

## Appendix C

# I U C L I D

## Data Set

**Existing Chemical** : ID: 75-35-4  
**CAS No.** : 75-35-4  
**EINECS Name** : 1,1-dichloroethylene  
**EINECS No.** : 200-864-0  
**TSCA Name** : Ethene, 1,1-dichloro-  
**Molecular Formula** : C2H2Cl2

**Producer Related Part**  
**Company** : The Dow Chemical Company  
**Creation date** : 20.03.2002

**Substance Related Part**  
**Company** : The Dow Chemical Company  
**Creation date** : 20.03.2002

**Memo** :

**Printing date** : 14.08.2002  
**Revision date** :  
**Date of last Update** : 02.08.2002

## 5.1.1 ACUTE ORAL TOXICITY

<b>Type</b>	:	LD50	
<b>Species</b>	:	rat	
<b>Strain</b>	:	other: Holtzman	
<b>Sex</b>	:	no data	
<b>Number of animals</b>	:	3	
<b>Vehicle</b>	:	other: corn oil	
<b>Value</b>	:	= 1510 mg/kg bw	
<b>Method</b>	:	other	
<b>Year</b>	:	1972	
<b>GLP</b>	:	no	
<b>Test substance</b>	:	no data	
<b>Method</b>	:	Adult rats were given VDC as a solution in corn oil via oral gavage at a dose volume of 2 ml/kg. All animals were sacrificed via cervical translocation and exsanguination.	
<b>Source</b>	:	The Dow Chemical Company, Midland, MI.	
<b>Reliability</b>	:	(2) valid with restrictions Study was conducted prior to advent of GLP, but provides adequate information based on the state of the science at the time.	
20.03.2002			(96) (97)
<b>Type</b>	:	LD50	
<b>Species</b>	:	rat	
<b>Strain</b>	:		
<b>Sex</b>	:		
<b>Number of animals</b>	:		
<b>Vehicle</b>	:		
<b>Value</b>	:	800 - 2000 mg/kg bw	
<b>Remark</b>	:	Rat: male, nonfasted	
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
20.03.2002			(98) (96)
<b>Type</b>	:	LD50	
<b>Species</b>	:	rat	
<b>Strain</b>	:		
<b>Sex</b>	:		
<b>Number of animals</b>	:		
<b>Vehicle</b>	:		
<b>Value</b>	:	= 1550 mg/kg bw	
<b>Remark</b>	:	Rat: male, nonfasted	
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
20.03.2002			(96) (99)
<b>Type</b>	:	LD50	
<b>Species</b>	:	rat	
<b>Strain</b>	:		
<b>Sex</b>	:		
<b>Number of animals</b>	:		
<b>Vehicle</b>	:		
<b>Value</b>	:	= 1800 mg/kg bw	
<b>Remark</b>	:	Rat: male, nonfasted	
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
20.03.2002			(96) (100)

**Type** : LD50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Value** : = 1500 mg/kg bw  
**Remark** : Rat: female, nonfasted  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 20.03.2002 (96) (100)

**Type** : LD50  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Value** : 201 - 235 mg/kg bw  
**Remark** : Mouse: male, nonfasted  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 20.03.2002 (101) (96) (102)

**Type** : LD50  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Value** : 171 - 221 mg/kg bw  
**Remark** : Mouse: female, nonfasted  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 20.03.2002 (101) (96) (102)

### 5.1.2 ACUTE INHALATION TOXICITY

**Type** : LC50  
**Species** : rat  
**Strain** : Sprague-Dawley  
**Sex** : male  
**Number of animals** : 16  
**Vehicle** : other: ambient air  
**Exposure time** : 4 hour(s)  
**Value** : = 6350 ppm  
**Method** : other  
**Year** : 1971  
**GLP** : no  
**Test substance** : other TS  
**Method** : Groups of 16 male Sprague-Dawley rats were exposed to 4900 or 6150 ppm VDC for 4 hours. The animals were returned to their cages and observed for 2 weeks. No food or water was provided during the exposure. Mortality was recorded, and the LD50 estimated using the method of Miller and Tainter (1944).

Atmospheres were generated by collecting high concentrations of the test material via passing air through a large fritted gas absorber containing the test material. A predetermined quantity of test material was then pumped into a 30-l exposure chamber (Leach, 1963) where it was diluted with

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ambient air to form a test atmosphere as specified with a flow rate of 6 l/min.

**Result** : Material Exposure Mortality LD50  
Conc. (ppm) (#dead/#treated) (ppm)

VDC 4900 1/16 6350  
6150 7/16

**Source** : The Dow Chemical Company, Midland, MI.  
**Test condition** : Commerically obtained.  
**Reliability** : (2) valid with restrictions  
Study was conducted prior to advent of GLP, but provides adequate information based on the state of the science at the time.

04.06.2002 (96) (103) (104) (105)

**Type** : LC50  
**Species** : mouse  
**Strain** : CD-1  
**Sex** : male  
**Number of animals** : 10  
**Vehicle** : other: ambient air  
**Exposure time** : 22 hour(s)  
**Value** : = 98 ppm  
**Method** : other  
**Year** : 1977  
**GLP** : no  
**Test substance** : other TS  
**Method** : Male CD mice were exposed to VDC for 22-23 hrs/day in stainless steel chambers 3.5 cubic meters in volume. Vapors were generated by bubbling nitrogen through a flask containing VDC. A stream of ambient air carried the vapors into the chamber. Sampling at various points in the chamber ensured that the distribution was uniform.

Mortality data were evaluated in terms of the LD50 (Weil, 1952) and LT50 (Lichfield, 1949).

**Source** : The Dow Chemical Company, Midland, MI.  
**Test condition** : Obtained from Aldrich Chemical Co. 99% purity, with 200 ppm hydroquinone monomethyl ether as an inhibitor.

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**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = 1.6 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Rat: male, fasted.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

20.03.2002 (107)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :

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**Exposure time** : 4 hour(s)  
**Value** : = 26 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Rat: female, fasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (107)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = 28.4 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Rat: male, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (108)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = 40.8 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Rat: female, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (108)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = 128 mg/l  
**Remark** : Rat: male, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (109) (96) (110)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :

## 5. Toxicity

**Id** 75-35-4  
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**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = 128 mg/l  
**Remark** : Rat: female, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (109) (96)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = 60 mg/l  
**Remark** : Rat: male, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (96) (111)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = 8 mg/l  
**Remark** : Rat: male, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (96) (112)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = 2.4 mg/l  
**Remark** : Rat: male, fasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (96) (111)

**Type** : LC50  
**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = 128 mg/l  
**Remark** : Rat: female, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
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**Type** : other: IRT

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**Id** 75-35-4  
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**Species** : rat  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 3 minute(s)  
**Method** : other: based on method described by Smith H.F et al: Am.Ind.Hyg.Ass.J. 23, 95-107 (1962)  
**Year** : 1962  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Mortality after 3 min exposure in an atmosphere enriched or saturated at 20 degrees C. Mortality was 8 of 12 animals.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (113)

**Type** : LC50  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = .2 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Mouse: male, fasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (114)

**Type** : LC50  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = .5 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Mouse: female, fasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (114)

**Type** : LC50  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = .46 mg/l  
**Method** :  
**Year** :  
**GLP** : no

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**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Mouse: male, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (115)

**Type** : LC50  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = .82 mg/l  
**Method** :  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Mouse: female, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (115)

**Type** : LC50  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = .42 mg/l  
**Remark** : Mouse: female, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (96) (116)

**Type** : LC50  
**Species** : mouse  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** :  
**Value** : = .14 mg/l  
**Remark** : Mouse: male, fasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (96) (116)

**Type** : LC50  
**Species** : hamster  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = 11.69 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Hamster: female, nonfasted

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (117)

**Type** : LC50  
**Species** : hamster  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = 6.59 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Hamster: male, nonfasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (117)

**Type** : LC50  
**Species** : hamster  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = .6 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Hamster: male, fasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (108)

**Type** : LC50  
**Species** : hamster  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Exposure time** : 4 hour(s)  
**Value** : = 1.8 mg/l  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Hamster: female, fasted  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (108)

### 5.1.3 ACUTE DERMAL TOXICITY

**5.1.4 ACUTE TOXICITY, OTHER ROUTES**

**Type** : LC50  
**Species** :  
**Strain** :  
**Sex** :  
**Number of animals** :  
**Vehicle** :  
**Route of admin.** :  
**Exposure time** :  
**Remark** : The LC50 for fasting rats could not be determined due to dose-response relationship.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 20.03.2002 (118) (96)

**5.2.1 SKIN IRRITATION**

**Species** : rabbit  
**Concentration** :  
**Exposure** :  
**Exposure time** :  
**Number of animals** :  
**PDII** :  
**Result** : irritating  
**EC classification** : irritating  
**Method** : other: BASF-Test  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 05.03.1993 (119)

**Species** : rabbit  
**Concentration** :  
**Exposure** :  
**Exposure time** :  
**Number of animals** :  
**PDII** :  
**Result** :  
**EC classification** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : There is no reliable information regarding the method. The boiling point of the substance is 31.7 0C. The irritating effect was possibly caused by the stabilizer (hydroquinone-monoethyl ether).  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 20.03.2002 (120)

**5.2.2 EYE IRRITATION**

**Species** : rabbit  
**Concentration** :

<b>Dose</b>	:	
<b>Exposure Time</b>	:	
<b>Comment</b>	:	
<b>Number of animals</b>	:	
<b>Result</b>	:	not irritating
<b>EC classification</b>	:	not irritating
<b>Method</b>	:	other: BASF-Test
<b>Year</b>	:	
<b>GLP</b>	:	no
<b>Test substance</b>	:	as prescribed by 1.1 - 1.4
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
05.03.1993		(119)
<b>Species</b>	:	rabbit
<b>Concentration</b>	:	
<b>Dose</b>	:	
<b>Exposure Time</b>	:	
<b>Comment</b>	:	
<b>Number of animals</b>	:	
<b>Result</b>	:	
<b>EC classification</b>	:	
<b>Method</b>	:	
<b>Year</b>	:	
<b>GLP</b>	:	
<b>Test substance</b>	:	
<b>Remark</b>	:	There is no reliable information regarding the method. The boiling point of the substance is 31.7 0C. The moderate irritating effect on the conjunctiva and reversible damage to the cornea is presumably caused by the stabilizer (hydroquinone monoethyl ether).
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
20.03.2002		(120)

**5.3 SENSITIZATION****5.4 REPEATED DOSE TOXICITY**

<b>Species</b>	:	rat
<b>Sex</b>	:	male/female
<b>Strain</b>	:	Sprague-Dawley
<b>Route of admin.</b>	:	inhalation
<b>Exposure period</b>	:	90 days
<b>Frequency of treatment</b>	:	6 hours/day; 5 days/week
<b>Post obs. period</b>	:	none
<b>Doses</b>	:	25, 75 ppm
<b>Control group</b>	:	yes, concurrent vehicle
<b>NOAEL</b>	:	< 25 ppm
<b>LOAEL</b>	:	= 25 ppm
<b>Method</b>	:	other
<b>Year</b>	:	1975
<b>GLP</b>	:	no
<b>Test substance</b>	:	other TS
<b>Method</b>	:	Groups of 20 male and female Sprague-Dawley rats (Spartan substrain) were exposed to vinylidene chloride (VDC) by inhalation for 90 days to assess toxicity of the subject test material. Rats were exposed to VDC concentrations of 25 and 75 ppm for 6 hours/day, 5 days/week. Exposures

were continued at these concentrations through the 90th day of the study after which the surviving animals were sacrificed.

Rats were exposed to the test material in 3.7 cubic meter stainless steel chambers under dynamic airflow conditions. VDC vapor, generated in a glass vaporization flask, was swept into the chamber by tempered, filtered air at a flowrate designed to produce the desired concentration. Analysis of chamber concentration was performed 2-3 times during each exposure period via IR spectrometry.

Animals were observed daily for signs of toxicity, with special attention given to signs of eye/nasal irritation. Body weights were recorded weekly for the first month of exposure, biweekly during the second month of exposure, and a minimum of monthly thereafter for the entire experimental period.

Clinical laboratory evaluations were conducted on animals sacrificed in interim evaluations (8/sex/dose at 30 days), as well as at study termination (12/sex/dose). Hematology tests conducted on blood collected from tail veins included red blood cell count, hemoglobin concentration, packed cell volume, and total and differential white blood cell counts. Urinalysis included determination of specific gravity, pH, glucose, protein, ketones, occult blood, bilirubin, and urobilinogen. Clinical chemistry determinations included SGPT, BUN, and AP.

All rats were submitted to a complete gross pathologic examination. A complete standard set of tissues was collected for each animal. Brain, heart, liver, kidneys, and testes were weighed. All tissues from the each animal in the control and high dose groups, as well as liver, kidneys, heart, lungs, trachea, spleen, thyroid gland, parathyroid gland, pituitary gland, adrenal glands, stomach, brain (cerebral cortex and cerebellum), and any grossly visible lesions were processed and examined histologically by light microscopy.

**Result** : There was no observable increase in mortality of rats of either sex attributable to VDC exposure. Likewise there were no clinical signs of toxicity observed in rats exposed to 25 or 75 ppm VDC during the 90 day exposure period. Clinical chemistry, hematology, urinalysis, body weight data and organ weights obtained at selected time intervals throughout the conduct of the study revealed no changes judged as a direct effect of the test material on these parameters or the function of the organ systems evaluated by them.

A target organ effect resultant from VDC exposure was observed in the liver of rats exposed to either 25 or 75 ppm VDC. This effect, characterized by a minimal increase in the degree of vacuolation in the cytoplasm of the hepatocytes, was observed in both male and female rats of both the 25 and 75 ppm exposure groups as early as the 30 day interim sacrifice in this study.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : Production grade vinylidene chloride from The Dow Chemical Company, Midland, MI. Minimum purity 99%, with hydroquinone monomethyl ether added as an inhibitor.

**Reliability** : (1) valid without restriction

04.06.2002

(96) (121) (122) (123)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 18 months

<b>Frequency of treatment</b>	: 6 hours/day and 5 days/week
<b>Post obs. period</b>	: 6 months
<b>Doses</b>	: 10, 40 ppm; after 5 weeks increased to 25 and 75 ppm, respectively
<b>Control group</b>	: yes, concurrent vehicle
<b>NOAEL</b>	: < 25 ppm
<b>LOAEL</b>	: = 25 ppm
<b>Method</b>	: other
<b>Year</b>	: 1982
<b>GLP</b>	: no
<b>Test substance</b>	: other TS
<b>Method</b>	: Groups of 103-104 male and female Sprague-Dawley rats (Spartan substrain) were exposed to vinylidene chloride (VDC) by inhalation for 18 months to assess chronic toxicity and oncogenic potential of the subject test material. Rats were exposed to VDC concentrations of 10 and 40 ppm for 6 hours/day, 5 days/week for the first 5 weeks of the study. Based upon the absence of observable treatment-related effects among rats sacrificed after one month of exposure, the exposure concentrations were increased to 25 and 75 ppm VDC. Exposures were continued at these concentrations through the 18th month of the study after which the surviving animals were held until 24 months and then sacrificed.
	<p>Rats were exposed to the test material in 3.7 cubic meter stainless steel chambers under dynamic airflow conditions. VDC vapor, generated in a glass vaporization flask, was swept into the chamber by tempered, filtered air at a flowrate designed to produce the desired concentration. Analysis of chamber concentration was performed 2-3 times during each exposure period via IR spectrometry.</p> <p>Animals were observed daily for signs of toxicity, with special attention given to signs of eye/nasal irritation. Body weights were recorded weekly for the first month of exposure, biweekly during the second month of exposure, and a minimum of monthly thereafter for the entire 24 month experimental period.</p> <p>Clinical laboratory evaluations were conducted on animals sacrificed in interim evaluations(5-10/sex/dose at 6 and 12 months), as well as at study termination (2-all/sex/dose). Hematology tests conducted on blood collected from tail veins included red blood cell count, hemoglobin concentration, packed cell volume, and total and differential white blood cell counts. Urinalysis included determination of specific gravity, pH, glucose, protein, ketones, occult blood, bilirubin, and urobilinogen. Clinical chemistry determinations included SGPT, BUN, and AP. Cytogenetic evaluation for chromosomal abberations was also conducted on 4 rats/sex/dose.</p> <p>All rats were submitted to a complete gross pathologic examination. A complete standard set of tissues was collected for each animal. Brain, heart, liver, kidneys, and testes were weighed. All tissues from the each animal in the control and high dose groups, as well as liver, kidneys, heart, lungs, trachea, spleen, thyroid gland, parathyroid gland, pituitary gland, adrenal glands, stomach, brain (cerebral cortex and cerebellum), and any grossly visible lesions suggestive of possible neoplastic process, were processed and examined histologically by light microscopy.</p>
<b>Result</b>	: There was no observable increase in mortality of rats of either sex attributable to VDC exposure. Likewise there were no clinical signs of toxicity observed in rats exposed to 25 or 75 ppm VDC during the 18 month exposure period. Clinical chemistry, hematology, urinalysis, body weight data and organ weights obtained at selected time intervals throughout the conduct of the study revealed no changes judged as a direct effect of the test material on these parameters or the function of the organ systems evaluated by them.

Cytogenetic evaluation of bone marrow preparations from rats of both sexes exposed to 0, 25 or 75 ppm VDC for 6 months did not reveal chromosomal aberrations in either the control or treated animals. A target organ effect resultant from VDC exposure was observed in the liver of rats exposed to either 25 or 75 ppm VDC. This effect, characterized by hepatocellular fatty change in the midzonal region of the hepatic lobule, was observed in both male and female rats of both the 25 and 75 ppm exposure groups as early as the 6 month interim sacrifice in this study. The midzonal fatty change was also observed at the 12 month sacrifice but no indication of progression of this lesion in either severity or incidence was apparent. During the last 6 months of the study, after exposures had been discontinued, this effect was no longer discernible; therefore this alteration was minimal in severity and readily reversible.

Although the incidence of several tumors and/or tumor types was found to be statistically increased or decreased in VDC exposed rats when compared to their respective control groups, none of these differences were judged to be attributable to VDC exposure. The observed absence of tumorigenic potential of VDC in rats is consistent with the findings of other investigators.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Production grade vinylidene chloride from The Dow Chemical Company, Midland, MI. Minimum purity 99%, with hydroquinone monomethyl ether added as an inhibitor.  
**Attached doc.** : VDC 2 Year Rat Inhalation Study Tables.pdf  
**Reliability** : (1) valid without restriction  
 04.06.2002 (124) (96) (125) (126) (127) (123)

**Species** : rat  
**Sex** : no data  
**Strain** : other: Long Evans or Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 90 days  
**Frequency of treatment** : Continuous or repeated  
**Post obs. period** :  
**Doses** : 20, 61, 101, 189 mg/m<sup>3</sup> (continuous); 395 mg/m<sup>3</sup> (repeated)  
**Control group** : yes, concurrent vehicle  
**NOAEL** : = 395 mg/m<sup>3</sup>?  
**Method** : other  
**Year** : 1967  
**GLP** : no  
**Test substance** : other TS  
**Method** : VDC vapor was metered into inhalation chambers (Fultyn, 1961) and diluted via a high pressure airstream to the desired concentration. Chamber concentrations were monitored continuously via IR spectrometry, gas chromatography, or chemical analysis.

Groups of 45 (low dose group) or 15 (remaining dose groups) rats were exposed to 20-189 mg/m<sup>3</sup> VDC continuously for 90 days or 395 mg/m<sup>3</sup> 8 hours/day for 6 weeks. Body weights were collected monthly. Total and differential leukocyte counts, hemoglobin concentration, and microhematocrits were obtained on all animals before and after exposure. Biochemical analyses conducted included assays for NADH, NADPH, SDH, LDH, ICD, G6PD, B-OHBD, AP, SGPOT, BUN, and liver lipid levels. All animals were routinely observed for signs of toxicity.

At study termination, a necropsy examination was performed on each animal, and sections of heart, lung, liver, spleen, and kidney were collected for histologic examination.

**Remark** : NOEL: Incomplete data in secondary source (ECETOC JACC No.5, 1985)

**Result** : Repeated exposure (30 exposures, 8 hours/day, 5 days/week): no mortality, signs of systemic toxicity or gross or histopathological changes. Other secondary source cites high incidence of pulmonary congestion (Environ. Health Criteria Vinylidene Chloride, 1990).  
Continuous exposure: Hepatotoxicity occurred at 189 mg/m<sup>3</sup>: fatty liver, focal necroses, haemosiderosis, lymphocyte infiltration, bile duct proliferation and fibrosis. Nuclear hypertrophy of the tubular epithelial cells of the kidney in all animals was apparent. AP and SGPT was elevated as compared to controls. In addition, body weight gain was decreased.  
Two rats died at 20 mg/m<sup>3</sup>. No other significant treatment-related changes were noted at the lower dose levels.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Uninhibited VDC with a minimum purity of 98%.  
**Attached doc.** : VDC 90 Day Rat Inhalation Tables.pdf  
**Reliability** : (2) valid with restrictions  
No reproductive organs were evaluated.

04.06.2002

(88) (96) (128)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : 90 days  
**Frequency of treatment** : daily  
**Post obs. period** :  
**Doses** : 60, 100 and 200 ppm  
**Control group** : yes, concurrent vehicle  
**NOAEL** : = 100 ppm  
**LOAEL** : = 200 ppm  
**Method** : other  
**Year** : 1975  
**GLP** : no  
**Test substance** : other TS  
**Method** : Analysis of Drinking Water: Samples of drinking water were analyzed via gas chromatography for VDC 16 times. The mean of the samples for each dose group were as follows:

Nominal Dose (ppm)	Analytical Mean Dose (ppm)
60	68+/-13
100	106+/-22
200	220+/-35

**General Design:**

Animals: Sprague-Dawley, Spartan substrain, SPF-derived rats 6-7 weeks of age were randomly divided by sex into treatment groups of 10. These rats were continued into the 2-year study, and rats used for the f0 generation of the concurrent reproduction study which were returned to the 2-year study once mating/gestation/lactation was completed. Additional groups of 8 rats/treatment group were added for sulfhydryl determinations. Rats were housed 2/cage in wire-bottom cages. Food (commercially available chow) and water (city tap water) were available ad libitum. Water was supplied from glass bottles with specially designed plastic screw caps fitted with stainless steel sipper tubes with stainless steel balls. The bottles were emptied and refilled each day from freshly prepared stock solutions. Because of the volatility of VDC, solutions were made up to exceed the nominal concentration, so that mean levels over 24 hours would be as near as possible to nominal concentrations.

Observations: Rats were observed at least twice weekly for signs of toxicity. Food consumption was recorded twice weekly. Water consumption was determined on 14 of the first 29 days on study and twice weekly for the remainder. Body weights were recorded weekly.

Clinical Studies: Clinical studies were conducted on blood collected via orbital sinus puncture on 5 rats/sex/dose on test days 30 and 86. Samples were also collected via decapitation at necropsy on day 90 from 10 rats/sex/dose for all groups.

Hematological parameters collected included packed cell volume, erythrocyte count, hemoglobin concentration, total and differential leukocyte counts (test day 181 samples only). Urine analysis was conducted on the same animals chosen for hematological analysis, and included specific gravity, pH, sugar, protein, ketones, occult blood, and bilirubin. Clinical parameters recorded included BUN, AP, SGPT, and glucose concentration. Non-protein free sulfhydryl content was measured in the livers and kidneys of 2 rats/sex/group killed on days 1, 3, 9, and 31, and 2 of the 10 rats/sex/group at necropsy.

Necropsy and Pathology: For all animals, a complete necropsy examination was performed and tissues preserved in 10% formalin. Histological examination was also performed on a standard set of tissues from all animals from controls and high dose. Selected target organs (liver and kidney) were examined from 5/sex/group for low and middle dose animals.

Rats were fasted overnight prior to necropsy. Rats were euthanized via decapitation after being weighed. Organ weights of brain, liver, kidney, heart and testes were recorded.

**Result** : There were no significant differences between the control group and the treated groups for the following parameters: appearance and demeanor, mortality, body weight, food consumption, water consumption, hematology, urinalysis, clinical chemistry determinations, non-protein free sulfhydryl content, organ weights, and organ-to-body weight ratios.

Gross pathologic examination and histopathologic observations showed both increases and decreases in the incidence of various nontumorous lesions in both sexes. Of the statistically significant deviations that were seen, only those affecting the liver were considered to be treatment-related. These lesions, visible only under microscopic examination, consisted of a minimal increase in cytoplasmic vacuolation of occasional individual hepatocytes for all males and most females given 200 ppm.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Commercial production sample from The Dow Chemical Company, Freeport, TX. Minimum purity 99.5%. Originally contained 180-220 ppm MEHQ as an inhibitor, but since VDC used to prepare various copolymers for food packaging is distilled to remove the inhibitor, these material used for the study was also distilled to decrease MEHQ to 1-5 ppm.

**Attached doc.** : VDC Rat Drinking Water Study Tables.pdf

**Reliability** : (1) valid without restriction

04.06.2002

(96) (121) (122) (123)

**Species** : rat  
**Sex** : male/female  
**Strain** : Fischer 344  
**Route of admin.** : gavage  
**Exposure period** : 90 days  
**Frequency of treatment** : 5 times/week  
**Post obs. period** : none

**Doses** : 0, 5, 15, 40, 100, 250 mg/kg/day  
**Control group** : yes, concurrent vehicle  
**NOAEL** : = 40 mg/kg bw  
**LOAEL** : = 100 ml/kg bw  
**Method** : EPA OTS 798.2650  
**Year** : 1982  
**GLP** : no data  
**Test substance** : other TS  
**Method** : Dosage Preparation: Appropriate amounts of VDC were weighed and then mixed with sufficient corn oil to give the desired concentrations. Rats received a dose volume of 5 ml/kg. The VDC-corn oil solutions were stored at 4 deg C for no longer than 7 days. Stability of 1% VDC in corn oil was found to be 7 days at room temperature. Samples of dosing solutions were analyzed every 2 months.

**Animals:** Four-week old Fischer 344 rats from the NCI Frederick Cancer Research Institute, Frederick, MD, were observed for 5 weeks for the presence of parasites or other diseases, and then assigned to treatment groups according to a table of random numbers. Rats were housed 5/cage in solid bottom polycarbonate cages covered with spun bonded fiberglass filter sheets and supplied with hardwood chip bedding. Cages and bedding were changed 2x/week. Diets of Wayne Lab Blox and tap water via an Edstrom automatic watering system were provided ad libitum. Feed hoppers were changed 1x/week.

**Treatment Groups:** Groups of 10 rats/sex/dose were given VDC in corn oil via gavage 5 days/week for 13 weeks. Vehicle control groups received corn oil alone. After 90 days, rats were killed using carbon dioxide and necropsied.

**Pathology:** A standard set of tissues was collected from each animal at the control and 250 mg/kg/day levels and examined microscopically. In addition, livers from rats in all other dose groups were examined microscopically.

**Result** : Three female rats receiving 250 mg/kg/day died during the first week of study. No other rats died.

Weight gain was depressed 20% for male rats receiving 250 mg/kg/day, when compared with controls. Severe centrilobular necrosis of the liver was seen in the 3 females that died. All other rats receiving 250 mg/kg/day had minimal to moderate hepatocytomegaly. Lesser degrees of the hepatocytomegaly were seen at 100 mg/kg/day.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : VDC (99% purity) was obtained in 2 batches from The Dow Chemical Company, Freeport, TX.

**Reliability** : (1) valid without restriction  
 02.08.2002

(129)

**Species** : mouse  
**Sex** : male/female  
**Strain** : B6C3F1  
**Route of admin.** : gavage  
**Exposure period** : 90 days  
**Frequency of treatment** : 5 times/week  
**Post obs. period** : none  
**Doses** : 0, 5, 15, 40, 100, 250 mg/kg/day  
**Control group** : yes, concurrent vehicle  
**NOAEL** : < 5 mg/kg bw  
**LOAEL** : = 5 mg/kg bw  
**Method** : EPA OTS 798.2650  
**Year** : 1982

**GLP** : no data  
**Test substance** : other TS  
**Method** : Dosage Preparation: Appropriate amounts of VDC were weighed and then mixed with sufficient corn oil to give the desired concentrations. Mice received a dose volume of 10 ml/kg. The VDC-corn oil solutions were stored at 4 deg C for no longer than 7 days. Stability of 1% VDC in corn oil was found to be 7 days at room temperature. Samples of dosing solutions were analyzed every 2 months.

Animals: Four-week old B6C3F1 mice from the NCI Frederick Cancer Research Institute, Frederick, MD, were observed for 5 weeks for the presence of parasites or other diseases, and then assigned to treatment groups according to a table of random numbers. Mice were housed 5/cage in solid bottom polycarbonate cages covered with spun bonded fiberglass filter sheets and supplied with hardwood chip bedding. Cages and bedding were changed 2x/week. Diets of Wayne Lab Blox and tap water via an Edstrom automatic watering system were provided ad libitum. Feed hoppers were changed 1x/week.

Treatment Groups: Groups of 10 mice/sex/dose were given VDC in corn oil via gavage 5 days/week for 13 weeks. Vehicle control groups received corn oil alone. After 90 days, mice were killed using carbon dioxide and necropsied.

Pathology: A standard set of tissues was collected from each animal at the control and 250 mg/kg/day levels and examined microscopically. In addition, livers from mice in all other dose groups were examined microscopically.

**Result** : All male mice receiving 250 mg/kg/day died within 24 hours; 9/10 females at the same dose died within 48 hours. Deaths occurred in 1 female at 5 mg/kg/day, 1 female at 15 mg/kg/day, 1 male at 40 mg/kg/day, and 2 males and 3 females at 100 mg/kg/day.

Weight gain was depressed in a dose-related fashion for male mice. Centrilobular necrosis, hemorrhage, and congestion of the liver were observed in the males and females that died at 250 mg/kg/day. Cellular atypia of the liver was seen in most mice at 100 mg/kg/day, but not in mice at 250 mg/kg/day. At 40, 15, and 5 mg/kg/day, the severity of the hepatic lesions was dose-related. The incidence of hepatic lesions in males was dose-related and higher than that in females. The most frequently encountered change at 40 mg/kg/day was slight to moderate fatty metamorphosis.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : VDC (99% purity) was obtained in 2 batches from The Dow Chemical Company, Freeport, TX.

04.06.2002

(129)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 52 weeks  
**Frequency of treatment** : 4 hours/day and 4-5 days/week  
**Post obs. period** :  
**Doses** : 0.040; 0.1; 0.2; 0.4; 0.6 and 0.8 mg/l  
**Control group** :  
**Result** : Histopathological liver changes (vacuolization, swelling, fatty degeneration and necrosis) were increased, compared to the control, at doses of 0.6 and 0.8 mg/l. The highest tolerated concentration for a long-term exposure in rats was reported as 0.6 mg/l.

**Source** : BASF AG Ludwigshafen

## 5. Toxicity

Id 75-35-4  
Date 14.08.2002

20.03.2002 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
(96) (130)

**Species** : rat  
**Sex** : male/female  
**Strain** : other: CD  
**Route of admin.** : inhalation  
**Exposure period** : 12 months  
**Frequency of treatment** : 6 hours/day and 5 days/week  
**Post obs. period** : 12 months  
**Doses** : 0.22 mg/l  
**Control group** :  
**Result** : Numerous measured parameters remained unaffected. The liver changes in the treatment group were described histopathologically as "mild to markedly severe focal disseminated vacuolization".

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
20.03.2002 (96) (131)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 6 weeks  
**Frequency of treatment** : 5 times/week for 6 hours  
**Post obs. period** : no  
**Doses** : 0.120 and 0.403 mg/l air  
**Control group** : yes, concurrent no treatment  
**NOAEL** : .12 mg/l  
**Method** :  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : 0.403 mg/l: Small impairment of body weight development in male animals. There were changes in clinical chemical parameters (increases in inorganic phosphate, glucose, total lipids and alkaline phosphatase), which however in part showed in only one animal. The absolute and relative kidney weights were increased, as was the relative liver weight (only female animals). The histopathological examinations showed numerous desquamated epithelial cells and detritus in the different kidney segments.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.06.2002 (132)

**Species** : rat  
**Sex** : male/female  
**Strain** : other: Alderley Park  
**Route of admin.** : inhalation  
**Exposure period** : 20 days  
**Frequency of treatment** : 6 hours/day  
**Post obs. period** :  
**Doses** : 0.2 and 0.8 mg/l air  
**Control group** :  
**Result** : 0.2 mg/l: Nose irritation and liver cell degeneration. 0.8 mg/l: Only minor nose irritation. Secondary source (ECETOC, JACC No.5, 1985) points to other studies in which the toxicity at comparable doses was considerably

## 5. Toxicity

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**Source** : more pronounced.  
: BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
21.03.2002 (88) (96) (133)

**Species** : rat  
**Sex** :  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 28 days  
**Frequency of treatment** : 4 hours/day; 4-5 days/week  
**Post obs. period** :  
**Doses** : 0.04 - 0.8 mg/l air  
**Control group** :  
**Result** : The highest dose rate had to be reduced to 0.6 mg/l due to pronounced toxicity. Liver and kidneys were the main target organs. In the comparative study the toxicity of different species and strains was described as follows in decreasing sequence: Swiss mouse > Balb/c mouse > C3H mouse > C57Bl mouse > rat, where the also tested hamster was not classified. With the exception of C3H mice, female animals reacted less sensitively.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
21.03.2002 (96) (134)

**Species** : rat  
**Sex** : male  
**Strain** : no data  
**Route of admin.** : inhalation  
**Exposure period** : 6 hours single treatment  
**Frequency of treatment** :  
**Post obs. period** : no data  
**Doses** : 10 ppm (8 mg/kg bw)  
**Control group** : yes, concurrent no treatment  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Result** : Only DNA turnover in liver and kidneys were determined, 48 hours after exposure 3H-TdR was injected and 4 hours later DNA turnover was determined. In the rat kidney turnover was 2.2 times the control value and in the liver turnover rate was less than that in controls.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Test substance** : 1,1 dichloroethylene was obtained from New England Nuclear with a purity of 99%.

04.04.1997 (135)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : 2 years  
**Frequency of treatment** :  
**Post obs. period** :  
**Doses** : 7; 10; 20 (male animals) and 9;14; 30 mg/kg bw (female animals)  
**Control group** :  
**Result** : Indications of minor hepatotoxicity in all dose groups in female animals and at 20 mg/kg for male animals were the only toxic effects observed.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
21.03.2002 (124) (96) (136) (126) (127)

**Species** : rat  
**Sex** : male/female  
**Strain** : other: F-344/N  
**Route of admin.** : gavage  
**Exposure period** : 104 weeks  
**Frequency of treatment** : 5 times/week  
**Post obs. period** :  
**Doses** : 1; 5 mg/kg bw in corn oil  
**Control group** : yes, concurrent vehicle  
**Result** : The only finding reported is kidney toxicity, which however is not more clearly specified.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
21.03.2002 (124) (137)

**Species** : rat  
**Sex** : male  
**Strain** : Wistar  
**Route of admin.** : gavage  
**Exposure period** : 4 weeks  
**Frequency of treatment** : 2 times/week  
**Post obs. period** :  
**Doses** : 125 (2 weeks) subsequently 200 mg/kg bw  
**Control group** :  
**Result** : Minor increase in sorbitol-dehydrogenase and aminotransferase is indicative of a hepatotoxicity. The additional administration of ethanol (5% in drinking water) increased the toxicity. A total of 6 out of 10 animals died at the high dose level. The simultaneous administration of dithiocarb and (+) catechol with VDC reduced the toxicity, so that no mortality occurred.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.06.2002 (96) (138)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : gavage  
**Exposure period** : 28 days  
**Frequency of treatment** : daily  
**Post obs. period** :  
**Doses** : 0,5; 5; 10; 20 mg/kg BW  
**Control group** : yes, concurrent no treatment  
**Result** : No mortality or clinical symptoms.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
21.03.2002 (96) (134)

**Species** : rat  
**Sex** : male/female  
**Strain** : other: BDIV  
**Route of admin.** : oral unspecified  
**Exposure period** : single in utero exposure on the 17th day of pregnancy and to 120 weeks postpartum  
**Frequency of treatment** : weekly

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**Date** 14.08.2002

**Post obs. period** :  
**Doses** : 50 mg/kg  
**Control group** :  
**Result** : Liver and kidney reported as target organs.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.06.2002 (96) (100)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : other: gastric feeding tube  
**Exposure period** : 52 weeks  
**Frequency of treatment** : 4-5 days/week  
**Post obs. period** : 95 weeks (0.5 mg/kg bw only 84 weeks)  
**Doses** : 0,5; 5; 10; 20 mg/kg bw  
**Control group** :  
**Result** : Secondary source (Env. Health Criteria Vinylidene Chloride, 1990) cites result as follows:  
"Hepatocyte vacuolization, cloudy swelling, fatty degeneration, necrobiosis and necrosis were found in some animals in treated as well as in control groups."  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
21.03.2002 (96) (130)

**Species** : mouse  
**Sex** : male/female  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : maximum 6 months  
**Frequency of treatment** : 6 hours/day and 5 days/week  
**Post obs. period** : 12 months  
**Doses** : 0.2 mg/l  
**Control group** : yes, concurrent no treatment  
**Result** : Compared to the control (11/56) the mortality after 6 months was increased in mice (11/24). Histopathological changes were not observed.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
21.03.2002 (96) (139)

**Species** : mouse  
**Sex** : male/female  
**Strain** : other: CD  
**Route of admin.** : inhalation  
**Exposure period** : 12 months  
**Frequency of treatment** : 6 hours/day and 5 days/week  
**Post obs. period** :  
**Doses** : 0.220 mg/l  
**Control group** :  
**Result** : Numerous measured parameters remained unaffected. Only from the 6 months-interval between sacrifices on, to the end of the experiment, liver damage was histopathologically described as "enlarged and basophilic hepatocytes with enlarged nuclei, focal degeneration and necrosis".  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

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(96) (131)

**Species** : mouse  
**Sex** : male/female  
**Strain** : Swiss Webster  
**Route of admin.** : inhalation  
**Exposure period** : from 6 hours to 8 days  
**Frequency of treatment** :  
**Post obs. period** :  
**Doses** : 0.04 and 0.2 mg/l air  
**Control group** :  
**Method** :  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Result** : In this experiment the toxicity to the mice strains mentioned above, was compared to male Sprague-Dawley rats (0.2 mg/l air), with numerous enzyme parameters (mono-oxygenase, epoxyde hydrolase, glutathion transferase) measured. A dose of 0.2 mg/l was lethal to male mice, but not to female mice or rats. Numerous enzyme parameters were changed. We should point out a decrease in the activity of cytosolic glutathione transferase in the kidneys of male mice, an organ in which tumors were observed in the male animals of this species. In female animals or rats the enzyme activity was not lowered. An effect on carcinogenesis is considered possible.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

04.06.2002

(140) (141)

**Species** : mouse  
**Sex** :  
**Strain** : Swiss  
**Route of admin.** : inhalation  
**Exposure period** : 28 days  
**Frequency of treatment** : 4 hours/day; 4-5 days/week  
**Post obs. period** :  
**Doses** : 0.04 - 0.8 mg/l air  
**Control group** :  
**Result** : The exposure duration had to be shortened at 0.2 mg/l and greater because of marked toxicity. Liver and kidneys were the main target organs. In the comparative study, the toxicity of various species and strains was rated as follows, in decreasing order: Swiss mouse > Balb/c mouse > C3H mouse > C57B1 mouse > rat, where the also tested hamster was not classified. With the exception of C3H mice, female animals reacted less sensitively.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

21.03.2002

(96) (134)

**Species** : mouse  
**Sex** :  
**Strain** : C3H  
**Route of admin.** : inhalation  
**Exposure period** : 28 days  
**Frequency of treatment** : 4 hours/day; 4-5 days/week  
**Post obs. period** :  
**Doses** : 0.04 - 0.8 mg/l air  
**Control group** :  
**Result** : The exposure duration had to be shortened at 0.6 mg/l

- and greater because of marked toxicity. Liver and kidneys were the main target organs. In the comparative study, the toxicity of various species and strains was rated as follows, in decreasing order: Swiss mouse > Balb/c mouse > C3H mouse > C57B1 mouse > rat, where the also tested hamster was not classified. With the exception of C3H mice, female animals reacted less sensitively.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.06.2002 (96) (142)
- Species** : mouse  
**Sex** :  
**Strain** : C57BL  
**Route of admin.** : inhalation  
**Exposure period** : 28 days  
**Frequency of treatment** : 4 hours/day; 4-5 days/week  
**Post obs. period** :  
**Doses** : 0.6-0.8 mg/l air  
**Control group** :  
**Result** : The exposure duration had to be shortened at 0.6 mg/l and greater because of marked toxicity. Liver and kidneys were the main target organs. In the comparative study, the toxicity of various species and strains was rated as follows, in decreasing order: Swiss mouse > Balb/c mouse > C3H mouse > C57B1 mouse > rat, where the also tested hamster was not classified. With the exception of C3H mice, female animals reacted less sensitively.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (96) (142)
- Species** : mouse  
**Sex** : male/female  
**Strain** : other  
**Route of admin.** : inhalation  
**Exposure period** : 2 weeks  
**Frequency of treatment** : 6 hours/day for 5 days/week  
**Post obs. period** :  
**Doses** : 0.22; 0.4; 0.8 mg/l  
**Control group** :  
**Remark** : Strains: Ha(ICR); CD-1; CF-W; B6C3F1  
**Result** : The toxicity was clearly different for the different strains and in terms of gender. Only the highest dose was lethal. Except for B6C3F1 mice, the female animals reacted less sensitively. The assumed cause of death was kidney toxicity in the male animals, based on macroscopic and histopathological studies, while for female mice (Ha(ICR) and B6C3F1) a hepatotoxic event was assumed as cause of death. CF-W mice (a strain derived from the Swiss Webster mouse, which is genetically related and supposed to be comparable to the Swiss mouse used by Maltoni in cancerogenicity studies) (Environ. Health Criteria Vinylidene Chloride, 1990).
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (96) (143)
- Species** : mouse  
**Sex** : male/female  
**Strain** : Swiss Webster  
**Route of admin.** : inhalation  
**Exposure period** : 4 hours

## 5. Toxicity

Id 75-35-4  
Date 14.08.2002

**Frequency of treatment** : s. above  
**Post obs. period** : 2 days  
**Doses** : 47 to 73 ppm (44 to 68.5 mg/kg bw )  
**Control group** : yes, concurrent no treatment  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Result** : Each group consisted of 5 animals, one female group were pretreated with 1.15 µmol/kg bw testosterone enantate. Pathological examination (48 hours after treatment): massive proximal tubular necrosis in kidneys of exposed male mice and of exposed and pretreated (testosterone) female mice. Urinary excretion of glucose, protein and gamma-glutamyl transpeptidase were significantly higher resp. lower (gamma-GTP) (p< 0.01) compared with control in 2 male groups (47, and 73 ppm exposure) and in the testosterone pretreated female group. The changes in these parameters were marked. No significant changes in these parameters occurred in untreated female mice.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : 1,1 dichloroethylene was purchased from Merck, no further data

02.08.2002

(144)

**Species** : mouse  
**Sex** : male  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : 6 hours, single treatment  
**Frequency of treatment** :  
**Post obs. period** : 8 days  
**Doses** : 10 and 50 ppm (resp. 17 and 85 mg/kg bw)  
**Control group** : yes, concurrent no treatment  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS

**Result** : Treatment related effects were seen in the kidneys: after 0 hour, 50 ppm: toxic nephrosis, after 8 and 24 hours: processing nephrosis, after 96 hours: regeneration apparent and after 8 days regeneration continuing. 10 ppm: 0 hour: slight dilation, swelling, after 96 hours: nephrosis variable 0-20% affected. In the liver at 10 and 50 ppm only minimal changes: slight centrilobular swelling. DNA turnover, kidneys, 48 hours after treatment injection of<sup>3</sup>H-TdR, 4 hours later examination: 50 ppm, 25 fold increase in the rate; 10 ppm 8 fold increase of the rate. Liver: 50 ppm: 2.4 fold increase; 10 ppm: 1.2 fold increase.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : 1,1 dichloroethylene was obtained from New England Nuclear with a purity of 99%.

06.04.1997

(135)

**Species** : mouse  
**Sex** : male/female

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

**Strain** : B6C3F1  
**Route of admin.** : gavage  
**Exposure period** :  
**Frequency of treatment** :  
**Post obs. period** :  
**Doses** : 2; 10 mg/kg bw in corn oil  
**Control group** : yes, concurrent vehicle  
**Result** : Liver necroses occurred at 2 and 10 mg/kg bw, but there were deficiencies in the conduct of the study that limit the validity of the study.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (124) (137)

**Species** : mouse  
**Sex** : male  
**Strain** : Swiss  
**Route of admin.** : gavage  
**Exposure period** : single dose  
**Frequency of treatment** :  
**Post obs. period** : 8 hours  
**Doses** : 200 mg/kg bw  
**Control group** : yes  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Remark** : 10 mice in each group were used. 8 hours after administration of 1,1 dichloroethylene the animals were killed and the kidneys were examined. DCE was diluted with corn oil.

**Result** : 50% of the proximal tubules of the kidneys were damaged after oral treatment with DCE.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : 1,1 dichloroethylene was purchased from Merck.  
02.04.1997 (145)

**Species** : mouse  
**Sex** : male/female  
**Strain** : B6C3F1  
**Route of admin.** : i.p.  
**Exposure period** : single dose  
**Frequency of treatment** :  
**Post obs. period** : up to 72 hours  
**Doses** : 5, 25, 50, 200 and 400 mg/kg bw  
**Control group** : yes  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Remark** : Each 4 mice, male were given 5, 20 and 50 mg/kg bw DCE and histopathologically examined. Female mice were given 200 mg/kg bw and examined as described. 400 mg/kg bw DCE 14C were administered to mice and the grade of covalently binding of DCE in the kidneys were determined.

**Result** : In female mice given a single dose of 200 mg/kg bw DCE no

morphological changes were observed in the mucosa of the nasal passages, lung or in the liver 1 or 3 days following treatment.

In male mice given a dose of 25 or 50 mg/kg bw DCE a mild tubular dilatation of the S1 and S2 segments of the proximal tubules was present. No morphological changes occurred in the 5 mg/kg bw group.

Autoradiography of <sup>14</sup>C DCE (400 mg/kg bw) in male mice revealed a selective covalent binding of radioactivity in the proximal tubules, in the midzonal part of the liver lobules and in the mucosa of the respiratory tract. The grade of binding were determined 3 hours after treatment with DCE.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Test substance** : <sup>14</sup>C 1,1 dichloroethylene was obtained from Amersham UK with a purity of 98%, 1,1 dichloroethylene was obtained from Merck, no further data.

02.08.2002

(146)

**Species** : rabbit  
**Sex** :  
**Strain** : New Zealand white  
**Route of admin.** : inhalation  
**Exposure period** : 90 days  
**Frequency of treatment** : Continuous or repeated  
**Post obs. period** :  
**Doses** : 0.101 mg/l (continuous); 0.395 mg/l (repeated)  
**Control group** : yes, concurrent no treatment  
**Remark** : NOEL: Incomplete information in secondary source (ECETOC JACC No.5, 1985)  
**Result** : Multiple exposures (30 exposures in 5-day/weeks at 8 hours each): no fatalities, systemic toxicity and histopathological changes. Other secondary source cites high incidence of pulmonary congestion (Environ. Health Criteria Vinylidene Chloride, 1990).  
Continuous exposure: considered not very relevant to workplace questions (8 hours/day at 5 day/week). (Environ. Health Criteria Vinylidene Chloride, 1990; ECETOC, JACC No.5, 1985). Hepatotoxicity occurred at 0.189 mg/l: fatty liver, focal necroses, haemosiderosis, lymphocyte infiltration, bile duct proliferation and fibrosis. According to secondary source, the findings in the lower dose rates were not substance-related (ECETOC, JACC No.5, 1985).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

22.03.2002

(88) (96) (147)

**Species** : rabbit  
**Sex** :  
**Strain** :  
**Route of admin.** : inhalation  
**Exposure period** : 4 months  
**Frequency of treatment** : 3 hours/day  
**Post obs. period** :  
**Doses** : 0.5 - 2 mg/l air  
**Control group** :  
**Result** : Bronchitis and degenerative changes in liver and kidneys.

- Source** : Increased proliferation rate in lymphatic tissue and spleen.  
: BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (96) (148)
- Species** : Chinese hamster  
**Sex** : male/female  
**Strain** :  
**Route of admin.** : inhalation  
**Exposure period** : 52 weeks  
**Frequency of treatment** : 4 hours/day and 4-5 days/week  
**Post obs. period** :  
**Doses** : 0.1 mg/l  
**Control group** :  
**Result** : No histopathological changes in animals that died spontaneously.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (96) (130)
- Species** : Chinese hamster  
**Sex** :  
**Strain** :  
**Route of admin.** : inhalation  
**Exposure period** : 28 days  
**Frequency of treatment** : 4 hours/day; 4-5 days/week  
**Post obs. period** :  
**Doses** : 0.1 mg/l air  
**Control group** :  
**Result** : Liver and kidneys were the main target organs. In the comparative study the toxicity of different species and strains was described as follows, in descending order: Swiss mouse > Balb/c mouse > C3H mouse > C57Bl mouse > rat, where the chinese hamster was not classified. With the exception of C3H mice, female animals reacted less sensitively.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
02.08.2002 (96) (134)
- Species** : dog  
**Sex** :  
**Strain** : Beagle  
**Route of admin.** : inhalation  
**Exposure period** : 90 days  
**Frequency of treatment** : continuous or repeated  
**Post obs. period** :  
**Doses** : 0.02; 0.061; 0.101; 0.189 mg/l (continuous) 0.395 mg/l (repeated)  
**Control group** : yes, concurrent no treatment  
**Remark** : NOEL: Incomplete information in secondary source (ECETOC JACC No.5, 1985)  
**Result** : Multiple exposures (30 exposures in 5-day/weeks) at 8 hours each): no fatalities, systemic toxicity and histopathological changes. Other secondary source cites high incidence of pulmonary congestion (Environ. Health Criteria Vinylidene Chloride, 1990). Continuous exposure: considered not very relevant to workplace questions (8 hours/day at 5 day/week). (Environ. Health Criteria Vinylidene Chloride, 1990;

		ECETOC, JACC No.5, 1985). Hepatotoxicity occurred at 0.189 mg/l: fatty liver, focal necroses, haemosiderosis, lymphocyte infiltration, bile duct proliferation and fibrosis. According to secondary source, the findings in the lower dose rates were not substance-related (ECETOC, JACC No.5, 1985).
<b>Source</b>	:	BASF AG Ludwigshafen
22.03.2002		EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) (88) (96) (147)
<b>Species</b>	:	dog
<b>Sex</b>	:	male/female
<b>Strain</b>	:	Beagle
<b>Route of admin.</b>	:	other: capsules
<b>Exposure period</b>	:	97 days
<b>Frequency of treatment</b>	:	daily
<b>Post obs. period</b>	:	
<b>Doses</b>	:	6.25; 12.5; 25 mg/kg bw in peanut oil
<b>Control group</b>	:	yes, concurrent no treatment
<b>Result</b>	:	No significant differences with untreated controls in terms of clinical symptoms, body weight and food consumption, hematological or clinical-chemical parameters and urine analysis. Also the organ weights were unaffected. A decrease in non-protein-bound SH groups in liver and kidneys was not observed.
<b>Source</b>	:	BASF AG Ludwigshafen
22.03.2002		EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) (124) (96) (136)
<b>Species</b>	:	guinea pig
<b>Sex</b>	:	
<b>Strain</b>	:	Hartley
<b>Route of admin.</b>	:	inhalation
<b>Exposure period</b>	:	90 days
<b>Frequency of treatment</b>	:	continuous or repeated
<b>Post obs. period</b>	:	
<b>Doses</b>	:	0.02;0.061;0.101;0.189 mg/l (continuous) 0.395 mg/l (repeated)
<b>Control group</b>	:	yes, concurrent no treatment
<b>Remark</b>	:	NOEL: Incomplete information in secondary source (ECETOC JACC No.5, 1985)
<b>Result</b>	:	Multiple exposures (30 exposures in 5-day/weeks) at 8 hours each): dose-dependent mortality, no systemic toxicity but histopathological changes in the liver (fatty degeneration and necrosis). Other secondary source cites high incidence of pulmonary congestion (Environ. Health Criteria Vinylidene Chloride, 1990). Continuous exposure: considered not very relevant to workplace questions (8 hours/day at 5 day/week). (Environ. Health Criteria Vinylidene Chloride, 1990; ECETOC, JACC No.5, 1985). Hepatotoxicity occurred at 0.189 mg/l: fatty liver, focal necroses, haemosiderosis, lymphocyte infiltration, bile duct proliferation and fibrosis. Also nuclear hypertrophia of the tubular epithelial cells of the kidney in all animals. According to secondary source, the findings in the lower dose rates were not substance-related (ECETOC, JACC No.5, 1985).
<b>Source</b>	:	BASF AG Ludwigshafen
22.03.2002		EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) (88) (96) (147)

**Species** : monkey  
**Sex** :  
**Strain** :  
**Route of admin.** : inhalation  
**Exposure period** : 90 days  
**Frequency of treatment** : continuous or repeated  
**Post obs. period** :  
**Doses** : 0.02; 0.061; 0.101; 0.189 mg/l (continuous) 0.395 mg/l (repeated)  
**Control group** : yes, concurrent no treatment  
**Remark** : NOEL: Incomplete information in secondary source (ECETOC JACC No.5, 1985)  
**Result** : Multiple exposures (30 exposures in 5-day/weeks) at 8 hours each): no fatalities, systemic toxicity and histopathological changes. Other secondary source cites high incidence of pulmonary congestion (Environ. Health Criteria Vinylidene Chloride, 1990).  
 Continuous exposure: considered not very relevant to workplace questions (8 hours/day at 5 days/week). (Environ. Health Criteria Vinylidene Chloride, 1990; ECETOC, JACC No.5, 1985). Hepatotoxicity occurred at 0.189 mg/l: fatty liver, focal necroses, haemosiderosis, lymphocyte infiltration, bile duct proliferation and fibrosis. According to secondary source, the findings in the lower dose rates were not substance-related (ECETOC, JACC No.5, 1985).  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 22.03.2002 (88) (96) (147)  
 04.06.2002  
 04.06.2002

### 5.5 GENETIC TOXICITY 'IN VITRO'

**Type** : Chromosomal aberration test  
**System of testing** : Chinese hamster lung fibroblast cell line  
**Concentration** : 0, 0.125, 0.25, 0.5, 1.0, 1.5 mg/ml  
**Cycotoxic conc.** : 2.0 mg/ml  
**Metabolic activation** : with and without  
**Result** : positive  
**Method** : other  
**Year** : 1987  
**GLP** : no data  
**Test substance** : other TS  
**Result** : VDC induced chromosomal aberrations in the presence of S9 activation, although its presumed metabolites did not induce aberrations either with or without S9 activation.  
**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Purchased from Aldrich Chemical Company, 99% purity.  
**Reliability** : (1) valid without restriction  
 22.03.2002 (149)  
**Type** : Sister chromatid exchange assay  
**System of testing** : Chinese hamster lung fibroblast line  
**Concentration** : 0, 0.025, 0.05, 0.075, 0.1 (with activation); 0, 0.025, 0.05, 0.2, 1.0 mg/ml (without activation)  
**Cycotoxic conc.** : 2.0 mg/ml

## 5. Toxicity

Id 75-35-4  
Date 14.08.2002

**Metabolic activation** : with and without  
**Result** : positive  
**Method** : other  
**Year** : 1987  
**GLP** : no data  
**Test substance** : other TS  
**Result** : VDC induced sister chromatid exchanges in the presence of S9 activation, although its presumed metabolites did not induce exchanges either with or without S9 activation.  
**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Purchased from Aldrich Chemical Company, 99% purity.  
**Reliability** : (1) valid without restriction  
22.03.2002 (149)

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA1535 TA1537 TA98 TA100 TA92 E. coli WP2 uvrA  
**Concentration** : 375 - 22500 ppm  
**Cycotoxic conc.** :  
**Metabolic activation** : with  
**Result** : positive  
**Method** : other: following Ames B.N. et al: Mutat.Res., 31, 347-364 (1975) Bartsch H. et al: Nature, 255, 641-643 (1975)  
**Year** :  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4  
**Remark** : Various formulations were tested:

a) S9 Mix mixed with NaDPH was mutagenic in decreasing order when using S9 mix with S9 Mix from mouse liver (Swiss and C 57 BL, both genders), and Chinese hamster liver > rat liver > human liver > kidneys of Chinese hamster > kidneys of male mice of both strains > kidneys of female mice and rats, with only occasional weak positive findings.  
b) The addition of epoxide hydrolase to the S9 Mix did not increase the frequency of mutations.  
c) In contrast, the addition of glutathion reduced it by approximately 50 %.  
d) The pretreatment by inhalation with VDC does not increase the frequency of mutation  
e) The different enzyme activities in the target tissues were discussed by the authors for the differentiated toxic and carcinogenic effects, for the various types of animals.  
The original report (BASF AG, 78/554 (1983), Oesch F. Et al, 1983) was published.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.06.2002 (140) (141)

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA100 TA1535  
**Concentration** : 0.2 - 20 % in air  
**Cycotoxic conc.** :  
**Metabolic activation** : with  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : Exposing the bacteria to an atmosphere with VDC. Metabolic activation by NADPH S9 Mix from OF-1 mice. TA100 was also positive after addition of S9 Mix from kidneys and lungs; here a mutagenic effect of the stabilizer (4-methoxy-phenol) was excluded. S9 Mix without NADPH addition was not mutagenic This proved the function of Cytochrom P 450 during

metabolic activation. The addition of S9 Mix for mice pretreated with phenobarbital (enzyme induction) led to an increase in the mutation rate. The addition of nucleophilic compounds (N-acetyl-cysteine and N-acetyl-methionine) reduced the mutagenic potential.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (150) (96)

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA100 TA1530  
**Concentration** : TA100 2 % in air; TA1530 2; 20 % in air  
**Cycotoxic conc.** :  
**Metabolic activation** : with  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : Metabolic activation by S9 Mix from the human liver and various animal species. Test batches with S9 Mix from human liver were mutagenic for TA 100, as was phenobarbital or 3-methyl-cholanthrene-induced S9 Mix from rat liver for TA 1530, where both compounds increased the mutation frequency up to 2-fold, compared to untreated S9 Mix. The opposite effect on the mutation frequency could be achieved with S9 Mix from rats pretreated with "alpha-carnonitrile, amino-acetonitrile, pregnenolone and disulfiram". The effective mechanism assumed was an accelerated detoxification of VDC or its metabolites. The mutation frequency of VDC when S9 Mix from diagnostic human liver specimens is used had approximately 1/5 the mutagenic activity of untreated S9 Mix mice for strain TA 100.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (151) (96)

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA1535  
**Concentration** : 5 % in air  
**Cycotoxic conc.** :  
**Metabolic activation** : with  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : Several different batches were tested during exposure to VDC. Weak positive results were obtained with S9 Mix from Alderley Park Swiss derived albino mice, where kidney homogenate had a stronger effect than liver homogenate.  
The induction of the animals with Arochlor reinforced the mutagenicity. With rat S9 Mix, positive results were observed only after pretreatment with Arochlor. Compared to similarly treated mice, here the mutation frequency was clearly lower.  
The use of S9 Mix from non-induced monkeys (marmoset) and man did not increase the mutation frequency. In contrast, for humans treated long-term with phenobarbital, the S9 Mix obtained from liver tissue was positive. Based on these results it was concluded that the strength of the metabolic activation in man was closer to that of rats than of mice.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.06.2002 (96) (152)

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA100  
**Concentration** : 2 % in air  
**Cycotoxic conc.** :  
**Metabolic activation** : with  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : The S9 Mix was mutagenic with or without phenobarbital induction from OF-1 mice (dose-dependent results regarding the exposure time with VDC): these results were confirmed in another study (Waskele L., 1978).  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 22.03.2002 (96) (153) (154)

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA1535 TA100  
**Concentration** : 1.6; 3 %  
**Cycotoxic conc.** :  
**Metabolic activation** : with  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : Secondary source (Environ. Health Criteria Vinylidene Chloride, 1990) cites "metabolically activated doses" as clearly positive.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 22.03.2002 (96) (155)

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA1950 TA1951 TA1952 TA1535 TA1538 TA100 TA98  
**Concentration** : 50 ul/plate einer 1; 10 oder 100 % Loesung  
**Cycotoxic conc.** :  
**Metabolic activation** : without  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : 100% VDC in 0.05 ml DMSO was mutagenic in the absence of S9 Mix.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 22.03.2002 (156) (96)

**Type** : Ames test  
**System of testing** : Salmonella typhimurium TA100  
**Concentration** :  
**Cycotoxic conc.** :  
**Metabolic activation** : with and without  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : S9 Mix from Arochlor-induced rats and man. The induction

with Arochlor increased the mutagenic activity.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 22.03.2002 (157) (158) (159) (96)

**Type** : Bacterial gene mutation assay  
**System of testing** : E. coli K12  
**Concentration** : 2.5 mmol/l  
**Cycotoxic conc.** :  
**Metabolic activation** :  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :

**Remark** : Mutagenic at a gene locus (retromutation). Not mutagenic at  
 2 other gene loci (retromutation). Not mutagenic at a gene locus (forward  
 mutation). Only one dose level was tested.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 22.03.2002 (96) (160)

**Type** : Cytogenetic assay  
**System of testing** : D6 Cells/Chinese hamster  
**Concentration** :  
**Cycotoxic conc.** :  
**Metabolic activation** : without  
**Result** : negative  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 22.03.2002 (101) (96) (102)

**Type** : Mouse lymphoma assay  
**System of testing** : L5178Y cells  
**Concentration** : 0.16, 4, 6, 8 and 15% v/v (40-603 mg/l)  
**Cycotoxic conc.** :  
**Metabolic activation** : with and without  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Result** : The lowest dose was 0.16% DCE where there was a 2fold  
 increase in mutant fraction and the RTG was 70%. Activation  
 did enhance both, cytotoxicity and mutagenicity of DCE.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Test substance** : 1,1 dichloroethylene was supplied from the NTP chemical  
 repository, Austin Texas, no further data

03.04.1997 (161)

**Type** : Sister chromatid exchange assay  
**System of testing** : CHO cells  
**Concentration** : 1.8 - 7 % in atmosphere  
**Cycotoxic conc.** :  
**Metabolic activation** :  
**Result** : negative

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : Dose-dependent increase in SCE rate.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (96) (155)

**Type** : Sister chromatid exchange assay  
**System of testing** : CHL cells of Chinese hamsters  
**Concentration** : 0 - 2 mg/l  
**Cytotoxic conc.** :  
**Metabolic activation** : with and without  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : S9 Mix from PCB-induced male Fischer 344 rats.  
Weakly statistically significantly increased SCE frequency  
in the test batch with metabolic activation. According to  
secondary source (Environ. Health Criteria Vinylidene  
Chloride, 1990) similar results were obtained during simultaneously  
performed chromosome analysis in vitro.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.06.2002 (96) (162)

**Type** : Unscheduled DNA synthesis  
**System of testing** : Hepatocytes from Long-Evans rats  
**Concentration** : 2.1 mmol /l  
**Cytotoxic conc.** :  
**Metabolic activation** : with  
**Result** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : A concentration of 2.1 mmol/l stimulated the unplanned  
DNS synthesis of hepatocytes obtained from  
phenobarbital-induced rats.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
22.03.2002 (163) (96)

**Type** : other: Ara test  
**System of testing** : Salmonella typhimurium BA 13  
**Concentration** : 10 to 40 ?mol/plate  
**Cytotoxic conc.** :  
**Metabolic activation** : with and without  
**Result** : ambiguous  
**Method** : other: according to Ruiz-Vazquez R. et al.: Mutation Research, 54, 121-129  
**Year** : 1978  
**GLP** : no data  
**Test substance** : other TS  
**Result** : No mutagenic effect was observed without S 9 mix.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Test substance** : 1,1 dichloroethylene was purchased from Fluka with a purity  
of 99.5%.

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

03.04.1997 (164)

**Type** : other: Host mediated assay  
**System of testing** : ICR Mouse (female) TA1590 TA1591 TA1592  
**Concentration** :  
**Cycotoxic conc.** :  
**Metabolic activation** :  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : The dosage reported was LD50 and 50% LD50, where the mutagenic effect as cited by the secondary source (Environ. Health Criteria Vinylidene Chloride WHO, 1990) was "inversely related to dose."  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

04.06.2002 (156) (96)

**Type** : other: Host mediated assay  
**System of testing** : Swiss albino CD mouse; yeast cells  
**Concentration** :  
**Cycotoxic conc.** :  
**Metabolic activation** :  
**Result** : positive  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : The experimental animals received VDC once (400 mg/kg) and in several doses (5 x 100 and 1 x 200 mg/kg). Positive results were obtained with yeast cells from the liver and kidneys. In contrast, yeast cells from the lung were not mutagenic.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

22.03.2002 (165) (96)

**Type** : other: Mitotic chromosome malsegregation  
**System of testing** : Aspergillus nidulans  
**Concentration** : 0.025 to 0.2 % vol/vol DMSO  
**Cycotoxic conc.** :  
**Metabolic activation** : without  
**Result** : positive  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Result** : At each concentration of 1,1 dichloroethylene chromosome malsegregation and mitotic growth arrest occurred. In the 4 highest dosed marked decrease in surviving of the mold occurred (0.125, -30%, 0.15, -50%, 0.175% - 59% and 0.2% -80%).  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Test substance** : 1,1 dichloroethylene was obtained from Aldrich with a purity of 99%.

02.04.1997 (166)

**Type** : other: Mutagenicity tests with yeast cells  
**System of testing** : Saccharomyces cerevisiae D7 and D61.M  
**Concentration** :

<b>Cycotoxic conc.</b>	:	
<b>Metabolic activation</b>	:	with and without
<b>Result</b>	:	positive
<b>Method</b>	:	
<b>Year</b>	:	
<b>GLP</b>	:	
<b>Test substance</b>	:	
<b>Remark</b>	:	Test procedure: Gene conversion, point mutation and aneuploidy in yeast cells. Positive results in the experiment with metabolic activation (S9 Mix from mice) on strain D7. For strain D61.M aneuploidy was described for the batch without metabolic activation.
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 22.03.2002 (167)
<b>Type</b>	:	other: Point mutation
<b>System of testing</b>	:	V 79 cells of Chinese hamsters
<b>Concentration</b>	:	
<b>Cycotoxic conc.</b>	:	
<b>Metabolic activation</b>	:	with
<b>Result</b>	:	negative
<b>Method</b>	:	
<b>Year</b>	:	
<b>GLP</b>	:	
<b>Test substance</b>	:	
<b>Remark</b>	:	Tested gene locus (8-azoguanine and ouabain) on V 79 cells. S9 Mix from rats and mice induced with phenobarbital were tested.
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 22.03.2002 (168) (96)
<b>Type</b>	:	other: Point mutation and mitotic gene conversion.
<b>System of testing</b>	:	Saccharomyces cerevisiae D7
<b>Concentration</b>	:	0 - 50 mmol/l
<b>Cycotoxic conc.</b>	:	
<b>Metabolic activation</b>	:	with and without
<b>Result</b>	:	positive
<b>Method</b>	:	
<b>Year</b>	:	
<b>GLP</b>	:	
<b>Test substance</b>	:	
<b>Remark</b>	:	With S9 Mix (Arochlor-induced mice) positive, without S9 Mix not mutagenic.
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 22.03.2002 (165) (96)
<b>Type</b>	:	other: according to Ames, but gaseous exposure
<b>System of testing</b>	:	E. coli WP2 uvrA , pKM 101
<b>Concentration</b>	:	0.05 and 0.1% (resp. 2 and 4 mg/l)
<b>Cycotoxic conc.</b>	:	
<b>Metabolic activation</b>	:	with and without
<b>Result</b>	:	ambiguous
<b>Method</b>	:	other
<b>Year</b>	:	
<b>GLP</b>	:	no data
<b>Test substance</b>	:	other TS
<b>Result</b>	:	No mutagenicity was observed for any strains without S9 mix! 2-3 fold increase of revertants after 48 hour compared with 1 hour exposure.
<b>Source</b>	:	BASF AG Ludwigshafen

EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : No further data about DCE (169)  
06.04.1997

**Type** : other: according to Ames, but plates were exposed to gaseous compound  
**System of testing** : Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538 and TA 2637

**Concentration** : 0.05 and 0.1%, presumable 500 and 1000 ppm; exposure time: 1, 3 and 48 hours

**Cycotoxic conc.** :  
**Metabolic activation** : with and without  
**Result** : ambiguous  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Result** : 1,1 dichloroethylene showed mutagenicity for the base pair type strains, but did not show mutagenicity for the frame shift type at 1 hour exposure. No mutagenicity were observed for any strains without S9 mix! 3 fold increase of revertants after 48 hour compared with 1 hour exposure.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : No further data about DCE (169)  
02.08.2002

## 5.6 GENETIC TOXICITY 'IN VIVO'

**Type** : Micronucleus assay  
**Species** : mouse  
**Sex** : male  
**Strain** : other: ddY, from Shizuoka Agricultural Co-op Assn.  
**Route of admin.** : gavage  
**Exposure period** : Once to 4 times  
**Doses** : 0 - 200 mg/kg  
**Result** : negative  
**Method** : other  
**Year** : 1987  
**GLP** : no data  
**Test substance** : other TS  
**Method** : Six mice were given either a single dose of 0, 25, 50, 100, or 200 mg VDC/kg or four daily doses of 0, 25, 50, or 100 mg VDC/kg in corn oil via oral gavage. Animals were killed by cervical dislocation 24 hrs after the last treatment, and femoral marrow cells were smeared, fixed with methanol and stained with 3% Giemsa. 1000 polychromatic erythrocytes (PCEs)/mouse were examined, and the number of micronucleated PCEs counted. The frequency of micronucleated normochromatic cells per 100 normochromatic cells was also recorded.

**Result** : Results: negative  
**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Purchased from Aldrich Chemical Company, Inc. 99% purity, with 200 ppm para-methoxyphenol as a stabilizer.

**Reliability** : (1) valid without restriction (96) (162)  
17.05.2002

**Type** : other: transplacental micronucleus assay  
**Species** : mouse  
**Sex** : female  
**Strain** : ICR

**Route of admin.** : i.p.  
**Exposure period** : single, on gestation day 18  
**Doses** : 0, 25, 50 and 100 mg/kg  
**Result** : negative  
**Method** : other  
**Year** : 1987  
**GLP** : no data  
**Test substance** : other TS  
**Method** : Pregnant mice were injected intraperitoneally with 0, 25, 50, or 100 mg VDC/kg on gestation day 18. 24 hrs after injection, fetal liver and fetal blood cells suspended in fetal calf serum were smeared and fixed with methanol. The cells were then stained with Acridine orange instead of Giemsa to distinguish micronuclei from RNA containing basophilic stippling that occasionally appeared in the fetal blood cells. 1000 erythrocytes emitting red fluorescence (which corresponds to PCEs in Giemsa staining) were observed per fetus and erythrocytes which emitted yellowish green fluorescence were scored.

**Result** : results: negative  
 No increased number of micronuclei in the fetal liver tissue or erythrocytes after single i.p. treatment of the maternal animals.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Purchased from Aldrich Chemical Company, Inc. 99% purity, with 200 ppm para-methoxyphenol as a stabilizer.

**Reliability** : (2) valid with restrictions  
 17.05.2002 (96) (162)

**Type** : Cytogenetic assay  
**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : 90 days  
**Doses** : 60, 100 and 200 ppm  
**Result** : negative  
**Method** : other  
**Year** : 1975  
**GLP** : no  
**Test substance** : other TS  
**Method** : Analysis of Drinking Water: Samples of drinking water were analyzed via gas chromatography for VDC 16 times. The mean of the samples for each dose group were as follows:

Nominal Dose (ppm)	Analytical Mean Dose (ppm)
60	68+/-13
100	106+/-22
200	220+/-35

**General Design:**

Animals: Sprague-Dawley, Spartan substrain, SPF-derived rats 6-7 weeks of age were randomly divided by sex into treatment groups of 10. These rats were continued into the 2-year study, and rats used for the f0 generation of the concurrent reproduction study which were returned to the 2-year study once mating/gestation/lactation was completed. Additional groups of 8 rats/treatment group were added for sulfhydryl determinations. Rats were housed 2/cage in wire-bottom cages. Food (commercially available chow) and water (city tap water) were available ad libitum. Water was supplied from glass bottles with specially designed plastic screw caps fitted with stainless steel sipper tubes with stainless steel balls. The bottles were emptied and refilled each day from freshly prepared stock solutions. Because of the volatility of VDC, solutions were made up to exceed the nominal concentration, so that mean levels over 24 hours would be as near

as possible to nominal concentrations.

Observations: Rats were observed at least twice weekly for signs of toxicity. Food consumption was recorded twice weekly. Water consumption was determined on 14 of the first 29 days on study and twice weekly for the remainder. Body weights were recorded weekly.

Clinical Studies: Clinical studies were conducted on blood collected via orbital sinus puncture on 5 rats/sex/dose on test days 30 and 86. Samples were also collected via decapitation at necropsy on day 90 from 10 rats/sex/dose for all groups.

Hematological parameters collected included packed cell volume, erythrocyte count, hemoglobin concentration, total and differential leukocyte counts (test day 181 samples only). Urine analysis was conducted on the same animals chosen for hematological analysis, and included specific gravity, pH, sugar, protein, ketones, occult blood, and bilirubin. Clinical parameters recorded included BUN, AP, SGPT, and glucose concentration. Non-protein free sulfhydryl content was measured in the livers and kidneys of 2 rats/sex/group killed on days 1, 3, 9, and 31, and 2 of the 10 rats/sex/group at necropsy.

Necropsy and Pathology: For all animals, a complete necropsy examination was performed and tissues preserved in 10% formalin. Histological examination was also performed on a standard set of tissues from all animals from controls and high dose. Selected target organs (liver and kidney) were examined from 5/sex/group for low and middle dose animals.

Rats were fasted overnight prior to necropsy. Rats were euthanized via decapitation after being weighed. Organ weights of brain, liver, kidney, heart and testes were recorded.

**Result** : There were no significant differences between the control group and the treated groups for the following parameters: appearance and demeanor, mortality, body weight, food consumption, water consumption, hematology, urinalysis, clinical chemistry determinations, non-protein free sulfhydryl content, organ weights, and organ-to-body weight ratios.

**Test substance** : Gross pathologic examination and histopathologic observations showed both increases and decreases in the incidence of various nontumorous lesions in both sexes. Of the statistically significant deviations that were seen, only those affecting the liver were considered to be treatment-related. These lesions, visible only under microscopic examination, consisted of a minimal increase in cytoplasmic vacuolation of occasional individual hepatocytes for all males and most females given 200 ppm.  
: Commercial production sample from The Dow Chemical Company, Freeport, TX. Minimum purity 99.5%. Originally contained 180-220 ppm MEHQ as an inhibitor, but since VDC used to prepare various copolymers for food packaging is distilled to remove the inhibitor, these material used for the study was also distilled to decrease MEHQ to 1-5 ppm.

**Attached doc.** : VDC 90 Day Rat Drinking Water Study Tables.pdf

**Reliability** : (1) valid without restriction

04.06.2002

(121) (122) (123)

**Type** : Dominant lethal assay

**Species** : rat

**Sex** : male

**Strain** : other: CD

**Route of admin.** : inhalation

**Exposure period** : 11 weeks with subsequent pairing

**Doses** : 0.22 mg/l (6 hours/day for 5 days/week)

**Result** :

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : Result: negative  
Pre and postimplantation loss was not affected.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
09.04.2002 (96) (170)

**Type** : Dominant lethal assay  
**Species** : mouse  
**Sex** : male  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : 5 days (6 hours/day)  
**Doses** : 0.04; 0.12 and 0.2 mg/l  
**Result** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : Result: negative  
The untreated female mice were examined 15 to 16 days after pairing with treated male mice,. At the highest dose level 14/20 animals died. At the intermediate dose, 2/20. There was no indication of a dominant lethal mutation. Pre- and postimplantation losses were not increased.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
09.04.2002 (171) (96)

**Type** : Drosophila SLRL test  
**Species** : Drosophila melanogaster  
**Sex** : male  
**Strain** : other: Canton S  
**Route of admin.** : other: feeding exposure and injection  
**Exposure period** : 3 days  
**Doses** : 5000 (injection) and 20000 and 25000 ppm (feeding)  
**Result** :  
**Method** : other: according to Woodruff et al. 1985  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Result** : Neither recessive lethals nor translocations occurred at both administration routes.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Test substance** : 1,1 dichloroethylene was obtained from E.M.I. with a purity of 98%.  
06.04.1997 (172)

**Type** : other: Chromosome analysis in vivo  
**Species** : rat  
**Sex** : male/female  
**Strain** :  
**Route of admin.** : inhalation  
**Exposure period** : 6 months  
**Doses** : 0, 0.1 and 0.3 mg/l  
**Result** :  
**Method** :  
**Year** :  
**GLP** :

**Test substance** :  
**Result** : Results: negative  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 09.04.2002 (96) (173)

**Type** : other: Chromosome analysis in vivo  
**Species** : mouse  
**Sex** : female  
**Strain** : ICR  
**Route of admin.** : i.p.  
**Exposure period** : Once or 5 times on sequential days  
**Doses** : See text  
**Result** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Remark** : Dose levels: The secondary source cites 1/2 the LD50  
 (single dose) or 1/6 of LD50 (multiple doses)

**Result** : Results: negative  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 09.04.2002 (156) (96)

**Type** : other: Chromosome analysis in vivo  
**Species** : mouse  
**Sex** :  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : 12 months (6 hours/day at 5 days/week)  
**Doses** : 0.22 mg/l  
**Result** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : Results: negative  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 09.04.2002 (96) (131)

**Type** : other: Chromosome analysis in vivo  
**Species** : rat  
**Sex** :  
**Strain** : other: CD  
**Route of admin.** : inhalation  
**Exposure period** : 12 months (6 hours/day at 5 days/week)  
**Doses** : 0.22 mg/l  
**Result** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : Results: negative  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 09.04.2002 (96) (131)

**Type** : other: DNA alkylation  
**Species** : mouse  
**Sex** : male

**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : 6 hours, once  
**Doses** : 10 and 50 ppm (17 and 85 mg/kg bw)  
**Result** :  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Remark** : Immediately after exposure to vinylidenechloride the mice were sacrificed and the DNA of liver and kidneys isolated.  
**Result** : The alkylation rate was very low (for example, treatment with dimethylnitrosoamine yielded in ca. 4000 alkylations per 10 exp 6 nucleotides) and in the kidneys higher than in the liver (29.6 resp. 6.06/10 exp 6 nucleotides, in the 50 ppm group and 11.4 resp. 0.94/10 exp 6 nucleotides). Using 3H thymidine DNA repair was measured in animals exposed to VDC, the only statistically significant slight increase was that occurring in the kidneys of the mice.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Test substance** : 1,1 dichloroethylene 14C was obtained from New England Nuclear with a purity of 99%.  
 06.04.1997 (135)

**Type** : other: DNA alkylation  
**Species** : rat  
**Sex** : no data  
**Strain** : no data  
**Route of admin.** : inhalation  
**Exposure period** : 6 hours  
**Doses** : 10 ppm (8 mg/kg bw)  
**Result** :  
**Method** :  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Remark** : Immediately after exposure the rats were sacrificed and the DNA were isolated from the liver and kidneys.  
**Result** : The DNA alkylation rate was very low and in the DNA of the kidneys higher than in the DNA of livers: 2 resp. 0.87 alkylations/10 exp 6 nucleotides (for example, the alkylation by treatment with dimethylnitrosoamine yielded in a alkylation rate of ca. 4000 per 10 exp 6 nucleotides). Using 3H thymidine, DNA repair was measured in animals exposed to VDC. No changes occurred in both target organs.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
**Test substance** : 1,1 dichloroethylene was obtained from New England Nuclear with a purity of 99%.  
 06.04.1997 (135)

**Type** : other: DNA binding study  
**Species** : rodent  
**Sex** :  
**Strain** :  
**Route of admin.** : inhalation  
**Exposure period** : 6 hours  
**Doses** : 0.04 mg/l (rat); 0.04 and 0.02 mg/l (mouse)  
**Result** :  
**Method** :  
**Year** :

<b>GLP</b>	:	
<b>Test substance</b>	:	
<b>Result</b>	:	Result: little adduct formation Adduct formation overall was small and again, more pronounced in mice than in rats. The kidneys appeared as the preferred organ, compared to the liver. In mice a dose-dependence was observed (30 Adducts/106 nucleotides at 0.2 mg/l, compared to 11 adducts/106 nucleotiden at 0.04 mg/l). DNA labeling during synthesis or contamination of it by labeled macromolecules cannot be excluded.
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 09.04.2002 (96) (174)
<b>Type</b>	:	other: bone-marrow-Test
<b>Species</b>	:	Chinese hamster
<b>Sex</b>	:	male/female
<b>Strain</b>	:	
<b>Route of admin.</b>	:	gavage
<b>Exposure period</b>	:	single gavage
<b>Doses</b>	:	178 ul/kg
<b>Result</b>	:	
<b>Method</b>	:	other: after Malaveille C. et al: Toxicol.appl.Pharmacol. 22, 269-275 (1972) Schmid W. et al: Humangenetik 11, 103-118 (1971)
<b>Year</b>	:	
<b>GLP</b>	:	no
<b>Test substance</b>	:	as prescribed by 1.1 - 1.4
<b>Result</b>	:	There were no clinical symptoms. In a preliminary study a dosage of 215 ul/kg was lethal to 2/6 animals. The report describes an increase in aberrant metaphases of bone marrow cells. A subsequent appraisal of coded bone marrow smears by an outside expert (Prof. Roehrborn, Duesseldorf University) concluded that the number of aberrant metaphases was not increased, but that the number of cells in anaphase was unusually high. A substance effect was discounted. The opinion was expressed that the cause could possibly be a non-optimum processing of the cells. This could raise questions on the validity of the study.
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 09.04.2002 (175)
<b>Type</b>	:	other: bone-marrow-Test
<b>Species</b>	:	Chinese hamster
<b>Sex</b>	:	male/female
<b>Strain</b>	:	
<b>Route of admin.</b>	:	inhalation
<b>Exposure period</b>	:	29 exposures, 6 hours/day for 5 days/week
<b>Doses</b>	:	0; 0.12 and 0.4 mg/l
<b>Result</b>	:	
<b>Method</b>	:	other: after Schmid E. at al: Humangeetik 11, 103-118, 1971 und Buckton K.E. WHO Genf, 1973
<b>Year</b>	:	
<b>GLP</b>	:	no
<b>Test substance</b>	:	as prescribed by 1.1 - 1.4
<b>Result</b>	:	Result: negative There were no systemic toxic or macroscopic findings. The report describes an increase in aberrant metaphases of bone marrow cells at both doses. A subsequent appraisal of coded bone marrow smears by an outside expert (Prof. Roehrborn, Duesseldorf University) concluded that the number of aberrant metaphases was not increased, but that the number of cells in anaphase was unusually high. A substance effect was discounted. The opinion was expressed that the cause could possibly be a

non-optimum processing of the cells. This could raise questions on the validity of the study.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
09.04.2002 (176)

**5.7 CARCINOGENITY**

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : 24 month  
**Frequency of treatment** : daily  
**Post. obs. period** : none  
**Doses** : 0, 50, 100, 200 ppm  
**Result** : negative  
**Control group** : yes, concurrent vehicle  
**Method** : other  
**Year** : 1978  
**GLP** : no  
**Test substance Method** : Analysis of Drinking Water: Samples of drinking water were analyzed via gas chromatography for VDC 16 times during the first 90 days of the study, and then 19 times at periodic intervals during the remainder of the study. The mean of the samples for each dose group were as follows:

Nominal Dose (ppm)	Analytical Mean Dose (ppm)
50	68+/-21
100	99+/-22
200	206+/-33

**General Design:**

Animals: Sprague-Dawley, Spartan substrain, SPF-derived rats 6-7 weeks of age were randomly divided by sex into treatment groups: 80/sex for controls, 48/sex/dose for treated groups. These rats included 10/sex/dose from a 90-day study which were continued into the 2-year study, and rats used for the f0 generation of the concurrent reproduction study which were returned to the 2-year study once mating/gestation/lactation was completed. Rats were housed 2/cage in wire-bottom cages. Food (commercially available chow) and water (city tap water) were available ad libitum. Water was supplied from glass bottles with specially designed plastic screw caps fitted with stainless steel sipper tubes with stainless steel balls. The bottles were emptied and refilled each day from freshly prepared stock solutions. Because of the volatility of VDC, solutions were made up to exceed the nominal concentration, so that mean levels over 24 hours would be as near as possible to nominal concentrations.

Observations: Rats were observed at least twice weekly for signs of toxicity and evidence of tumor formation. Food consumption was recorded twice weekly from 5 cages/sex/dose for the first 3 months, then 25 cages/sex/dose for controls and 14 cages/sex/dose for treated groups 2 times during one week for the remainder of the study (as far as surviving numbers of rats would permit). Water consumption, recorded for the same cages as food consumption, was determined daily for the first 3 weeks, then 2 times/week for the next 12 weeks, then twice during one week of each month thereafter. Body weights were recorded weekly for the first 14 weeks and monthly thereafter.

Clinical Studies: Clinical studies were conducted on blood collected via orbital sinus puncture on 5 rats/sex/dose on test days 181, 184, 366, 541, and on 10 rats/sex/dose on day 707. Samples were also collected at necropsy on day 710 from 10 rats/sex/dose for all groups having more than 10 animals remaining.

Hematological parameters collected included packed cell volume, erythrocyte count, hemoglobin concentration, total and differential leukocyte counts (test day 181 samples only). Urine analysis was conducted on the same animals chosen for hematological analysis, and included specific gravity, pH, sugar, protein, ketones, occult blood, and bilirubin. Clinical parameters recorded included BUN, AP, SGPT, and glucose concentration.

Necropsy and Pathology: During the 24-month experimental period, every effort was made to choose and submit animals to necropsy prior to natural death to minimize loss of data to autolysis. For all animals, a complete necropsy examination was performed and tissues preserved in 10% formalin. Histological examination was also performed on a standard set of tissues, as well as any suspect tumorous lesions, from all animals from controls and high dose. Selected target organs and any suspect tumorous lesions were examined from low and middle dose animals.

Rats were fasted overnight prior to necropsy. Rats were euthanized via decapitation after being weighed. Organ weights of brain, liver, kidney, heart and testes were recorded.

**Result**

: There were no significant differences between the control group and the treated groups for the following parameters: appearance and demeanor, mortality, body weight, food consumption, water consumption, hematology, urinalysis, clinical chemistry determinations, organ weights, and organ-to-body weight ratios.

Gross pathologic examination and histopathologic observations showed both increases and decreases in the incidence of various nontumorous lesions in both sexes. Of the statistically significant deviations that were seen, only those affecting the liver were considered to be treatment-related. These lesions, visible only under microscopic examination, consisted of a minimal amount of hepatocellular fatty change and periportal hepatocellular hypertrophy, and were present in females at all dose levels and in males only at the high dose level. A similar trend was present in males at 100 ppm, although the change was not statistically identified. All other statistically significant deviations were considered to be within the normal variation encountered in lifetime studies with this strain of rat.

The only statistically significant tumorous changes noted were a decrease in pancreatic nodules in males at 100 ppm and an increase in mammary gland fibroadenomas/adenofibromas in females at 50 ppm. Because of the lack of a dose response, these were not considered treatment-related, and no other increases in tumorous lesions were found.

**Source**

**Test substance**

: The Dow Chemical Company, Midland, MI.  
 : Commercial production sample from The Dow Chemical Company, Freeport, TX. Minimum purity 99.5%. Originally contained 180-220 ppm MEHQ as an inhibitor, but since VDC used to prepare various copolymers for food packaging is distilled to remove the inhibitor, these material used for the study was also distilled to decrease MEHQ to 1-5 ppm.

**Attached doc.**

**Reliability**  
 04.06.2002

: VDC Rat 2 Year Drinking Water Study Tables.pdf  
 : (1) valid without restriction  
 (124) (96) (136) (126) (127) (123)

**Species**

: rat

**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 18 months  
**Frequency of treatment** : 6 hours/day, 5 days/week  
**Post. obs. period** : 6 months  
**Doses** : 10, 40 ppm; after 5 weeks increased to 25 and 75 ppm, respectively  
**Result** : negative  
**Control group** : yes, concurrent vehicle  
**Method** : other  
**Year** : 1975  
**GLP** : no  
**Test substance** : other TS  
**Method** : Groups of 103-104 male and female Sprague-Dawley rats (Spartan substrain) were exposed to vinylidene chloride (VDC) by inhalation for 18 months to assess chronic toxicity and oncogenic potential of the subject test material. Rats were exposed to VDC concentrations of 10 and 40 ppm for 6 hours/day, 5 days/week for the first 5 weeks of the study. Based upon the absence of observable treatment-related effects among rats sacrificed after one month of exposure, the exposure concentrations were increased to 25 and 75 ppm VDC. Exposures were continued at these concentrations through the 18th month of the study after which the surviving animals were held until 24 months and then sacrificed.

Rats were exposed to the test material in 3.7 cubic meter stainless steel chambers under dynamic airflow conditions. VDC vapor, generated in a glass vaporization flask, was swept into the chamber by tempered, filtered air at a flowrate designed to produce the desired concentration. Analysis of chamber concentration was performed 2-3 times during each exposure period via IR spectrometry.

Animals were observed daily for signs of toxicity, with special attention given to signs of eye/nasal irritation. Body weights were recorded weekly for the first month of exposure, biweekly during the second month of exposure, and a minimum of monthly thereafter for the entire 24 month experimental period.

Clinical laboratory evaluations were conducted on animals sacrificed in interim evaluations(5-10/sex/dose at 6 and 12 months), as well as at study termination (2-all/sex/dose). Hematology tests conducted on blood collected from tail veins included red blood cell count, hemoglobin concentration, packed cell volume, and total and differential white blood cell counts. Urinalysis included determination of specific gravity, pH, glucose, protein, ketones, occult blood, bilirubin, and urobilinogen. Clinical chemistry determinations included SGPT, BUN, and AP. Cytogenetic evaluation for chromosomal aberrations was also conducted on 4 rats/sex/dose.

All rats were submitted to a complete gross pathologic examination. A complete standard set of tissues was collected for each animal. Brain, heart, liver, kidneys, and testes were weighed. All tissues from the each animal in the control and high dose groups, as well as liver, kidneys, heart, lungs, trachea, spleen, thyroid gland, parathyroid gland, pituitary gland, adrenal glands, stomach, brain (cerebral cortex and cerebellum), and any grossly visible lesions suggestive of possible neoplastic process, were processed and examined histologically by light microscopy.

**Result** : There was no observable increase in mortality of rats of either sex attributable to VDC exposure. Likewise there were no clinical signs of toxicity observed in rats exposed to 25 or 75 ppm VDC during the 18 month exposure period. Clinical chemistry, hematology, urinalysis, body weight data and organ weights obtained at selected time intervals throughout the

conduct of the study revealed no changes judged as a direct effect of the test material on these parameters or the function of the organ systems evaluated by them.

Cytogenetic evaluation of bone marrow preparations from rats of both sexes exposed to 0, 25 or 75 ppm VDC for 6 months did not reveal chromosomal aberrations in either the control or treated animals.

A target organ effect resultant from VDC exposure was observed in the liver of rats exposed to either 25 or 75 ppm VDC. This effect, characterized by hepatocellular fatty change in the midzonal region of the hepatic lobule, was observed in both male and female rats of both the 25 and 75 ppm exposure groups as early as the 6 month interim sacrifice in this study. The midzonal fatty change was also observed at the 12 month sacrifice but no indication of progression of this lesion in either severity or incidence was apparent. During the last 6 months of the study, after exposures had been discontinued, this effect was no longer discernible; therefore this alteration was minimal in severity and readily reversible.

Although the incidence of several tumors and/or tumor types was found to be statistically increased or decreased in VDC exposed rats when compared to their respective control groups, none of these differences were judged to be attributable to VDC exposure. The observed absence of tumorigenic potential of VDC in rats is consistent with the findings of other investigators.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Production grade vinylidene chloride from The Dow Chemical Company, Midland, MI. Minimum purity 99%, with hydroquinone monomethyl ether added as an inhibitor.

**Attached doc.** : VDC 2 Year Rat Inhalation Study Tables.pdf  
 04.06.2002 (124) (96) (136) (126) (127) (123)

**Species** : mouse  
**Sex** : female  
**Strain** : Swiss  
**Route of admin.** : dermal  
**Exposure period** : until spontaneous death or morbidity  
**Frequency of treatment** : 3 times/week  
**Post. obs. period** :  
**Doses** : 40 doses, 121 mg/animal in Acetone (0.2 ml)  
**Result** :  
**Control group** : other: Acetone (0.1 ml)  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : No treatment-related tumors were found.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 09.04.2002 (124) (96) (177)

**Species** : mouse  
**Sex** : female  
**Strain** : other: ICR/Ha Swiss  
**Route of admin.** : dermal  
**Exposure period** : single  
**Frequency of treatment** :  
**Post. obs. period** : until spontaneous death  
**Doses** : 121 mg/animal; subsequently, 5ug PMA/animal 3 times/week  
**Result** :  
**Control group** :  
**Method** :  
**Year** :

**GLP** :  
**Test substance** :  
**Result** : This is an initiation test on skin, administering phorbol myristyl acetate (PMA) as promotor after a single VDC treatment. Papillomas were significantly increased in 8/30 animals. A skin cancer could be observed in 1/30 animals. According to the secondary source (DFG MPC values, 1985) it must be taken into account that the papillomas appeared also in the PMA controls in the test, which is confirmed by results from earlier studies with the phorbol ester (Jaeger R.J. et al., 1973), and hence questions arise as to the results of the study. In addition, in the study, in which 14 other substances besides VDC were tested for tumor initiation, individual squamous cell cancers appeared exclusively in PMA-treated controls.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 09.04.2002 (124) (96) (178) (177)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : two years  
**Frequency of treatment** : daily  
**Post. obs. period** :  
**Doses** : 5-12, 8-20 and 16-40 mg/kg bw day  
**Result** :  
**Control group** : yes, concurrent no treatment  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Result** : Negative results, the only statistically significant tumorous changes detected, i.e., the decrease in pancreatic nodules in male rats of the middle dose group and the increase in mammary gland fibroadenomas/adenofibromas in the females of the lower dose group, were considered not to be treatment related.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : 1,1 dichloroethylene was obtained from Dow Chemical Midland with a purity of 99.5%.  
 09.04.2002 (179)

**Species** : rat  
**Sex** : male/female  
**Strain** : other: BDIV  
**Route of admin.** : gavage  
**Exposure period** : lifetime  
**Frequency of treatment** : 1 time/week  
**Post. obs. period** :  
**Doses** : 50 mg/kg in olive oil  
**Result** :  
**Control group** : other: olive oil  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : The number of liver tumors, 1/81 (male) and 3/81 (female), was slightly higher than the control (0/49 and 0/47, respectively). The

number of meningeal tumors was 6/81 in male animals compared to 1/48 for the controls and thus not statistically significantly higher. A dose dependence can not be ruled out, but according to the secondary source (Costa, A.K., and Ivanetich, K.M., 1984) is not very likely. It must furthermore be taken into account that the animals were already exposed in the embryonic phase via the mother.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
09.04.2002 (163) (96) (100)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : gavage  
**Exposure period** : 52 weeks  
**Frequency of treatment** : 4-5 times/week  
**Post. obs. period** : Until spontaneous death  
**Doses** : 0.5; 5; 10 and 20 mg/kg in olive oil  
**Result** :  
**Control group** : other: olive oil  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : No treatment-related tumors were observed.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
09.04.2002 (124) (180) (181) (182)

**Species** : rat  
**Sex** : male/female  
**Strain** : other: F-344/N  
**Route of admin.** : gavage  
**Exposure period** : 104 weeks  
**Frequency of treatment** :  
**Post. obs. period** :  
**Doses** : 1 and 5 mg/kg in corn oil  
**Result** :  
**Control group** : other: corn oil  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : No treatment-related tumors were observed.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
09.04.2002 (124) (137)

**Species** : mouse  
**Sex** : male/female  
**Strain** : other: B6C3F1/N  
**Route of admin.** : gavage  
**Exposure period** : 104 weeks  
**Frequency of treatment** :  
**Post. obs. period** :  
**Doses** : 2 and 10 mg/kg in corn oil  
**Result** :  
**Control group** : other: corn oil  
**Method** :

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

**Year** :  
**GLP** :  
**Test substance** :  
**Result** : No treatment-related tumors were observed.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
09.04.2002 (124) (137)

**Species** : mouse  
**Sex** : male/female  
**Strain** : no data  
**Route of admin.** : gavage  
**Exposure period** : no data  
**Frequency of treatment** : no data  
**Post. obs. period** : no data  
**Doses** : no data  
**Result** :  
**Control group** : yes  
**Method** :  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Result** : No cancerogenic potential in males and females  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (183)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 52 weeks  
**Frequency of treatment** : 4 hours/day, 4-5 times/week  
**Post. obs. period** : Until spontaneous death  
**Doses** : 0.04, 0.101, 0.202, 0.403, 0.604, 0.805 mg/l air  
**Result** :  
**Control group** : yes, concurrent no treatment  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : The highest dose could be administered only on 2 treatment days, because of severe toxicity. No treatment-related tumors appeared in any treatment groups.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
09.04.2002 (124) (180) (181) (182)

**Species** : rat  
**Sex** : male/female  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : 52 weeks  
**Frequency of treatment** : 6 hours/day, 5 times/week  
**Post. obs. period** :  
**Doses** : 0.222 mg/l air  
**Result** :  
**Control group** : yes, concurrent no treatment  
**Method** :

**Year** :  
**GLP** :  
**Test substance** :  
**Result** : In parallel with this experiment with VDC, the same lab tested VC (vinyl chloride). On 2 of 36 VDC-treated male rats the typical findings for VC (hemangiosarcomas) were observed. The possibility of crosscontamination was discussed (DFG MPC values, 1985). Other tumors that could be considered treatment-related did not occur.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 13.05.2002 (124) (96) (131) (184)

**Species** : rat  
**Sex** :  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : 1-10 months, depending on experimental group  
**Frequency of treatment** : 6 hours/day, 5 times/week  
**Post. obs. period** :  
**Doses** : 0.222 mg/l air  
**Result** :  
**Control group** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : The tumors observed in the preceding experiments (Lee C.C. et al., 1977; Lee C.C. et al., 1978) in rats (hemangiosarcomas) were not observed, with one exception. Because of the lack of a dose-response relationship and the fact that no other treatment-related tumors were observed, a carcinogenic effect for VDC was not assumed in this study (Costa A.K. und Ivanetich K.M., 1984).

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 13.05.2002 (163) (124) (96) (185) (131) (184)

**Species** : rat  
**Sex** : male/female  
**Strain** : Wistar  
**Route of admin.** : inhalation  
**Exposure period** : 12 months  
**Frequency of treatment** : 4 hours/day, 5 days/week  
**Post. obs. period** : Until spontaneous death (22-24 months)  
**Doses** : 0.403 and 0.805 mg/l air  
**Result** :  
**Control group** : yes, concurrent no treatment  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : No treatment-related tumors were observed.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 14.05.2002 (124) (96) (186)

**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 12th day of pregnancy or young animals

<b>Frequency of treatment</b>	:	104 weeks, 7 hours/day, 5 days/week
<b>Post. obs. period</b>	:	
<b>Doses</b>	:	0.4 mg/l air
<b>Result</b>	:	
<b>Control group</b>	:	yes, concurrent no treatment
<b>Method</b>	:	
<b>Year</b>	:	
<b>GLP</b>	:	
<b>Test substance</b>	:	
<b>Result</b>	:	The authors report that the total number of malignant tumors (per 100 animals) and leukemias in animals was increased compared to the control group, when they were previously exposed in utero and after birth were treated for 104 weeks by VDC inhalation. The publications show no statistical evaluation or a comparison with historical control data. For descendants treated only for 15 weeks by VDC inhalation, or maternal animals that after littering received VDC over the rest of their lifespan, the authors report possible indications of a minor increase in the tumor rate.
<b>Source</b>	:	BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA) 02.08.2002 (187)
<b>Species</b>	:	mouse
<b>Sex</b>	:	male/female
<b>Strain</b>	:	Swiss
<b>Route of admin.</b>	:	inhalation
<b>Exposure period</b>	:	52 weeks
<b>Frequency of treatment</b>	:	4 hours/day, 4-5 times/week
<b>Post. obs. period</b>	:	Until spontaneous death
<b>Doses</b>	:	0.04; 0.101 and 0.202 mg/l air
<b>Result</b>	:	
<b>Control group</b>	:	yes, concurrent no treatment
<b>Method</b>	:	
<b>Year</b>	:	
<b>GLP</b>	:	
<b>Test substance</b>	:	
<b>Result</b>	:	Because of the marked toxicity (kidneys, liver), the high dose group was treated for only 4 days and then remained under observation until spontaneous death (after 121 weeks). Of 18 surviving male animals in this experimental group, 2 had kidney adenocarcinomas. These were also observed in the middle dose group in 28/119 male and 1/138 of the female animals. These tumors were not observed in the other experimental groups. A relationship between the chronic-toxic effect and these tumors is discussed (DFG MPC values, 1985) is discussed. A mixed exposure to mono and dichloro-acetylene that occurred as impurity up to 0.02 g/kg in the VDC tested and that can be formed from it under the effects of heat and using alkaline cleaning agents on metal surfaces, is also discussed. Dichloro-acetylene even at very low dosages causes cystadenomas in the area of the proximal kidney tubuli that are very similar to kidney tumors in VDC exposures. (DFG MPC values, 1985).  The question of the high gender and species specificity was examined in more recent studies (Speerschneider P. und Dekant W., 1994). It is assumed that Cytochrome P450 2E1 converts vinylidene chloride to nephrotoxic metabolites in the kidneys. In studies with rats or mice, and in vitro with man, it was shown that this metabolic path and this activation of vinylidene chloride plays a role only in male mice.
<b>Source</b>	:	BASF AG Ludwigshafen

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

04.06.2002 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
(124) (180) (181) (182) (188)

**Species** : mouse  
**Sex** : male/female  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : 52 weeks  
**Frequency of treatment** : 6 hours/day, 5 days/week  
**Post. obs. period** : none  
**Doses** : 0.222 mg/l air  
**Result** :  
**Control group** : yes, concurrent no treatment  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : In parallel with this experiment with VDC, the same lab tested VC (vinyl chloride). In 2/35 VDC-treated male mice and 1/35 female mice the typical findings for VC (hemangiosarcomas of the liver) were observed. The possibility of cross-contamination was discussed (DFG MPC values, 1985). Other tumors that could be considered treatment-related did not occur.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
14.05.2002 (124) (96) (131) (184)

**Species** : mouse  
**Sex** : male/female  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : 1-6 months, depending on experimental group  
**Frequency of treatment** : 6 hours/day, 5 times/week  
**Post. obs. period** : 52 weeks  
**Doses** : 0.222 mg/l air  
**Result** :  
**Control group** : yes, concurrent no treatment  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : The tumors observed in the preceding experiments (hemangiosarcomas) were not found in this experiment, with one exception. Because of the lack of a dose-response relationship and the fact that no other treatment-related tumors were observed, a carcinogenic effect of VDC is not assumed in this study (DFG, MPC values, 1985).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
14.05.2002 (124) (185)

**Species** : Chinese hamster  
**Sex** : male/female  
**Strain** :  
**Route of admin.** : inhalation  
**Exposure period** : 52 weeks  
**Frequency of treatment** : 4 hours/day, 4-5 times/week  
**Post. obs. period** : Until spontaneous death  
**Doses** : 0.101 mg/l air  
**Result** :

**Control group** :  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : No treatment-related tumors were observed.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 14.05.2002 (124) (180) (181) (182)

**Species** : mouse  
**Sex** : female  
**Strain** : other: ICR/Ha Swiss  
**Route of admin.** : s.c.  
**Exposure period** : 548-636 days  
**Frequency of treatment** : 1 time/week  
**Post. obs. period** :  
**Doses** : 2 mg/animal in 0.05 ml trioctanoin  
**Result** :  
**Control group** : other: 0.05 ml Trioctanoin  
**Method** :  
**Year** :  
**GLP** :  
**Test substance** :  
**Result** : No treatment-related tumors were observed.  
**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
 14.05.2002 (124) (96) (177)

## 5.8 TOXICITY TO REPRODUCTION

**Type** : Fertility  
**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : Multigeneration study (3 generations with 6 litters)  
**Frequency of treatment** : continuous  
**Premating exposure period**  
**Male** : 100 days before mating, then until end of generation  
**Female** : 100 days before mating, then until end of generation  
**Duration of test** : 3 generation  
**Doses** : 50; 100 and 200 ppm (drinking water)  
**Control group** : yes, concurrent vehicle  
**NOAEL Parental** : = 50 ppm  
**NOAEL F1 Offspr.** : = 200 ppm  
**NOAEL F2 Offspr.** : = 200 ppm  
**Method** : other  
**Year** : 1979  
**GLP** : no  
**Test substance** : other TS  
**Method** : Analysis of Drinking Water: Samples of drinking water were analyzed via gas chromatography for VDC 16 times during the first 90 days of the study, and then 19 times at periodic intervals during the remainder of the study. The mean of the samples for each dose group were as follows:

Nominal Dose (ppm)      Analytical Mean Dose (ppm)

50	68+/-21
100	99+/-22
200	206+/-33

**General Design:**

Animals: Sprague-Dawley, Spartan substrain, SPF-derived rats 6-7 weeks of age were randomly divided by sex into treatment groups. Male and female F0 generation rats used in this study were part of a concurrent 2-year toxicity study. All rats saved for mating in any generation were uniquely identified by an ear tag.

Observations: All animals were observed frequently for signs of toxicity. Body weights were recorded on a weekly basis. Water consumption was recorded twice weekly during pre-mating periods. Food consumption was recorded. Reproductive parameters including mating day, parturition day, number of live/dead pups on lactation days 0, 1, 7, 14, and 21, litter weights on lactation days 1, 7, and 14, pup body weight on lactation day 21, and the sex of each weanling on lactation day 21. The following indices were calculated for each group of rats: fertility index (number pregnant/number mated), gestational survival index (live pups/litter size), and the 24-hour, 7-day, 14-day, 21-day survival indices.

Dose Groups: Ten male and 20 female rats per dose group received 50, 100, or 200 ppm VDC in the drinking water; 15 male and 30 female rats in the control group received drinking water without VDC. 200 ppm was chosen as the highest dose since it represents the limit of VDC solubility in water. The equivalent mg/kg/day doses for male and female rats ingesting 50, 100, or 200 ppm were 6, 10, or 19 mg/kg/day and 8, 13, or 26 mg/kg/day, respectively. Water was continuously available during pre-mating, mating, gestation, and lactation.

f0 Mating: The female rats were housed 2 per cage for the first 100 days of the study, then housed 2 females and 1 male per cage for a 15-day mating period (3 estrus cycles). After the mating period, males were returned to their original cages in the 2-year study. Because low fertility rates were obtained during the first (f1a litters) mating period, the mating procedure for the second (f1b litters) mating period was altered. Females were singly housed with males, and the area under each cage was observed daily for evidence of vaginal plugs resulting from copulation. Females were separated from males when evidence of copulation was found. If after 10 days no evidence of copulation was found, the female was rotated to a different male for another 10-day period. The maximum period of cohabitation was 30 days: 10 days with each of 3 different males.

f0 Delivery: After the mating period, females were individually housed in metal delivery cages having a layer of ground corn cob as nesting material. At the end of the first week of lactation, a screen was placed in the bottom of the cage. Dams and pups remained in delivery cages until pups were necropsied, after which the females were returned to their original cages. After a period of no less than 10 days after weaning of the f1a litters, the mating procedure outlined previously was followed to produce the f1b litters.

f1 Generation: The rats to be raised as the f1 generation were selected randomly from the f1b weanlings.

f1 Mating: At 110 days of age, the f1 females were singly housed with f1 males, and the area under each cage was observed daily for evidence of vaginal plugs resulting from copulation. Females were separated from males when evidence of copulation was found. If after 6 days no evidence

of copulation was found, the female was allowed to be alone for 6 days, then rotated to a different male for another 6-day period. The cohabitation period was shortened from that used to produce the f1b litters because generally no evidence of copulation was observed after 6 days.

f1 Delivery: After the mating period, females were individually housed in metal delivery cages having a layer of ground corn cob as nesting material. At the end of the first week of lactation, a screen was placed in the bottom of the cage. Dams and pups remained in delivery cages until pups were necropsied, after which the females were returned to their original cages.

f2 Generation: The rats to be raised as the f2 generation were selected randomly from the f2 weanlings.

f2 Mating: At 110 days of age, the f2 females were singly housed with f2 males, and the area under each cage was observed daily for evidence of vaginal plugs resulting from copulation. Females were separated from males when evidence of copulation was found. If after 6 days no evidence of copulation was found, the female was allowed to be alone for 6 days, then rotated to a different male for another 6-day period.

f2 Delivery: After the mating period, females were individually housed in metal delivery cages having a layer of ground corn cob as nesting material. At the end of the first week of lactation, a screen was placed in the bottom of the cage. Dams and pups remained in delivery cages until pups were necropsied, after which the females were returned to their original cages. Because of decreased survival in the VDC-treated animals, after a period of no less than 10 days after weaning of the f3b litters, the mating procedure outlined previously was followed to produce the f3c litters.

Post-Mortem Examination: All pups not selected to continue to the next generation were sent to necropsy at 21-24 days of age. Gross pathological examination was conducted on all pups. Bone marrow smears were collected from 5 pups/sex/dose from the f1b, f2, and f3b generations. Weights of kidney and liver from 2-7 pups of different litters/sex/dose were collected for the f1b, f2, and f3b generations. Sections of these organs were preserved for microscopic examination.

At the time of weaning the f2 and f3c litters, the f1b and f2 adults, respectively, were necropsied and examined for gross pathological alterations. BUN, SGPT, and AP levels were determined for 10 rats/sex/dose of the f2 generation.

Weights of brain, heart, liver, kidneys, and testes were taken for at least 10 males and 10 females in each dose group.

For the f1b adults, microscopic examination of sections of liver and kidney was conducted on at least 10 rats/sex/dose. For the f2 adults, liver, kidney, and all grossly visible macroscopic lesions were examined microscopically. Gross pathological examination was conducted on all f3b generation animals at 185-213 days of age.

**Result**

: Clinical Observations: Approximately 30 days prior to mating the f0 generation, sialodacryoadenitis infection (viral origin) was observed among the rats, as evidenced by swollen salivary glands. The rats appeared to have recovered prior to mating to produce the f1b litters. The infection also appeared in f2 rats during lactation of the f3a litters. The infection was uniformly spread among rats in all dose levels. The rats appeared to have recovered prior to mating for the f3b litters. No other clinical signs were noted.

Body Weights: No consistent, compound-related alterations in body weight

were observed in any generation.

Food/Water Consumption: Among male rats, there was no effect on food consumption. Females had a slight, sometimes statistically significant decrease in food consumption at all treatment levels; this was not dependent on concentration of VDC or duration of test. There were no alterations in water consumption at any dose level.

Fertility: A low fertility rate was observed in the f0 generation in 3/4 dose groups, including controls. Because of this, the f0 rats were remated. The fertility rate was still decreased in dams ingesting 200 ppm, but was not decreased in the remaining groups. No overall decrease in fertility was observed in subsequent matings to produce the f2, f3a, f3b, or f3c generations. There were no effects on average litter size or pup growth.

Survival: Although neonatal survival was decreased in the f2 and f3a litters, the survival indices of the f2 litters were within the range of control values seen with this strain in this laboratory. The apparent effect seen in the f3a litters was not replicated in subsequent matings of the same adults to produce the f3b and f3c litters. Consequently, the decreased neonatal survival seen in the f3a litters was attributed to chance.

Pup NOEL/NOAEL: Alterations seen among pups, during both gross and microscopic examination, were random in nature and not significantly different in treated animals from those seen in controls.

Adult NOEL/NOAEL: Histopathologic examination of tissues from f1 and f2 adult rats revealed mild pathologic changes in the liver which were considered to be of a reversible nature. Kidney disease, common among male rats of this strain, was slightly exacerbated at the 200 ppm level in males.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Commercial production sample from the Dow Chemical Company, Freeport, TX. Purity of 96.95%.  
**Reliability** : (1) valid without restriction  
 17.05.2002 (101) (88) (96) (189) (190)

## 5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

**Species** : rat  
**Sex** : female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : Days 6-16 of pregnancy  
**Frequency of treatment** : 7 hours/day  
**Duration of test** :  
**Doses** : 0, 20, 80, 160 ppm  
**Control group** : other: each dose group had its own control group  
**NOAEL Maternalt.** : = 20 ppm  
**NOAEL Teratogen** : = 160 ppm  
**NOAEL Fetotoxicity** : = 20 ppm  
**other: NOAEL Maternal** : = 200 ppm  
**Tox. (Drinking Water Study)**  
**other: MOAEL** : = 200 ppm  
**Teratogenicity/Fetotoxicity (Drinking Water Study)**  
**Method** : other

**Year** : 1977  
**GLP** : no  
**Test substance** : other TS  
**Method** : Animals: Sprague-Dawley rats, adults, ~250 g. The day on which sperm was found in a vaginal smear was considered day zero of pregnancy. The animals were uniquely identified by means of an ear punch. Animals were housed individually in wire-bottom cages. Animals had unlimited access to commercially available feed and city tap water, except when they were housed in exposure chambers. Feed and water consumption were monitored at intervals of 3 days or less.

Experimental Design: Groups of 30 bred rats were exposed to 80 or 160 ppm for 7 hours/day on days 6-15 of gestation. Because some embryotoxicity was observed at 80 ppm, and additional 44 bred rats were exposed to 20 ppm. Groups of 20-47 bred rats were exposed in chambers to filtered room air to serve as controls.

Pregnant animals were exposed in stainless steel and glass Rochester-type exposure chambers of 4.3 cubic meters. The chamber atmosphere was generated by metering VDC at a known rate into a heated vaporization flask and then into the airstream being drawn into the chamber. The concentration of VDC in the chamber was continuously analyzed during exposure using an infrared spectrometer. Time-weighted averages were as follows:

Nominal Concentration (ppm)	Analytical Concentration (ppm)
20	20+/-1
80	80+/-5
160	158+/-6

For the ingestion study, 26 bred rats were given tap water containing 200 ppm VDC on days 6-15 of gestation. A group of 24 bred rats was given tap water without VDC. The water was supplied from 16 ounce glass bottles with plastic screw caps fitted with stainless steel sipper tubes containing stainless steel balls. The bottles were emptied and refilled daily from freshly prepared stock solutions. In another study, VDC was determined to be stable in water for 24 hours.

Maternal and Fetal Observations: Animals were observed daily for indications of toxicity. Maternal body weights were recorded on days 6, 10 and 16 of gestation. In addition, maternal body weight and liver weight were recorded at cesarean section on day 21 of gestation. On the day of cesarean section, the females were sacrificed by carbon dioxide inhalation; the uterine horns were exteriorized through a midline incision in the abdominal wall, and the number and position of live, dead and resorbed fetuses recorded. The uteri of apparently non-pregnant animals were stained with a 10% solution of sodium sulfide to check for the presence of early resorptions. After being weighed, measured for crown-rump length, and sexed, all fetuses were examined for external alterations and cleft palate. One-third of each litter, selected at random, was immediately examined for evidence of soft tissue alterations via dissection under a low-power stereoscope. The head of each animal chosen for soft tissue examination was preserved in Bouin's solution and subsequently examined using a razor sectioning technique. All of the fetuses in each litter were then eviscerated, stored in 95% ethanol, and stained with alizarin-red S to facilitate examination for skeletal alterations.

**Result** : Inhalation Study:  
 Maternal Toxicity: No deaths were seen in any dose group via inhalation or drinking water. Single rats in the 80 or 160 ppm dose group delivered litters early on days 18 and 21 of gestation, respectively; no other early deliveries were seen. Sialodacryoadenitis was seen in one female at 20 ppm and in

one control female; this disease, viral in origin, was not observed in any other animal.

Mean body weight gain of rats exposed to 80 or 160 ppm was significantly decreased, as was food consumption; water consumption was significantly increased, as was mean liver weight (only at 160 ppm). At 20 ppm, the only maternal effects noted were minor changes in body weight and water consumption.

Embryo- and Fetotoxicity: No major malformations occurred at incidences significantly different from controls. In addition, the collected incidence of major malformations was not significantly different from controls. The few major malformations which did occur in VDC exposed rats have been known to occur in control animals in this species. There was a significantly increased incidence of skeletal alterations (such as wavy ribs and various delayed ossifications) at 80 and 160 ppm, maternally toxic concentrations. There was a significant increase in incidence of resorptions at 80 ppm; however, this increase was due to a single litter which was totally resorbed. Also, a similar increase was not seen at 160 ppm, so the increase was not considered treatment-related. No effects were seen at 20 ppm.

Feeding Study:

Maternal Toxicity: No evidence of toxicity was observed at 200 ppm.

Embryo- and Fetotoxicity: No evidence of teratogenicity, embryotoxicity, or fetotoxicity was observed at 200 ppm. An increase in crown-rump length was statistically identified, but this effect was not considered toxicologically significant.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Production grade VDC from The Dow Chemical Company, Midland, MI. Minimum purity of 99.5%; contained 200-400 ppm monomethylether of hydroquinone (MEHQ) to inhibit polymerization. Since vinylidene chloride used in various copolymers for food applications is distilled to remove MEHQ, a similar process was used to prepare the VDC used for the feeding portion of the study.

**Reliability** : (1) valid without restriction  
 03.06.2002 (96) (189)

**Species** : rat  
**Sex** : female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : pregnancy plus 2 months prior  
**Frequency of treatment** : continuous  
**Duration of test** : gestation +  
**Doses** : 0.15 or 110 ppm  
**Control group** : yes, concurrent vehicle  
**NOAEL Maternalt.** : = 100 ppm  
**Method** : other  
**Year** : 1993  
**GLP** : no data  
**Test substance** : other TS  
**Method** : Sexually mature female Sprague-Dawley rats were mated to a very limited number of mature males. Day 0 of pregnancy was assessed from the presence of sperm in a vaginal smear. Females were placed with males for mating during estrus, as determined via vaginal smear.

0.15 or 110 ppm VDC were given via foil-covered glass drinking bottles, which were changed and cleaned every 24 hours. Water consumption was recorded daily; body weights were recorded throughout pregnancy. Females received VDC in the drinking water for 2 months prior to and

throughout pregnancy or for only the 2 months prior to pregnancy.

On day 22, pregnant rats were sacrificed via carbon dioxide inhalation. Gravid uterus and ovaries were removed through a midline incision and examined. Each uterine horn was opened along its length, allowing visualization of all fetuses, implantation and resorption sites. Placental weight, crown-rump length, and weight of each fetus was recorded.

A v-type incision was made in each fetus from sternum to axilla, exposing the thoracic cavity. The great cardiac veins and arteries were examined in situ under magnification. The heart was then removed, flushed with 2% glutaraldehyde, fixed for 24 hours, then removed to 0.1 mol/liter phosphate buffer for storage.

Hearts were dissected under light microscopy for gross abnormalities prior to excising the right atrial appendage to check for atrial septal defects. The atrial appendages were then completely removed to examine the mitral, pulmonary, aortic, and tricuspid valves. Incisions were made to allow visualization of the ventricular septum to examine for defects.

**Result** : All maternal rats were healthy throughout the study and there was no evidence of toxicity. There was no significant difference between any of the treated groups and the control group as determined by percentage of live births, implants, and resorptions. No differences were found between groups in congenital abnormalities other than cardiac.

3% of the control group had cardiac anomalies, while 13% of the group that received 110 ppm both before and during pregnancy, 12% of the group that received 0.15 ppm both before and during pregnancy had cardiac defects. No differences were seen between controls and groups that were treated only prior to pregnancy. A variety of defects were observed, with no particular combination of defects or syndromes predominating.

However, a similar finding by this group with trichloroethylene have not been reproduced in a high-dose bolus dosing study at 500 mg/kg by Fisher et al. (2001) nor in a guideline inhalation developmental toxicity study in rats inhaling up to 3.22 mg/L (600 ppm) by Carney et al. (2001). In addition, the study has been criticized by the IRIS Peer Review Workshop (2001) for lack of dose-response, high control incidence rates, lack of specificity and a number of quality control problems.

**Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Dichloroethylene, purity unspecified, was obtained from Aldrich Chemical.  
**Reliability** : (3) invalid

Similar findings by this group with trichloroethylene have not been reproduced in a high-dose bolus dosing study at 500 mg/kg by Fisher et al. (2001) nor in a guideline inhalation developmental toxicity study in rats inhaling up to 3.22 mg/L (600 ppm) by Carney et al. (2001). In addition, the study has been criticized by the IRIS Peer Review Workshop (2001) for lack of dose-response, high control incidence rates, lack of specificity and a number of quality control problems.

10.07.2002

(191)

**Species** : rat  
**Sex** : female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : Days 6-16 of pregnancy  
**Frequency of treatment** : 22-23 hours/day  
**Duration of test** : 21 days  
**Doses** : 0.06-1.796 mg/l air  
**Control group** : other: 2 groups (normal and rationed feed)  
**Result** : Embryo/fetotoxic and weakly teratogenic effects in the range

of maternal toxicity.

Based on the original literature, the following evaluation can be made: dose-dependent, clear maternal toxicity and mortality and body weight loss during the exposure period, for the fetuses.

At the end of the experiment, delayed bone maturation and dose-dependent (in part statistically significant) increase in the incidence of various forms of hydrocephalia was observed in all groups treated with VDC. Results were confounded by the pronounced maternal toxicity; the total number of litters and fetuses in the experimental groups was very low. In another study on pregnant Wistar rats the skeletal retardation was qualitatively confirmed, but not the occurrence of hydrocephalia (Murray F.J. et al., 1979). A direct comparison of the two studies was not possible because of the different exposure durations (7 and 22-23 hours/day, respectively).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
04.06.2002 (96) (189) (192)

**Species** : rat  
**Sex** : male/female  
**Strain** : CD-1  
**Route of admin.** : inhalation  
**Exposure period** : Days 8-20 of gestation  
**Frequency of treatment** : 22-23 hours/day  
**Duration of test** :  
**Doses** : 0.2; 1.1 mg/l air  
**Control group** : other: 2 groups, one with rationed feed  
**Remark** : Maternal tox.: in both dosage groups dose-dependent.  
**Result** : The goal of this study was a behavioral study of young animals to day 21 post-partum, following inhalation treatment of the parent animals during days 8-20 of the gestation period. Based on the original literature, it is possible to make the following evaluation: the maternal toxicity manifested as a dose-dependent impairment of body weight gain. At the high dose the number of live fetuses trended lower and body weight of the newborn was depressed. In numerous behavioral tests no treatment-related effect was observed in the young animals, even when the VDC treatment of the maternal animals caused toxicity. The delayed skeletal ossification in the fetuses observed even at lower dosages in a separate experiment with animals of the same rat strain had no effect on the development of the young animals (for instance, in the swim test, grip strength and endurance test, as well as dental development) in this experiment; however, no examination (skeletal staining) was performed regarding developmental skeletal delays.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (96) (192)

**Species** : rat  
**Sex** : female  
**Strain** : Sprague-Dawley  
**Route of admin.** : inhalation  
**Exposure period** : 7 hours, 10 days  
**Frequency of treatment** : daily, GD 6-15  
**Duration of test** : 16 days  
**Doses** : 20, 80 and 160 ppm (18.5, 74 and 148 mg/kg bw day)  
**Control group** : yes, concurrent no treatment  
**Method** : other  
**Year** :  
**GLP** : no data

<b>Test substance</b>	: other TS	
<b>Remark</b>	: The 160 and the 80 ppm group consisted of 30 animals, the 20ppm group of 44 animals.	
<b>Result</b>	: The level of significance chosen for all cases was $p < 0.05$ . Maternal toxicity: No maternal deaths occurred. Single dams in the 80 or 160 ppm group delivered litter prematurely on days 18 and 21 of gestation. The mean body weight of pregnant in the 20 and 160 ppm groups was significantly less than that of the control on day 10 GD, at 80 ppm a significant decrease was observed on GD 16. Maternal weight gain on GD 6-9 was decreased in a dose dependant manner at 80 and 160 ppm. A significant increase in maternal weight gain was noted during the post exposure period among the dams exposed to 160 ppm. No effects on bodyweight gain was observed in the 20 ppm group. Only at 160 ppm VDC a significant increase in relative liverweight were recorded. Food consumption: 160 ppm: decreased significantly food consumption on GD 6-8, increased significantly on GD 12-14 and 18-20. 80 ppm: significant decreased GD 6-17. Water consumption: 160 ppm: significantly greater throughoutthe GDs 6-20, 80 ppm: significantly increased GD 15-17, 20 ppm: significantly increased GDs 12-17.  Embryo- and fetotoxicity: No significant effect on the number of implantation or on the number of live and dead fetuses was discerned. Fetal sex ratio or body weight was not altered. The incidence of major malformations was not significantly different from that of the control litters. No external or soft tissue alteration occurred more often than among controls. At 80 and 160 ppm several minor skeletal changes occurred significantly more often (delayed ossification of the interparietal bone of the skull, wavy ribs).	
<b>Source</b>	: BASF AG Ludwigshafen EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)	
<b>Test substance</b>	: 1,1 dichloroethylene was obtained from Dow Chemical Midland with a purity of 99.5% and traces of hydrochinon monomethylether (200-400 ppm).	
02.08.2002		(193)
<b>Species</b>	: mouse	
<b>Sex</b>	: female	
<b>Strain</b>	: CD-1	
<b>Route of admin.</b>	: inhalation	
<b>Exposure period</b>	: Days 6-16 of gestation	
<b>Frequency of treatment</b>	: 22-23 hours/day	
<b>Duration of test</b>	:	
<b>Doses</b>	: 0.06-1.796 mg/l air	
<b>Control group</b>	: other: 2 groups (normal and rationed feed)	
<b>Remark</b>	: Maternal tox.: at doses $> 0.06$ mg/l	
<b>Result</b>	: Embryo/fetotoxic effect. Based on the primary literature it is possible to make the following evaluation: VDC is embryo/fetotoxic at all dosages. Only the lowest dosage proved non-lethal to the fetuses. Maternal toxicity manifested as mortality, delayed body weight gain to body weight decrease in the exposure period and reduced food intake. At 0.06 mg/l no maternal toxicity was observed, but a delayed skeletal ossification was noted	

in the fetuses (no NOEL). The fertility index was low in all experimental groups, including the controls. Because of the high mortality of the mother animals and the embryoletality the number of fetuses seems insufficient in this study for an assured evaluation of possible teratogenic properties. Numerous additional experiments were performed, besides the main experiment (controls with rationed feed, different exposure intervals). The authors concluded that VDC is weakly teratogenic, with a small primary effect. In a review article prepared in collaboration with the USEPA (1,1-dichloroethene, Agency for Toxic Substances and Disease, 1989), a MRL (minimal risk level) of 0.9 ppm (0.004 mg/l) was derived, based on the skeletal changes mentioned above.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (194) (96) (192)

**Species** : rabbit  
**Sex** : female  
**Strain** : New Zealand white  
**Route of admin.** : inhalation  
**Exposure period** : Days 6-18 of gestation  
**Frequency of treatment** : 7 hours daily  
**Duration of test** :  
**Doses** : 0.32; 0.64 mg/l air  
**Control group** : other: each dose group was assigned its own control group  
**NOAEL Maternal.** : .32 mg/l  
**Result** : Not teratogenic but embryo/fetotoxic.  
Increased resorption rate and delayed ossification in the high dose group (0.64 mg/l). The authors report that the resorption observed correlates closely with the body weight of the corresponding mother animal; it was not possible to decide whether this was a direct embryotoxic effect or an indirect effect due to maternal toxicity. In contrast to the rat study, the determination of food and drinking water consumption was not performed in this study.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (96) (189)

**Species** : rabbit  
**Sex** : female  
**Strain** : New Zealand white  
**Route of admin.** : inhalation  
**Exposure period** : 7 hours per day, on GD 6-18  
**Frequency of treatment** : daily  
**Duration of test** : 24 days  
**Doses** : 80 and 160 ppm (36 and 72 mg/kg bw day)  
**Control group** : yes, concurrent no treatment  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Remark** : The 160 ppm group consisted of 18, and the 80 ppm group of 22 animals.  
**Result** : The level of significance chosen for all cases was  $p < 0.05$ .  
Maternal toxicity: Single deaths occurred in all groups including control group, this did not appear to be dose related (infections did lead to deaths).

Body weight gain was significantly decreased in the 160 ppm group at GD 6-18 and on days 19-28 post exposure, in the 80 ppm group on day 1 of exposure.

The absolute and relative liver weight were increased but only in the 80 ppm group and not in the higher dose group.

Embryo- and fetotoxicity:

No significant effect on the number of corpora lutea, implantations, or live and dead fetuses was noted.

Four exhibited litters in which all or most of implantations were resorbed were observed in the 160 ppm group (significant).

The incidence of major malformations was not significantly affected by exposure of VDC. The soft tissue examination revealed a statistically significant decrease in the occurrence of minor satellite vessels, only in the 160 ppm group.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : 1,1 dichloroethylene was obtained from Dow Chemical Midland with a purity of 99.5% and traces of hydroquinone monomethylether (200-400 ppm).

06.04.1997

(195) (193)

**Species** : rat  
**Sex** : female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : Days 6-15 of gestation  
**Frequency of treatment** : daily  
**Duration of test** :  
**Doses** : 200 mg/l (ca. 40 mg/kg)  
**Control group** : yes, concurrent vehicle  
**Remark** : Maternal tox.: not observed  
**Result** : Not embryo/fetotoxic nor teratogenic.

The goal of the study was to establish whether VDC in the drinking water could cause prenatal toxicity. To this end the rats were offered the technically maximum water-soluble concentration of 200 ppm. The authors report that the thereby orally incorporated amount of VDC corresponded to an inhalation exposure of 120 ppm (0.48 mg/l) over 7 hours. The results show that for the same rat strain VDC is more toxic in inhalation exposure. The authors attribute this possibly to glutathione levels that fluctuate with the time of day, and the related detoxification mechanism. These are particularly high in the late evening and early morning and correlate with food and drinking water intake. In inhalation the substance uptake is spread over a relatively long period (7 hours), where conceivably the amount of glutathione available was not always enough for detoxification.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.05.2002

(96) (189)

**Species** : rat  
**Sex** : female  
**Strain** : Sprague-Dawley  
**Route of admin.** : drinking water  
**Exposure period** : 10 days GD 6-15  
**Frequency of treatment** : daily

**Duration of test** : 16 days  
**Doses** : 200 ppm (40 mg/kg bw day)  
**Control group** : yes, concurrent no treatment  
**Method** : other  
**Year** :  
**GLP** : no data  
**Test substance** : other TS  
**Remark** : Each group consisted of 24 to 26 animals.  
**Result** : The level of significance for all cases was  $p < 0.05$ .  
 Maternal toxicity:  
 No maternal deaths were seen. No effect on maternal body weight gain or mean body weight and on the absolute and relative liver weight. No changes in food or water consumption.  
 Embryo- and fetotoxicity:  
 Statistically significant increase in the average number of corpora lutea was observed. Implantation number, number of death and live fetuses, fetal sex ratio, fetal body weight and incidence of major/minor malformations were not altered by treatment with VDC.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

**Test substance** : 1,1 dichloroethylene was obtained from Dow Chemical Midland with a purity of 99.5% and traces of hydroquinone monomethylether (200-400 ppm).

05.04.1997

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**5.10 OTHER RELEVANT INFORMATION**

**Type** : Biochemical or cellular interactions  
**Remark** : DNA damage in female rat liver was chosen as an experimental parameter, a dose of 120 mg/kg 1,1 dichloroethylene did not produce rat liver DNA damage.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

17.05.2002

(196)

**Type** : Biochemical or cellular interactions  
**Remark** : The effect of 1,1 dichloroethylene on hepatic DNA damage, hepatic ornithine decarboxylase activity, serum alanine aminotransferase activity, and hepatic cytochrome P450 content (female rats, CD; 0/7 animals died after treatment with 40 mg/kg bw) was determined. No significant changes in these parameters were observed. At treatment with 120 mg/kg bw 0/9 died and only the ornithine decarboxylase activity increased significantly.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

03.04.1997

(197) (198)

**Type** : Biochemical or cellular interactions  
**Remark** : Pulmonary cytochrome P450 2E1 bioactivates 1,1 dichloroethylene in male and female mice. CYP 2B1 and CYP 1A1 did not mediate the bioactivation of DCE. This bioactivation occurred in a greater extent in lung microsomes from female than from male mice.

**Source** : BASF AG Ludwigshafen  
 EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)

03.04.1997

(199)

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

- Type Remark** : Biochemical or cellular interactions  
: Adenosine 5'-phosphosulfate kinase activity was decreased in male rats (Sprague-Dawley, liver, after treatment with 500 mg/kg bw orally) 77% of that of control.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (200)
- Type Result** : Biochemical or cellular interactions  
: Apart from a very small induction of cyt P450 at the dose level (15% increase, at a level of 0.125x LD50 dose) all enzymatic markers were clearly reduced after treatment of mice with this olefin. (Enzymatic markers: Aminopyrine N-demethylase activity, Cytochrom content, Nitrophenol hydroxylase activity, Pentoxyresorufin O-dealkylase activity and Ethoxyresorufin O-dealkylase activity).
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- Test substance** : 1,1 dichloroethylene was of analytical grade purity.  
03.04.1997 (201)
- Type Result** : Biochemical or cellular interactions  
: No induction of cytochrom P 450 2B1 in livers of treated Swiss albino CD-1 mice whereas halogenated ethans and methans induce cytochrom P450 2B1.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (202)
- Type Remark** : Distribution  
: Distribution of 14C after inhalation of 14C 1,1-dichloroethylene in different tissues of rats exposed 6 hours to 200 ppm VDC: values in ug/g; liver: 15.75, kidney: 3.15, lung: 5.19, fat tissue: 0.74, muscle: 0.91, skin: 3.78, carcass: 1.68 and plasma: 3.15.  
Another finding in these studies: about 60% VDC were metabolized the rest were bounded in tissues and then metabolized.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
06.04.1997 (203)
- Type Remark** : Metabolism  
: Toxicological study of metabolites:  
The metabolite chloroacetic acid was checked for mutagenic effect. Point mutation in vitro in V79 cells (Chinese hamster) with S-9 Mix from phenobarbital-induced rats and mice was negative (Drevon C. and Kuroki T., 1979). This was confirmed in another study (Huberman E. et al., 1975). In addition, according to the Ames test on 5 different strains, with and without metabolic activation, VDC was not mutagenic (McCann et al., 1975). The strain TA1530 was checked in another Ames test with S-9 Mix from phenobarbital-induced mice and was negative (Malaveille C. et al., 1975).
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (168) (96) (204) (205) (206)
- Type Remark Source** : Metabolism  
: 1,1 dichloroethylene is metabolized to chloroaldehyde.  
: BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (207)

- Type Result** : Metabolism  
: Metabolism rate (in kidney microsomes) of 1,1 dichloroethylene increased markedly (8-fold) compared to female and castrated male CD1 mice in male, castrated and testosterone treated male and female mice.  
Expression of cytochrom P450 2E1 was found in male mice, male castrated and testosterone treated male mice and in female testosterone treated mice. The authors conclude that the expression of this cytochrom P450 was regulated by testosterone.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- Test substance** : 1,1 dichloroethylene was obtained from Merck, no further data
- 06.04.1997 (144)
- Type Remark** : Metabolism  
: Glutathione conjugation serves to activate 1,1 dichloroethylene, the putative product S-(2-chloroethyl)-DL-cysteine has been implicated as the reactive intermediate involved in induced nephrotoxicity and mutagenicity.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- 03.04.1997 (208)
- Type Method** : Metabolism  
: Male Sprague-Dawley rats (~250 g) were exposed for 6 hours to 10 or 200 ppm of [14C] VDC vapor under dynamic airflow conditions in all-glass inhalation chambers modified from an original design by Leach (Atomic Energy Project Report UR-629, 1963). Rats were deprived of solid food ~18 hours prior to exposure.  
[14C] VDC vapor was generated either by metering liquid [14C] VDC at a controlled rate into a warmed (25 C) vaporization flask (200 ppm) or by dilution of a concentrated [14C] VDC atmosphere prepared in a Saran bag (10 ppm). In both cases sufficient [14C] VDC was added to provide a constant concentration of ~200 dpm of [14C] VDC/ml of the inhalation chamber atmosphere. Concentration was monitored continuously via infrared spectroscopy. In addition, samples of chamber air were collected hourly and analyzed via gas chromatography. Analysis of the 14 C activity in the inhalation chamber atmosphere was achieved by bubbling 1 ml air samples into a liquid scintillation vial containing Concifluor, 2-methoxyethanol, and toluene (6:11:83) and assaying for radioactivity by liquid scintillation spectrometry.
- Immediately after exposure, the rats were placed into Roth-type metabolism chambers designed for separate collection of urine, feces, and expired [14C] VDC and 14CO<sub>2</sub>. 72 hours after exposure, rats were decapitated and exsanguinated, and samples of tissue (liver, kidney, lung, perirenal fat, skeletal muscle, skin, whole blood) and the remaining carcass were saved for analysis of 14C activity. Samples of 0-12 and 12-24 hour (postexposure) collections of urine from 2 rats in each treatment group were subjected to high-pressure liquid chromatography to fractionate urinary 14C activity. Anion exchange chromatography of urinary metabolites of [14C] VDC was carried out.
- Covalent binding of 14C activity to tissue constituents was determined in livers collected at necropsy. Concentration-time data obtained for the excretion of 14C activity in expired air or urine from each individual animal were characterized by a 2-compartment open model, and the best pharmacokinetic parameter estimates were obtained using a least-squares

**Result**

nonlinear parameter estimation routine on a digital computer.

: The accumulation of <sup>14</sup>C activity in the body during inhalation exposure to [<sup>14</sup>C] VDC depends primarily on metabolism to nonvolatile metabolites. If the absorption, metabolism, and elimination of the material could be described by first-order kinetic processes over the exposure ranges selected, then accumulation of <sup>14</sup>C activity would be proportional to the exposure concentration, and this does not appear to be the case. Furthermore, although there were no significant alterations in either the routes or the rates of excretion of <sup>14</sup>C activity, the total fractions of the body burden eliminated by these pathways were influenced by concentration. Thus, the dose-dependent character of the pharmacokinetics appears to be due to saturation of one or more metabolic pathways rather than an effect on elimination of the parent compound or its metabolites.

An 18-hour fast also influenced the fate of inhaled [<sup>14</sup>C] VDC in the rat. Fasted rats had lower end-exposure body burdens of <sup>14</sup>C activity and were less capable of metabolizing their accumulated burden of VDC than fed rats. Fasted, but not fed, rats showed definite signs of VDC-induced renal and hepatic toxicity. Also, fasted rats had higher normalized concentrations of <sup>14</sup>C activity in liver, kidneys, and lungs, indicating that total metabolism does not correlate directly with toxicity. Toxicity may be more closely reflected in the balance between detoxification and those metabolic pathways leading to toxicity.

N-acetyl-S-(2-hydroxyethyl) cysteine and thiodyglycolic acid account for 25-30% and 9-17% of the metabolized <sup>14</sup>C activity, respectively, thus supporting the hypothesis that conjugation with GSH is an important pathway for VDC detoxification. Hepatic GSH concentrations may determine the extent of the retention and metabolism of inhaled VDC.

**Source****Test substance**

: The Dow Chemical Company, Midland, MI.  
 : Redistilled vinylidene chloride (VDC, 99.5% purity) was obtained from The Dow Chemical Company, Freeport, TX. [<sup>14</sup>C] VDC was obtained from New England Nuclear, Boston, MA (Lot No. 777259, sp act, 0.475 mCi/mmol, purity >98%).

**Attached doc.**

: VDC Inhal Pharma 1.txt  
 VDC Inhal Pharma 2.txt  
 VDC Inhal Pharma 3.txt

10.07.2002

(209)

**Type****Method**

: Metabolism  
 : Male Sprague-Dawley rats (~250 g) were given 1 or 50 mg/kg [<sup>14</sup>C] VDC in USP corn oil at a dose volume not exceeding 5 ml/kg body weight. Rats were deprived of solid food ~18 hours prior to exposure.

The desired amount of [<sup>14</sup>C] VDC in xylene was added to a sealed 2-ml glass vial connected by polyethylene tubing to a septum-stoppered serum bottle containing 12 g of USP corn oil. The glass vial was warmed to 45 C and the [<sup>14</sup>C] VDC in the head space over the xylene was bubbled into the corn oil. The appropriate amount of cold-carrier VDC was then added to the corn oil to obtain the desired concentration. Dosing solutions were analyzed via gas chromatography. Analysis of the <sup>14</sup>C activity in the dose solutions was conducted via liquid scintillation spectrometry.

Immediately after exposure, the rats were placed into Roth-type metabolism chambers designed for separate collection of urine, feces, and expired [<sup>14</sup>C] VDC and <sup>14</sup>CO<sub>2</sub>. 72 hours after exposure, rats were decapitated and exsanguinated, and samples of tissue (liver, kidney, lung, perirenal fat, skeletal muscle, skin, whole blood) and the remaining carcass were saved for analysis of <sup>14</sup>C activity. Samples of 0-12 and 12-24 hour (postexposure) collections of urine from 2 rats in each treatment group were subjected to high-pressure liquid chromatography to fractionate urinary <sup>14</sup>C activity. Anion exchange chromatography of urinary

- metabolites of [14C] VDC was carried out.
- Covalent binding of 14C activity to tissue constituents was determined in livers collected at necropsy. Concentration-time data obtained for the excretion of 14C activity in expired air or urine from each individual animal were characterized by a 2-compartment open model, and the best pharmacokinetic parameter estimates were obtained using a least-squares nonlinear parameter estimation routine on a digital computer.
- Result** : Results of this study indicate that the fate of VDC ingested by rats is dependent upon both the dose administered and the nutritional state of the animal. After a single oral dose of 1 mg/kg, only 1-3% of the dose is expired as VDC, the remainder being retained and metabolized to non-volatile metabolites which are then excreted, primarily in the urine. Conversely, a greater percentage of the 50 mg/kg dose is expired (20-30%). Therefore, VDC metabolism in the rat appears to be a saturable process in which a finite limit attained for the uptake and/or biotransformation, irrespective of a further increase in the dose administered to the animal.
- An 18-hour fast also influenced the fate of ingested [14C] VDC in the rat. Fasted rats show a diminished capacity to metabolize VDC as indicated by an increased excretion of unchanged [14C] VDC in expired air as well as a decreased urinary output of 14C activity in the form of nonvolatile metabolites.
- N-acetyl-S-(2-hydroxyethyl) cysteine and thiodyglycolic acid account for the metabolized 14C activity, thus supporting the hypothesis that conjugation with GSH is an important pathway for VDC detoxification. Hepatic GSH concentrations may determine the extent of the retention and metabolism of ingested VDC.
- Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : Redistilled vinylidene chloride (VDC, 99.5% purity) was obtained from The Dow Chemical Company, Freeport, TX. [14C] VDC was obtained from New England Nuclear, Boston, MA (Lot No. 777259, sp act, 0.475 mCi/mmol, purity >98%).
- Attached doc.** : VDC Oral Pharma 1.txt  
VDC Oral Pharma 2.txt
- 02.08.2002 (210)
- Type** : Toxicokinetics  
**Remark** : VDC is readily absorbed via the inhalation or oral routes. No information on absorption through the skin is available.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)
- 17.05.2002 (101)
- Type** : Toxicokinetics  
**Remark** : Analogous to the other chlorinated ethenes, VDC is first converted to oxirane (epoxide) by microsomal mono-oxygenase (Costa A.K. und Ivanetich K.M., 1982; Bonse G. et al., 1975; Henschler D., 1977). Metabolization continues via spontaneous transposition of the dichloroethene oxide to chloroacetyl chloride and after hydrolysis, to chloroacetic acid, which can be conjugated with glutathione. The resulting S-(2-carboxymethyl)-cysteine forms dithioglycolic acid, thio-glycolic acid and thiodiglycolic acid (Hathway D.E., 1977; Jaeger R.J., 1975). The pathway that is significant for toxicity and genotoxicity proceeds through a conjugation of the reactive oxirane and the unstable glutathione-acetyl chloride to N-acetyl--S-cysteinyl-acetyl derivative (Jones B.K. and Hathway D.E., 1978; Jones B.K. und Hathway D.E., 1978). In mice this metabolic path predominates, probably due to the higher GSH-epoxide transferase activity, compared to that in rats. In rats

and mice a drop in the hepatocellular GSH content leads to reduced metabolism of the oxirane, resulting in higher toxicity (Andersen M.E. et al., 1989). Disulfiram, tetramethylthiuram disulfide, 3-aminotriazole, inhibitors of microsomal monooxygenase and hence, of oxirane formation, decrease the bonding of VDC metabolites to cellular macromolecules of the liver and kidneys (Buccafusco R.J. et al., 1981; Dawson G.W., 1975).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (211) (212) (87) (213) (214) (88) (96) (215) (216) (217) (102) (218)

**Type** : Toxicokinetics  
**Remark** : In principle VDC is more toxic to mice than to rats, since mice metabolize the substance quantitatively more rapidly (Dow Chemical, 1980; Jones B.K and Hathway .E., 1978). Correspondingly, the alkylation rate of proteins is higher in mice than in rats (Dow Chemical, 1980).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (219) (96) (102)

**Type** : Toxicokinetics  
**Remark** : Studies with rats following oral administration of 1-50 mg/kg or 40-800 mg/m<sup>3</sup> (10-200 ppm) 14C-VDC in respiratory air showed that the metabolism can be saturated at higher exposure levels. Correspondingly, at 1 mg/kg, or 40 mg/m<sup>3</sup> (10 ppm), no difference between normally fed and fasting animals could be observed, while at 50 mg/kg, or 800 mg/m<sup>3</sup> (200 ppm), there was a relative increase in the exhalation of the substance through the lungs, combined with a relative decrease in the urinary excretion of radioactivity (Norris J.M., 1977). At high levels of VDC exposure to rats, the hepatocellular glutathione content was reduced (Jaeger R.J. et al., 1973; Jaeger R.J. et al., 1973). These effects apparently do not occur in mice and rats at 100 mg/m<sup>3</sup> (25 ppm), while after 7 days of inhalation of 320 mg/kg (80 ppm) for 22-23 h/d mice showed a stronger hepatotoxic effect than rats (Short R.D. et al., 1977; Short R.D. et al., 1977).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
02.08.2002 (101) (96) (178) (220) (121) (221) (116)

**Type** : Toxicokinetics  
**Remark** : Because of its stability, the oxirane generated in the first metabolic step forms alkylation products with DNA both in vitro and in vivo (Bolt H.M. et al., 1982). This corresponds to the positive findings in metabolic mutagenicity tests in vitro and in the "host mediated assay" by isolation of the microorganisms of the liver (Bronzetti G. et al., 1981).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (222) (165) (96)

**Type** : Toxicokinetics  
**Remark** : After a 6 hour exposure of mice to 14C-VDC, there were 6 and 30 alkylations per 10<sup>6</sup> nucleotides in liver and kidney DNA, respectively. At the same time, the DNA repair activity in the kidneys - but not in the liver - was increased. After exposure to 40 mg/m<sup>3</sup> (10 ppm), in the kidney there were 11, in the liver 0.94 alkylations per 10<sup>6</sup> nucleotides, in both organs without increasing the DNA repair activity (Reitz R.H. et al., 1980). Correspondingly, the kidneys at least of mice appear to be more sensitive towards the genotoxic effect of VDC than the liver. At 50 mg/m<sup>3</sup> (12.5 ppm), the

## 5. Toxicity

Id 75-35-4  
Date 14.08.2002

glutathione-S-transferase activity in the kidneys of male mice was clearly decreased, compared to rats. A PBPK [physiologically based pharmacokinetic] model was described (D'Souza R.W. and Andersen M.E., 1988).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (223) (96) (224)

**Type** : Toxicokinetics  
**Remark** : Data on VDC metabolism in man are not available.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101)

**Type** : Toxicokinetics  
**Remark** : Analogous to the other chlorinated ethenes, VDC is first converted to oxirane (epoxide) by microsomal mono-oxygenase (Costa A.K. und Ivanetich K.M., 1982; Bonse G. et al., 1975; Henschler D., 1977). Metabolization continues via spontaneous transposition of the dichloroethene oxide to chloroacetyl chloride and after hydrolysis, to chloroacetic acid, which can be conjugated with glutathione. The resulting S-(2-carboxymethyl)-cysteine forms dithioglycolic acid, thio-glycolic acid and thiodiglycolic acid (Hathway D.E., 1977; Jaeger R.J., 1975). The pathway that is significant for toxicity and genotoxicity proceeds through a conjugation of the reactive oxirane and the unstable glutathione-acetyl chloride to N-acetyl--S-cysteinyl-acetyl derivative (Jones B.K. and Hathway D.E., 1978; Jones B.K. und Hathway D.E., 1978). In mice this metabolic path predominates, probably due to the higher GSH-epoxide transferase activity, compared to that in rats. In rats and mice a drop in the hepatocellular GSH content leads to reduced metabolism of the oxirane, resulting in higher toxicity (Andersen M.E. et al., 1989). Disulfiram, tetramethylthiuram disulfide, 3-aminotriazole, inhibitors of microsomal monooxygenase and hence, of oxirane formation, decrease the bonding of VDC metabolites to cellular macromolecules of the liver and kidneys (Buccafusco R.J. et al., 1981; Dawson G.W., 1975).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (211) (212) (87) (213) (214) (88) (96) (215) (216) (217) (102) (218)

**Type** : Toxicokinetics  
**Remark** : In principle VDC is more toxic to mice than to rats, since mice metabolize the substance quantitatively more rapidly (Dow Chemical, 1980; Jones B.K and Hathway .E., 1978). Correspondingly, the alkylation rate of proteins is higher in mice than in rats (Dow Chemical, 1980).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (219) (96) (102)

**Type** : Toxicokinetics  
**Remark** : Studies with rats following oral administration of 1-50 mg/kg or 40-800 mg/m<sup>3</sup> (10-200 ppm) 14C-VDC in respiratory air showed that the metabolism can be saturated at higher exposure levels. Correspondingly, at 1 mg/kg, or 40 mg/m<sup>3</sup> (10 ppm), no difference between normally fed and fasting animals could be observed, while at 50 mg/kg, or 800 mg/m<sup>3</sup> (200 ppm), there was a relative increase in the exhalation of the substance through the lungs, combined with a relative decrease in the urinary excretion of radioactivity (Norris J.M., 1977). At high levles of VDC exposure to rats, the

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

**Source** : hepatocellular glutathione content was reduced (Jaeger R.J. et al., 1973; Jaeger R.J. et al., 1973). These effects apparently do not occur in mice and rats at 100 mg/m<sup>3</sup> (25 ppm), while after 7 days of inhalation of 320 mg/kg (80 ppm) for 22-23 h/d mice showed a stronger hepatotoxic effect than rats (Short R.D. et al., 1977; Short R.D. et al., 1977).  
: BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (96) (178) (220) (121) (221) (116)

**Type** : Toxicokinetics  
**Remark** : Because of its stability, the oxirane generated in the first metabolic step forms alkylation products with DNA both in vitro and in vivo (Bolt H.M. et al., 1982). This corresponds to the positive findings in metabolic mutagenicity tests in vitro and in the "host mediated assay" by isolation of the microorganisms of the liver (Bronzetti G. et al., 1981).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (222) (165) (96)

**Type** : Toxicokinetics  
**Remark** : After a 6 hour exposure of mice to 14C-VDC, there were 6 and 30 alkylations per 10<sup>6</sup> nucleotides in liver and kidney DNA, respectively. At the same time, the DNA repair activity in the kidneys - but not in the liver - was increased. After exposure to 40 mg/m<sup>3</sup> (10 ppm), in the kidney there were 11, in the liver 0.94 alkylations per 10<sup>6</sup> nucleotides, in both organs without increasing the DNA repair activity (Reitz R.H. et al., 1980). Correspondingly, the kidneys at least of mice appear to be more sensitive towards the genotoxic effect of VDC than the liver. At 50 mg/m<sup>3</sup> (12.5 ppm), the glutathione-S-transferase activity in the kidneys of male mice was clearly decreased, compared to rats. A PBPK [physiologically based pharmacokinetic] model was described (D'Souza R.W. and Andersen M.E., 1988).

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
02.08.2002 (101) (223) (96) (224)

**Type** : Toxicokinetics  
**Remark** : Data on the metabolism of VDC in man are not available.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101)

**Type** : Toxicokinetics  
**Method** : Male Sprague-Dawley rats weighing 250-300 g were fasted for 18 hours prior to being given 10, 25, 50, or 100 mg/kg VDC either via i.v. injection (0.5 ml) or oral intubation (0.5 ml).

VDC was injected directly into a sealed vial containing 1.5 ml of 50% aqueous PEG 400. The contents were vortexed for 1 min. For i.v. injection, a 0.5 ml withdrawal was made into a chilled tuberculin syringe and injected into the dorsal vein of the penis. For oral dosing, a 0.5 ml aliquot was administered via blunt-tipped intubation needle.

Blood samples were collected at selected intervals for 6-8 hrs following dosing. For most experiments, rats were maintained in a lightly etherized state during the first 15 min of blood sampling. Thereafter, the rats were etherized just prior to blood sampling. At each interval, 0.1 ml of blood was withdrawn from the caudal artery into a tuberculin syringe. In one experiment, rats were cannulated into the jugular vein in order to compare toxicokinetics in unanesthetized vs. etherized rats.

- The concentration of VDC in blood samples was determined via gas chromatographic head-space analysis.
- Blood concentration vs. time data obtained from i.v. dosing experiments were evaluated by ESTRIP and NONLIN computer programs. The total body clearance, apparent volume of distribution, biological half-life, volume of distribution for the central compartment, and bioavailability were calculated.
- Result** : The results of this study demonstrate that VDC is very rapidly and completely absorbed from the GI tract. Peak arterial blood levels were observed just 2-8 min after dosing.
- Bioavailability of orally administered VDC was comparable to that of the i.v.-administered. The elimination of iv and orally administered VDC followed a triexponential pattern. An increase in apparent volume of distribution and total body clearance was observed with increasing iv dose. The data suggest that the fraction of dose subjected to pulmonary first-pass elimination is larger at higher dose levels, resulting in an increase in total body clearance.
- Although fasting did not alter the rate of elimination, accessibility to food and route of administration did influence the biological half-life, which was consistently shorter in iv-dosed rats than in their oral counterparts. It is likely that prolonged absorption is responsible for the longer half-life, rather than a decreased rate of elimination.
- Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : VDC (98% minimum purity) was purchased from Mathson, Coleman, and Bell (Norwood, OH).
- Attached doc.** : VDC OralIV Pharma 1.txt  
10.07.2002 (225)
- Type** : Toxicokinetics  
**Method** : Adult male Sprague-Dawley rats were anesthetized and exposed via tracheostomy to inhaled VDC at levels of 25, 75, 150, or 300 ppm. Rats were allowed to acclimate to a breathing valve inserted into the tracheostomy for 10 min prior to exposure, or until a stable breathing rate was reached. Rats were exposed to a given dose level for 3 hours. Blood samples were periodically withdrawn from the femoral vein over the course of the exposure.
- Measured volumes of VDC was generated in a Mylar bag, which was then attached to a breathing valve inserted in the tracheostomy. Exhaled air was collected in another Mylar bag, thus creating a closed system.
- The respiratory rate of each rat was measured continuously using a pneumotachograph. Alveolar levels of solvent were calculated from VDC levels in inhaled and exhaled air, which were sampled at 2-8 min intervals and were determined via gas chromatography. Blood levels of VDC were determined via gas chromatographic headspace analysis.
- Result** : Findings in this study indicate that the rat's capacity to metabolize and eliminate VDC can be exceeded during the course of inhalation of 150 ppm or more. Inhalation of 300 ppm definitely exceeds the rat's capability to assimilate the chemical.
- Departures from linearity during the final hour in plots of cumulative uptake also suggest that inhalation of 150 ppm for ~2 hours can result in saturation kinetics.
- Source** : The Dow Chemical Company, Midland, MI.  
**Test substance** : VDC (98% minimum purity) was obtained from Mathson, Coleman, and Bell (Norwood, OH).

- Attached doc.** : VDC Inhal Toxico 1.txt  
VDC Inhal Toxico 2.txt  
10.07.2002 (226)
- Type Remark** : other: Computer automated structure evaluation  
: Using the carcinogenic potency database (CDBP), 233 chemicals (rodent carcinogens) were analyzed with CASE and electrophilic substructure alert analysis as well as data of Salmonella assay in order to more exact description of carcinogenicity.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
06.04.1997 (227)
- Type Result** : other: Effect of exposure route on potency of carcinogens  
: Inhalation of 1,1 dichloroethylene were less effective than oral intake of the substance in mice and rats.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (228)
- Type Remark** : other: QSAR analysis  
: The QSAR analysis indicated that toxic effects induced by chlorinated aliphatics in *Aspergillus nidulans* are mainly dependent on steric factors. An involvement of free radicals, generated by the reductive mechanism of haloalkanes and haloalkenes is hypothesized as an explanation of the data.  
Note: 1,1 dichloroethylene were evaluated as positive in chromosome malsegregation induction among other chlorated alkenes.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
02.04.1997 (166)
- Type Remark** : other: Quantitative Prediction of Human Cancer Risk  
: In case of 1,1 dichloroethylene the human evidence is inconsistent with the prediction (predicted human cancer incidence is much higher than what is actually observed).
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
02.04.1997 (229)
- Type Remark Source** : other: Review  
: Summarizing descriptions  
: BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (230) (124) (88) (96)
- Type Remark Source** : other: Summarizing descriptions  
: Summarizing descriptions  
: BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (101) (230) (124) (88) (96)
- Type Remark Result** : other: cardiac teratogenicity of dichloroethylene in a chick model  
: 3 days old chick embryos were treated with 3.8, 3 and 0.8 mg1,1 trichloroethylene, the compound was injected (dissolved in mineral oil) into the eggs. On day 18 the embryos were harvested and examined.  
: The results suggested that DCE is a more potent cardiac teratogen than a general teratogen in the chick. It is

- noteworthy that in the highest dose group less abnormalities occurred than in the control.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
02.04.1997 (231)
- Type** : other: compendium of chemicals organized by target organs  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
02.04.1997 (232)
- Type** : other: drinking water levels of 1,1 DCE  
**Remark** : An estimated 4,789,000 individuals are exposed to levels of DCE in drinking water at or above 0.2 microg/l, while 52,000 are exposed to levels above 5 microg/l DCE in drinking water supply systems (public) in USA.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (203)
- Type** : other: levels of 1,1 DCE in the air  
**Remark** : Median air levels in USA for urban/suburban areas and source dominated areas are 20 ng/cubic m and 14 microg/cubic m respectively.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (203)
- Type** : other: list of compounds (cancer risk assessment)  
**Remark** : 1,1 dichloroethylene have been submitted to carcinogenicity bioassays at the Bentivoglio Laboratories, DCE is characterized as intermedial potency carcinogen.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (233)
- Type** : other: list of teratogenicity of plastic and rubber chemicals  
**Remark** : 1,1 dichloroethylene did not produce any teratogenic effect in rabbit, mouse, and rats.  
Source: presumable Murray et al. chapter 5.9 in this sheet.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (234)
- Type** : other: photoreaction products from 1,1 dichloroethylene and NO<sub>2</sub>  
**Remark** : Slightly mutagenic products were generated by UV reaction with NO<sub>2</sub> and 1,1 dichloroethylene.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (235)
- Type** : other: relationships among chemical structure and carcinogenicity/mutagenicity  
**Remark** : 1,1 dichloroethylene is characterized to be non-alerting to DNA-reactivity and as non carcinogenic in rat and mice. 1,1 dichloroethylene is 1 of 301 chemicals which were analysed with the view of finding relationships among chemical structure and carcinogenicity/mutagenicity. Similar publications of theoretical views of different compounds can be found in 2 other references (both containing 1,1 dichloroethylene).

- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
01.07.2002 (236) (237) (238)
- Type** : other: review  
**Remark** : Report about carcinogenicity of alkenes.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (239)
- Type** : other: summarizing report  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (240)
- Type** : other: summarizing report  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (241)
- Type** : other: summarizing report  
**Remark** : A very detailed and comprehensive report for the 3  
dichloroethylenes, 1,1 and cis/trans 1,2 dichloroethylene.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (203)
- Type** : other: summarizing review/handbook  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
03.04.1997 (242)

**5.11 EXPERIENCE WITH HUMAN EXPOSURE**

- Remark** : Depression of the central nervous system with drunkenness to  
unconsciousness, in acute exposures over 1000 ppm.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (243)
- Remark** : Moderate skin and mucosal irritation from liquid vinylidene  
chloride.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (244)
- Remark** : No liver damage in man due to VDC.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (245)
- Remark** : The odor threshold lies near 50 ppm.  
Mucosal irritation in the eyes and upper respiratory tract from approx. 25  
ppm.  
**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (246)
- Remark** : No liver damage in 98 workers with long-term exposure of up to 25 years at  
exposure levels between 5 and 300 ppm.

- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (247)
- Remark** : No increased mortality rate in mortality studies on 629 workers with mixed exposure to vinylidene chloride, vinyl chloride and acrylonitrile, with estimated average concentrations of approx. 50 ppm between 1955 and 1965, less than 10 ppm between 1965 and 1975 and less than 5 ppm from 1975 on. In the age group under 50 years there was an accumulation of cerebral hemorrhages, brain atheroscleroses with apoplexy, acute cardiovasculae diseases and bronchial carcinomas in 2 employees after a short exposure duration (14-25 months).
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (248)
- Remark** : High doses of vinylidene chloride (e.g. 4000 ppm) cause sudden loss of consciousness. Brief anaesthetic effect after short exposure.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (249)
- Remark** : Significantly higher mortality due to cardiovasculae diseases (for instance cardiac infarction) in follow-up study with 535 persons over 6 months, who in the years from 1965 on had average exposures of 50 ppm.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (250)
- Remark** : Cohort study on 4806 chemical workers exposed to 19 different chemicals between 1942 and 1973: no increased incidence of pulmonary cancer that could be traced to vinylidene chloride.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (251)
- Remark** : High concentrations of vinylidene chloride around 4000 ppm cause reversible CNS depression, up to unconsciousness. Skin irritation, especially after prolonged contact. Long-term exposure to non-anaesthetic doses and repeated short-term exposure may cause liver and kidney damage.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (252)
- Remark** : Persistent cranial nerve disturbance (trigeminal damage, cervical and auricular skin nerves, nervus hypoglossus and masticatory and ocular muscles) in 2 tank-cleaning workers due to mixed exposure to vinylidene chloride and dichloroacetylene or monochloroacetylene during work in extreme heat.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (253)
- Remark** : Skin irritation, painful eye irritation, temporary corneal erosion and iritis due to liquid vinylidene chloride or phenolic stabilizers (MEHQ). Eye and trachea irritation at 25 ppm.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (254)
- Remark** : Moderate skin and mucose irritation due to liquid vinylidene

- chloride.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (255)
- Remark** : No liver damage in man due to VDC.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (245)
- Remark** : The odor threshold lies near 50 ppm.  
Mucosal irritation in the eyes and upper respiratory tract from approx. 25 ppm.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (246)
- Remark** : No liver damage in 98 workers with long-term exposure of up to 25 years at exposure levels between 5 and 300 ppm.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (247)
- Remark** : No increased mortality rate in mortality studies on 629 workers with mixed exposure to vinylidene chloride, vinyl chloride and acrylonitrile, with estimated average concentrations of approx. 50 ppm between 1955 and 1965, less than 10 ppm between 1965 and 1975 and less than 5 ppm from 1975 on. In the age group under 50 years there was an accumulation of cerebral hemorrhages, brain atheroscleroses with apoplexy, acute cardiovascular diseases and bronchial carcinomas in 2 employees after a short exposure duration (14-25 months).
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (248)
- Remark** : High doses of vinylidene chloride (e.g. 4000 ppm) cause sudden unconsciousness. Brief anaesthetic effect following short-term exposure.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (249)
- Remark** : Significantly higher mortality due to cardiovascular illness (for instance cardiac infarction) in follow-up study on 535 persons over 6 months, who in the years from 1965 on had exposures averaging 50 ppm.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (250)
- Remark** : Cohort study on 4806 chemical workers exposed to 19 different chemicals between 1942 and 1973: no increased incidence of pulmonary cancer that could be traced to vinylidene chloride.
- Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (251)
- Remark** : High concentrations of vinylidene chloride around 4000 ppm cause reversible CNS depression, up to unconsciousness. Skin irritation, especially after prolonged contact. Long-term exposure to non-anaesthetic doses and repeated short-term exposure may cause liver and kidney damage.

## 5. Toxicity

**Id** 75-35-4  
**Date** 14.08.2002

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (252)

**Remark** : Persistent cranial nerve disturbance (trigeminal damage, cervical and auricular skin nerves, nervus hypoglossus and masticatory and ocular muscles) in 2 tank-cleaning workers due to mixed exposure to vinylidene chloride and dichloroacetylene or monochloroacetylene during work in extreme heat.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (253)

**Remark** : Skin irritation, painful eye irritation, temporary corneal erosion and iritis due to liquid vinylidene chloride or phenolic stabilizers (MEHQ). Eye and trachea irritation at 25 ppm.

**Source** : BASF AG Ludwigshafen  
EUROPEAN COMMISSION - European Chemicals Bureau Ispra (VA)  
17.05.2002 (254)

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