FOREWORD INTRODUCTION

1,1'-DIFLUOROETHYLENE (VDF,VF2)

CAS N°: 75-38-7

SIDS Initial Assessment Report for 13th SIAM

(Bern, Switzerland, November 6-9, 2001)

Chemical Name : 1,1-difluoroethylene (VDF, VF2)

CAS No. : 75-38-7

Sponsor Country : United States of America

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History :

The work and review process undertaken for this chemical was done by industry and the United States Environmental Protection Agency. Documents were prepared and reviewed by industry prior to submission to sponsor country. Sponsor country conducted reviews of submitted data and offered comments to industry. Industry prepared and resubmitted documents for consideration at SIAM 13. All data were obtained within the consortia's archives and libraries. In addition, databases that were searched may be found in section 7 of the SIAR.

Testing : No testing (X)
Testing ( )

Comments :

Deadline for Circulation : September 14, 2001

Date of Circulation :

SIDS INITIAL ASSESSMENT PROFILE

CAS No.	75-38-7
Chemical Name	1,1-Difluoroethylene or vinylidene fluoride
Structural Formula	$F_2C=CH_2$

RECOMMENDATIONS

The chemical is currently of low priority for further work.

SUMMARY CONCLUSIONS OF THE SIAR

Human Health

Metabolic/kinetic studies with vinylidene fluoride (VF2) in rats and mice indicate that during inhalational exposure, VF2 reaches a maximum level in blood at 15 minutes. Some metabolism takes place in the liver. It has been hypothesized that some fluoroacetic acid may be formed during metabolisation of VF2, which in turn may interfere with the citric acid cycle. However, mammalian toxicity study results do not indicate that this leads to structural or functional pathological changes.

Acute toxicity of VF2 is low with 1 hr LC00 of 200,000 ppm (524,000 mg/m^3) in rats. Only slight CNS effects were noted at very high concentrations (80% in air). Cardiac sensitization studies were negative. Several inhalation exposure studies have been conducted in rats and mice exposed 6h/d, 5d/week for 13 weeks. No target organs were consistently identified although effects on the kidney, spleen and testes were reported in various studies. In rats and mice the LOEC of 500 ppm (13,100 mg/m^3) was identified, based on body, organ weight and clinical chemistry changes in the absence of histopathological changes. A NOEC of 250 ppm (6,550 mg/m3) was identified in rats. At 40,000 - 50,000 ppm (104,8000 – 131,000 mg/m^3) effects on the nasal epithelium were noted in rats.

In chronic toxicity/carcinogenicity inhalation studies, rats and mice were exposed 6 h/d, 5d/week for 24 and 18 months, respectively at concentrations up to 10,000 ppm (26,200 mg/m^3). Neoplastic findings were comparable in control and treated animals. An earlier 52 week study in rats exposed orally to VF2 indicated increased lipomas/liposarcomas. However, this study was performed according to a protocol with significant deviations from currently prescribed guidelines and was reported in insufficient detail for proper evaluation. In genotoxicity studies, VF2 has shown some activity in bacterial assays, but was negative in the *in vitro* chromosomal aberration and gene mutation study in mammalian cells. *In vivo*, VF2 was negative in a mouse micronucleus and Drosophila SLRL test. Thus there is no evidence of genotoxicity *in vivo*. Overall, the results suggest that VF2 does not present a genotoxic hazard to man.

VF2 did not induce teratogenic or embryofetal toxicity effects in developmental toxicity studies in rats exposed up to 10,000 ppm during gestation days 6 –15. The NOEL for reproductive effects is $\geq$ 7000 ppm (18,340 mg/m^3) in rat studies.

Environment

VF2 is a gas at ambient temperatures and atmospheric pressure. Emissions will only occur during production and processing of VF2 and will partition nearly exclusively to air (>99%). Its low log P_{ow} does not indicate any significant bioaccumulative potential. In air, VF2 will be degraded by reaction with hydroxyl radicals. A half-life of 3.3 days has been calculated. Likely primary products resulting from the tropospheric degradation of VF2 are COF_2 and formaldehyde. Fluorogyloxal (CFOCHO) may also be a product of the degradation of VF2. The ultimate degradation products are formaldehyde, HF and CO2.

No biodegradation studies in water have been performed for VF2, however, related gaseous materials (tetrafluoroethane, pentafluoroethane, difluoromethane, 1-chloro-1,1-difluorethane, vinylidine chloride) generally

showed < 10% degradation indicating that transformation to metabolites in soil or the water compartment may be considered very low. Based on these analogous substances, VF2 is not expected to be readily biodegradable and testing is not recommended. Due to specific physico-chemical properties of VF2 its production and use pattern, and its nearly exclusive partitioning to air, no aquatic toxicity testing has been performed. Using QSAR, the LC50 (96 hr) for fish is 245 mg/L, the daphnia LC50 (48 hr) is 250 mg/L and the green algae EC50 (96 hr) is 149 mg/L.

Exposure

VF2 is almost exclusively used as a monomer for the production of fluoropolymers (polyvinylidene flouride) and as copolymer with hexafluoropropylene and chlorotrifluoroethylene. In the United States, production is performed in closed systems and is anticipated to be representative of global production methods based on the chemicals physical chemical properties. Global production in 1999 was approximately 33,000 tonnes (72,600,000 pounds). The emissions of VF2 come exclusively from production and processing installations of VF2. The segment of the population exposed directly or indirectly to VF2 is very limited: workers during production and processing. Consumers manipulating goods made of VF2 (polymers) are not exposed to VF2. Possible emissions during production and processing are low and lead to very low atmospheric concentrations. VF2 is not expected to be released to water systems but in case of emissions will totally partition to air. It will not partition to the water from the air. VF2 is a flammable gas at ambient temperature (limits 4.7 % to 25.1%). Its flammability constitutes its most important physical danger.

NATURE OF FURTHER WORK RECOMMENDED

No recommendation.

FULL SIDS SUMMARY

CAS N° 75-38-7		SPECIES	PROTOCOL	RESULTS
PHYSICO-CHEMICAL				
2.1	Melting point		handbook	-144°C
2.2	Boiling point		handbook	-83 to –85.7°C
2.3	Density			0.67 to 0.92 gm/cm ^{3} at 20°C
2.4	Vapour pressure		handbook	35700 hPa at 20°C
2.5	Partition coefficient		calculated	1.24
2.6	Water solubility		handbook	254 mg/l at 25°C
2.11	Oxidising properties	Not considered to have oxidising properties		
2.12	Additional remark Soil Koc	Henry's law constant: 0.226 atm.m3/mol 7.12		
ENVIRONMENTAL FATE AND PATHWAY				
3.1.1	Photodegradation		calculated	Rate cst: 2*10^{-12} to 2.04*10^{-13} cm^3/molecule/sec T1/2: 3.3 days
3.1.2	Stability in water	No data. VF2 will quickly evaporate to the atmospheric compartment (see Mackay modeling)		
3.2	Monitoring data	No data		
3.3	Transport and Distribution	According to the Mackay model (level 1) more than 99.6% of emitted VF2 will collect in the atmosphere with negligible amounts remaining in water, sediment and soil.		
3.5	Biodegradation	No data. VF2 will evaporate from soil and surface waters before any significant degradation can take place.		
ECOTOXICOLOGY				
4.1	Acute/prolonged toxicity to fish			No data
4.2	Acute toxicity to aquatic invertebrates			No data
4.3	Toxicity to aquatic plants e.g. algae			No data
4.4	Toxicity to micro-organisms e.g. bacteria			No data
4.5.1	Chronic toxicity to fish			No data
4.5.2	Chronic toxicity to aquatic invertebrates			No data
TOXICOLOGY				
5.1.1	Acute Oral			Not applicable
5.1.2	Acute Inhalation		Lester at al., 1950	> 80% v/v
5.1.3	Acute Dermal			Not applicable
5.2.1	Skin irritation/corrosion			Not applicable

5.2.2	Eye irritation/Corrosion			No specific test results but no irritation observed during other tests.
5.4	Repeated dose	Rat, 2 weeks, inhalation	Dupont Cy. OTS0215306, 1977	NOEL < 25000 ppm
		Mouse, 2 weeks, inhalation	Newton, 1988	NOEL = 40000 ppm
		Rat, 13 weeks, inhalation	Reuzel, 1986	NOEL: 1000 ppm LOEL: 7000 ppm
		Mouse, 13 weeks, inhalation	Newton, 1989	NOEL: 7000 ppm LOEL: 40000 ppm
5.5	Genetic Toxicity In vitro			
	Bacterial test	S.typhimurium	Russell, 1979	Positive only for TA1535 strain in presence of S9
		S.typhimurium TA 100	Bartch, 1979	Negative with and without S9
	Non-bacterial test	CHO cells/ HGPRT	Rickard, 1986	Negative with and without S9
		CHO cells/chromos. Aberration	Rickard, 1986	Negative with and without S9
5.6	Genetic Toxicity In vivo	Mouse, micronucleus, inhalation	Hodson-Walker, 1988	Negative
		D.melanogaster, sex linked recessive lethal test	Sernau, 1988, 1989	Negative
5.7	Carcinogenicity	Rat, 52 weeks, oral	Maltoni, 1979	NOEC < 4.12 mg/kg
		Rat, 104 week, inhalation	Arts, 1991	NOEC: 10000ppm
		Mouse, 78 weeks, inhalation	Newton, 1991	NOEC: 10000 ppm
5.8	Reproduction Toxicity	Rat, 13 weeks, inhalation	Reuzel, 1986	NOEC: = or >7000 ppm
		Rat, 13 weeks, inhalation	Koeter,	NOEC: = or > 7000 ppm
5.9	Development / Teratogenicity	Rat, gestation day 5 to 15, inhalation	Mecler, 1978	NOEC: = or > 10 000 ppm
5.11	Human experience	No data.		

SIDS INITIAL ASSESSMENT REPORT

1,1-Difluoroethylene

1. Identity

Purity Molecular weight	99.5 % (does not contain any additives for stabilization.) 64
Melting point	– 144°C
Boiling point	– 83 to – 85°C
Vapor pressure	35700 hPa (26960 mmHg) at 20°C
Water solubility	254 mg/L at 25C
Partition Coefficient (Log K_{ow})	1.24
Henry's Law Constant	0.226 atm.m^3/mole
Other:	Colorless, flammable gas at ambient temperature

2 General Information on Exposure

Production volume

Solvay, Atofina, and Ausimont are the major producers of VF2. The production sites are located in France and the USA. Global production in 1999 was approximately 33,000 metric tons (72,600,000 pounds).

Production method

Several methods for manufacture of VF2 are based on pyrolysis including the dechlorination of 1,2-dichloro-1,1 – difluoroethane in the presence of a catalyst and the dehydrofluorination of 1,1,1-trifluoroethane. Based on physico-chemical properties VF2 is produced in closed systems.

Uses and function of VF2

VF2 is used to manufacture polyvinylidene fluoride and elastomeric copolymers with chlorotrifluoroethylene and hexafluoropropylene. The polymerisation process is performed in closed systems. VF2 is usually polymerised above its critical temperature of 30.1°C and at pressures above 3 Mbars (30 atm). VF2 is a closed system intermediate.

Form of Marketed Product

Manufacturers of VF2 either polymerize the compound on-site or sell and transport the substance in bulk quantities as liquefied gas under pressure (100 gallon gas cylinders or tube trailers).

Information on Safe Handling Procedures (Storage)

VF2 is stored in open air and protected from direct sunlight in steel containers (typical 50 to 100 m^3) fitted with a safety valve or vent and pumps are monitored by explosimeters. These containers are stored away from ignition and heat sources. Equipment and piping containing VF2 is grounded to avoid static build up and electrostatic discharges.

2.1. Sources of Releases to the Environment

Production and processing releases

VF2 is handled in closed systems under high pressure. Exposure during handling is considered to be negligible since it is carried out in sealed pipes and vessels. Emissions will therefore be incidental during equipment failures and maintenance operations. Monitoring systems are in place and capable of detection at levels of 0.1 ppm. Leaks are therefore quickly revealed and corrected.

Release from polymer use

Polymers made from the monomer VF2 do not contain unreacted monomer above 1 ppm. The polymers, which are thermally, chemically, and UV-light resistant, are used for tank linings, pumps, valves and lined pipes in chemical or food processing equipment. When the polymer product is used with compatible materials, the decomposition of the polymer is minimal, leading to negligible concentrations in food, when used in food processing equipment, or to the environment.

2.2 Human exposure

VF2 is a gas at room temperature. Therefore, the main route of human exposure is via inhalation. The two main exposure groups assessed for possible VF2 inhalation are occupational groups and populations residing in locations in the vicinity of producing and processing facilities.

2.2.1. Occupational exposure

Potential exposure to VF2 is limited to its production and polymerization. The American Conference of Governmental Industrial Hygienists', Threshold Limit Value (TLV), Time Weighted Average (2001) for VF2 is 500 ppm.
In a survey of a VF2 production plant in 1992-1993, a mean work place VF2 concentration of 0.9 ppm was determined. During 0.7% of the working time a level in the work atmosphere of 22.7 ppm was reached. (Solvay, unpublished data, ref 58) In the mid 1980's, two polymerization plants in the USA were monitored for exposures to VF2 during the polymerization process. In one plant, there were no exposures noted above 1.2 ppm VF2 (TWA). In the second plant (personal sampling), depending on the function of the person involved, VF2 atmospheric measurements ranged between < 0.1 ppm and 40 ppm. All measurements above 10 ppm were from incidental exposures (other than normal working conditions and maintenance) and of short duration. For example, the 40 ppm (personal sampling) value was obtained during non-routine work or maintenance. An emergency repair of a malfunctioning pump required that a vapor line be bleed resulting in a short-term elevated exposure to the maintenance worker. (US EPA, draft 1999, ref 57) Since the performance of these surveys, process controls and structural production conditions have been improved, so that possibility of exposure of workers to VF2 has further decreased.
No monitoring data are available for other VDF manufacturers/processors in other countries. Since manufacturing/processing is similar world-wide for VF2, it may be assumed that exposure values would be within the same range.

2.2.2. Consumer Exposure

Consumer exposure is not anticipated based on the physico-chemical properties and use of VF2. There are no direct consumer uses of fluoroalkenes. In addition, final products for which VF2 is used do not contain unreacted VF2 above 1 ppm. Thus, consumer exposure is not anticipated.

2.2.3. Indirect Exposure via the Environment.

VF2 is a gas, has a low calculated log Kow (1.24) and is thus considered to have no significant bioaccumulation potential. Records indicate that during manufacturing and processing of VF2, under normal operating conditions, releases to the environment are anticipated to be minimal. Therefore, indirect human exposure is not expected.

2.3 Environmental Fate

2.3.1. Distribution in Air, Water, Soil

VF2 is a gaseous substance at ambient temperature (BP: -83 to -85.7°C, VP: 35700 hPa at 20°C) with a limited solubility in water (254 mg/l at 20°C and 1 bar atmospheric pressure). Under natural conditions, this compound will evaporate from water and almost completely enter the atmospheric compartment. This is indicated by the results of the Level I and III Mackay modeling based on the physico-chemical data as mentioned in the SIDS dossier. Estimated values indicate that more than 99.94 % of emitted VF2 will partition to the air compartment.

The remaining amount (0.05%) will distribute to the aquatic compartment.
VF2 is unlikely to persist in water due to its high vapour pressure (35700 hPa). The EPIWIN model calculates the half life ($T_{1/2}$) in river water as 0.8 hours and $T_{1/2}$ in lake water as 76 hours (See IUCLID Dossier). Due to its density in the liquid phase (0.67 g/cm3 at 25°C), VF2 will float on water rather than dissolve in it if it is accidentally released under supercooled conditions. Its leaching into soil and ground water in such circumstances will also be negligible.
Its (calculated) log Kow (1.24) indicates that the substance would not significantly partition to organic material in soil or water. The calculated soil Koc (partition coefficient organ carbon- water) is 7.12. Hence the presence of organic matter would not contribute significantly to increased concentrations in these compartments over those determined by its solubility and volatility.

2.3.2. Abiotic and Biotic Degradation in Air, Water and Soil

No experimental data are available on the degradation of VF2. The Biowin program in the EPIWIN model indicates that VF2 will degrade in water and soil (timeframe of days to weeks). However, under the natural conditions prevailing in soil, natural waters and under standard temperature and pressure, VF2 and similar compounds will partition completely to the atmospheric compartment before any significant degradation could take place.
In the atmosphere, VF2 is considered to be degraded by reaction with OH radicals. Howard (1976) calculated a Rate constant for this reaction of $2*10^{-12}$. Life-time calculation by the Prahter and Spivakovsky procedure yields a half life for VF2 of 3.3 days. The AOP program (See IUCLID Dossier for details) in the EPIWIN model yields similar results: T ½ (OH radicals): 4.7 days and T ½ (O3): 40.9 days.

Likely primary products resulting from the tropospheric degradation of vinylidene fluoride are COF_2 and formaldehyde. Within a few weeks, COF_2 will be hydrolyzed to CO_2 and HF after uptake into cloud droplets. Fluorogyloxal (CFOCHO) may also be a product of the degradation of VF2, but this remains uncertain. If fluorogyloxal is formed, it will disappear rapidly from the atmosphere, probably mainly by photolysis on a time scale of a few hours, ultimately giving HF and carbon oxides.

2.3.3. Bioaccumulation in Different Environmental Compartments

VF2 has a calculated log Kow of 1.24 (KOWWIN program in the EPI WINN model). This value indicates that possible bioaccumulation in the food chain is not significant. Moreover, the limited solubility of VF2 as well as its almost total distribution to air and its short half life in that compartment makes significant contact with the organisms in the food chain negligible. This is supported by the BCF program results in the EPIWIN model (BCF: 1.8). (See IUCLID Dossier for details.)
Therefore, it is considered that bioaccumulation of VF2 in the food chain is of low concern.

2.4 Predicted Environmental Concentration.

No environmental monitoring data are available.
In view of the similar production and processing conditions of VF2 worldwide (closed systems), its physico-chemical properties, and its predicted distribution and degradation in air and water, the environmental concentrations of VF2 in the different environmental compartments are considered to be negligible.

3.0 Human Health Hazards

3.1. Effects on Human Health

3.1.1. Toxicokinetics / Metabolism

Cellular interactions

Rats exposed to VF2 concentrations up to 25000 ppm for up to 6 hrs, did not show hepatotoxic signs as measured by liver weight, histology and serum sorbital dehydrogenase activity. (Conolly, et al, 1979, ref 43)
Fed and fasted rats exposed to VF2 concentrations of up to 82000 ppm for 4 hrs did not show a toxicologically significant increase in serum alanine alpha-ketoglutarate transaminase. (Jaeger et al, 1975, ref 44)

Toxicokinetics/Metabolism

VF2 was found to inactivate P450 enzyme and heme only to 17% in primed and unprimed rat hepatic microsomes when exposed to 60µM for 30 minutes. Fluor was only minimally released in this test. (Baker et al., 1987, ref 46)
When rats were exposed to VF2 concentrations of 2200 ppm for 30 minutes, the animals showed an increased Fluor urinary excretion for 7 days post exposure. Creatinine excretion and urinary volume were not increased. The medulla of the kidneys showed hyperemia and a pale whitish band in the cortex, but no histopathological changes were observed in that organ. (Dilley et al., 1974, ref 47)
After 8 hrs exposure to VF2 concentrations of 500 ppm, rats exhaled acetone, which was considered by the authors as an indication that VF2 is partly metabolized to fluoroacetate and that VF2 interacts with hepatic cytochrome P450. (Filser et al., 1980, ref 50)
Metabolism seems saturated at the 100 ppm exposure concentration. Vmax was calculated to be 1.1 µM/hr/kg. (Filser et al., 1978, ref 48) Filser suggested that an epoxide intermediate is formed with subsequent rearrangement to halogenated acetaldehyde or acyl halide and formation of fluoroacetic acid; the latter could interfere with the citric acid cycle.(Filser et al., 1980, ref 50) Zwart (1985, ref 52) observed a saturation of VF2 metabolism in rats at an exposure concentration of 400 ppm. Stoeckle et al., (1979, ref 51) found a similar metabolism rate for VF2 as that observed by Filser in rats and observed that exposure to 2000 ppm VF2 for 14 weeks induced only a minimal ATPase deficiency in rat hepatocytes. Bolt et al., (1979, ref 60) reported that interaction with P450 with slowly metabolized compounds like VF2 may lead to inhibition of metabolism of drugs and other xenobiotics. Inhibition of p-hydroxylation of aniline and demethylation of aminopyrine by VF2 served as indicator reactions.
Medinski et al., (1990, ref 54) calculated kinetic parameters for VF2 in rats. Steady state blood levels of VF2 in rats were 15 ng/ml at 30 ppm exposure and 2400 ng/ml at 16,000 ppm exposure. Tmax was 15 minutes for all concentrations tested. After exposure blood levels decreased to 10% of Cmax in 1 hr. VF2 tissue air partition coefficients were: 0.07, 0.18, 0.8, 1.0 and 0.29 for water blood, liver, fat and muscle respectively.
Kinetic values measured and calculated for mice seemed to be lower than those found for rats. (Bechtold et al.,1988, ref 55)

Comments on the toxicokinetic and metabolism studies

The above-mentioned studies give a fair idea of the molecular behavior of VF2 in the mammalian organism, and indicate that some metabolism of the molecule takes place. The long-term toxicity/carcinogenocity studies mentioned below show that the metabolic fate of VF2 in animals

does not lead to structural nor functional adverse effects at the concentrations tested (up to 10000 ppm for 2 years in the rat).

3.1.2 Acute toxicity

Several acute inhalation toxicity tests have been performed, which are more or less comparable to LC50 studies.
In a series of acute inhalation experiments, the lethal concentration for rats and mice after 1-hour exposure was greater than 200,000 ppm. Animals were observed for 7 days post exposure. Only the mice showed some minor behavioral changes. (Pennwalt, 1982, ref 15) In another test, rats were exposed to levels up to 80% (+20% oxygen) for up to 19 hours. No mortality was observed. At exposures to a concentration of 80%, some minor CNS effects were noted. No pathological changes were reported. (Lester et al. 1950, Ref 17) Dogs and cats survived exposure to 50% in air without cardiac sensitizing effects. (Burgison, 1955, ref 18) Other test reports mentioned mortality of mice at 128000 ppm after a four-hour exposure but results are difficult to interpret because of variable exposure periods and the possibility of inadequate oxygen supply. (Carpenter et al, 1949, ref 16)
In an acute hepatotoxicity test with Holtzman rats, animals were exposed to concentrations of 0, 500, 15000 and 25000 ppm for 4 to 6 hrs. No mortality was observed. Only animals pretreated with polychlorinated biphenyls showed increased liver weights, increased serum sorbital dehydrogenase activity and hepatocellular damage at VF2 concentrations of 500 ppm VF2 and above. (Conolly et al, 1979, ref 43)
Although none of the mentioned studies were performed according to currently prescribed standard protocols, the Pennwalt data indicate clearly that VF2 has a low acute toxicity. The other acute studies corroborate the weight of evidence for low acute toxicity.
Since the substance is a gas at ambient temperature, no specific primary cutaneous or ocular irritation studies were performed, but other toxicity study results indicate that VF2 has no significant irritancy to skin and eyes. Accidental releases of liquefied VF2 gas may cause frostbite when in contact with skin.

3.1.3 Repeated Dose Toxicity

CD1 mice were exposed by inhalation to VF2 concentrations of 0, 1000, 5000, 15000 and 40000 ppm for 2 weeks (6hrs/d, 5d/wk). No mortality was noted. There were no treatment-related effects on body weight, organ weights. No pathological changes were observed. The NOEL in this study was considered to be 40000 ppm VF2. (Newton, 1988, ref 24)
In an older 2-week inhalation study in albino rats, in which animals were exposed to 25000 ppm VF2 (6hrs/d, 5d/wk), a slight increase in urinary fluoride excretion, changes in RBC count and respiratory structural changes were noted. Due to lack of details of the study procedure these findings cannot be properly evaluated. Impurities in the test substance and/or a preexisting infection may have contributed to the observed effects. (Dupont, 1977, ref 20)
Weanling and young adult Sprague-Dawley rats were exposed by inhalation to VF2 concentrations of 0, 250, 1000 and 7000 ppm for 13 weeks (6hrs/d, 5d/wk). This study was combined with a fertility/reproduction study. (see also Koeter, 1986, ref 39) An interim sacrifice and evaluation was made at 4 weeks. Satellite groups were subjected to a recovery period of 10 weeks after exposure. Compared to control no treatment related changes were observed regarding body weight, hematology, urinalysis, mortality, estrus cycle, and organ weights. Gross pathology revealed no changes; on histopathology, no treatment-related effects were noted on sperm concentration, number of sperm cells with deformed heads/tails or on numbers of isolated heads/tails in weanlings or young adults. A slight degeneration of the vomeronasal organ in animals exposed to 7000 ppm was observed. At four weeks, the change was noticed both in weanlings and in young adults. At 13 weeks, it occurred only in weanlings. After 10 weeks recovery, it was not observed in any animal.

(Reuzel, 1986, ref 19) A simple fertility study was also conducted as part of the study, in which male and female rats that had been exposed to VF2 in the 13-week subchronic portion of the study were mated with untreated partners. No effects of potential reproductive significance were observed. (Koeter et al., 1986, ref 39)
CD1 mice were exposed by inhalation to VF2 concentrations of 0, 1000, 7000 and 40000 ppm for 13 weeks (6hrs/d, 5d/wk). Treatment-related, but not dose-related, increase in locomotor activity was noted. The increase was observed in both sexes and was prominent in mid study. It declined afterwards. Increased sensitivity to touch was seen in the 40000 ppm males during the last week of exposure and in mid and high dose females in the last 2 weeks of exposure. Dose-related rough haircoat was observed in males after eight weeks of exposure.
An increase in mean corpuscular Hb was seen in the high dose males. There were no-treatment related effects on body weight, food consumption nor on organ weights. No treatment related macroscopic or microscopic pathological changes were observed. Since the (subjective) clinical symptoms are not related to pathological changes the NOAEL is considered to be 7000 ppm. (Newton, 1989, ref 25)

Fisher 344 rats were exposed by inhalation for 90 days (6hrs/d, 5d/wk) to 0, 500, 1500, 5000, 15000 and 50000 ppm VF2. Transient body weight changes were observed which had subsided at the end of the study. Unexplained body weight changes were also seen in the controls. RBC counts, Hb levels and hematocrit decreased in males of the 1500 and 50000 ppm group. No such changes were observed in the females. In this study, some changes in clinical chemistry (9 SGPT, 8 SGOT, 8 SDH, 8 creatinine, 8 BUN) and organ weights (relative and/or absolute: 8 liver, 8 kidney, 8 thymus, 9 brain, 9 heart, 9 testis) were observed. However, there was no dose relationship nor clear relation to gender. Histopathological examination only revealed one animal with serous rhinitis and erosion of the eptelium of the nasal cavity (50000 ppm). The authors concluded that the NOEC in this study was < 500 ppm, and although observable effects were noted at all exposure levels, dose related effects were only apparent at the highest concentration. (Manus et al., 1984, ref 21)

In another study, Manus et al., (1984, ref 22) exposed BCF mice by inhalation for 13 weeks (6hrs/d, 5d/wk) to similar VF2 concentrations as in the above mentioned rat study. Some mortality and transient bodyweight loss during the study was observed which was suspected to be related to a failing watering system. In this study body weight changes were seen in females. Liver weight changes occurred (1500 ppm males and 15000 ppm females) but were not dose related. On histopathology, only mild renal changes indicative of regeneration was observed in very low incidence in all dosed males and high dose females and was not evidently related to dose. The authors concluded that the NOEC in this study was < 500 ppm.
An inhalation study was performed with Sprague-Dawley rats, whereby animals were exposed for 13 weeks (6hrs/d, 5d/wk) to VF2 concentrations of 0, 1000, 7000 and 40000 ppm. Interim sacrifices and observations were made at 2 and 4 weeks. In this study changes in body weight (transient in males and females), hematological parameters (from 7000 ppm in males and in 40000 ppm in females), clinical chemistry (in mid and high dose males and high dose females), urinalysis (in high dose males and transient in mid and high dose females) and organ weight changes (heart, lungs, spleen,) were observed.
These occurred at different concentrations, were not evidently concentration related and were sometimes transient. Microscopic examination of testis and epidydimis showed treatment related changes in mid and high dose groups throughout the study; these were characteristic of impaired spermatogenesis. The spleen showed treatment related changes characterized by lymphocytic depletion of the marginal zone, in males and females of the mid and high dose groups and in females of the low dose group at week 2. Vacuolar degeneration of the vomeronasal organ in the nose was observed in all treatment groups. Mineralization of the kidneys was increased in males of the high dose group after week 4. The NOEL in this study was considered to be < 1000 ppm.

(Appelman et al., 1985, ref 23)

3.1.4 Genetic Toxicity

Several in-vitro and in-vivo genotoxicity tests were performed with VF2.

In vitro studies
In an Ames test, in which *S. typhimurium* strains TA 1535, TA 100, TA1537 and TA98 were exposed (with and without the S9 activation system) to concentrations up to 50% VF2 in the gas phase, only strain TA 1535 reverted significantly at concentrations of 10% VF2 and above and only in presence of the activation system (number of revertant colonies increased maximally 2.6 time those of controls). (Russell, 1979, ref 29)
Bartsch et al, (1979, ref 30) exposed *S. typhimurium* TA 100 24 hrs to VF2 concentrations ranging from 20 to 50% in the gas phase; a marginal non-significant increase in revertant colonies were noted at 50% and only in the presence of the S9 activation system.
In an HGPRT test, Chinese Hamster Ovary (CHO) cells were exposed to VF2 concentrations of 0, 20, 40, 60, 80 and 100% in the gas phase for 19 and 5 hours (without and with S9 activation system). No mutant frequency increase was observed at any concentration. (Rickard, 1986, ref 31)
In a separate study, the same author (Rickard et al., 1986, ref 32) also exposed CHO cell to investigate the occurrence of chromosomal aberrations. VF2 concentrations were 0, 25, 50, 75 and 100% in the gas phase. Exposure period was 5 and 2 hours (without and with S9 activation system). No chromosomal aberrations were observed at any concentration in the presence or absence of the activation system. VF2 had no toxic properties to the cells at any concentration (as measured by replication delay in subcultures).
In some older in-vitro tests (an *E. coli* test (Landry et al., 1968, ref 26) an Ames test (Jagannath, 1977, ref 27) and a BALB/3T3 cell transformation test (Matheson, 1978, ref 28)) mutagenic effects were observed. Since the exposure concentrations were not described or unknown and in some cases the studies were not adequately detailed the results are not as reliable as the more recent studies mentioned above.

In vivo studies
Male and female mice were exposed to 0, 5000, 15000 and 40000 ppm VF2 for 6 hrs. Their bone marrow was collected at 24, 48 and 72 hrs after initiation of the exposure for microscopic evaluation of incidence of micronuclei in erythrocytes. VF2 was found not to be toxic to bone marrow nor influence the incidence of micronuclei at any concentration tested. (Hodson-Walker, 1988, ref 33)
A Sex Linked Recessive Lethal test was performed in male *Drosophila melanogaster* (fruit flies). Animals were exposed for 24 hrs to 0, 4.95, 22.8 and 43% VF2. After exposure, males were mated with non-exposed females. There was no significant difference in lethality of the progeny between controls and exposed males. Therefore, VF2 was not considered to be mutagenic to the X chromosome of *D. melanogaster*. (Sernau, 1988, 1989, refs 34, 35)
From all the presented genotoxicity tests it can be concluded that VF2 does not significantly interfere with the genome of organisms. The marginal, but positive finding in *S. typhimurium* TA1535 ($\geq$10% VF2 in presence of an activation system) cannot be explained: it may indicate that some metabolite of VF2 may interfere directly or indirectly with the genomic integrity of some selected protocaryotic organisms.

3.1.5. Carcinogenicity

Sprague-Dawley rats were exposed by inhalation to VF2 concentrations of 0, 150, 600, 2500, 10000ppm for 104 weeks (6hrs/d, 5d/wk). At 12 months of exposure an interim sacrifice and examination was performed. No treatment-related effects were noted on survival, clinical

symptoms, ophthalmology, body weight gain, hematology, urinalysis, macroscopic and microscopic pathology. Food consumption tended to be lower in treated animals than in controls. Relative organ weights (brain, heart, epididymis) of the 150 ppm males only were decreased at study termination. There were no treatment related shifts in benign or malignant tumor incidence, total number of tumors, or total number of tumor bearing animals. (Arts, et al., 1991, ref 36)
Newton (1991, ref 37) exposed mice by inhalation for 18 months to VF2 concentrations of 0, 600, 2500 and 10000 ppm. (6hrs/d, 5d/wk). No treatment- related effects were observed in survival, clinical symptoms, ophthalmology, body weight food consumption, hematology, nor in macroscopic or microscopic pathology. Incidence of observed benign and malignant neoplasms in exposed animals was not different from controls and was not considered related to treatment.
In a one year study, Sprague-Dawley rats were fed 0, 4.12 and 8.25 mg/kg BW by gavage for 52 weeks (4 to 5 d/wk) VF2 was dissolved in olive oil. Animals were allowed to die naturally. Lipoma and liposarcomas were observed at necropsy after natural death. The number of lipomas was increased in the high dose group compared to controls. None were seen in the low dose group. There was a dose-related trend in the numbers of liposarcoma's. However, this study was performed according to a protocol with significant deviations from currently prescribed guidelines (number of animals, exposure period, route of administration, statistical evaluation). The study was not reported in great detail, which impedes proper interpretation of the results. Moreover liposarcomas were found in fat tissue of different embryonal origin but considered as one type of tumor. (Maltoni et al., 1979, ref 38)

3.1.6. Reproductive/developmental toxicity

As previously mentioned in the repeat dose section, studies on male fertility have been documented. In Appelman et al., 1985 (ref 23), upon microscopic examination of the testis and epidydimis, it was noted that treatment related changes in the mid and high dose groups were observed. Observations were characteristic of impaired spermatogenesis. However, these findings were not reproduced in a subsequent study by Reuzel et al (1986, ref 19). In this male fertility study, males were exposed to VF2 for 13 weeks then specially evaluated for effects on the gonads: (organ weights, weeks 5 and 13: coagulating glands, epididymis, prostate, seminal vesicles, testes, uterus and testes of animals in the 10 week recovery group. Microscopic evaluation: Sperm morphology at week 14, histological eximination of testis and epididymis (all animals), ovaries and uterus (control and high dose). The gross and microscopic pathology evaluations revealed no treatment-related effects on sperm concentration, on number of sperm cells with deformed heads/tails, or on numbers of isolated heads/tails in weanlings or young adults. Reuzel established a NOEL of 7000 ppm for those fertility effects.
Koeter at al (1986, ref 39) exposed male and female rats for 15 weeks prior to mating and 2 weeks during mating to 0, 250, 1000 and 7000 ppm VF2. After mating females were exposed until day 15 of gestation to the same concentrations. No effects were observed at any concentration on mortality, parental body weight, fertility indices, reproductive performance, male reproductive organ weights, or on histopathology. There were no treatment-related effects on ovary weights, or on litter data. The NOEL was considered to be greater than or equal to 7000 ppm.
In a teratology study female pregnant rats were exposed to 0, 2000 and 10000 ppm VF2 during gestation days 6 to 15. Mothers were sacrificed on day 20 of pregnancy. No effects were observed at any concentration on maternal body weight, food consumption, nor on number of implantation sites, corpora lutea live and dead fetuses resorption sites. No treatment-related effects were seen at any concentration tested on fetal soft tissues of head, thoracic and visceral organs, nor on skeletal structures. The NOEC for teratogenicity was considered to be greater than or equal to 10000 ppm. (Meckler et al., 1978, ref 40)

3.1.7 Physical hazard

VF2 is a flammable gas.
This property constitutes the substance's most important physical hazard.

3.1.8 Initial assessment for human health.

Due to the conditions of production and use of VF2 (closed system intermediate), resulting occupational concentrations are considered to be low. This is corroborated by, albeit limited, occupational exposure surveys (exposure normally below 10 ppm).
In this hazard evaluation, the primary studies to be used to determine the chemical's hazard are the chronic toxicity/carcinogenicity studies. It is believed that the overall quality, detailed description and length of the studies, provides a more sound basis for determining the hazard of VF2. Many of the subacute/subchronic studies do not have the level of detail provided in the more recent GLP chronic studies. In addition, many of the effects observed in the subchronic studies were not considered to be dose related or transient and in many cases not related to organ pathology. The overall weight of evidence regarding the studies and the inability to reproduce the same effects in the chronic GLP studies should be taken into consideration. The Arts and Newton studies are considered to be the key studies for the evaluation of VDF. These two studies were performed according to currently accepted guidelines and GLP standards. Since they are lifetime studies which are reported in great detail, they are considered as the most reliable representation of the toxicological effects of VF2 in animals. It can be concluded from the results that lifetime exposure to 10000 ppm does not induce effects of any toxicological significance for rats and mice, and does not increase incidence of any type of cancer in these species over their incidence in non-exposed animals.
No published data were retrieved on possible adverse health effects resulting from human exposure to VF2 in the more than 40 years of industrial use of the substance.

4. Hazards to the Environment

Data are not available concerning aquatic effects. However, exposure models determined that >99% of VF2 would be present in the air compartment. The Log Kow indicates that bioaccumulation is not likely. Thus, because of VF2's physical chemical properties, its nearly exclusive partitioning to air, and its use pattern, the conduct of aquatic toxicity testing was not necessary.

4.1. Aquatic effects

As explained above, no aquatic toxicity testing has been performed. However, a possible toxicity of VF2 was calculated with the ECOSAR program in the EPIWIN model and the details of this model are included in the dossier. The LC50, 96 hrs for fish is estimated to be 245 mg/l; the Daphnia LC50, 48 hrs is estimated to be 250 mg/l; .the green algae EC50, 96 hrs is estimated to be 149 mg/l.
Using the Mackay fugacity Model (level I and III)(See IUCLID dossier), it was determined that about 0.05% of discharged VF2 would be partitioned to the water compartment and less than 0.0002% would be partitioned to the sediment compartment.
In addition, QSAR modeling was performed with the structural analogues vinylidene chloride and 1,2 difluoroethylene. It should be noted that the approach to compare halogenated alkanes and alkenes is of limited reliability. Vinylidene chloride is a water-soluble liquid at ambient temperature (BP: 32°C, Water solubility: 2.5 gm/l) and vinylidene fluoride has a (BP: -83°C and water solubility: 250 mg/l) . No ecotoxicological data were retrieved on 1,2 difluoroethylene. 1,1 Dichloroethylene was found to be only harmful to Crustaceans. The 48 hrL C50 for Daphnia magna was 11.6 mg /l. For both fish and algae the predicted aquatic toxicity values (LC/EC 50 > 100 mg/L) indicate low acute aquatic toxicity concern in these species.

4.2 Terrestrial effects

A possible toxicity of VF2 was calculated with the ECOSAR program in the EPI WIN model. The LC50 for the earthworm, 14 days, is calculated to be 675 mg/kg.
The Mackay Level I and III models calculated that >99% of the emitted VF2 would partition to the air compartment and negligible amounts to soil. The calculated half-life of VF2 in the atmosphere is 3.3 days. Therefore, VF2 is not expected to deposit onto soil and crops to any significant degree. Consequently, concentrations of VF2 to which certain mammals, birds and other terrestrial organisms could be exposed are considered to be negligible.
Effects on plants via atmospheric contact are not anticipated. The half-life of VDF in atmosphere is 3.3 to 4.7 days, which results in a complete transformation of VDF in atmosphere in a few weeks time.
Supposed ultimate degradation products of VF2 are CO2 and HF. The expected low VDF concentrations in the atmosphere in the vicinity of an emission source and the relatively short half life of the substance will render the representative testing of the effect of VDF on plants technically difficult and its results at least questionable when extrapolated to the natural environment.

4.3 Initial Assessment for the environment

Due to the physical-chemical properties of VF2, the conditions of its production and use (closed system intermediate), its predicted partitioning to air with negligible partitioning to other compartments and its predicted fast degradation, resulting environmental concentrations are considered to be very low.
No toxicity data for aquatic and terrestrial organisms have been generated, but are considered to be of low concern.

5. Conclusions and Recommendations

5.1. Conclusions

Conclusion for human health

VF2 has been tested for acute toxicity, genotoxicity and for toxicity after repeated exposure, including its toxic potential on fertility, prenatal development reproduction as well as for its chronic toxicity and carcinogenic potential.
Although in earlier repeated exposure tests, some effects were observed on the hematopoietic system, the liver, the kidneys and the testes, these effects were not reproduced in more recent lifetime exposure tests in mice and rats. General signs of systemic toxicity were observed in rats and mice at 500 ppm in several 13-week inhalation studies. Overall, a LOEC of 500 ppm based on body weight, organ weight and clinical chemistry changes in the absence of histopathological changes can be identified for rats and mice. A NOEC of 250 ppm can be identified for rats. At 40,000 – 50,000 ppm effects on the nasal epithelium were noted in rats.
In genotoxicity studies, VF2 has shown some activity in bacterial assays, but was negative in the *in vitro* chromosomal aberration and gene mutation study in mammalian cells. *In vivo*, VF2 was negative in a mouse micronucleus and Drosophila SLRL test. Thus there is no evidence of genotoxicity *in vivo*.
The chronic toxicity/carcinogenicity tests and the tests on fertility and reproduction are the key studies for evaluation of the SIDS endpoints. It can be concluded from the results that for rats and mice, the lifetime exposure to 10000 ppm does not induce effects of any toxicological significance, and does not increase incidence of any type of cancer in these species over their incidence in non-exposed animals.
Since VF2 is produced and processed in closed systems, occupational exposure is low. Monitoring of occupational exposure to VF2 during production and processing indicates that typical average exposure concentrations are below10 ppm with incidental exposure above these values.
Residents in the vicinity of production and processing plants are expected be exposed to much lower concentrations than those found on the work floor. In view of the use of VF2, production of various polymers with VF2 residual <1 ppm, consumer exposure is not expected.

Conclusion for the Environment

Based on its physical-chemical properties and its predicted fate in the environment, VF2 is not expected to have significant toxic properties for aquatic organisms. Modeling data indicate a possible degradability in the aquatic compartment. However, its short residence time (few hours to few days) in the aquatic compartment will not lead to the formation of any significant metabolite concentration in that compartment. VF2 is only used for production of polymers in closed systems whereby emissions to the aquatic environment are not a concern.

Emissions of VF2 will partition almost completely to air and will be degraded swiftly by reaction with OH radicals (calculated half-life: 3.3 days). Therefore, atmospheric VF2 will not contribute significantly to global warming and does not constitute a significant concern for animals and man exposed via that compartment.

5.2. Recommendations

Human health

The performed toxicity test programs on VF2 cover adequately all endpoints to be considered in this SIAR. Therefore no additional toxicity tests are recommended.

Environment

No further environmental testing is deemed necessary for following reasons :
VF2 is a gas with limited water solubility and a low Log Kow.
Mackay level I and III modelling indicate that VF2 will partition nearly completely to air.
Where aquatic and terrestrial toxicity testing and biodegradation testing is concerned following considerations are made. In order to obtain and maintain adequate concentrations in such test systems, specific containment techniques have to be used (semi static, flow through, closed vessels without head space) which may lead to artificial changes in itself (e.g. lack of CO2 in algal media, increased oxygen depletion in closed systems...), which in turn may lead to artifacts in the effects observed.
Moreover, such artificial conditions may not be at all representative of those in the natural environment.
Another important consideration is the pattern of use. The material is used only as a chemical intermediate in the production of polymers, in closed systems. VF2 is not expected to be released to water systems, but in any case emissions will partition to air >99%.

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7. Databases

Following databases were consulted to update and verify the available physico-chemical, toxicological and environmental information on VF2:

TOXLINE
TOXLIT
GENETOX
CCRIS
DART/ETIC
EMIC
HSDB
RTECS
AQUIRE
GIABS
MEDLINE
TSCATS
CHRIS
NIOSHTIC
DATALOG
ENVIROFATE
BIODEG
BIOLOG
PHYTOTOX
TERETOX
CHAPMAN & HALL
MERCK INDEX

I U C L I D Data Set

Existing Chemical	:	ID: 75-38-7
CAS No.	:	75-38-7
EINECS Name	:	1,1-difluoroethylene
EC No.	:	200-867-7
Molecular Weight	:	64.04
Molecular Formula	:	CH2=CF2

Producer related part

Company	:	Solvay S.A.
Creation date	:	06.12.1994

Substance related part

Company	:	Solvay S.A.
Creation date	:	06.12.1994
Status	:	
Memo	:	JPE
Printing date	:	12.03.2002
Revision date	:	
Date of last update	:	12.03.2002
Number of pages	:	297
Chapter (profile)	:	
Reliability (profile)	:	
Flags (profile)	:	

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBS TANCE IDENTIFICATION

1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	
Substance type	:	Organic
Physical status	:	Gaseous
Purity	:	> 99.7 % w/w
Colour	:	
Odour	:	
Remark	:	The dataset was prepared i n collaboration with the following co-producers. Chap. 2 -5 are sent by Solvay on their behalf: - ELF ATOCHEM 4, Cours Michelet 92091 Paris La Defense 10 Cedex France

04.05.1995

1.1.2 SPECTRA

Type of spectra	:	other:
Remark	:	Mass : 11 Reliability criteria: Not assignable: secondary literature (4b)

14.03.2001 (1)

1.2 SYNONYMS AND TRADENAMES

Difluoro 1.1 ethene
09.01.1995

Difluoro 1.1 ethylene
09.01.1995

Difluoroethene
22.03.1995

VF2
09.01.1995

Vinylidene fluoride
08.12.2000

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

Labelling	:	provisionally by manufacturer/importer
Specific limits	:	
Nota	:	, ,
R-Phrases	:	(10) Flammable
S-Phrases	:	(21) When using do not smoke

09.01.1995

1.6.2 CLASSIFICATION

Classified	:	provisionally by manufacturer/importer
Class of danger	:	flammable
R-Phrases	:	(10) Flammable
Specific limits	:	
1st Concentration	:	
2nd Concentration	:	
3rd Concentration	:	
4th Concentration	:	
5th Concentration	:	
6th Concentration	:	
7th Concentration	:	
8th Concentration	:	
1st Classification	:	
2nd Classification	:	
3rd Classification	:	
4th Classification	:	
5th Classification	:	
6th Classification	:	
7th Classification	:	
8th Classification	:	

09.01.1995

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use	:	Type
Category	:	Use in closed system
21.02.1995		
Type of use	:	Industrial
Category	:	Polymers industry
21.02.1995		
Type of use	:	Use
Category	:	Anti-static agents

21.02.1995

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Type of limit : other: SAEL
Limit value : 1000 other: ppm
Remark : SAEL = Solvay acceptable exposure limit in 1995.
08.12.2000 (2)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

Remark : Because vinylidene fluoride is a gas under all environmental conditions, it is expected to be approx.100 % in air. See also derogation statement.

08.12.2000

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Remark : Country where Solvay production plant is located in EU :
- France

14.03.1995

1.11 ADDITIONAL REMARKS

Remark : MAK classification: IIIB (1983).
18.01.1995

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value : = -144 °C
Remark : Reliability criteria: reliable with restriction: handbook (2g)
18.06.2001 (3) (1)

2.2 BOILING POINT

Value : = -85.7 °C at 1013 hPa
Reliability : (4) not assignable
13.03.2001 (3) (4)

Value : = -85.7 °C at
Reliability : (4) not assignable
13.03.2001 (3)

Value : = -83 °C at
Remark : Reliability criteria: reliable with restriction: handbook (2g)
18.06.2001 (1) (5)

Value : -83 °C at
Remark : Reliability criteria: Reliable with restrictions: Data from handbook or collection of data (2g)
25.04.2001 (5)

2.3 DENSITY

Type : Density
Value : = .92 g/cm³ at -20 °C
Source : Elf Atochem
24.04.1995 (6)

Type : Density
Value : = .67 g/cm³ at 20 °C
Source : Elf Atochem
24.04.1995 (7)

Type : Density
Value : = 617 kg/m3 at 23.6 °C
Method : other: calculated
Year : 1955
GLP :
Test substance :
Remark : Liquid density.
Reliability criteria: reliable with restrictions:Accepted calculation method (2f)
20.08.2001 (8)

Type :
Value : 617 kg/m3 at 24 °C
Remark : as liquified gas

reliability criteria: reliable witrh restrictions: collection of data (2g)
14.03.2001 (1)

Type : relative density
Value : = 2.2 at 25 °C
Remark : Vapour density (air=1).

reliability criteria: not assignable: documentation insufficient for assessment (4e)
10.05.1995 (9)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : = 35700 hPa at 20 °C
Remark : Reliability criteria: reliable with restrictions: data from handbook or collection of data.(2g)
25.04.2001 (5)

2.5 PARTITION COEFFICIENT

Partition coefficient :
Log pow : = 1.24 at °C
pH value :
Method : other (calculated)
Year : 1979
GLP :
Test substance :
Remark : Reliability criteria: reliable with restrictions: acceptable calculation method (2f)
18.06.2001 (10)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in :
Value : = 165 mg/l at 25 °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :
Deg. product :
Method : other: no data
Year : 1990
GLP : no data
Test substance :
Remark : Reliability criteria: reliable with restrictions: handbook (2g)
Solubility at 1 atm.
25.06.2001 (4)

Solubility in	:	
Value	:	180 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	
Remark	:	Reliability criteria: Not assignable: secondary literature (4b)

18.06.2001 (1)

2.6.2 SURFACE TENSION

Test type	:	Other
Value	:	at °C
Concentration	:	
Remark	:	Is a gas at ambient temperature and atmospheric pressure.

13.03.2001

2.7 FLASH POINT

Remark	:	None Reliability criteria: Not assignable: documentation insufficient for assessment (4e)

14.03.2001

2.8 AUTO FLAMMABILITY

Value	:	= 390 °C at
Method	:	other: no data
Year	:	
GLP	:	no data
Test substance	:	
Remark	:	Reliability criteria: Not assignable: documentation insufficient for assessment (4e)
Reliability	:	(4) not assignable

14.03.2001 (9)

2.9 FLAMMABILITY

Result	:	flammable
Method	:	other: no data
Year	:	
GLP	:	no data

Test substance :
Remark : Flammability limits in air : lower limit: 4.7 %
upper limit : 25.1 %
Reliability criteria: Not assignable: documentation insufficient for assessment (4e)
20.08.2001 (9)

2.10 EXPLOSIVE PROPERTIES

Method : other: no data
Year :
GLP : no data
Test substance :
Remark : Explosive limits: 5.8-20.3 vol % in air.
Reliability criteria:reliable with restrictions: handbook (2g)
Reliability : (4) not assignable
18.06.2001 (3)

2.11 OXIDIZING PROPERTIES

Result : no oxidizing properties
Remark : Reliability criteria: Not assignable: documentation insufficient for assessment (4e)
19.06.2001 (11)

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

Remark : Henry's Law Constant: 0.226 atm.m3/mole
Based on the EPIWIN model (SRC).
Henry's law constant: 5.09E-3 atm Cu M/mole.

Reliability criteria: reliable with restrictions: accepted calculation method (2f)
10.03.1995 12)

Remark : Critical temperature: Tc = 30 degC
Critical pressure : Pc = 4.43 MPa
Soluble in chlorinated solvents, ethanol, ether.
Source : Elf Atochem
24.04.1995 (7)

3.1.1 PHOTODEGRADATION

INDIRECT PHOTOLYSIS		
Sensitizer	:	O3
Conc. of sensitizer	:	700000000000 molecule/cm³
Rate constant	:	.00000000000000000028 cm³/(molecule*sec)
Degradation	:	% after
Remark	:	T 1/2: 40.9 days Calculated with SRC calculation method. P/C data as mentioned in the IUCLID data set. Reliability criteria: reliable with restrictions: accepted calculation method (2f)
Source	:	EPI WINN, (SRC method), EPA
21.08.2001		
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	.0000000000022667 cm³/(molecule*sec)
Degradation	:	% after
Remark	:	T 1/2: 4.7 days Calculated with the SRC model. P/C data as mentioned in the IUCLID data base Reliability criteria:reliable with restrictions: accepted calculation method (2f)
Source	:	EPI WINN, (SRC model), EPA, 2001
21.08.2001		
Conc. of substance	:	at 25 °C
DIRECT PHOTOLYSIS		
Halflife t1/2	:	= 3.3 day(s)
Degradation	:	% after
Quantum yield	:	
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	cm³/(molecule*sec)
Degradation	:	% after
Deg. product	:	
Method	:	other (calculated)
Year	:	2001
GLP	:	
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The atmospheric lifetime of VF2 has been calculated by the Prather and Spivakovsky procedure for deriving the tropospheric OH lifetime of a gven compound by scaling to that of CCl3CH3 at the temp of 277°K For VF2 this atmospheric T1/2 is calculated to be 3.3 days. Reliability criteria: reliable with restriction: acceptable calculation method (2f)
Reliability	:	(3) invalid
20.08.2001		(13)

3.1.2 STABILITY IN WATER

Deg. product	:	
Method	:	other:
Year	:	
GLP	:	
Test substance	:	
Remark	:	No experimental data are available. Half-life in surface waters was calculated by the appropriate model provided by the Syracuse Research Corporation. Half-life (by evaporation) in river water is 0.9 hrs; from lake water is 77 hours P/C data as mentioned in the IUCLID data set. River Lake Depth in m 1 1 Wind veloc. m/sec 5 0.5 Current veloc. m/sec 1 0.05
	:	EPI WINN, (SRC model), EPA, 2001

21.08.2001

3.1.3 STABILITY IN SOIL

Type	:	other:
Radiolabel	:	
Concentration	:	
Soil temperature	:	°C
Soil humidity	:	
Soil classification	:	
Year	:	
Remark	:	No experimental data are available, but due to its low boiling point and its low logP value, the compound will evaporate from soil and collect in the atmosphere. (see also biodegradation and Mackay modeling.)

14.03.2001

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONM ENTAL COMPARTMENTS

Type	:	Volatility
Media	:	other: air
Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	

Year :
Remark : Henry's law constant: 1270 kPa m3/mol (20 degC calculated).
10.05.1995 (9)

Type : Volatility
Media : other: water
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method :
Year :
Remark : Water evaporation: t 1/2, 23 hours (20 degC calculated).
10.05.1995 (9)

Remark : Because vinylidene fluoride is a gas under all environmental conditions, it is e xpected to be 100 % in air.(see also Mackay modeling)
14.03.2001

3.3.2 DISTRIBUTION

Media : other: soil adsorption
Method : other (calculation)
Year :
Remark : Reliability criteria: Reliable with restrictions: accepted calculation method (2f)
Result : Koc = 7.12 (calculated on the basis of MW: 64.O3, Water solubility of 250 mg/l, BP: -83°C, MP: -144°C)
12.03.2002 (14)

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Remark : No experimental data are available.

The biodegradability was calculated with the SRC model.
Linear biodegradation probability is 0.7
Non-linear biodegradability is 0.9
Both values indicate that biodegradability is probably fast

Primary and ultimate biodegradation is 3.7 to 3 and indicates biodegradation in a period of weeks.

In an STP, the biodegradation accounts for 0.04 % of the removal of the original imput.(63 % evaporates)

Reliability criteria: reliable with restrictions: accepted calculation model (2f)
Source : EPI WINN (SRC model) , EPA, 2001
21.08.2001

3.6 BOD5, COD OR BOD5/COD RATIO

Remark : No experimental data are available.
21.08.2001

3.7 BIOACCUMULATION

BCF	:	= 1.8
Elimination	:	
Method	:	other: calculated with SRC model
Year	:	
GLP	:	
Test substance	:	
Remark	:	No experimental data are available.

Reliability criteria: Reliable with restrictions: accepted calculation method
21.08.2001 (15)

3.8 ADDITIONAL REMARKS

21.08.2001

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other: calculated
Species	:	other: fish
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	ca. 246
Remark	:	no experimental data available.
Source	:	EPI WINN, (SRC model), EPA, 2001

21.08.2001

4.2 ACUTE TOXICITY TO AQUATIC INVERTEB RATES

Type	:	other: calculated
Species	:	Daphnia sp. (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	ca. 250
Remark	:	no experimental data are available.
		Reliability criteria; reliable with restrictions: accepted calculation method (2f)
Source	:	EPI WINN, (SRC model), EPA, 2001

21.08.2001

Type	:	other: calculated
Species	:	other: mysid shrimp
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	ca. 122
Remark	:	No experimental data are available.
		Reliability criteria: Reliable with restrictions: accepted calculation method (2f)
Source	:	EPI WINN, (SRC model), EPA, 2001

21.08.2001

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	
Endpoint	:	other: calculated
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	ca. 149
Method	:	other:
Year	:	
GLP	:	
Test substance	:	
Remark	:	No experimental data are available.
		Reliability criteria: reliable with restrictions: accepted calculation method (2f)
Source	:	EPI WINN, (SRC model), EPA, 2001

21.08.2001

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Remark : no data.
21.08.2001

4.5.1 CHRONIC TOXICITY TO FISH

Method : other
Year :
GLP :
Test substance :
Remark : no experimental data.
21.08.2001

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

Method : other
Year :
GLP :
Test substance :
Remark : no experimental data.
21.08.2001

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

Method : other
Year :
GLP :
Test substance :
Remark : no data.
21.08.2001

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

Type : other: calculated
Species : other: earthworm
Endpoint :
Exposure period : 14 day(s)
Unit : Mg/kg soil dw
LC50 : ca. 675
Method : other
Year :
GLP :
Test substance :
Remark : no experimental data.

Reliability criteria: reliable with restrictions: accepted calculation method (2f)
Source : EPI WINN, (SRC model), EPA, 2001
21.08.2001

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

Method	:	other
Year	:	
GLP	:	
Test substance	:	
Remark	:	no data

21.08.2001

4.7 BIOLOGICAL EFFECTS MONITORING

Remark	:	No data.

22.03.1995

4.8 BIOTRANSFORMATION AND KINETICS

Remark	:	No data.

22.03.1995

4.9 ADDITIONAL REMARKS

Remark	:	Due to specific physico chemical properties of VF2, no aquatic nor terrestrial toxicity testing has been performed. In order to obtain and maintain adequate concentrations in such test systems, specific containment techniques have to be used (semi static, flow through, closed vessels without head space...) which may lead to artefactal changes in itself (e.g. lack of CO2 in algal media, increased oxygen depletion in closed systems...), which in turn may lead to artefacts in the effects observed. Moreover, such artificial conditions may not be at all representative of those in the natural environment. (e.g. maintained test concentrations during fixed exposure times versus naturally decreasing concentrations by more than half in less than 24 hrs..) Another important consideration is the pattern of use. The material is used only as in manufacturing as a chemical intermediate in the production of polymers, in closed systems. It is not expected to be released to water systems, and it will not partition to the water from the air.

21.08.2001

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo	:	In vivo
Type	:	Metabolism
Species	:	Rat
Number of animals		
Males	:	
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	
Remark	:	Male Holtzman rats were exposed to VF2 concentrations ranging from 0 to 25000 ppm for 4 to 6 hrs. Animals were either not pretreated, or pretreated with phenobarbital or with PCB. The goal was to evaluate the hepatotoxicity of VF2 by measurement of liver weight, serum sorbital dehydrogenase (SDH) activity and by histology of the liver. No effects were seen in non-pretreated animals nor in animals pretreated with phenobarbital. 4-Hrs exposure of animals pretreated with PCB caused increased liver weight at all concentrations. (statistically significant at 15000 and 25000 ppm , but not at 500 ppm). The increase was not really dose-dependent. SDH values were significantly elevated in a dose-dependent fashion at all test concentrarions. Histologically, the 15000 + PCB and 25000 ppm + PCB group showed showed balloonig of hepatocytes, centrilobular and mide-zonal necrosis surrounded by hemorrhagic and inflammatory zones. Lesions were considered to be distinctly different from those seen in similar tests with VCM. This is not considered to be a key study for SIDS evaluation and is therefore not further detailed in this document. Reliability criteria: reliable with restrictions: well documented, acceptable scientific principles, acceptable for assessment.(2e)

21.11.2001

In Vitro/in vivo	:	In vivo
Type	:	Metabolism
Species	:	rat
Number of animals		
Males	:	
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	
Remark	:	Fed and fasted male Holzman rats were exposed to 26000 and

82000 ppm of VF2 for 4 hrs (5 animals per feeding status and per test concentration. Controls were exposed to air.)
Actual exposure concentrations were monitored with gas chrom atography.
The hepatic enzyme alanine-alpha-ketoglutarate transaminase (AKT) in all animals were measured after exposure.
Exposure to 82000 ppm had no appreciable effect at 24 hrs on serum AKT activity either in fed or fasted rats. Althuogh there was a small statistically significant rise in serum AKT among fed rats after the 82000 ppm exposure, it was not considered to be a meaningfull elevation.
This concentration was without apparent central nervous system depressant effect.
No mortality occurred during exposure.

Reliability criteria: reliable with restrictions: xell documented, acceptable scientific principles, acceptable for assessment.

21.11.2001

In Vitro/in vivo : In vitro
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Remark : Rat liver microsomes exposed to concentrations up to 7 kPa (partial pressure) VF2 in the gas phase.
VF2 showed a progressive inhibition of aminopyrine demethylation with increasing VF2 concentrations.
The authors conclude that VF2 may persist at the enzymic site and thus exhibit inhibition of oxygenation of drugs and xenobiotics.

This is not a key study for SIDS evaluation and is therefore not further detailed in this document.

Reliability criteria: reliable with restrictions: well documented, acceptable scientific principles, acceptable for assessment (2e)

21.11.2001

In Vitro/in vivo : In vitro
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Remark : Rat hepatic microsomes(unprimed or primed with beta naphtoflavone or phenobarbital) were exposed to variuos gaseous VF2 concentrations up to 60 µM for up to 30 minutes.
A negative control was run concurrently.

The capacity of VF2 to destroy P 450 and heme were measured.

The release o f Fluor ion was minimal (to approx. 3 nM F- / nM P 450) in uprimed as well as in primed microsomes at different times and at different concentrations of VF2.

VF2 inactivates P 450 and heme noly tyo 17% under the conditions of these test.

This is not considered a key study in the SIDS evaluation and is therefore not further detailed in this document.

Reliabilty criteria: reliable with restrictions: well documented, acceptable scientific principles, acceptable for assessment.(2e)

21.11.2001

In Vitro/in vivo : In vivo
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Remark : Male sprague-Dawley rats were exposed for 30 minutes to 2200 ppm VF2.
VF2 exposed rats showed increased urinary fluor excretion during days 1 to 7 post exposure.
Urinary potassium excretion was only increase on day 6 after exposure.
Creatine excretion and urinary volume were not significantly altered.
Kidneys showed macroscopic changes: marked hyperemia of the medulla, pazle whitish band in the cortex near the corticomedullary junction.
No histological changes.

Since this is not a key study no more details of the s tudy have been described in this document.

Reliability criteria: Reliable with restrictions: well documented, meets scietific principles (2e)

21.11.2001

In Vitro/in vivo : In vivo
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Remark : Male Sprague-Dawley rats were whole body exposed to 500 ppm VF2 for 8 hrs.
Actual test concentrations were monitored by GC -MS.

Animals exhaled acetone at amounts of between 1.2 and 2.5 µmol/hr/Kg body weight. (controls: 0.05 µM/hr/kg)

Subsequently similar experiments were conducted by the same group that corroborated and refined the previous findings.

Metabolism of VF2 after inhalation seems to be saturated at 100 ppm concentration
The Vmax for metabolism of VF2 was calculated to be 1.1 µM/hr/kg BW.

The authors conclude that VF2 may interact with hepatic microsomal cytochrome P 450.
The acetone formation may partly be explained by the hypothesis that VF2 is metabolised to fluoroacetate.
Filser et al., (1980) put forward the hypothesis that all halogenated ethylenes share following metabolic steps:
-epoxidation of the ethylene double bond
-rearrangement to the halogenated acetaldehyde or halogenated acyl halide
- partial transformation of the latter to halogenated acetic acid
One possible mechanism which is thought to contribute to acetone formation is that the halogenated acetic acid formed(fluoroacetic acid) inhibits the enzymes of the citric acid cycle as suggested by others.

These studiesare not considered key studies for SIDS evaluation .

Reliability criteria: reliable with restriction: well documented, acceptable scientific principles, acceptable for assessment (2e)

21.11.2001

In Vitro/in vivo : In vivo
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Remark : Female newborn Wistar rats were whole-body exposed to 2000 ppm for 4,6,8 and 10 weeks (8hr/d, 5d/wk).
A replicate was done with same strain at the same dosage and at the same regimen for 8, 10, 12 and 14 weeks.
Recovery period for both replicates was 2 weeks.
Negative controls were run in a similar way.
Test concentration was monitored with GC.

ATPase content in liver cells was evaluated.
After 14 weeks of exposure the number of ATPase deficient hepatic foci was low and 2 orders of magnitude lower than the number of foci observed after 4 weeks exposure to VCM.

In an experiment with Wistar rats exposed to VF2 at different concentrations, it was concluded that the metabolisation rate of VF2 was approx. 1.1 µM /hr/kg BW.

This is not a keystudy for SIDS evaluation and is therefore

not further detailed in this document.

Reliability criteria: reliable with restrictions: well documented, acceptable scientif principles, acceptable for assessment (2e)

21.11.2001

In Vitro/in vivo	:	In vivo
Type	:	Metabolism
Species	:	rat
Number of animals		
Males	:	
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	
Remark	:	Male Sprague-Dawley rats were exposed for 6 hrs to VF2 concentrations ranging from 20 to 1800 ppm. It appeared that the maximum metabolism of VF2 vapour in these rats is reached at a level of approx. 400 ppm using the calculation method of Filser and Bolt. This is not a key study for SIDS evaluation and is therefore not further detailed in this document. Reliabilty criteria: reliable without restriction: in accordance with generally accepted scientific standards and described in sufficient detail (1d)

21.11.2001

In Vitro/in vivo	:	In vivo
Type	:	Toxicokinetics
Species	:	rat
Number of animals		
Males	:	
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	
Remark	:	Male Fisher344/N rats were exposed nose only for 6 hrs to concentrations of VF2 ranging from 30 to 16000 ppm. Actual test concentrations were monitored by GC every 10 minutes. Tidal volume and breathing frequency were not affected by any concentration. Experimentally determined steady-state blood levels of VF2 (GC) increased linearly with increasing exposure concentration from 15 ng VF2/ ml (30 ppm) to 2400 ng VF2/ ml at 16000 ppm. VF2 tissue/air partition coefficients were 0.07, 018, 0.8, 1.0, and 0.29 for water, blood, liver, fat and muscle respectively. These values and published values for metabolism of VF2, Km

and Vmax, were incorporated in a physiological model.
Model predictions agreed with experimentally determined data. Time to Cmax was less than 15 minutes for all concentrations.
After end of exposure, VF2 blood levels decreased to 10% of Cmax in 1 hr.
Simulation of the metabolism of VF2 indicated that the amount of VF2 metabolised per 6 hrs exposure period increased with increasing concentration of VF2 approaching a maximum at
about 2000 ppm VF2.
This air concentration results in a blood level of 260 ng VF2/ml at steady state.

This is not considered a key study in the SIDS evaluation and is therefore not further detailed in this document.

Reliability criteria: reliable with restrictions: well documented, acceptable scientific principles, acceptable for assessment (2e)

21.11.2001

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species : mouse
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Remark : Male B6C3F1 mice were exposed to VF2 concentrations of 250, 3750 and 15000 ppm for 6 hrs (nose only).
Exposure concentrations were monitored by GC at 10 minutes intervals. (No control was exposed).

Concentrations of VDF were measured in the blood.
A physiological model to simulate blood levels of VF2 in rats was adapted to mice by incormorating physiologcally realistic parameters for mice where appropriate. and by assuming that chemical specific parameters such as blood tissue partition coefficients determined for rats could also be applied to mice.
Measured steady state levels of VF2 in blood of mice increased with increasing exposure concentration.
For both the 3750 and 15000 ppm VF2 exposures, the experimentally determined fell within the 95% confidence interval predicted by the physiological model.
For the 250 ppm VF2 exposure, the experimentally determined values for VF2 in blood were lower than predicted by the model.
At the lowest concentration it was not possible to detect VF2 in blood taken 15 minutes after cessation of exposure, (suggesting that VF2 concentrations were below the LOD of 4 ng VF2/ml).
For 15000 ppm exposure, VF2 could be detected in blood at 15 minutes post exposure.

This is not considered at key study for SIDS evaluation and

is therefore not further detailed in this document.

Reliability criteria: reliable with restrictions: well documented, acceptable scientific principles, acceptable for assessment.(2e)

21.11.2001

In Vitro/in vivo	:	In vivo
Type	:	Toxicokinetics
Species	:	rat
Number of animals		
Males	:	
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	
Remark	:	F344 rats were exposed to VF2 concentrations of 3750 and 5000 ppm for 6 hrs inorder to develop a new method for measurnig VF2 in blood. At 3750 ppm and 5000 ppm the steady-state blood concentrations of VF2 were 240 and 626 ng/ml. This is not considered to be a key study for SIDS evaluation and is therefore not further detailed in this document. Reliability criteria: reliable with restrictions: well documented, acceptable scientific principles, acceptable for assessment.(2e)

21.11.2001

5.1.1 ACUTE ORAL TOXICITY

Method	:	other: not applicable : the compound is a gas at ambient temperature
Year	:	
GLP	:	
Test substance	:	

16.03.2001

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LCLo
Value	:	> 200000 ppm
Species	:	other: wistar rat
Strain	:	
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	
Exposure time	:	1 hour(s)
Method	:	
Year	:	1982
GLP	:	
Test substance	:	no data
Remark	:	5 male and 5 female rats were exposed to 200000 ppm VF2 for 1 hr.

Animals were observed for 7 days after exposure.

No mortality was observed; no respiratory, skeletal reflex, or gross pathological changes were observed in these rats.

Reliability criteria: reliable with restriction: comparable to guideline study with acceptable restrictions (2c)

28.08.2001 (16)

Type	:	LCLo
Value	:	> 200000 ppm
Species	:	other: CF1 mouse
Strain	:	
Sex	:	Male
Number of animals	:	5
Vehicle	:	
Doses	:	
Exposure time	:	1 hour(s)
Method	:	
Year	:	1982
GLP	:	
Test substance	:	no data
Remark	:	5 males per concentration were exposed to 4000, 8000, 20000,40000, 100000 and 200000 ppm for 1 hour Animals were observed for 7 days after exposure Exposures were under static conditions. All mice survived the highest concentration (200000 ppm). it produced excessive grooming behaviour. There were no loss in body weight, no respiratory changes, abnormal reflexes, or gross pathological changes. Reliability criteria: reliable with restrictions: comparable to guideline study with acceptable restrictions (2c)

28.08.2001 (16)

Type	:	LCLo
Value	:	ca. 128000 ppm
Species	:	Rat
Strain	:	
Sex	:	Male/female
Number of animals	:	6
Vehicle	:	Other: air
Doses	:	
Exposure time	:	
Method	:	
Year	:	1949
GLP	:	No
Test substance	:	
Remark	:	Animals were exposed to undescribed concentrations of VF2 in a dessicator (flow through) with variable exposure times, during which onset of first symptoms was noted. The actual concentration was not monitored but calculated. According to the authors, a 4 hrs exposure period to a concentration of approx. 128000 ppm of VF2 killed 2/6, 3/6, or 4/6 animals. The authors do not exclude that animals died of inadequate oxygen supply.

A necropsy was performed but not reported.

Reliability criteria: not reliable: significant methodological deficiencies (3b)

28.08.2001 (17)

Type	:	Other: comparable to current acute inhalation toxicity test guidelines
Value	:	
Species	:	Rat
Strain	:	
Sex	:	no data
Number of animals	:	
Vehicle	:	Other: oxygen
Doses	:	
Exposure time	:	19 hour(s)
Method	:	
Year	:	1950
GLP	:	no data
Test substance	:	no data
Remark	:	Tested concentrations were: 10, 20, 30, 40 50 and 80% VF2 Exposure time: from 30 minutes up to 19 h (some animals). The carrier gas was oxygen No deaths were noted; no loss of righting reflex, postural reflex or corneal reflex was observed at any tested concentration. slight intoxication at concentration 40 % and above.At 80 % by volume in air, unsteady gait but no loss of postural reflex. No progressive signs of intoxication were noted at prolonged exposures to 19 hrs. At necropsy, no signs of pulmonary irritation were observed. Since animals were not observed for a 14 day period after exposure, no reliable LC50 value can be determined. Reliability criteria: not reliable: insufficient documentation (3a)

28.08.2001 (18)

Type	:	
Value	:	
Species	:	dog
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	
Method	:	
Year	:	1990
GLP	:	
Test substance	:	
Remark	:	Inhalation, 25 to 50 % for 5 to 15 minutes (primed with epinephrine): no cardiac sensitization. Reliability criteria: reliable with restrictions: well documented, acceptable scientific principles, acceptable for assessment (2e)

16.05.2001 (19)

Type :

Value	:	
Species	:	cat
Strain	:	
Sex	:	
Number of animals	:	
Vehicle	:	
Doses	:	
Exposure time	:	
Method	:	
Year	:	1990
GLP	:	
Test substance	:	
Remark	:	Inhalation, 25 to 50 % for 5 to 15 minutes (primed with epinephrine): no cardiac sensitization. Reliability criteria: reliable with restrictions: well documented, acceptable scientific principles, acceptable for assessment (2e)

16.05.2001 (19)

5.1.3 ACUTE DERMAL TOXICITY

Method	:	other: not applicable : the compound is a gas.
Year	:	
GLP	:	
Test substance	:	

16.03.2001

5.1.4 ACUTE TOXICITY, OTHER ROUTES

16.03.2001

5.2.1 SKIN IRRITATION

Species	:	
Concentration	:	
Exposure	:	
Exposure time	:	
Number of animals	:	
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	other: not applicable (gas)
Year	:	
GLP	:	
Test substance	:	

10.03.1995

5.2.2 EYE IRRITATION

Species	:	
Concentration	:	
Dose	:	

Exposure time	:	
Comment	:	
Number of animals	:	
Vehicle	:	
Result	:	
Classification	:	
Method	:	other:
Year	:	
GLP	:	
Test substance	:	
Remark	:	No experimental data are available but data from acute, repeated and prolonged exposure by the inhalation route did not reveal any sign of eye irritation.

16.03.2001

5.3 SENSITIZATION

Number of animals	:	
Vehicle	:	
Result	:	
Classification	:	
Method	:	other: not applicable (gas)
Year	:	
GLP	:	
Test substance	:	

10.05.1995

5.4 REPEATED DOSE TOXICITY

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	13 weeks
Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	
Doses	:	250, 1000, 7000 ppm
Control group	:	
NOAEL	:	= 1000 ppm
Method	:	other: comparable to m odified OECD guideline 422
Year	:	1985
GLP	:	yes
Test substance	:	
Remark	:	The subchronic toxicity part of a combined subchronic toxicity/reproduction/fertility study is described here. weanling rats (180 per sex)and young adult rats (180 per sex) were whole-body exposed. An interim kill was performed at week 4. A group of animals was retained for a recovery period of 10 weeks. Parameters evaluated:

Clinical observations were made 2 X / day.
Once per week close clinical evaluation was made on each animal.

Body weight was measure at the start of the study and weekly thereafter.

Hematology was evaluated in week 4 and 13

Urinalysis was performed in the males in week 4 and 13.

Vaginal smears were performed in control and high dose animals in weeks 3 and 4 and weeks 12 and 13.

Pathology:
Organ weights of all animals killed at week 5 and 13 of adrenals, brain, coagulating glands, epididymis, heart, kidney, liver, lung, ovaries, pituitary, prostate, simal vesicles, spleen, testes, uterus.
Testes of animals killed after the 10 week recovery period were also weighted.

Microscopic evaluation:
Sperm morfology at week 14
Histological eximination of testis and epididymis(all animals), lungs and nasal turbinates (all animals), adrenals and pituitary (controls and high dose), ovaries and uterus (control and high dose)

Statistical methods:

Body weight: analysis of covariance foolowed by Dunnett's test
organ weights, hematological, biochemical data: analysis of variance, followed by Dunnett's test
Incidences of pathological changes: Fisher's exact test.

Results:

Compared to controls, no treatment related changes were observed in treated animals regarding body weight, heamatology, urinalysis, mortality, oestrus cycle, organ weights.

Pathology:
No treatment related effects were observed on marcoscopic examination.

Microscopic examination revealed treatment related changes in the nose, in animals of both subsets. The changes occurred in the vomeronasal epithelium which cobvers partly the wall of the vomeronasal organ. The ciliated epithelium, which covers the other part of the wall , looked normal.

Weanlings:
At day 28 a varying number of large vacuoles was observed in the vomeronasal epithelium and, in the more severe cases, the vomeronasal epithelium showed a complete vacuolar change. The abnormality was noticed in 4 males and in all females exposed to 7000 ppm VF2. At day 91, similar degenerative lesions were observed, but they were distinctly less pronounced and were restricted to 3 females of the 7000 ppm group only.

Young adults:
At day 28, a varying number of large vacuoles was observed in the vomeronasal epithelium and in more severe cases, the vomeronasal epithelium showed a complete vacuolar change. The abnormality was noticed in 6 males and 9 females exposed to 7000 ppm VF2. At day 91 such degenrative changes were not found; the vomeronasal organ looked normal in all male and all female rats.

In animals of both subsets signs of rhinitis, characterised by varying numbers of inflammatory cells and a skight hyperplastic reaction of the local epithelium were observed in a number of male and female rats of all groups (including the controls). There was no concentration-response relationship.

NOEC rat 13 weeks: 1000 ppm.

Note:

The findings in the vomeronasal organ of rats is considered to be of doubtfull biological significance.

Reliability criteria: reliable without restrictions: comparable to guideline study (1b)

Remark: Key study for SIDS evaluation

05.03.2002 (20)

Type	:	
Species	:	rat
Sex	:	male
Strain	:	other: Albino ChR-CD
Route of admin.	:	inhalation
Exposure period	:	2 weeks
Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	
Doses	:	25000 ppm
Control group	:	
Method	:	
Year	:	1977
GLP	:	
Test substance	:	
Remark	:	Slight increase in total fluoride in urine after the last exposure; slightly higher erythrocyte count; tracheitis, mucosal hyperplasia and an increase in murine pneumonitis.

Reliability criteria: not assignable: documentation insufficient for assessment (4e)

19.06.2001 (21)

Type	:	
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	inhalation
Exposure period	:	90 days
Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	
Doses	:	500, 1500, 5000, 15000, 50000 ppm
Control group	:	
Method	:	other: comparable to OECD guideline 413

Year : 1984
GLP : no data
Test substance :
Remark : 10 animals per sex and per concentration were whole-body exposed.

Results:

Body weight gain.

Statistically significant bodeweight changes were seen during the first half of the exposure period when compared to controls. There was none at study termination.
There was an unexplained BW depression in the controls with an actual body weight loss in the controls of both sexes at week 5 of the study

Clinical observations

none that were considered related to treatment

Haematology

Statistically significant decrease in RBC counts, hemoglobin levels and hematocrit levels for males of the 1500 and 50000 ppm dose groups. No changes in females.

Males	0 ppm	1500 ppm	50000 ppm
RBC	9310	8470	8483
HGB	16.32	15.12	15.17
HCT	47.34	42.94	43.50

Clinical chemistry

Significant increase of creatinine levels in the 500 (+ 24%) and 1500 ppm (+18%) females.
Significant increase in SGOT levels in 50000 ppm males (+20%) and females (+56%).
Significant increase in SDH levels in 15000 ppm males (+22%) and females (+28%)
Significant increase in BUN levels in 1500ppm and 5000 ppm males (+ 16 and +21% resp) and in 5000 and 50000 ppm females (+21 and +15% rep.).
Significant decrease in SGPT levels in 15000 ppm males (- 13%) and females (- 18%).

Organ weights

Absolute organ weights

Significant increase in liver weights in the 500, 5000 and 15000 ppm males (+13,+17, +14% resp) and in the 500 and 15000 ppm females.(+11, +16% resp)
Significant increase in thymus weights in the 1500, 5000, and 50000 ppm females.(+22,+24, +22%)
Significant increase in (right) kidney weights in all treated males (+16, +12, +17, +14, +12% resp) and in 15000 ppm females.(+13%)
Significant decrease in the (right) testes weights in the 50000 ppm males. (-7%)

Relative organ weights

Significant increase in rel. liver weights in the 5000 and 15000 ppm males (+7, +7% resp) and in 500 and 15000 ppm females (+5, +7% resp).
Significant decrease in rel. brain weight in 15000 ppm males (-7%).
Significant decrease in rel. heart weight in 1500 and 5000 ppm males (-9, -10% resp).
Significant decrease in rel. testes weight in 5000 and 50000 ppm males (-8, -11%).
Significant increase in rel. kidney weight in 500 and 5000 ppm males (+9, +7% resp) .

Histopathology

One rat in the 50000 ppm exhbited serous rhinitis, of which could not be excluded to be related to treatment.
Other pathological findings were incidental and considered not to be related to treatment.
Reliability criteria: reliable without restriction: Comparable to guideline study (1b)

21.11.2001 (22)

Type :
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : inhalation
Exposure period : 13 weeks
Frequency of treatm. : 6 h/d, 5 d/wk
Post exposure period :
Doses : 500, 1500, 5000, 15000, 50000 ppm
Control group :
Method :
Year : 1984
GLP : no data
Test substance :
Remark : 10 animals per sex and per concentration (including control) were whole-body exposed to VF2.

Results

Clnical observations

Few mice at various concentrations showed body w eight loss and/or thinness.

Mortality

6 animals died during the study (two 5000 ppm males, one 500 ppm female, three 5000 ppm females)
There were no treatment related deaths in the 15000 and 50000 ppm groups.

Hematology

Significant decrease in WBC counts in the 500 ppm females.

Significant decrease in lymphocytes in the 500, 5000 and 50000 ppm males.(not considered biologically significant)
Significant increase of the hematocrit in the 50000 ppm females.
The latter may by caused by increased erythropoiesis that may be due to mild hypoxia.

Body weight

Statistically significant body weight depression was observed in 500 ppm females at week 9 and 10, in 1500 ppm females at weeks 9, 11 and 13, in 5000 ppm females at week 5 and in 15000 ppm females at week 11.
During the second half of the study, the males had no statistically significant changes in their body weights.
It should be noted that several animals with marked BW loss during week 5 and 6 rapidly recovered in the next week.
This has partially been attributed to a malfunction in the watering system. Also 3 deaths are suspected to be caused by the same failure.
At study termination, only the 1500 ppm females showed a statistically significant decrease in BW (-13%). Males of the 500, 15000 and 50000 ppm and females of all VF2 dose groups showed a decreasing trend in BW.

Organ weights

Absolute organ weight

Significant increase in liver weight of the 1500 ppm males (+13%).
Significant decrease in liver weights of the 15000 ppm females.(-10%)

Relative organ weight

Statistically significant increase in rel. liver weight in 500 and 1500 ppm males.(+10, +10% resp)

Pathology

Gross necropsy
No findings that could be related to treatment.

Histopathology

A small number of of exposed mice had renal changes, kidney/tubule regeneration. This was seen in a very low incidence in all dosed males, except the 5000 ppm males and was also noted in the 5000 and the 50000 ppm females.
All lesions were of minimal severity. There was no evidence of renal degeneration or necrosis.

The NOEC is considered by the authors to be < 500 ppm.
Reliability criteria: reliable without restrictions: Comparable to guideline study (1b)

21.11.2001 (23)

Type :
Species : rat

Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	13 weeks
Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	
Doses	:	1000, 7000, 40000 ppm
Control group	:	yes
Method	:	other: comparable to OECD guideline 413
Year	:	1985
GLP	:	yes
Test substance	:	no data
Remark	:	30 animals per sex and per concentration were used in this study.

Following parameters were evaluated:
Condition and behaviour, ophatalmology, body weight, food consumption, heamatology, clinical chemistry, urinalysis, organ weights, gross and microscopic pathology.
Interim kills were performed at 2 and 4 weeks.

Decreased BW gain from 7000 ppm in males and females but not statistically significant at the end of the study.
A transient (first weeks only) decreased food consumption in males and femals at 40000 ppm.

Heamatology:
statistically significant anemia in 40000 ppm males (-7%) and females (-11%).
Statistically significant increase of mean corpuscular volumes troughout the study in the 40000 ppm males (+5%) and at study termination in the 40 000 ppm females (+6%).
Statistically significant increase of mean corposucular haemoglobin in 40 000 ppm males and females at study termination(+8 and +8% resp).
Statistically significant decrease in WBC counts at study termination from 7000 ppm in males (-34,-25% resp) and at 40000 ppm in females (-28%) (mainly decrease of lymphocytes)

Clinical chemistry:
In the first few weeks of the study there was a statistically significant decrease of serum alkaline phosphatase in the mid and high dose males and the high dose females. This effect was transient.
Alpha2 globulins were increased in mid and high dose males at study termination (+7,+10% resp).
Several transient and not dose related changes were noted in some other serum enzymes (GPT, GOT, OCT) , in Ca, Na, Cl , K, triglycerides and cholesterol were observed but were not considered to be related to the test compound.

Urinalysis:
gamma glutamyl tranferase activity was increased during the study and decreased at study termination in high dose males.
A similar but transient effect was seen during the study in mid and high dose females.

Organ weight changes:

Absolute and relative h eart weights were increased in all high dose animals troughout the study (males:abs:+16;rel:+19%;

females:abs:+19;rel:+13%), and in females of the mid dose group in the first 4 weeks. Also the relative heart weight of the females of the low dose group was higher as compared with that of the control group on the 4th week.
The absolute spleen weight was decreased in males and females of the high dose group throughout the study (. When the spleen weight was expressed relative to body weight, the decrease was only observed in males of the high dose group on week 2 and in females of ther high dose group on week 2 and week 13 and in females of the mid dose group on week 2.
Relative lung weights were increased in males and females of the high dose group during the study but not at termination.

Absolute and relative testes weights were decreased in the mid and high dose groups on week 4 and at study termination (end study:-23,-65% resp)
Relative testes weights were decreased in high dose group at study termination (-64%)
In addition, the absolute testes weight of the high dose males was decreased on week 2.
Absolute epididymis weight was decreased in the high dose group on week 4 and in the mid and high dose groups at study termination (end study: -20,-42% resp).
Relative weight of the epididymes was decreased in the high dose group at study termination (-42%).

Pathology:
Autopsy revealed soft testes and epididymes in the high dose group on week 4 and at study termination.

Microscopic examination revealed treatment related changes in testes and epididymes of males of mid and high dose groups throughout the study.
The changes were characterised by impairment of spermatogenesis.

The spleen showed treament related changes, characterised by lymphocytic depletion of the marginal zone, in males and females of the mid and high dose groups and in females of the low dose group at week 2.
Vacuolar degeneration of the Vomeronasal organ in the nose was observed in all treatment groups.
Changes appeared to decrease in severity with time.
Mineralisation of the kidneys was increased in males of the high dose group after week4 and at study termination.

NOEC 90 day , rat: < 1000 ppm

Note: the summarised conclusions mentioned in the report do not coincide with the tabulated results.
Reliability criteria: reliable with restrictions:Comparable to guideline study with acceptable restrictions. (inconsistent reporting)(2b)

22.11.2001 (24)

Type :
Species : mouse
Sex : male/female
Strain : CD-1
Route of admin. : inhalation
Exposure period : 2 weeks

Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	
Doses	:	1000, 5000, 15000, 40000 ppm
Control group	:	
NOAEL	:	= 40000 ppm
Method	:	other: comparable to OECD guideline 412
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	5 animals /sex/group were whole-body exposed to 0, 1000, 5000, 15000 and 40000 ppm. The gas concentration in the chambers were monitored by GC four times per exposure day. There was no mortality. There were no clinical symptoms observed which were related to the treatment. There was no treatment related effect on body weight or BW gain. Absolute and relative organ weights were not affected by treatment. Macroscopic examination at necropsy revealed no treatment related changes. The NOEC in this study was considered to be 40000 ppm. Reliability criteria: reliable without restrictions: Comparable to guideline study (1b)

22.08.2001 (25)

Type	:	
Species	:	mouse
Sex	:	male/female
Strain	:	CD-1
Route of admin.	:	inhalation
Exposure period	:	13 weeks
Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	
Doses	:	0, 1000, 7000, 40000 ppm
Control group	:	
NOAEL	:	= ppm
Method	:	other: comparable to OECD guideline 413
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	10 animals per sex and per group were whole-body exposed. Exposure concentrations were measure by GC four times per exposure day. Clinical observations: Treatment related, but not dose related increased locomotor activity. It was observed in both sexes and was prominent in mid study and declined afterwards. Increased sensitivity to touch (aggressivity) in 40000 ppm males during the last week of exposure, in 7000 and 40000 ppm females during the last 2 weeks of exposure. Dose related rough coat in males after eight weeks of exposure. Body weight and food consumption:

No treatment related effects

Hematology:

Significant increase in mean corpuscular hemoglobin content in the 40000 ppm males.

Absolute and relative organ weights:

No treatment related effects

Pathology:

No treatment related macro- and microscopic pathological changes observed.

The NOEC is 7000 ppm
Reliability criteria: reliable without restrictions: Comparable to guideline study (1b)

22.08.2001 (26)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Escherichia coli reverse mutation assay
System of testing	:	exposure to maximally soluble concentration in aqueous medium.
Test concentration	:	Unknown
Cycotoxic concentr.	:	
Metabolic activation	:	
Result	:	
Method	:	
Year	:	1968
GLP	:	No
Test substance	:	no data
Remark	:	E; Coli strain B and strain Sd-4 were cultured exposed to gaseous VF2 in their liquid medium by bubbling the gas trough the medium for 10 minutes (It is assumed that microorganisms were exposed to the max disolved VF2 concentration in the medium which is unknown). E Coli strains were plated 24 hrs after exposure on agar. Viability decreased to 62% of control for strain B and to 94 % for Sd-4. Mutation rate was 1000 higher than control for strain B and 100 times higher for strain Sd-4 This test procedure is not standard and results are therfore difficult to interpret. Since this study is not considered as a key study, further details of the study procedure are not described. Reliability criteria: Not reliable: Unsuitable test system (3c)

26.04.2001 (27)

Type	:	Ames test
System of testing	:	exposure to the gas

Test concentration	:	Unknown
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	
Method	:	
Year	:	1977
GLP	:	no data
Test substance	:	no data
Remark	:	Histidine dependent Salmonella typhimurium strains TA 1535 , TA 1537, TA 1538, TA 98 and TA 100 were used Tests were carried out in the presence and absence of rat liver derived S -9 mix activation system. Positive controls were tested with different mutagens. The cultures were exposed to unknown gaseous concentrations for1, 24, 48 and 72 hrs. The revertant colonies were counted in all concentration groups and compared to the number of revertant colonies in the control group. Statistical methods: not mentioned Results: Positive in TA 1535 only in the in absence (after 72 hrs)and in presence of S-9 activation (from 24 hrs exposure on) Negative in TA 1537, 1 538 TA 98, TA 100 Reliability criteria: Not reliable: documentation insufficient for assessment (3a)

26.04.2001 (28)

Type	:	Other: cell transformation
System of testing	:	
Test concentration	:	unknown
Cycotoxic concentr.	:	
Metabolic activation	:	without
Result	:	negative
Method	:	
Year	:	1978
GLP	:	no data
Test substance	:	no data
Remark	:	BALB/3T3 cells were cultured in bottles with our without culture medium.The test with culture medium was run in duplo. The test without culture medium was run once. Bottles were gassed (concentrations not described) and cells were exposure for 0, 0.5, 1, 2, 4, 6, 24, and 48 hrs. A positive control was run with3-methylcholanthrene. The test without the culture medium did not show any transformation of cells. There was a slight increase in incidence of transformed cells in one of two replicates of the test with culture medium.

In this test VF2 was considered not mutagenic to BALB/3T3 cells under the conditions of the test.

The concentrations used are not mentioned in the test report.
Therefore the observed effects cannot be interpreted.
A lack of oxygen may have influenced the outcome of the test.

Reliability criteria: Not reliable: documentation insufficient for evaluation (3a)

26.04.2001 (29)

Type	:	Ames test
System of testing	:	exposure to gas
Test concentration	:	up to 50 %
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	
Method	:	
Year	:	1979
GLP	:	no data
Test substance	:	no data

Remark : Histidine dependent Salmonella typhimurium strains TA 1535 and TA 100 were used to detect base-pair substitution mutations and strains TA 1537 and TA 98 to detyect frame-shift mutations.

Tests were carried out in the presence and absence of rat liver derived S-9 mix activation system.
The cultures were exposed to gaseous concentrations from 0 to 50% VF2 for 48 hrs.
Test concentrations were measured at the beginning and at the end of the exposure by GC.
The revertant colonies were counted in all concentration groups and compared to the number of revertant colonies in the control group.

Statistical methods:

number of revertants for each dose group: z-test
Dose dependency: Spearman rank test.

Results:

Positive in TA 1535 only in the presence of S-9 activation, from 10 %,
Negative in TA 1537, TA 98, TA 100 upto 50 % with or without S9.

Reliability criteria: reliable without restriction: comparable to guideline study (1b)

26.04.2001 (30)

Type	:	Ames test
System of testing	:	exposure to the gas
Test concentration	:	up to 50%
Cycotoxic concentr.	:	
Metabolic activation	:	with and without

Result	:	negative
Method	:	
Year	:	1979
GLP	:	no data
Test substance	:	no data
Remark	:	Histidine dependent Salmonella typhimurium strain TA 100 was exposed up to 24 hrs to gaseous concentrations of 0, 20, and 50 % VF2. Exposure was made with and without rat liver derived S9 activation. Exposure was measured by GC. There was a marginal but not significant increase in revertant colonies at 24hrs exposure at 50% and only in the presence of S9. Reliability criteria: Not reliable: significant methodological deficiencies (3b)

26.04.2001 (31)

Type	:	HGPRT assay
System of testing	:	exposure to the gas phase
Test concentration	:	
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	
Year	:	1986
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Cell cultures of the BH4 clone of Chinese hamster overy cells were exposed to gaseous concentrations of VF2 Concentrations tested were 0(nitrogen), 20, 40, 60, 80 and 100% VF2. Actual test concentration werez measured at the beginnig and at the end of the exposure by GC. Each concentration was tested on cell cultures in the presence or absence of rat liver derived S9 activation system. Exposure period: 18 - 19 hrs for non-activated cultures 5 hrs for activated cultures Evaluated parameters: Cytotoxicity: after exposure by survival of subcultured cells for seven days. Mutagenicity: incidence transformation of the HGPRT gene locus by measuring incidence of cells with resistance to 6-TG. Statistical analysis: for effect of of each concentration in comparison with control: mutant frequency: t- test of significance for concentration-responce relationship: ANOVA for linear, quadratic or higher order effects: F-test of significance. Results:

The mutant frequency of none of the sample concentrations tested was significantly greater than that of the negative controls ($p<0.05$)
and
The correlation between mutant frequency and the concentration of the test sample was not significantly greater than 0 ($p< 0.05$)

Thus under the conditions of the test VF2 was considered not a mutagen in this test.

This is considered as a key study for SIDS evaluation.
Reliability criteria: reliable without restriction:
comparable to guideline study (1b)

26.04.2001 (32)

Type	:	Cytogenetic assay
System of testing	:	exposure to gaseous VF2
Test concentration	:	0, 25, 50, 75 and 100%
Cycotoxic concentr.	:	
Metabolic activation	:	with and without
Result	:	
Method	:	
Year	:	1986
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	This test was performed according to accepted EPA and OECD guidelines. Cell cultures of the BH4 clone of the CHO cell line were exposed to different concentration of VF2 in the gas phase. The exposure was done in presence and absence of rat liver derived S-9 activation system. Exposure periods were 5 hrs (without activation) and 2 hrs (with activation). negative control consis of nitrogen exposure only. Positive control was done with exposure to ethylmethane sulphonate. Evaluated parameters: Cytotoxicity by measurement of delay of cell replication after end of exposure. Genotoxic effect by measurement of incidence of chromosomal aberrations. Statistical evaluation: Aberrations per cell (dose vs control): Mann-Withney U test Dose responce relation: Jonckheere test Percent abnormal cells and cells with more than one aberration: dose vs control: Fisher exact test dose response relation: Cochran-Armitage for trend. Results: No cell replication delay in any of the tested concentrations. No treatment related chromosomal aberrations in the trials without S9 activation.

No treatment related chromosomal aberrations in the trials with S9 activation.

VF2 was considered not to cause chromosomal aberrations under the conditions of the test.

Reliability criteria: reliable without restriction: GLP guideline study.(1a)

26.04.2001 (33)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	:	Micronucleus assay
Species	:	mouse
Sex	:	male/female
Strain	:	CD-1
Route of admin.	:	inhalation
Exposure period	:	6 h
Doses	:	5000, 15000, 40000 ppm
Result	:	
Method	:	
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	5 male and 5 female CD1 mice were exposed (nose-only) to 0, 5000, 15000 and 40000 ppm VF2 for 6 hrs. A positive control treated with chlorambucyl was concurrently evaluated. Test concentrations were monitored by GC every 1/2 hr during the exposure. Bone marrow smears of treated and control animals were made at 24, 48 and 72 hrs after initiation of the exposure. Parameters evaluated: systemic bone marrow toxicity: ratio polychromatic erythrocytes vs mature cells. Mutagenicity: incidence of micronuclei in polychromatic erythrocyte. Statistical evaluation: Incidence of micronuclei in erythrocytes of treated animals vs control: Mann-Withney U test Results: No evidence of toxicity of VF2 for the murine bone marrow of animals exposed to up to 40000 ppm VF2. No difference in frequency of micronuclei in polychromatic erythrocytes between treated and control animals (both sexes). It was considered that under the conditions of the test VF2 did not cause chromosomal or other damage leading to micronucleus formation in polychromatic erythrocytes of exposed mice.

Reliability criteria: Reliable without restriction:
comparable to guideline study (1b)

18.05.2001 (34)

Type	:	Drosophila SLRL test
Species	:	Drosophila melanogaster
Sex	:	
Strain	:	
Route of admin.	:	inhalation
Exposure period	:	24 h
Doses	:	4.95, 22.8 and 43 %
Result	:	negative
Method	:	
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	VF2 was evaluated for mutagenic activity using the Oregon-R strain of Drosophyla melanogaster. Preliminary tests indicated that VF2 was neither toxic nor affected the fertility of the treated males compared to the negative controlat concentrations up to 50% the main test was conducted using 3 mixtures of 4.95, 22.8 and 43% of VF2 with 20% oxygen and the balance made by N2. 200 male flies were exposed for 24 hrs. Negative control was 20% O2 and 80% N2 The positive control was ethyl methane sulphonate in the feed. Actual test atmosphere was monitored by GC. 24 hrs after end exposure treated males were mated to virgin Basc females. Statistical evaluation: Lethality per dose vs control: ? lethality-concentration relation: Cochran-Artmitage trend analysis. Results: The differences in lethality in progeny of males between control and VF2 treated groups were not statistically different . VF2 was considered not to be mutagenic to the X chromosome of Drosophyla melanogaster under the conditions of the test. Reliability criteria: Reliable without restriction: comparable to guideline study (1b)

26.04.2001 (35) (36)

5.7 CARCINOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	104 weeks
Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	

Doses	:	150, 600, 2500, 10000 ppm
Result	:	
Control group	:	yes
Method	:	other: OECD guideline 453
Year	:	1991
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Control group consisted of 140 animals of each sex. In the exposed groups, each group consisted of 80 animals of each sex.(including 20 animals/sex /group as satellites) All animals were whole-body exposed. Exposure concentrations were monitored by GC analysis Interim kill of 20 animals per sex and per group was performed at 12 months. Parameters observed: Clinical observation was made twice per day. Ophtalmoscopy was perform prior to study on all animals killed at 12 months (satellite), on 10 animals/sex of control and high dose group at six months. Serological examination was made on receipt of animals, at start of exposure, at week 22, at week 26, one year after start, at 18 months and at 2 years . Body weight was recorded once every week until week 13 and every four week thereafter. Food consumption was determined during the first 13 weeks in all groups (measured per cage) Hematology was performed on 20 animals/sex/group on weeks 13, 26, 52 Clinical chemistry was performed on blood drawn from 20 animals/sex/group on weeks 13 and 26 and on weeks 53 and 54 on the animals killed at 12 months. Urinalysis was performed on satellite animals on weeks 13, 26, and 52 Pathology: Macroscopic examination was performed on all animals. Organ weights were measured on all satellite animals killed at 12 months and on 10 animals/sex/group at study termination. Weighted organs included: adrenals, brain, epididymis, heart, kidneys, liver, lungs with mediastinal lymphnodes, trachea and larynx, ovaries, pituitary, spleen, testes thyroid. Histological examination was performed on following tissues of controls and high dose animals: adrenals, aorta, axillary lymphnodes, brain, ceacum, coagulating glands, colon, epididymis, eye, femur with joint and bone marrow, heart, kidney, larynx, liver, lung, mammary gland, mesenteric lymph nodes, sciatic nerve, nose,

oesofagus, ovaries, pancreas, parathyroid, parotid salvary gland, pharynx , pituitary.
In the 600 ppm animals following tissues were examined: adrenals, brain, kidney, liver, larynx, lung, nose, ovary, partathyroids , pituitary.

Statistical methods used:

Body weights: analysis of covariance, Dunnetts multiple comparison test,
Body weight and BW gain: Bartlet's test, Dunnet's test.
Food intake: Bartlett's test, LSD
Absolute and relative organ weights, hematological data, urine data: Bartlett's test, Dunnett's test
WBC counts, Reticulocyt counts, blood globulins, urine pH: Kruskal-Wallis method
Incidences in histopathological changes, mortality: Fishers test
All pairwise comparisons were two-tailed.

Results:

No treatment-related mortality was observed.

Clinical observation:

No treatment-related changes were noted.

Ophtalmology:

No treatment-related effects were observed.

Body weight gain and food consumption:

No treament-related effects on BW gain was observed, but food consumption tended to be lower in treated animals than in controls.

Hematology:

No consistent and clear changes were observed which could be related to treatment

Urinalysis:

No treatment-related changes were observed.

Organ weights:

Absolute organ weights after 12 months were similar in all groups.
Relative organ weights (brain , heart, epidydimis) of the 150 ppm males were decreased compared to control at study termination.

Pathology:

Macroscopic and microscopic examination at necropsy did not reveal treatment related effects.
Some differences in incidence of minor nasal changes were

considered as of negligible toxicological concern.

Evaluation of the observed neoplasms did not reveal treatment related shifts in benign or malignant tumor incidence, total number of tumors, or total number of tumor bearing animals.

Key study for SIDS evaluation.

Reliability criteria: reliable without restriction: GLP Guideline study (1a)

22.08.2001 (37)

Species	:	mouse
Sex	:	male/female
Strain	:	CD-1
Route of admin.	:	inhalation
Exposure period	:	18 months
Frequency of treatm.	:	6 h/d, 5 d/wk
Post exposure period	:	
Doses	:	0, 600, 2500, 10000 ppm
Result	:	
Control group	:	
Method	:	other: OECD guideline 451
Year	:	1991
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	82 animals per sex and per group were whole- body exposed. Actual exposure concentrations were measured by GC, 6 times per exposure day.

Parameters observed:

Gross clinical observations were made twice daily.
Detailed physical eximinations were performed pretest and weekly thereafter.

Ophtalmology was performed pretest and on moths 6, 12 and at study termination

Body weight was measured twice pretest, weekly til week 13, monthly til week 52, then weekly til end study.

Food consumption was measured weekly til week 13 the, monthly til week 52, then weekly thereafter.

Hematology and clinical chemistry were evaluated at 12 and 18 months

Pathology:
Macroscopic examination on all animals.
Histology on respiratory tract,and tissue masses in all animals of all dose groups.
In controls and high doses: abdominal aorta, adrenals, bone and bone marrow, brain, oesofagus, eyes with optic nerve, gall bladder, heart, cecum, colon, rectum ileum, jejunum, duodenum, kidney, larynx, liver, lungs, lymph nodes, nasopharynx, sciatic nerve, ovaries, pancreas pharynx, pituitary, prostate, salivary gland, seminal vesicles, skin, spinal cord, skin, mammary gland, spleen, stomach, testes,

epididymis, thymus, thyroid, parathyroid, trachea, urinary bladder, uterus.

Statistical methods:

Chi-square: proportion of incidences between groups,
fishers exact test: comparison of treatment group with control
bonferroni inequality: overall test of stated significance level
armitage test: for linearity trend in dose groups

Results:

Survival was similar amongst groups at study termination

Clinical observations:

No treatment related effects observed.

Ophtalmology:

No treament related effects observed.

Body weight gain and foor consumption:

No treatment related effects observed.

Hematology:

No treatment related effects observed.

Pathology:

No treatment related m acroscopic or microscopic lesions observed.

When observed benign and malignant neoplasms in VF2 exposed animals were compared to respective controls, none were considered to be related to exposure to the test substance.

Overall the morphological findings in the animals from this study were not considered to be of any toxicological or oncological significance with respect to VF2.

VF2 is not considered to be a carcinogen for the mouse.

Key study for SIDS evaluation

Reliability criteria: reliable without restriction:
comparable to guideline study (1b)

21.11.2001 (38)

Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	gavage
Exposure period	:	52 weeks
Frequency of treatm.	:	4 to 5 d/wk
Post exposure period	:	until natural death

Doses	:	4.12, 8.25 mg/kg (dissolved in olive oil)
Result	:	
Control group	:	yes, concurrent vehicle
Method	:	other: is not comparable to accepted study guidelines
Year	:	1979
GLP	:	no
Test substance	:	no data
Remark	:	In the high dose group 35 animals per sex were used. In the low dose and in control 30 animaLs of each sex were used per group. Parameters evaluated: Body weight: eve ry 2 weeks during treament, every eight weeks after treatment. Clinical evaluation: every 2 weeks Pathology: macroscopic and histological examination on all animals. Following tissues were evaluated: Zymbal glands, intrascapular brown fat, salivary glands, tongue, lungs, liver, kidney, adrenals, spleen stomach, intestines, bladder, brain, every organ with pathological lesions. No statistical evaluation was performed. Results: Lipomas and liposarcomas were observed: number of lipomas were increased in the high dose group compared to the number found in controls but no lipomas were found in the low dose group. There was a dose- related trend in the numbers of liposarcomas.(0% in controls versus 1.7% in low dose versus 4.3% in high dose. No other pathological effects were mentioned Reliability criteria: Not reliable: documentation insufficient for assessment (3a) .

22.08.2001 (39)

5.8.1 TOXICITY TO FERTILITY

Type	:	Fertility
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	13 weeks
Frequency of treatm.	:	6 hrs/d 5 d/wk
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	13 weeks
No. of generation studies	:	
Doses	:	250, 1000, 7000 ppm

Control group	:	yes
NOAEL parental	:	7000 ppm
Method	:	other: comparable to modified OECD guideline 422
Year	:	1985
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The male fertility part of a combined subchronic toxicity/reproduction/fertility study is described here. weanling rats (180 per sex and per concentration)and young adult rats (180 per sex and per concentration) were whole-body exposed . An interim kill was performed at week 4. A group of animals was retained for a recovery period of 10 weeks. Parameters evaluated: Clinical observations were made 2 X / day. Once per week close clinical evaluation was made on each animal. Body weight was measure at the start of the study and weekly thereafter. Hematology was evaluated in week 4 and 13 Urinalysis was performed in the males in week 4 and 13. Vaginal smears were performed in control and high dose animals in weeks 3 and 4 and weeks 12 and 13. Pathology: Organ weights of all animals killed at week 5 and 13 of adrenals, brain, coagulating glands, epididymis, heart, kidney, liver, lung, ovaries, pituitary, prostate, simal vesicles, spleen, testes, uterus. Testes of animals killed after the 10 week recovery period were also weighted. Microscopic evaluation: Sperm morfology at week 14 Histological eximination of testis and epididymis(all animals), lungs and nasal turbinates (all animals), adrenals and pituitary (controls and high dose), ovaries and uterus (control and high dose) Statistical methods: Body weight: analysis of covariance foolowed by Dunnett's test organ weights, hematological, biochemical data: analysis of variance, followed by Dunnett's test Incidences of pathological changes: Fisher's exact test. Results: Compared to controls, no treatment related changes were observed in treated animals regarding body weight, heamatology, urinalysis, mortality, oestrus cycle, organ weights.

Pathology:
No treatment related effects were observed on marcoscopic examination.

The results did not show any treatment related effect on sperm concentration, number of sperm cells with deformed heads/tails or on numbers of isolated heads/tails either in weanlings or in young adults.

NOEC rat 13 weeks, fertility end point: 7000 ppm.

Reliability criteria: reliable without restrictions: comparable to guideline study (1b)

Remark: Key study for SIDS evaluation

21.11.2001 (20)

Type	:	Fertility
Species	:	rat
Sex	:	male/female
Strain	:	Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	0-5 d (pregnancy) 2 wk (mating period)
Frequency of treatm.	:	6 h/d, 7 d/wk (mating period) or 5 d/wk (premating period)
Premating exposure period		
Male	:	15 weeks
Female	:	15 weeks
Duration of test	:	
No. of generation studies	:	
Doses	:	250, 1000, 7000 ppm
Control group	:	
NOAEL parental	:	7000 ppm
NOAEL F1 offspring	:	7000 ppm
Method	:	other: comparable to modified OECD guideline 422
Year	:	1985
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	

The female fertility part of a combined subchronic toxicity/fertility/reproduction toxicity study is described here.

20 animals per sex and per dose group were whole body exposed as described above. Monitoring of test atmosphere was done by GC.

Exposed males and females were mated for 2 weeks with untreated partners. During mating exposed animals were also exposed during 6hrs/d and 7d/wk.
Pregnant females were exposed during first 5 days of gestation.

Pregnant females were sacrificed at day 15 of gestation.

Evaluated parameters:

Clinical symptoms:
Cage-side inspection, twice daily
Individual inspection , once per week.

Body weights:
Body weights were recorded prestudy,once per week and at sacrifice.

Organ weights:
after kill, in treated and untreated animals following
organs were weighted: testes epididymes, seminal vesicles,
prostate, ovaries.

Fertility evaluation and reproductive performance:
in treated animals and in untreated males and females which
were mated with de former following parameters were
recorded:
mating index, male fertility index, female fertility index,
fecundity index, pre-coital time.
In treated and untreated females: number of corpora lutea,
number of implantation sites, number of early and late
resorptions.

Statistical methods:
Body weights of parent rats: analysis of variance
Number of females mated, number of pregnant females, number
of females bearing live fetusses: Chi-square test
Difference in median pre-coital times: Mann-Withney U test
mean pre-coital time including only females mated: Student t
test
organ weights, litter data, pre-implantation loss: analysis
of variance followed by Dunnett's Multiple comparison test.

Results:

No mortality nor clinical symptoms in any group.

Body weight of parents similar in all groups

No treatment related differences in fertility indices or in
reproductive performance

No treatment related autopsy findings, difference in ovary
weights and in litter data

Reproductive organ weights of treated males were similar in
all groups.

NOEC : = or > 7000 ppm

This is a key study for SIDS evaluation.

Reliability criteria: Reliable without restriction:
Comparable to guideline study (1b

22.08.2001 (40)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	other: CRL:COBS CD (SD) BR

Route of admin.	:	inhalation
Exposure period	:	6-15 days of gestation
Frequency of treatm.	:	6 h/d
Duration of test	:	
Doses	:	2000, 10000 ppm
Control group	:	yes
NOAEL maternal tox.	:	= 10000 ppm
NOAEL teratogen.	:	= 10000 ppm
Method	:	
Year	:	1978
GLP	:	no
Test substance	:	no data
Remark	:	20 females per dose group were mated with males of the same strain. From days 6 through 15 females were whole-body exposed for 6hrs per day. Test atmosphere concentrations were monitored by GC. At day 20 of gestation feti were delivered by cesarean section. Parameters evaluated: Clinical observations: daily Body weight measured at days 0, 6, 15, 20 of gestation. Food consumption: recorded periods: days 0-6,6-15, 15-20. At day 20: number of implantation sites, corpora lutea, live and dead fetuses, resorption sites Feti: weight, external examination and externally visible abnormalities. Changes in soft tissues of head, thoracic and visceral organs, skeletal abnormalities. Statistical methods: differences in means and near-normal distribution of body weights, food consumption, mean pup weight: Dunnett's t test sex- and pregnancy ratio: 2X2 contingency tables with Yates'correction Number of abnormal fetusses within a litter: Wilcoxon Rank Sum. Results: No mortality. Mothers did not show treatment related external or macroscopic features. No changes in body weight or food consumption. No treatment related effects on number of implantation sites, corpora lutea, live and dead fetuses, resorption sites. No treatment related effects on the soft tissues of head or on thoracic and visceral organs. No treatment related effects on the fetal skeleton. It was concluded that exposure to 10000 ppm VF2 of pregnant rats during gestation days 6 through 15 did not cause an adverse effect on dams nor their progeny.

Reliability criteria:reliable with restrictions: Study well documented, meets generally
accepted scientific principles , acceptable for
assessment.(2e)

This is a key study for SIDS evaluation.

22.08.2001 (41)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

Remark : Vinylidene fluoride measurements were made in working atmosphere using a MIRAN apparatus (infra-red). The sensitivity is about 1 ppm and precision is about 0.5 ppm. Background values represent 0.1 ppm. Mean value measured in 1992-1993 in a vinylidene fluoride synthesis pilot plant was 0.9 ppm. During 0.7 % of working time an alarm level of 22.7 ppm was reached.
In a laboratory, the general mean was 0.5 ppm with an alarm level mean of 20 ppm representing 0.5 % of total working time.
In a polymerization unit the monthly mean ranged from 0.038 ppm to 2.09 ppm. The number of alarm levels above 50 ppm was about 2 per month.

10.05.1995 (42)

Remark : Within the frame of an industrial hygiene monitoring programme (organised by the Fluoroalkene industry Group on request of US EPA), personal sampling were performed for various jobs within tw o VF2 polymerization plants in the US.

All sampling was performed with a 100 ml "Critical Orifice Personell Sampler" (personal sampling).(flow rate range: 0.06 to 0.08 ml/min). COPS were worn by different persons with specific jobs for a full shift.
VF2 concentrations in the samples were measured with GC.

In one plant (Dupont), no exposure data were noted above the detection limit of 1.2 to 1.9 ppm. Jobs included supervisor, polymerizing operator, finishing operator, laboratory technician, mechanical jobs.

In the second plant (Pennwalt), personal sampling during a workshift (LOD: 0.01 to 0.03 ppm)
indicated the following values (range)
- finished product operator: < 0.03 - 30 ppm
- control room operator : < 0.01 - 40 ppm
- polymer operator : < 0.01 - 38.4 ppm
- maintenance jobs : < 0.03 - 0.71 ppm
- plant supervisor : < 0.03 ppm
- laboratory technician : < 0.01 - 1.21 ppm
- field service operator : < 0.01 - 10.3 ppm
- field service operator : < 0.01 - 10.3 ppm

All values measured above 10 ppm were incidental and related to specific situations: valve relief, plugging of a line.

Further details on this exposure survey are described in, a confidential report that was submitted to EPA in 1985.

27.08.2001 (43)

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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