	Number of animals			
per gro	oup	-		-
3.2.7	Satellite group(s)	-		
3.3 expos	Administration/			
3.3.1	Dose route			
Durati	on of test/exposure			
3.3.3 exposi	Frequency of tre			
3.3.4 period	Post exposure			

		DDACarbonate	February 2009
Section Annex	1 6.7(1) Point ПА 6.7	Carcinogenicity study in mice	
3.3.5	Concentration		_
3.3.6	Vehicle		
3.3.8 receive	Actual dose d		
3.3.9	Controls		
3.4	Examinations		
3.4.1	Observations		
3.4.2	Clinical signs		
3.4.3	Mortality		
3.4.4	Bodyweight		
3.4.5	Food consumption		
3.4.6	Water consumption		
3.4.7	Ophthalmoscopic		
examin	ation		
3.4.9	Clinical Chemistry		
3.4.10	Urinalysis		
3.5 pathole	Sacrifice and ogy		
3.5.1	Organ weights		
3.5.2 histopa	thology		
3.5.3	Statistical analysis		
41	Framinations	4. RESULTS	
4.1.1	Observations		
4.1.2	Clinical signs		
4.1.3	Mortality		
4.1,4	Bodyweight		
4.1.5	Food consumption		7

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Section Annex	n 6.7(1) Point IIA 6.7	Carcinogenicity study in mice	
4.1.6	Water consumption		
4.1.7	Ophthalmoscopic		
examin	ation	54	-
4.1.8	Haematology		_
4.1.9	Uninclucia Chemistry		
4.1.10	Crimarysis		-
4.2 pathol	ogy		
4.2.1	Organ weights		
4.2.2	Gross and		
histopa	thology		-
4.2.3	Statistical analysis		-
4.3	LOAEL		
4.4	NOAEL		
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	Materials and		
metho	us		
52	Results and		-
discuss	sion		
5.3	Conclusion	NOEL = 500 ppm (equivalent to 76.3 and 93.1 mg/kg/d for males and	
		females, respectively)	
		The test substance is not considered to be carcinogenic in this strain of	
5.3.1	Reliability	mice under the conditions of this study.	-
5.3.2	Deficiencies		-
			-
		Evaluation by Competent Authorities	
		EVALUATION DV DADBODTEUD MEMBER CTATE	
Date		EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	Land M. d 1	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date Materia	als and Methods	EVALUATION BY RAPPORTEUR MEMBER STATE	

	DDACarbonate	February 2009
Section 6.7(1) Annex Point IIA 6.7	Carcinogenicity study in mice	
Results and discussion		
Conclusion		
Reliability		
Acceptability		
Remarks		
	Comments from other member state (specify)	
Date		
Materials and Methods		
Results and discussion		
Conclusion		(
Reliability		
Acceptability		

	й. —		DDACarbonate	February 2009
Sectio Annex	n 6.7(2) : Point IIA 6.7	Carcino	ogenicity study in rats	
		1.	REFERENCE	Official use only
1.1	Reference	toxicity/ in rats. U Ref No.	(1991) Chronic dietary (oncogenicity study with Union Carbide, Report No. 53-566. (Unpublished) LON 1755	-
1.2	Data protection			
1.2.1	Data owner			
1.2.2	Criteria for data	Data sul	omitted to the MS before 14 May 2000 on existing a.s. for th	ie
protect	tion	purpose	of its entry into Annex I/IA	
C.		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes USEPA 1988	Guideline 83-5; OECD Guideline 453	
2.2 (only y	GLP where required)	Yes		
2.3	Deviations	No		
		3.	MATERIALS AND METHODS	
3.1	Test material	1	_	
311	Lot/Batch number			
3.1.2	Specification			
3.1.3	Description	1		
3.1.4	Purity			
3.1.5	Stability			
3.2	Test Animals			
3.2.1	Species			
3.2.2	Strain			
3.2.3	Source			
3.2.4	Sex			
3.2.5 initiati	Age/weight at study on	=		
3.2.6	Number of animals per group			
3.2.8	Control animals			
3.3 exposi	Administration/ are			
3.3.1	Route of exposure			
3.3.2	Duration of			
treatm	ent C	-		
5.5.5 exposi	rrequency of	12		
3.3.4 period	Post exposure			

		DDACarbonate	February 2009
Section Annex	1 6.7(2) Point IIA 6.7	Carcinogenicity study in rats	
3.3.5	Concentration		
3.3.6	Vehicle		
3.3.7 applied	Total volume		
3.3.8	Controls		
3.4	Examinations		
3.4.1	Observations		
3.4.2	Clinical signs		
3.4.3	Mortality		
3.4.4	Bodyweight		
3.4.5	Food consumption		
3.4.6	Water consumption		
3.4.7 examin	Ophthalmoscopic		
3.4.8	Haematology		
3.4.9	Clinical Chemistry		
3.4.10	Urinalysis		
35 patholo	Sacrifice and		
3.5.1	Organ weights		
3.5.2 histopat	Gross and thology		
3.5.3	Other examinations		
3.5.4	Statistics		
41	Examinations	4. RESULTS	
111	Observations		
4.1.1	Clinical signs		
4.1.3	Mortality		
4.1.4	Body weight gain		

		DDACarbonate	February 2009
Section Annex	n 6.7(2) Point IIA 6.7	Carcinogenicity study in rats	
4.1.5	Food consumption		
4.1.6	Water consumption		
4.1.7	Opthalmoscopic		
examin	nation		
4.1.8	Haematology		
4.1.9	Clinical chemistry		
4.1.10	Cimarysis		
4.2 nathol	Sacrifice and		
421	Organ weights		-
4.2.2	Gross and		
histopa	athology		
122	Other examinations		
4.2.4	Other examinations		
4.2.4			
4.3	LO(A)EL		
4.4	NO(A)EL		
5.1 metho	Materials and ds		
5.2 discus	Results and sion		
5.3	Conclusion	NOEL = 750 ppm (equivalent to 32 and 41 mg/kg/d for males females respectively) The test substance is not carcinogenic in this strain of rats und	and er the
531	Reliability	conditions of this study.	
532	Deficiencies		1
2.2.2	Denciencies		
		Evaluation by Competent Authorities	
		EVALUATION BY RAPPORTEUR MEMBER STATE	





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Section 6.8.1(1) Annex Point IIA 6.8.1		Terat	togenicity test in rats	
		1.	REFERENCE	Official use only
1.1	Reference	(Sprag (unpu Ref N	(1991) Developmental toxicity evaluation of administered by gavage to CD [®] gue-Dawley) rats. Union Carbide, Project No: 53-534. blished) Jo.: LON 1781	
1.2	Data protection			
1.2.1	Data owner			
1.2.2	Criteria for data			
protec	tion			
		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes U.S. I 1991	EPA Guideline 83-3; OECD Guideline 414	
2.2 (only	GLP where required)	Yes		
2.3	Deviations	No		
		3.	MATERIALS AND METHODS	
3.1	Test material	1		
3.1.1	Lot/Batch number	1		
3.1.2	Specification			
3.1.3	Description			1
3.1.4	Purity			1
3.1.5	Stability			
3.2	Test Animals			1
3.2.1	Species			-
3.2.2	Strain			
3.2.3	Source	1		
3.2.4	Sex			
3.2.5	Age/weight at study			
3.2.6	Number of animals	1		-
per gro	oup			
3.2.7	Control animals			
3.3 exposi	Administration/ ure			
331	Route of exposure			
3.3.2	Duration of			-
treatm	ent			
3.3.3	Frequency of	1		
exposi	ıre			
3.3.4	Vehicle			

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	2	DDACarbonate	February 2009
Sectio Annez	n 6.8.1(1) x Point IIA 6.8.1	Teratogenicity test in rats	
3.3.5	Dose levels		
3.3.6 vehicle	Concentration in e	3	
3.3.7 admin	Actual dose istered		
3.3.8 period	Post exposure		
3.4 exami	Adult nations		
3.4.1	Clinical signs		
3.4.2	Mortality		
3.4.3	Bodyweight		
3.4.4	Food consumption		
3.4.5	Water consumption		
3.5 exami	Sacrifice and	T	
351	Maternal findings		
352	Gross nectonsy		
finding	or of the second		
3.5.3	Organ weights		
3.5.4	Other		
3.5.5	Foetal findings		
3.5.6	Bodyweight		
3.5.7	Gross necropsy		
finding	gs		
3.5.8	Skeletal		
examin	nations		
3.5.9	Visceral		
examin	nations		
4.6	Statistics		
4.7	Further remarks		1 mar 10
		4. RESULTS	
4.1 observ	Maternal vations		
4.1.1	Clinical signs		
4.1.2	Mortality		
4.1.3	Body weight gain		
4.1.4	Food consumption		
4.1.5	Gross findings at		
necrop	osy		
4.1.6	Other		
4.2 observ	Foetal vations	1	
421	Bodyweight		
422	Gross findings at		
necror	STOSS Intomigs at		

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Section Annex	n 6.8.1(1) Point IIA 6.8.1	Teratogenicity test in rats	
4.2.3	Skeletal findings		
4.2.4	Visceral findings		
4.3	Remarks		
(*E.@*	(1) (1) (1) (1)		_
		5. APPLICANT'S SUMMARY AND CONCLUSION	
5.1	Materials and		
metho	ds		
5.2	Results and		
discuss	sion		
5.3	Conclusion	No developmental toxicity including teratogenicity was observed at any	
		dosage employed. The "no observable effect level" (NOFL) for maternal toxicity was 1	
		mg/kg/day; the NOEL for developmental toxicity was at least 20	
1.1	1.00	mg/kg/day	
5.3.1	Reliability		
5.3.2	Deficiencies		
-			_
		Evaluation by Competent Authorities	
			1
1.1		EVALUATION BY RAPPORTEUR MEMBER STATE	
Date			
Matari	als and Mathada		-
Materia	ars and methods		
			2
Doculto	and discussion		-
Results	s and discussion		
0 1			-
Conclu	151011		
Reliabi	ility		ľ
Accept	tability		
Remar	ks		
an and		Comments from other member state (marif.)	_
Date		Comments from other member state (specify)	-
Date			
Materia	als and Methods		

1

	DDACarbonate	February 2009
Section 6.8.1(1) Annex Point IIA 6.8.1	Teratogenicity test in rats	
Results and discussion		
Conclusion		
Reliability		
Acceptability		

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Section 6.8.1(2) Annex Point IIA 6.8.1		Tera	togenicity test in rabbits	
		1.	REFERENCE	Official use only
1.1	Reference		. (1989) Developmental toxicity study of	
		Zeala Ref N	administered by gavage to New nd white rabbits. Union Carbide, Project No: 51-590 (unpublished) Io.: LON 1770	
1.2	Data protection			
1.2.1	Data owner			
1.2.2	Criteria for data			
protect	tion	-	OUDELINES AND OUALITY ASSUDANCE	-
í		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes U.S. 1 1989	EPA OPP 83-3	
2.2 (only v	GLP where required)	Yes		
2.3	Deviations	No		
		3.	MATERIALS AND METHODS	
3.1	Test material	1		
3.1.1	Lot/Batch number	1		
3.1.2	Specification			1
3.1.3	Description			
3.1.4	Purity			5
3.1.5	Stability			
3.2	Test Animals			
3.2.1	Species			1
3.2.2	Strain			
3.2.3	Source	1		
3.2.4 3.2.5	Age/weight at study			
3.2.6 per gro	Number of animals	1		
3.2.7	Control animals			
3.3 exposi	Administration/ 1re			
3.3.1	Route of exposure			
3.3.2	Duration of			
treatm	ent	-		
3.3.3 expos	Frequency of	-		
3.3.4	Vehicle			
335	Dose levels			

	i contra de la con	DDACarbonate	February 2009
Section Annex	n 6.8.1(2) Point IIA 6.8.1	Teratogenicity test in rabbits	
3.3.6 vehicle	Concentration in		
3.3.7 admini	Actual dose stered		
3.3.8 period	Post exposure		
3.4 examin	Adult	1	
2 / 1	Clinical signs		
3.4.1	Mortality		
3.4.2	Roduweight		
311	Food consumption		
3.4.4	Water consumption		
3.4.3	water consumption		
3.5	Sacrifice and	. Contraction of the second se	
2.5.1	Matamal findings		
3.5.1	Maternal findings		
5.5.2 finding	Gross necropsy		
2 5 2	Organ weights		
3.5.3	Ofgan weights		
355	Foetal findings		
356	Bodyweight		
3.5.7	Gross necropsy		
finding	gs		
3.5.8	Skeletal		
examin	ations		
3.5.9	Visceral		
2 5 10	Statistics		
5.5.10			
3.5.10	Further remarks		
		4. RESULTS	
4.1 observ	Maternal vations		
4.1.1	Clinical signs		
4.1.2	Mortality		
4.1.3	Body weight gain		
4.1.4	Food consumption		
4.1.5	Gross findings at necropsy		
4.1.6	Other		
4.2	Foetal	1	
UDServ	D 1 1		
4.2.1	Bodyweight		
417	tross findings at		

	2	DDACarbonate	February 2009
Sectio Annez	n 6.8.1(2) x Point IIA 6.8.1	Teratogenicity test in rabbits	
1. T	necropsy		
4.2.3	Skeletal findings		
4.2.4	Visceral findings		
4.3	Remarks		
1		5. APPLICANT'S SUMMARY AND CONCLUSIO	N
5.1 Materials and			
metho	ods		
			-
5.2 discus	Results and		
uiscus	301		
5.3	Conclusion	Not teratogenic; increased incidence of dead foetuses and red weight at the maternal lethal dose of 10 mg/kg b.w. The "no observable effect level" (NOEL) for maternal toxici 1 mg/kg/day; the NOEL for developmental toxicity was at lea	uced fatal ity was ist
521	Dallability	10 mg/kg/day.	
532	Deficiencies		
5.5.2	Denenencies		
-			
-		Evaluation by Competent Authorities	
1		EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	Section 2010		
Materi	ials and Methods		
Result	s and discussion		
Conch	usion		
Reliab	ility		
Accep	tability		
Rema	ks		
- connu	1999) 1997	Comments from other sector date (
Date		Comments from other member state (specify)	
June	1 11/1 1		
Mater	ais and Methods		

	DDACarbonate	February 2009
Section 6.8.1(2) Annex Point IIA 6.8.1	Teratogenicity test in rabbits	
Results and discussion		
Conclusion		
Reliability		
Acceptability		



	2e	_	DDACarbonate	February 2009
Section 6.8.2(1) Two generations rep Annex Point IIA 6.8.2			generations reproduction study	
1		1.	REFERENCE	Official use only
1.1	Reference	Sprag admir (unpu Ref N	(1991) Two-generation reproduction study in gue-Dawley (CD [®]) rats with nistered in the diet, Union Carbide, Report No. 52-648 iblished) No.: LON 1777	
1.2	Data protection		· · · · · · · · · · · · · · · · · · ·	
1.2.1	Data owner	1		
1.2.2	Criteria for data			
protec	tion			1
		2.	GUIDELINES AND QUALITY ASSURANCE	
2.1	Guideline study	Yes U.S. 1991	EPA OPP 83-4	
2.2 (only)	GLP where required)	Yes		
2.3	Deviations	No		
	10.19.00100141	3.	MATERIALS AND METHODS	
3.1	Test material	1		
3.1.1	Lot/Batch number	1		
5.1.2	opeemeaton			
3.1.3	Description			
3.1.4	Purity			
3.1.5	Stability			
3.2	Test Animals			
3.2.1	Species			
3.2.2	Strain			
3.2.3	Source			
3.2.4	Sex			
3.2.5 initiati	Age/weight at study on			
3.2.6	Number of animals			
3.2.7	Control animals			
3.3	Administration/			
exposi	ure			
3.3.1	Route of exposure	- Ĵ		
3.3.2	Duration of			
treatm	ent			






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Section 6.8.2(1) Annex Point IIA 6.8.2	Two generations reproduction study	
Date		
Materials and Methods		
Results and discussion		
Conclusion		
Reliability		1
Acceptability		





	DDACarbonate	February 2009
Section 6.9 Annex Point IIA 6.9	Neurotoxicity study	
Date Evaluation of applicant's justification Conclusion		

Section 6.10(1)	Mechanistic study	
Annex Point IIA 6.10	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Detailed justification:		
	Evaluation by Competent Authorities	_
Data	EVALUATION BY RAPPORTEUR MEMBER STATE	
Evaluation of applicant's ustification		_
conclusion		
Remarks		
Date Evaluation of applicant's	Comments from other Member State (<i>specify</i>)	
ustification		

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a correction of	

Section 6.11 Other routes of administration

Section 6.11(1) Annex Point IIA 6.11	Other routes of administration	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Detailed justification:		
		i -
	Evaluation by Competent Authorities	
		•
Date	EVALUATION BY RAPPORTEUR MEMBER STATE	-
Evaluation of applicant's justification		
Conclusion		
Remarks		
Date	Comments from other Member State (specify)	
Evaluation of applicant's justification		

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Section 6.12 Annex Point IIA. 6.12	Medical data in anonymous form	Official use only
6.12.0 Introductory remark		
6.12.1 Medical surveillance data on manufacturing plant personnel if available		
6.12.2 Direct observation, e.g. clinical cases, poisoning incidents if available		-
6.12.3 Health records, both from industry and any other available sources		
6.12.4 Epidemiological studies on the general population, if available		
6.12.5 Diagnosis of poisoning including specific signs of poisoning and clinical tests, if available		
6.12.6 Sensitisation/ allergenicity		

Section 6.12 Medical data in anonymous form

	DDACarbonate	February 2009
Section 6.12 Annex Point IIA. 6.12	Medical data in anonymous form	Official use only
observations, if available		
6.12.7 Specific treatment in case of an accident or poisoning: first aid measures, antidotes and medical treatment, if known		
6.12.8 Prognosis following poisoning		
	Evaluation by Competent Authorities	
Date Evaluation of applicant's justification Conclusion	EVALUATION BY RAPPORTEUR MEMBER STA	ATE
Remarks		
Date Evaluation of applicant's justification Conclusion	Comments from other Member State (specify)	

Section 6.13 Toxic effects on livestock and pets

Section 6.13 Annex Point IIA 6.13	Toxic effects on livestock and pets	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Detailed justification:		•
		•
	Evaluation by Competent Authorities	
Date Evaluation of applicant's justification Conclusion	EVALUATION BY RAPPORTEUR MEMBER STATE	
Remarks		
Date Evaluation of applicant's justification Conclusion	Comments from other Member State <i>(specify)</i>	

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Section 6.15.1 **Residues in food/feedstuffs** Annex Point III-A.6.15.1 JUSTIFICATION FOR NON-SUBMISSION OF DATA Official use only **Detailed justification: Evaluation by Competent Authorities** EVALUATION BY RAPPORTEUR MEMBER STATE Date **Evaluation of applicant's** justification Conclusion Remarks Comments from other Member State (specify) Date Evaluation of applicant's justification Conclusion Remarks

Section 6.15 Food and feedingstuffs







	DDACarbonate	February 2009
Section 6.15.5 Annex Point III-A.6.15.5	Other relevant information (ADI, MRL, etc.)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
		•
Detailed justification:		
		_
		-
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date Evaluation of applicant's justification		•
Conclusion		
Remarks		
Date Evaluation of applicant's justification	Comments from other Member State (specify)	
Conclusion Remarks		



Section 6.16 Annex Point IIA 6.16	Any other tests related to the exposure of the active substance to humans, in its proposed biocidal products that are considered necessary may be required	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
		-
	Evaluation by Competent Authorities	
Date Evaluation of applicant's	EVALUATION BY RAPPORTEUR MEMBER STATE	
justification Conclusion		
ustification Conclusion Remarks		

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Section 6.17 Toxic effects of metabolites from treated plants

Section 6.18 Annex Point IIA. 6.18	Summary of mammalian toxicology and conclusions (in Doc. II-A)	Official use only
Pharmacokinetics		
Acute Toxicity		
Irritation and Sonsitization		
ITTRATION AND SENSILIZATIO		
Repeated dose toxicity, neurotoxicity and carcinogenicity		

Section 6.18 Summary of mammalian toxicology and conclusions

Lonza GmbH

