VINYLIDENE FLUORIDE

Data were last reviewed in IARC (1986) and the compound was classified in *IARC Monographs* Supplement 7 (1987).

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Nomenclature*

Chem. Abstr. Reg. Serv. No.: 75-38-7

Systematic name: 1,1-Difluoroethene

1.1.2 *Structural and molecular formulae and relative molecular mass*

$C_2H_2F_2$ Relative molecular mass: 64.04

1.1.3 *Physical properties* (for details, see IARC, 1986)

(*a*) *Boiling-point*: –83°C

(*b*) *Melting-point*: –144°C

(*c*) *Conversion factor*: mg/m^3 = 2.62 × ppm

1.2 Production, use and human exposure

Vinylidene fluoride has been produced commercially since the 1940s. It is used in the manufacture of polyvinylidene fluoride and elastomeric copolymers. Human exposure can occur in the manufacture of the monomer and its use in polymer production (IARC, 1986).

2. Studies of Cancer in Humans

No data were available to the Working Group.

3. Studies of Cancer in Experimental Animals

In a limited study in one strain of rats by oral administration, a small number of liposarcomas was observed in treated animals (IARC, 1986).

4. Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

No data were available to the Working Group.

4.1.2 *Experimental systems*

Vinylidene fluoride is taken up rapidly via the pulmonary route in rats, but at equilibrium the mean concentration (by volume) in rats was only 23% of that in the gaseous phase. Metabolism proceeded very slowly and was saturable at exposure concentrations of about 260 mg/m^3. Its maximum rate was 1% that of vinyl chloride and less than 20% that of vinyl fluoride; there has been a report of an increase in the urinary excretion of fluoride in exposed rats. No alkylating intermediate was demonstrated after passage through a mouse-liver microsomal system. However, vinylidene fluoride inhibits mixed-function oxidase activity *in vitro* and, like similar halogenated compounds that are transformed to reactive metabolites, it alters rat intermediary metabolism, leading to acetone exhalation (IARC, 1986).

Male Fischer 344/N rats were exposed via the nose only for 6 h to concentrations of vinylidene fluoride ranging from 27 to 16 000 ppm [71–42 000 mg/m^3]. Tidal volume (mean, 1.51 mL/breath) and respiratory frequency (mean, 132 breaths/min) were not influenced by exposure concentration. Steady-state blood levels of vinylidene fluoride increased linearly with increasing exposure concentration up to 16 000 ppm. Vinylidene fluoride tissue/air partition coefficients were determined experimentally to be 0.07, 0.18, 0.8, 1.0, and 0.29 for water, blood, liver, fat and muscle, respectively. Previously published determinations (Filser & Bolt, 1979) for the maximum velocity of metabolism (V_{max} in mg/h/kg) and Michaelis–Menten constant (K_m in mg/L) are 0.07 and 0.13, respectively. Time to reach steady-state blood levels of vinylidene fluoride was less than 15 min for all concentrations. After cessation of exposure, blood levels of vinylidene fluoride decreased to 10% of steady-state levels within 1 h. Simulation of the metabolism of vinylidene fluoride indicated that although blood levels of vinylidene fluoride increased linearly with increasing exposure concentration, the amount of vinylidene fluoride metabolized per 6-h exposure period approached a maximum at about 2000 ppm [5240 mg/m^3] vinylidene fluoride (Medinsky *et al*., 1988).

Concentrations of vinylidene fluoride were measured in blood of B6C3F$_1$ mice during 6-h exposures to nominal concentrations of 250, 3750 or 15 000 ppm [650, 9800 or 39 000 mg/m^3] vinylidene fluoride. Measured steady-state levels of vinylidene fluoride in blood of mice increased with increasing exposure concentration. At the two lower exposure concentrations, vinylidene fluoride was not detected in blood taken 15 min or longer after cessation of exposure, suggesting that the post-exposure levels were at or below the detection limit (4 ng vinylidene fluoride/mL blood). For the 15 000 ppm

exposure, vinylidene fluoride was detected in blood up to 15 min after exposure (Medinsky *et al*., 1990).

4.2 Toxic effects

4.2.1 *Humans*

No data were available to the Working Group.

4.2.2 *Experimental systems*

Exposure of rats to 215 000 mg/m^3 vinylidene fluoride for 3.5 h produced no sign of hepatoxicity. However, treatment of rats with Aroclor 1254 on three consecutive days followed by exposure for 6 h to 65 500 mg/m^3 did produce some hepatotoxicity. No excess ATPase-deficient foci were observed in the livers of Wistar rats that had been exposed from birth to 5200 mg/m^3 for 8 h per day on five days per week for 10–14 weeks (IARC, 1986).

4.3 Reproductive and developmental effects

No data were available to the Working Group.

4.4 Genetic and related effects

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems*

Vinylidene fluoride (50% v/v in air for 24 h) gave equivocal results for mutagenicity to *Salmonella typhimurium* when tested in the presence of an exogenous metabolic system (IARC, 1986).

5. Evaluation

No epidemiological data relevant to the carcinogenicity of vinylidene fluoride were available.

There is *inadequate evidence* for the carcinogenicity of vinylidene fluoride in experimental animals.

Overall evaluation

Vinylidene fluoride is *not classifiable as to its carcinogenicity to humans (Group 3).*

6. References

Filser, J.G. & Bolt, H.M. (1979) Pharmacokinetics of halogenated ethylenes in rats. *Arch. Toxicol.*, **42**, 123–136

IARC (1986) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*, Vol. 39, *Some Chemicals Used in Plastics and Elastomers*, Lyon, pp. 227–235

IARC (1987) *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*, Supplement 7, *Overall Evaluations of Carcinogenicity: An Updating of* IARC Monographs *Volumes 1 to 42*, Lyon, p. 73

Medinsky, M.A., Bechtold, W.E., Birnbaum, L.S., Chico, D.M., Gerlach, R.F. & Henderson, R.F. (1988) Uptake of vinylidene fluoride in rats simulated by a physiological model. *Fundam. appl. Toxicol.*, **11,** 250–260

Medinsky, M.A., Bechtold, W.E., Birnbaum, L.S. & Henderson, R.F. (1990) Measurement of steady-state blood concentrations in B6C3F_1 mice exposed by inhalation to vinylidene fluoride. *Toxicology*, **64,** 255–263