

2.3 Analysis

No information was available to the Working Group on methods for determining PVC residues in foods or other parts of the environment.

A rapid and simple way of identifying fifteen packaging films, including PVC, has been described in which the films were treated with ten different solvents and the solubility and physical appearance of the film at room temperature and at the boiling-points of the solvents were noted (Van Gieson, 1969).

Plastics, including PVC, have been identified by measurement of the pH of an aqueous solution of the pyrolysis products, followed by thin-layer chromatography, and by reaction of PVC with pyridine (Braun & Nixdorf, 1972).

PVC has been separated from plasticizers, stabilizers, modifiers, fillers, pigments and other inorganic additives by gel permeation chromatography or sequential solvent extraction. The resulting additive-free fraction has been analysed by chlorine analysis, infra-red spectroscopy, molecular-weight determination by viscosity measurements and thermal gravimetry and differential thermal analysis (Brookman, 1974).

Pyrolysis-gas chromatography has been proposed to identify PVC in polymers used in medical applications (Nematollahi *et al.*, 1970), in three commercial polymers (in this case, pyrolysis-gas chromatography was used in combination with thermogravimetric analysis and differential thermal analysis) (Boettner *et al.*, 1969), and among some chlorine-containing polymers (Tauge *et al.*, 1969). Pyrolysis-gas chromatography has also been used to identify polymers, including PVC, among 37 commercial polymers (Okumoto & Takeuchi, 1972), in plastics and rubbers (Fischer, 1967) and in adhesives used in building (in this case, pyrolysis-gas chromatography was used in combination with thermogravimetry, differential thermogravimetry and differential thermal analysis) (Rona, 1971).

Thin-layer chromatography of pyrolysis products has been used to identify high polymers, including PVC (Pastuska, 1969).

Thermogravimetry and infra-red spectral analysis have been used to determine PVC in floor tiles (Powell, 1974).

3. Biological Data Relevant to the Evaluation of Carcinogenic Risk to Humans

3.1 Carcinogenicity studies in animals¹

Subcutaneous or intraperitoneal administration

Rat: A group of 45 adult Wistar rats were given s.c. implants in the abdominal wall of squares or discs of a commercial PVC known to contain some additives; the implants were 0.04 mm thick and 15 mm wide. At the appearance of the first tumour, 44 animals were still alive. Seventeen (38.6%) malignant tumours (fibrosarcomas and 1 liposarcoma) developed at the site of film implantation, with a latent period of 189-727 days; a similar but perforated film did not produce local tumours in 27 rats at risk. No local tumours were found in a group of 50 rats given a s.c. implant of cotton (Oppenheimer *et al.*, 1952, 1955). With a pure PVC film of 0.03 mm thickness, 4 malignant tumours were obtained after 533 days in a similar group (Oppenheimer *et al.*, 1955) [The Working Group noted that the reporting of this experiment was preliminary and that final results were never forthcoming].

Groups of 35 (male and female) Wistar rats were given a s.c. implant into the abdomen of PVC film 4 x 5 x 0.16 mm. A group of 25 control rats received an implant of glass of similar size. After 300 days, 30 and 20 animals were still alive in the two groups, respectively; all surviving rats were killed 800 days after implantation. One sarcoma and one fibroma were found after 580 days in the PVC-treated rats, whereas no local tumours developed in the control group (Russell *et al.*, 1959).

A group of 80 outbred albino rats (sex unspecified) received implants (of unstated size) of PVC film by laparotomy to surround the kidney. The animals were sacrificed at 3, 10, 15, 30, 90, 195, 285, 300 and 380 days after the implantation. Of rats that survived 285-375 days, 6/16 developed fibrosarcomas at the site of implantation (Raikhlin & Kogan, 1961).

In rats implanted in the kidney with either PVC capsules, whole PVC films or perforated PVC films, 5/16, 2/5 and 1/5 sarcomas were observed (Kogan & Tugarinova, 1959).

¹The Working Group was aware of a study in progress to assess the carcinogenicity of PVC powder by inhalation exposure and intrapleural administration to rats (IARC, 1978a).

3.2 Other relevant biological data(a) Experimental systems

Rats and guinea-pigs exposed continuously to PVC dust for 24 hours/day for periods varying from 2-7 months were found to have extensive lung damage (Frongia *et al.*, 1974).

The growth of granulation tissue around PVC particles implanted into the muscles of rabbits has been reported (Guess & Stetson, 1968). Severe fibroblastic reactions were found in rats (Calnan, 1963) and dogs (Harrison *et al.*, 1957) which received PVC sponge implants into the s.c. tissue of the anterior abdominal wall.

Ingested and rectally absorbed PVC particles (5-110 μ m) were found to be transported by both the lymphatic and the portal system from the intestinal wall of rats, guinea-pigs, rabbits, chickens, dogs and pigs (Volkheimer, 1975).

In rats, inhalation of fumes from heated PVC produced interstitial oedema, as well as focal bronchial and intra-alveolar haemorrhage in the lungs of some animals (Cornish & Abar, 1969).

No data on the embryotoxicity, teratogenicity, metabolism or mutagenicity of this compound were available to the Working Group.

(b) Humans

Workers exposed to PVC dust during the manufacture of articles made from PVC showed alterations in the respiratory organs (e.g., changed bronchovascular pattern, increased pulmonary ventilation at rest) (Vertkin & Mamontov, 1970).

Pneumoconiosis due to inhalation of PVC dust was suggested following pulmonary biopsies in a male patient who had inhaled PVC dust for 1 year and exhibited granulomatous lesions due to foreign bodies. The severity of the disease was shown by the observed dyspnoea, secondary polyglobulia and reduced respiratory function (Szende *et al.*, 1970).

Fibrotic lung changes and altered pulmonary function tests have been reported in 96 workers exposed to PVC dust; the changes were more pronounced in those with long exposure (Lilis *et al.*, 1976; Waxweiler *et al.*, 1976).

Reduced pulmonary function and an enhancement of pulmonary function defects associated with an increased risk of respiratory impairment were noted in a number of nonsmoking workers exposed to an occupational environment contaminated with vinyl chloride fumes and PVC dust (Miller, 1975; Miller *et al.*, 1975).

In 15 polyvinyl production workers employed in 'PVC-processing industries', where stabilizers, colours and bulk materials were added to and mixed with the basic PVC powder, the following pathological findings were reported: in 7, slight to moderate thrombocytopenia; in 7, increased bromosulphalein retention; in 6, reticulocytosis; in 1, leucopenia; and in 1, slight splenomegaly. Neither scleroderma-like skin changes nor Raynaud's syndrome were observed (Lange *et al.*, 1975). A large proportion of abnormal liver function tests and platelet counts were found in a group of 37 PVC process workers: 20% had abnormal alkaline phosphatase, 60% abnormal lactic dehydrogenase, 30% abnormal serum glutamic-oxaloacetic transaminase, 10% abnormal serum glutamic-pyruvic transaminase, and 35% abnormal platelets (Wegman, 1975).

Cases of 'meat-wrappers' asthma have been reported, in which meat wrappers developed respiratory symptoms when exposed to fumes of PVC film sealed and cut with a hot wire. The identity of the causative agent(s) has not been established (Brooks & Vandervort, 1977; Falk & Portnoy, 1976; Polakoff *et al.*, 1975; Sokol *et al.*, 1973).

During the period 1970-1975, 175 fire-fighters experienced respiratory distress due to the toxicity of hydrogen chloride gas released from the combustion of PVC plastics (Dyer & Esch, 1976). Carbon monoxide, hydrochloric acid and phosgene (Cornish & Abar, 1969; Dyer & Esch, 1976) have been reported as the major PVC pyrolysis products of toxicological importance, although more than 75 components have been identified following the thermal degradation of PVC (Dyer & Esch, 1976).

The few cases of dermatitis that have been reported are believed to be caused by sensitivity to plasticizers in polyvinyl plastics (Morris, 1953).

3.3 Case reports and epidemiological studies¹

A proportional mortality study was carried out using death certificates from 1970-1972 of 707 male plastic workers (extruding, moulding, cutting, turning or otherwise machining plastics, and including PVC fabricating). A statistically significant excess of stomach cancer mortality was found (24 observed versus 16.4 expected, $P < 0.05$) (Baxter & Fox, 1976) [The study is limited by the use of proportionate mortality methodology and by the fact that not all deaths studied were among workers engaged in activities directly involving PVC].

¹The Working Group was aware of a study in progress on workers exposed to PVC (IARC, 1978c).

In a cross-sectional mortality study of 4341 deaths during 1964-1973 among current and former employees of 17 PVC fabricators, an excess in total cancer mortality, particularly that of the digestive system, was reported among both white males and white females. The risk of cancer of the breast and urinary organs was also reported to be in excess among white females (Chiazze *et al.*, 1977) [The study is limited by the use of proportionate mortality methodology and by the fact that not all deaths were among workers engaged in activities directly involving PVC].

Casterline *et al.* (1977) reported a case of a 22-year-old male who developed a squamous-cell carcinoma of the buccal mucosa as a result of a habit, acquired at the age of 8 years, of chewing plastic materials containing PVC. No prior history of mouth or lip lesions, of smoking tobacco or drinking alcohol, or of occupational exposure to vinyl chloride was noted.

Vinyl chloride-vinyl acetate copolymers

1. Chemical and Physical Data

1.1 Synonyms and trade names

Chem. Abstr. Services Reg. No.: 9003-22-9

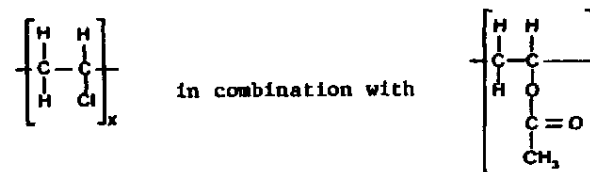
Chem. Abstr. Name: Acetic acid ethenyl ester polymer with chloroethene

Acetic acid vinyl ester polymer with chloroethylene; chloroethylene-vinyl acetate polymer; polyvinyl chloride-polyvinyl acetate; vinyl acetate-vinyl chloride copolymer; vinyl acetate-vinyl chloride polymer; vinyl chloride-vinyl acetate polymer

A 15; A 15 (polymer); A 15-0; A 15S; Bakelite LP 70; Bakelite VLPV; Bakelite VMCC; Bakelite VSJD 10; Bakelite VYHD; Bakelite VYHH; Bakelite VYNS; Bakelite VYNW; Breon 351; Breon 425; Breon AS 60/41; Corvic 51/83; Corvic 236581; Corvic R 46/88; Denkalac 41M; Denka Vinyl MM 90; Diamond Shamrock 744; Diamond Shamrock 7401; Exon 450; Exon 454; Exon 470; Exon 481; Exon 760; Flovic; Geon 100x150; Geon 130x10; Geon 135; Geon 351; Geon 400x47; Geon 421; Geon 427; Geon 434; Geon 103EP-J; Geon 440L2; Geon 450x150PN; Geon 150XML; Geon 103ZX; Hostalit PVP; Leucovyl PA 1302; Lucovyl GA 8502; Lucovyl MA 6028; Lucovyl PA 1208; Marvinol VP 56; 50ME;

Norvinyl P 6; Opalon 400; Pevikon C 870; Pliovac A0; Pliovic A0; PVC Cordo; Resin 4301; Rhodopas 6000; Rhodopas AX; Rhodopas AX 30/10; Rhodopas AX 85/15; Sarpifan HP 1; Solvic 523KC; Solvic PA 513; Solvic 513PB; Sumilit PCX; Tennus 0565; VA 3 (copolymer); VAGD; VH 10/60; Vilit 40; Vinnol H 10/60; Vinnol H 15/45; Vinnol H 40/60; Vinylite VGHH; Vinylite VYDR; Vinylite VYDR 21; Vinylite VYFS; Vinylite VYHD; Vinylite VYHH; Vinylite VYNS; Vinylite VYNW; Vinyon; VLVF; VMCC; VYHH; VYNS; VYNW

1.2 Structural and molecular formulae and molecular weight



1.3 Chemical and physical properties of the copolymers

(a) Description: White powder

(b) Stability: Sensitive to excessive exposure to heat and light in the absence of added stabilizers. Hydrogen chloride gas is a decomposition product of degradation.

1.4 Technical products and impurities

Low levels of vinyl acetate are copolymerized with vinyl chloride to obtain resins with specific properties. Depending upon the use, the vinyl acetate level may vary from 2-20%, with an average of 11-12%. As described in the monograph on polyvinyl chloride, p. 405, various additives are used to aid in processing the resins.

No detailed information on the possible presence of unreacted monomers in the copolymers was available to the Working Group.

3.2 Other relevant biological data

(a) Experimental systems

An aqueous dispersion of a vinyl chloride-vinyl acetate copolymer administered orally at a dose of 10 ml/day to rats or rabbits decreased the reticulocyte count and caused changes in the blood serum protein fractions and histological changes in the stomach and liver. Inhalation of the dry residue at concentrations of 4.2 mg/m³ in air decreased body-weight gain and caused pneumonia and peribronchitis. Application of this preparation to the skin decreased reticulocyte and leucocyte counts and haemoglobin levels (Ivanova & Shamina, 1973).

In rats, inhalation of fumes from heated vinyl chloride-vinyl acetate copolymer produced focal oedema and intra-alveolar haemorrhages of the lung (Cornish & Abar, 1969).

No toxic effects were reported in Wistar albino rats of both sexes following daily intakes of 0.61 or 5.75 g/kg bw vinyl resin (copolymer of 95% vinyl chloride and 5% vinyl acetate) for 2 years (Smyth & Well, 1966).

No data on the embryotoxicity, teratogenicity, metabolism or mutagenicity of this compound were available to the Working Group.

(b) Humans

Two cases of dermatitis have been reported in people wearing Elastiglass garters (vinyl chloride-vinyl acetate copolymer) (Zelsler, 1940).

3.3 Case reports and epidemiological studies

No data were available to the Working Group.

4. Summary of Data Reported and Evaluation

4.1 Experimental data

Vinyl chloride was tested in rats by oral, subcutaneous and intraperitoneal administration and in mice, rats and hamsters by inhalation exposure. Following oral and inhalation exposure, vinyl chloride was carcinogenic in all three species, producing tumours at different sites, including angiosarcomas of the liver. Vinyl chloride was carcinogenic in rats following prenatal exposure. A dose-response effect has been demonstrated.

The results of subcutaneous and intraperitoneal injection studies in rats are incomplete and cannot be evaluated.

Vinyl chloride is mutagenic.

Polyvinyl chloride was tested in rats by subcutaneous and intraperitoneal implantation; local sarcomas were induced, the incidence of which varied with the size and form of the implant.

Vinyl chloride-vinyl acetate copolymers were tested in rats by subcutaneous implantation as films or powder; local sarcomas were induced following implantation of films.

4.2 Human data

Vinyl chloride is manufactured on a vast scale, and exposure involves workers in the production, polymerization and processing industries. Also, large sections of the general population may have some exposure to vinyl chloride, particularly through direct or indirect contact with polymer products.

Several independent but mutually confirmatory studies have shown that exposure to vinyl chloride results in an increased carcinogenic risk in humans, involving the liver, brain, lung and haemo-lymphopoietic system.

In one epidemiological study, an excess of foetal mortality was reported among wives of workers who had been exposed to vinyl chloride, indicating a possible mutagenic effect in human germ cells. Several investigations have detected an increase in chromosomal aberrations in the lymphocytes of workers exposed to vinyl chloride. Increased rates of birth defects among children of parents residing in communities where vinyl chloride-polyvinyl chloride or other chemical processing plants are located have been reported in several other studies. These suggest teratogenic and/or mutagenic effects of vinyl chloride in humans.

In two proportionate mortality studies, in which death certificates of workers who had been involved in the fabrication of plastics, including polyvinyl chloride, were analysed, there appeared to be an increased proportion of cancer of the digestive system in both sexes and possibly of the urinary system and of the breast in women.

4.3 Evaluation

Vinyl chloride is a human carcinogen. Its target organs are the liver, brain, lung and haemo-lymphopoietic system. Similar carcinogenic effects were first demonstrated in rats and were later confirmed in mice and hamsters. Although evidence of a carcinogenic effect of vinyl chloride in humans has come from groups occupationally exposed to high doses of vinyl chloride, there is no evidence that there is an exposure level below which no increased risk of cancer would occur in humans.

Epidemiological reports regarding clastogenic effects among vinyl chloride-exposed workers and a single study of increased foetal mortality among the wives of workers who had been exposed to vinyl chloride suggest that vinyl chloride could be mutagenic to humans. Additional support for this suggestion derives from experimental evidence of its mutagenicity.

Studies which indicate increased rates of birth defects among the children of parents residing in communities where vinyl chloride production and polymerization plants are located indicate the necessity for further investigation of the teratogenicity of vinyl chloride and its polymers in both animals and humans.

The available studies on polyvinyl chloride, which indicate an elevated proportion of digestive system cancer in male and female workers and possibly of cancers of the breast and urinary organs in female workers involved in the fabrication of plastics, including polyvinyl chloride, are insufficient to evaluate the carcinogenicity of this compound.

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VINYLLIDENE CHLORIDE and
VINYLLIDENE CHLORIDE-VINYL CHLORIDE COPOLYMERS

Vinylidene chloride

1. Chemical and Physical Data

1.1 Synonyms and trade names

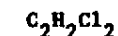
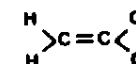
Chem. Abstr. Services Reg. No.: 75-35-4

Chem. Abstr. Name: 1,1-Dichloroethene

1,1-Dichloroethylene; *asym*-dichloroethylene

Sconatex

1.2 Structural and molecular formulae and molecular weight



Mol. wt: 97.0

1.3 Chemical and physical properties of the pure substance

From Weast (1976), unless otherwise specified

- (a) Description: Clear liquid with a sweet odour (Hardie, 1964; Windholz, 1976)
- (b) Boiling-point: 32°C (Windholz, 1976)
- (c) Melting-point: -122.1°C
- (d) Density: d^{20}_{20} 1.218; vapour density, 3.4 (air = 1) (Anon., 1972)
- (e) Refractive index: n^{20}_D 1.4249
- (f) Spectroscopy data: λ vapour <200 nm; infra-red, nuclear magnetic resonance and mass spectral data have been tabulated (Grasselli & Ritchey, 1975).