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Degussa Corporation
May 6, 1994

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Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street, S. W.
Washington, D.C. 20460

(A)



INIT 05/10/94

Attn.: Section 8(e) Coordinator

Re: Substantial Risk Notification
Pursuant to TSCA Section 8(e)

Dear Sir:

This Substantial Risk Notification is being submitted in accordance with Section 8(e) of the Toxic Substances Control Act (TSCA) by Degussa Corporation. The substance is a "new" chemical, 1,3-dioxolane, 2-ethenyl- (which we call 2-vinyl-1,3-dioxolane) CASRN 3984-22-3. This new chemical substance has been imported under a Research & Development exemption.

We just became aware of an acute oral toxicity study in rats and were informed about an ongoing acute dermal toxicity study in rabbits. A summary of each study and a printout from the STN Chemical Abstracts Service Registry File follows.

Acute Oral Toxicity Study In Rats

Dosage/route/duration: The test material diluted with water was administered by gavage to male and female rats at a dose range between 46.4 and 215 mg/kg. The post-exposure observation was 14 days.

Results: After oral administration, hypokinesia, stilted gait, coordination disturbances, piloerection and sunken sides were observed in surviving rats. In deceased animals additionally restrained gait, low temperature of the body surface, mydriasis and lacrimation were recorded. Ante mortem decrease of muscle tone, loss of righting, pinna, corneal, and pain reflexes and strenuous respiration occurred.

At necropsy deceased animals showed reddening of the mucous membranes of the intestines and the stomach. Additionally the stomach was distended with liquid.

The LD₅₀ for both sexes together was 84.7 mg/kg.

A copy of the study is attached.



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Acute Dermal Toxicity Study In Rabbits

In a preliminary notice from the contract laboratory, a LD₅₀ value of approximately 25 mg/kg of an acute dermal toxicity test was reported. No additional data are available at this time, but the study will be submitted when it is available.

Sincerely,



John Lewinson, Ph.D.
Manager, Product Regulatory Compliance

JL-94-156

cc: R. Marion, DCA
Dr. Pieter, DCRP
B. Santoro, DCRP

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Study No.: 887624
Report

DEGUSSA AG - US-IT - NR.		
92	0006	D ^N OT

2-VINYL-1,3-DIOXOLANE

Acute Toxicity

**Testing the Acute Toxicity
after Single Oral Administration
in Rats**

R E P O R T

July 13, 1992

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The report comprises 22 pages.

1. GENERAL INFORMATION

1.1 Study Specification

Sponsor : Degussa AG/ZN Wolfgang
Industrielle Toxikologie (US-IT)
Postfach 13 45
D-6450 Hanau 1

Testing Facility : ASTA Medica AG
Institute of Toxicology
Kantstraße 2
D-4802 Halle-Künsebeck

Study Director : Dr. rer. nat. K. Berthold
Veterinary Care : Dr. med. vet. H.-J. Zechel
Study Performance : M. Beste

Quality Assurance : K.E. Fichtner
Representative: Dr. B. Wilker, formerly Roos

Test Substance : 2-Vinyl-1,3-dioxolane

Objective : Testing the acute toxicity after single oral
administration in rats.

Test Guidelines : OECD Guideline No. 401 (1)
EEC Guideline 84/449/EEC (2)

Study No. : 887624

Time Schedule : Protocol Feb. 5, 1992
and 1 amendment
First day of administration Feb. 25, 1992
End of study Mar. 12, 1992
Final report July 13, 1992

Quality Assurance : The study was performed according to the
principles of Good Laboratory Practice (GLP)
(3).

Archivation : The approved protocol, all raw data obtained
in the course of the study, as well as a copy
of the final report are kept in the archives
of the Institute of Toxicology at least
30 years (starting with the report date).
Afterwards the sponsor will decide on further
use.

1.2 Authentication

I, the undersigned, hereby declare that to the best of my knowledge the study was performed under my supervision in accordance with current Good Laboratory Practice (as laid down in the German Chemicals Act).

In line with normal practice in this type of short-term study, the protocol did not require analysis of the dose form.

This report represents a true and accurate record of the results obtained.

Study Director : K. Berthold 13.7.92
Dr. rer. nat. K. Berthold

Report Review

Head of Institute
of Toxicology

: H. Jahn 27/07/92
Dr. med. vet. H. Jahn

1.3 ASTA Medica AG
Corporate Quality Assurance
Section GLP/GCP

Quality Assurance Statement

The non-clinical laboratory study

2-Vinyl-1,3-dioxolane
Testing the acute toxicity after single oral administration in rats

performed at ASTA Medica AG, Halle-Künsebeck,

was inspected and audited for conformance to the principles of
Good Laboratory Practice (GLP).

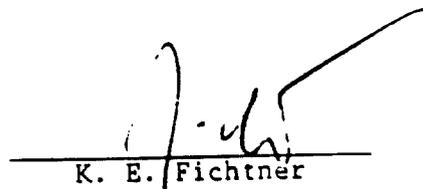
The dates of inspections and reports to study director and management
are given below.

<u>Phase of Study</u>	<u>Date of QA Inspection</u>	<u>Date of QA Report</u>
Protocol Review	Feb. 6, 1992	
Experimental Period	Feb. 24, 1992	
	Feb. 25, 1992	
	Feb. 26, 1992	
	Mar. 3, 1992	Mar. 3, 1992
Final Report Audit	July 16, 1992	July 16, 1992

Date:

July 27, 1992

Signed:


K. E. Fichtner

2. SUMMARY

2-Vinyl-1,3-dioxolane was studied for acute toxicity after single oral administration in rats. The test substance, available as a colourless liquid, was diluted with deionized water. As the doses were 46.4, 100, and 215 mg/kg and the administration volume was 10.0 ml/kg, the concentration varied between 4.64 and 21.5 mg/ml in male and female rats.

Intoxication was characterized by hypokinesia, stilted gait, coordination disturbances, and sunken sides. Additionally piloerection, restrained gait, and low temperature of the body surface were recorded. In individuals also mydriasis and lacrimation were observed. Antemortem decrease of muscle tone, loss of righting, pinna, corneal, and pain reflexes and strenuous respiration occurred.

The symptoms appeared within 12 minutes after treatment and lasted for up to 15 days.

Deaths occurred 2 to 24 hours after administration.

At necropsy only deceased animals showed reddening of the mucous membranes of the intestines and the stomach. Additionally the stomach was distended with liquid.

The LD 50 values were

for male rats: 85.5 (39.6 - 165) mg/kg
for female rats: 85.5 (39.6 - 165) mg/kg
and for male and female rats: 84.7 (61.6 - 116) mg/kg

The slopes of the dose response curves were

for male rats: 4.49 (0.85 - 8.14)
for female rats: 4.49 (0.85 - 8.14)
and for male and female rats: 5.85 (2.37 - 9.33)

3. INTRODUCTION

The study was conducted to investigate the acute toxicity of 2-vinyl-1,3-dioxolane after single oral administration in rats.

The objective of the study was to determine the signs of toxicity (clinical observations, macroscopical examination), the progress of intoxication, and the time of death (1, 2, 4). The observation period was 14 days. The findings obtained were supplemented by determination of the LD 50.

This study was conducted in accordance with the OECD Guideline No. 401 (1) and the EEC Guideline 84/449/EEC (2).

4. METHODS

4.1 Test Substance

Test Substance/
Trade Name/Identity : 2-Vinyl-1,3-dioxolane

Chemical Name/Synonym : VDL
Acroleine-ethyleneglykol-acetale

CAS No. : 3984-22-3

Batch No. : Kö 1659 /Fr: 3

Physical Appearance : Colourless liquid

Content/Purity : > 99% (GC)

Solubility : 11.5 g in 100 ml water (20°C)

Density : 0.97 g/ml

Storage : The test substance was kept in a closed container in a refrigerator.

Stability : According to information from the sponsor the test substance was stable throughout the experimental period.

Additional Information : See attachment 1 and under substance No. 91008 on file in Institute of Toxicology.

4.2 Test System

4.2.1 Animal Species : Rat

Strain : Bor: WISW (SPFCpb)

Origin/ Breeder : Winkelmann Versuchstierzucht GmbH & Co. KG., D-4799 Borchten

Justification for the Selection of the Test System : The test system was selected on the basis of international recommendations. According to these, rats are suitable for detecting toxic properties of test substances in rodents.

Age of the Animals at Treatment : Males 8 weeks Females 9 weeks

Body Weight of the Animals at Treatment : Males 144 - 170 g Females 134 - 156 g

Total Number of Animals : Males 15 Females 15

4.2.2 Husbandry

- Location : ASTA Medica AG
Institute of Toxicology
Kantstraße 2
D-4802 Halle-Künsebeck
- Caging : Macrolon cages, type II
- Number of
Animals per Cage : 1
- Bedding : Animal bedding chips, supplied by Jelu-Werk,
J. Ehrler, Industriemehle, D-7092 Rosenberg/
Württ.
- Diet : Standard diet ad libitum, ssniff R, Special
diet for rats (composition of the diet see
attachment 2)
supplied by ssniff Spezialdiäten GmbH,
D-4770 Soest
According to information from the manufac-
turer contaminant analyses of the diet are
performed in appropriate intervals. Certifi-
cates of analyses are on file in the testing
facility.
- Water : Water was provided ad libitum in drinking
water quality from the Stadtwerke Halle,
using drinking bottles.
According to information from the Stadtwerke
Halle the water is investigated in appropria-
te intervals. Certificates of analyses are on
file in the testing facility.
- The known contaminants present in diet and
water are toxicologically insignificant in
the quantities detected for the experiment
performed.
- Room Temperature : 20.5 - 23.0°C
- Relative Humidity : 50 - 65% (for a short period up to 87%, this
deviation was without any influence
on the results of the study)
- Room Lighting : 6 a.m. - 6 p.m. CET artificial lighting
6 p.m. - 6 a.m. CET darkness
- Room Hygiene,
Cage Cleaning : The room was cleaned regularly with commer-
cial antiseptics and cages with the cage
washing machine type HAMO-R-T-500D (supplied
by Hamo AG, CH-Biel-Bienne) or type K 850/500
(supplied by Netzsch Newamatic GmbH, D-8264
Waldkraiburg).

- 4.2.3 Randomization : At arrival the animals were randomized using a computerized random figure generator.
- 4.2.4 Identification of the Animals and Cages : The animals were individually identified with colour codes and ear notches. The cages were labelled with: Study number, name of the test substance, animal species, animal number, sex, dose, day of administration.
- 4.2.5 Acclimatization Period : The animals were kept at least 5 days under test conditions before administration of the test substance. Veterinary supervision of the animals was done before start of study.

4.3 Procedure

- Diet Withdrawal : Approx. 16 hours before treatment
- Administration of the Test Substance : Single oral administration by gavage (Nelaton catheter, red rubber, supplied by Willy Rüsck, D-7053 Rommelshausen/Stuttgart)

Justification for the Selection of the Route of Administration

- : The test substance was examined on its toxicity after single oral administration because of the potential oral exposition of man.

Solvent/Vehicle

- : Deionized water, supplied by ASTA Medica AG, D-4800 Bielefeld 14

Preparation of the Solution

- : Aqueous solutions were prepared immediately before dosing.

Dose/Dose Groups :

Dose (mg/kg)	Concentration (mg/ml)	Administration Volume (ml/kg)	Animals per Dose
Males			
46.4	4.64	10.0	5
100	10.0	10.0	5
215	21.5	10.0	5
Females			
46.4	4.64	10.0	5
100	10.0	10.0	5
215	21.5	10.0	5

4.4 Observations/Findings

4.4.1 Clinical Examinations

Behaviour, General
Condition, and
Clinical Symptoms

: The animals were continuously observed for the first 4 to 6 hours after administration and then once daily. The nature of the toxicity as well as the onset, the intensity, and the duration of the signs were recorded (1, 2, 4).

Mortality

: Mortality was checked twice daily (a.m. and p.m.), on Saturdays, Sundays, on national and business holidays only once daily. If ascertainable, the time of death of the deceased animals was documented. Animals found dead were recorded correspondingly.

Body Weight

: The body weights were recorded at the beginning and also 7 and 14 days after administration or after death of the animals on days 2 to 14.

Observation Period

: 14 days after administration

4.4.2 Pathology

Sacrifice

: At the end of the observation period the animals were sacrificed with CO₂.

Gross Necropsy

: A gross necropsy was performed on all animals. Macroscopical examination included external appearance, body orifices, body cavities (thoracic and abdominal), and their contents.

4.5 Evaluation of Data

: The LD 50 values were determined for each sex and for both sexes together with 95% confidence interval by probit analysis (5 - 8).

The dose groups used for determination of the LD 50 value were marked with * in table 3.

4.6 Protocol Adherence

: The study was conducted in accordance with the original protocol and the 1 amendment with the following exception:

Instead of an automatic watering system, drinking bottles were used.

5. RESULTS

Clinical Observations and Necropsy

About one hour after treatment animals of the low dose group (46.4 mg/kg) began to show slight to moderate hypokinesia, coordination disturbances, and stilted gait. Five animals, predominantly females also exhibited sunken sides. Two days afterwards all animals had recovered.

At necropsy none of these animals exhibited any findings.

After treatment with 100 mg/kg of the test substance rats additionally showed severe hypokinesia and piloerection. In one male rat lacrimation was observed also. Ante mortem decrease of muscle tone and loss of righting and corneal reflexes was detected. Symptoms were recorded already 12 minutes after treatment and lasted up to 15 days. Eight of 10 rats died between 3 and 24 hours after administration.

At necropsy all deceased rats showed reddening of the mucous membranes of the gastro-intestinal tract and distention of the stomach by a liquid.

In the high dose group (215 mg/kg) the same signs of toxicity were recorded as in the mid dose group. The only additional symptoms were restrained gait, loss of pinna and pain reflexes, and moderate to severe mydriasis. Ante mortem low temperature of the body surface and strenuous respiration were noticed. All animals died within about 2 to 3.3 hours.

At necropsy the same changes as in the deceased rats of the mid dose group were recorded.

Clinical symptoms are shown in table 1 separately for surviving and deceased animals. The individual body weights are listed in table 2. Mortality data are given in table 3.

The macroscopic findings for deceased animals are given in table 4.

Statistics

The LD 50 values and the slopes of the dose response curves for male and female rats and for both sexes together were determined by probit analysis with a confidence interval of 95%.

LD 50-values

Male animals: 85.5 (39.6 - 165) mg/kg
Female animals: 85.5 (39.6 - 165) mg/kg
Male and female animals: 84.7 (61.6 - 116) mg/kg

Slopes

Male animals: 4.49 (0.85 - 8.14)
Female animals: 4.49 (0.85 - 8.14)

Table 2 Acute Toxicity - Body Weights (g) - Individual Values

Test Substance : 2-Vinyl-1,3-Dioxolane
 Species : Rat
 Administration : Oral

Dose (mg/kg)	Animal No.	Day 0	Day 7	Day 14
Male Animals				
46.4	21	164	198	229
	22	165	205	245
	23	170	207	242
	24	147	174	202
	25	167	199	230
100	11	164		
	12	156		
	13	156		
	14	159		
	15	162	184	208
215	1	152		
	2	144		
	3	153		
	4	150		
	5	154		
Female Animals				
46.4	26	153	177	190
	27	138	153	162
	28	145	170	179
	29	155	178	191
	30	145	168	179
100	16	145		
	17	143		
	18	142		
	19	144	159	170
	20	134		
215	6	136		
	7	143		
	8	139		
	9	137		
	10	156		

6. TABLES

Table 1a Acute Toxicity - Clinical Symptoms

Test Substance : 2-Vinyl-1,3-Dioxolane
 Species : Rat
 Administration : Oral

Sex : Male, Surviving Animals

Symptoms	Dose mg/kg	
	46.4 x/5	100 x/1
Hypokinesia slight	3	1
moderate	2	
Coordination disturbances	1	1
Stilted gait	1	
Piloerection		1
Sunken sides	1	1

Sex : Male, Deceased Animals

Symptoms	Dose mg/kg	
	100 x/4	215 x/5
Hypokinesia moderate	2	1
severe	2	4
Coordination disturbances	1	2
Stilted gait	2	1
Restrained gait		3
Decrease of muscle tone AP	1	3
Loss of righting reflex LP	1	1
DP	1	1
Loss of corneal reflex	1	3
Lacrimation	1	1
Piloerection	1	1
Strenuous respiration		1
Sunken sides		4
Low temperature of body surface		3

AP = Abdominal Position, LP = Lateral Position, DP = Dorsal Position

Table 1b Acute Toxicity - Clinical Symptoms

Test Substance : 2-Vinyl-1,3-Dioxolane
 Species : Rat
 Administration : Oral

Sex : Female, Surviving Animals

Symptoms	Dose mg/kg	
	46.4 x/5	100 x/1
Hypokinesia slight moderate	3	1
Coordination disturbances	3	1
Stilted gait	3	1
Piloerection		1
Sunken sides	4	1

Sex : Female, Deceased Animals

Symptoms	Dose mg/kg	
	100 x/4	215 x/5
Hypokinesia slight	1	
moderate	2	3
severe	1	2
Coordination disturbances	3	2
Stilted gait	2	2
Restrained gait		3
Decrease of muscle tone AP	2	5
Loss of righting reflex LP	1	4
DP	1	4
Loss of pinna reflex		3
Loss of pain reflex		2
Loss of corneal reflex	3	5
Lacrimation		1
Mydriasis moderate		1
severe		2
Piloerection	3	
Strenuous respiration		3
Sunken sides	2	5

Table 3 Acute Toxicity - Mortality Data

Test Substance : 2-Vinyl-1,3-Dioxolane
 Species : Rat
 Administration : Oral

Dose (mg/kg)	Mortality Rate		Time of Survival until																		
			Hours p. appl.						Days p. appl.												
	x/n	%	0.5	1	2	4	6	24	2	3	4	5	6	7	8	9	10	11	12	13	14
Male Animals																					
46.4*	0/5	0																			
100*	4/5	80				2		2													
215*	5/5	100				5															
Female Animals																					
46.4*	0/5	0																			
100*	4/5	80				2		2													
215*	5/5	100			2	3															

* Dose groups used for calculation of the LD 50 value.

Table 4 Acute Toxicity - Macroscopical Examination

Test Substance : 2-Vinyl-1,3-Dioxolane
 Species : Rat
 Administration : Oral

Sex : Male, Deceased Animals

Organ/Finding	Dose mg/kg				
	100 x/4	215 x/5	x/	x/	x/
Stomach					
- reddened		5			
- distended with liquid	4	4			
Glandular stomach					
- mucous membrane reddened	4				
Intestine					
- reddened	2	5			
Small intestine					
- reddened	2	3			

Sex : Female, Deceased Animals

Organ/Finding	Dose mg/kg				
	100 x/4	215 x/5	x/	x/	x/
Stomach					
- reddened		4			
- distended with liquid	4	1			
Glandular stomach					
- mucous membrane reddened	4				
Intestine					
- reddened	2	4			
Small intestine					
- reddened	2	1			

Table 5 Acute Toxicity - LD 50 Values

Test Substance : 2-Vinyl-1,3-Dioxolane
Species : Rat
Administration : Oral

Method : Probit Analysis (5 - 8), Confidence Limit 95%

	LD 50 (mg/kg)	Slope
Male Animals	85.5 (39.6 - 165)	4.49 (0.85 - 8.14)

Female Animals	85.5 (39.6 - 165)	4.49 (0.85 - 8.14)

Male and Female Animals	84.7 (61.6 - 116)	5.85 (2.37 - 9.33)

7. REFERENCES

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8. ATTACHMENTS 1 - 2

Attachment 1 Data on the Test Substance

Attachment 2 Composition of the Diet

Attachment 2

s s n i f f R
Special Diet for RatsIngredients (in % Diet)

Raw Protein	21.00%	Calcium	1.10%
Raw Fat	3.00%	Phosphorus	0.80%
Raw Fiber	4.80%	Sodium	0.30%
Raw Ash	6.70%	Magnesium	0.20%
		Potassium	1.00%

Amino Acids (in 1 kg Diet)

Lysine ⁸	1.20%
Methionine	0.35%
Cystine	0.30%
Glycine	1.00%
Leucine	1.70%
Isoleucine	1.00%
Arginine	1.40%
Phenylalanine	1.00%
Tryptophane	0.35%
Histidine	0.50%
Alanine	1.00%
Tyrosine	0.70%
Aspartic Acid	1.60%
Glutamic Acid	3.00%
Valine	1.00%

Vitamins (in 1 kg Diet)

A	20,000 I.E.
D ₃	2,000 I.E.
E ₃	60 mg
C	500 mg
B ₁	15 mg
B ₂	30 mg
B ₆	12 mg
B ₁₂	60 mcg
Biotin	200 mcg
Pantothenic Acid	40 mg
Choline	1,600 mg
Folic Acid	2 mg
Nicotinic Acid	120 mg
K ₃	5 mg

Trace Elements (in 1 kg Diet)

Manganese	75 mg
Copper	12 mg
Zinc	80 mg
Iodine	1 mg
Ferrum	320 mg
Fluorine	10 mg

Fatty Acids

Data available on request