DICHLORVOS

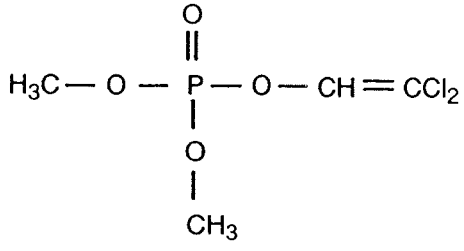
This substance was considered by a previous Working Group in 1978 (IARC, 1979a). Since that time, new data have become available, and these have been incorporated into the monograph and taken into consideration in the present evaluation.

1. Exposure Data

1.1 Chemical and physical data

1.1.1 *Synonyms, structural and molecular data*

Chem. Abstr. Serv. Reg. No.: 62-73-7
Replaced CAS Reg. Nos.: 8023-22-1; 8072-21-7; 8072-39-7; 8076-16-2; 11095-17-3; 11096-21-2; 11111-31-2; 11126-72-0; 12772-40-6; 55819-32-4; 62139-95-1; 62655-59-8; 95828-55-0; 116788-91-1
Chem. Abstr. Name: Phosphoric acid, 2,2-dichloroethenyl dimethyl ester
IUPAC Systematic Name: 2,2-Dichlorovinyl dimethyl phosphate
Synonyms: 2,2-Dichloroethenol, dimethyl phosphate; dimethyl dichlorovinyl phosphate; dimethyl 2,2-dichloroethenyl phosphate; dimethyl 2,2-dichlorovinyl phosphate; *O,O*-dimethyl 2,2-dichlorovinyl phosphate; 2,2-dichloroethenyl dimethyl phosphate; phosphoric acid, 2,2-dichlorovinyl dimethyl ester



$C_4H_7Cl_2O_4P$ Mol. wt: 221.0

1.1.2 *Chemical and physical properties*

From AMVAC Chemical Corp. (1986), otherwise specified

(*a*) *Description*: Clear, colourless to pale yellow, almost odourless liquid
(*b*) *Boiling-point*: 117°C at 10 mm Hg [1.33 kPa]
(*c*) *Melting-point*: < -60°C (AMVAC Chemical Corp., 1990)
(*d*) *Density*: 1.422 at 25°C/4°C
(*e*) *Spectroscopy data*: Infrared (prism [7721]; grating [44551P]) spectroscopy data have been reported (Sadtler Research Laboratories, 1980).

(*f*) *Solubility*: Completely miscible with aromatic hydrocarbons, chlorinated hydrocarbons, alcohols, ketones and esters; slightly soluble in water (approx. 1%) and glycerine (approx. 0.5%); insoluble in kerosene and aliphatic hydrocarbons
(*g*) *Volatility*: Vapour pressure, 0.012 mm Hg [1.6×10^{-3} kPa] at 20°C
(*h*) *Stability*: Hydrolysed by water and readily decomposed by strong acids and bases; breaks down on standing in the presence of traces of moisture, with the formation of acidic products that catalyse further decomposition; corrosive to black iron and mild steel (WHO, 1989)
(*i*) *Octanol/water partition coefficient (P)*: log P, 1.47 (WHO, 1989)
(*j*) *Half-time in water*: 301 min at pH 8; 462 min at pH 7; 2100 min at pH 6; 4620 min at pH 5.4 (Latif *et al.*, 1984)
(*k*) *Conversion factor for airborne concentrations*[1]: $mg/m^3 = 9.04 \times ppm$

1.1.3 *Trade names, technical products and impurities*

Some examples of trade names are: Atgard; Bibesol; Brevinyl; Canogard; Chlorvinphos; DDVP; Dedevap; Des; Dichlofos; Dichlorman; Dichlorovos; Divipan; ENT 20738; Equigard; Equigel; Estrosel; Estrosol; Fecama; Fekama; Insectigas D; Mopari; Nefrafos; Nerkol; Nogos; Novotox; Nuan; Nuvan; OKO; OMS 14; Panaplate; Phosvit; Prima U; SD 1750; Szklarniak; TAP 9VP; Task; Unifos; Unitox; Vapona; Vapona Insecticide; Vaponite; Vinylofos; Vinylophos; Winylophos

WHO (1985, 1989) specifications for technical-grade dichlorvos for public health use require a minimum purity of 97%; the value was previously 93% (WHO, 1967).

Dichlorvos is available in the USA as a technical-grade product with a minimal purity of 93 or 96% (AMVAC Chemical Corp., 1986, 1990). In the past, 2-4% epichlorohydrin (see IARC, 1987a) was added to stabilize the technical-grade product; other stabilizers may now be used in some products, but improved technology and purity has largely eliminated the need for them (WHO, 1989). Analysis of a sample of commercial-grade dichlorvos (produced in about 1970) showed the following constituents (%): dichlorvos, 95-97; dipterex (trichlorfon; *0,0*-dimethyl 2,2,2-trichloro-1-hydroxyethylphosphonate) (see IARC, 1983a, 1987b), 1.5-3; *O,O*-dimethyl 2-chlorovinyl phosphate, 0.4-0.7; *O,O*-dimethyl methylphosphate, trace-0.1; *O,O,O*-trimethyl phosphate, 0.3-0.8; and chloral (trichloroacetaldehyde), 0.1-0.5 (Santodonato *et al.*, 1985).

In the USA and Europe, registered formulations include dusts, granules, pellets/tablets, impregnated resin strips, emulsifiable concentrates, soluble concentrates, wettable powders and pressurized formulations (Royal Society of Chemistry, 1986; US Environmental Protection Agency, 1987). In the USSR, dichlorvos is formulated as emulsion concentrates, pellets and aerosols (Izmerov, 1984). Dichlorvos is also formulated in combination with dimethoate, dinocap, fenchlorphos, fenitrothion, iodofenphos, lindane (see IARC, 1987c), malathion (see IARC, 1983b, 1987d), methoxychlor (see IARC, 1979b, 1987e), phosalone,

[1]Calculated from: mg/m^3 = (molecular weight/24.45) × ppm, assuming standard temperature (25°C) and pressure (760 mm Hg [101.3 kPa])

piperonyl butoxide (see IARC, 1983c, 1987f), pirimiphos-methyl, propoxur, tetrasul, pyrethrins and trichlorfon (Royal Society of Chemistry, 1986).

1.1.4 *Analysis*

Selected methods for the analysis of dichlorvos in various matrices are given in Table 1. Dichlorvos residues can be determined by gas chromatography; the same method can be used for product analysis. Alternative methods include infrared spectrometry and reaction with excess iodine, with estimation by titration (WHO, 1989). Several other methods in various media have been reviewed (Porter, 1964; Anon., 1972; Vevai, 1974; Worthing & Walker, 1987; WHO, 1989).

Table 1. Methods for the analysis of dichlorvos

Sample matrix	Sample preparation	Assay procedure[a]	Limit of detection	Reference
Air	Collect vapours on polyurethane foam; extract with 5% diethyl ether in hexane	GC/ECD	Not reported	US Environmental Protection Agency (1988a)
	Adsorb on XAD-2; desorb with toluene	GC/FPD	0.2 µg/sample	US National Institute for Occupational Safety and Health (1979)
Water	Extract with dichloromethane; isolate extract; dry; concentrate with methyl *tert*-butyl ether	GC/NPD	2.5 µg/l	US Environmental Protection Agency (1988b)
Groundwater, soil, wastes	Extract with dichloromethane; dry; concentrate; clean-up using Florisil column or gel permeation; exchange into hexane	GC/MS	0.1 µg/l	US Environmental Protection Agency (1986)
Formulations	Dissolve in chloroform; concentrate using evaporation (baits & emulsifiable concentrate forms)	IR	Not reported	Williams (1984)
	Extract with sodium hydroxide; dry using anhydrous sodium sulfate (spray solutions & sprays in hydrocarbon solvents)	IR	Not reported	Williams (1984)
Fruits and vegetables	Acidify with hydrochloric acid; extract with hexane; clean-up on silicic acid column	GC/MCD	0.05 ppm (mg/kg)	US Food and Drug Administration (1989a)
Animal tissues, crops, milk	Acidify with hydrochloric acid; extract with hexane; clean-up with anhydrous sodium sulfate	GC/TD or GC/ECD[b]	0.01-0.02 ppm (mg/l or mg/kg) (milk & tissues)	US Food and Drug Administration (1989a)

Table 1 (contd)

Sample matrix	Sample preparation	Assay procedure[a]	Limit of detection	Reference
Animal tissues, crops, eggs, milk	Extract into hexane; clean-up on silicic acid column with dichloromethane:hexane (3:2) eluant	GC/FPD	0.002 ppm (mg/l milk)	US Food and Drug Administration (1989b)

[a]Abbreviations: GC/ECD, gas chromatography/electron capture detection; GC/FPD, gas chromatography/flame photometric detection; GC/MS, gas chromatography/mass spectrometry; GC/NPD, gas chromatography/nitrogen-phosphorus detection; GC/MCD, gas chromatography/microcoulometric detection; GC/TD, gas chromatography/thermionic detection; IR, infrared spectrophotometry

[b]Used if interfering organophosphorus or organochlorine pesticides are present

1.2 Production and use

1.2.1 *Production*

Dichlorvos was first synthesized in the late 1940s (Tinker, 1972). It has been commercially manufactured and used throughout the world since 1961 (WHO, 1989). It was first found as a highly insecticidal impurity of trichlorfon (chlorophos) in 1955; trichlorfon is rapidly converted to dichlorvos at above pH 6 (Eto, 1974). Dichlorvos is manufactured by the dehydrochlorination of trichlorfon in aqueous alkali at 40-50 °C or by the reaction between chloral and trimethyl phosphite (WHO, 1989).

Dichlorvos is produced currently in Argentina, Brazil, Germany, India, Israel, Japan, the Republic of Korea, Mexico, the Netherlands, Spain, Sweden, Switzerland and the USA (Meister, 1990). The present worldwide production of dichlorvos is about 4000 tonnes per year (WHO, 1989). Worldwide production figures for 1984 were as follows (tonnes): eastern Europe, 220; western Europe, 300; Latin America, 400; south-east Asia, 500; USA, 500; Japan, 1100; Middle East, India and Pakistan, 1200 (WHO, 1989).

1.2.2 *Use*

Dichlorvos is a contact and stomach insecticide with fumigant and penetrant action. It is used as granules or impregnated resin to control internal and external parasites (especially fleas and ticks) in livestock and as aerosols or liquid sprays or as impregnated cellulose, ceramic or resin strips to control insects in houses, buildings and outdoor areas (especially flies and mosquitos). It is also used to protect certain crops (and other plants) from insects in the field and in storage. Dichlorvos is not generally applied directly to soil, but it is added to water to control parasites in the case of intensive fish farming (WHO, 1989). It is used as an antihelminthic by incorporation in animal feeds (Worthing & Walker, 1987).

Worldwide, it is estimated that 60% is used in plant protection, 30% for public health and vector control and 10% to protect stored products (WHO, 1989).

In the USA, in 1971, 16 tonnes of dichlorvos were used on crops (mainly tobacco) and 1100 tonnes were used on livestock and livestock buildings; in 1976, 50 tonnes were used on crops and 390 on livestock. In 1975, 80% of the dichlorvos produced in the USA was formulated into polyvinyl chloride resin strips containing 20% by weight of dichlorvos, which were used primarily in households. These strips were first marketed in 1967 to control flies

and mosquitoes in the home; they were introduced earlier in dairy and poultry operations. Flea collars containing dichlorvos, for dogs and cats, have also been commercially marketed (Santodonato *et al.*, 1985).

In the USA in 1980, the yearly agricultural usage of dichlorvos (active ingredient) was estimated as follows (tonnes): dairy cattle, 340; beef cattle, 30; hogs, 6; poultry, 2; and other livestock, 14; about 50 tonnes were used for treatment of tobacco. Overall, 680-1200 tonnes of dichlorvos were used for agricultural uses, 450 tonnes for public health and about 450 tonnes for household use (US Environmental Protection Agency, 1980). Less than 450 tonnes of dichlorvos (active ingredient) are believed to have been used in the USA in 1989.

In Finland, about 1500 kg (active ingredient) of dichlorvos were sold in 1988 (Agrochemical Producers' Association of Finland, 1989).

1.3 Occurrence

1.3.1 *Air*

Dichlorvos is degraded rapidly in air, the rate depending on humidity. The method of application is an important factor in determining its concentration in air (Gillett *et al.*, 1972a).

Examples of indoor air concentrations resulting from household and public health use are shown in Table 2 (WHO, 1989).

The highest exposure recorded in a vaporizer production plant and its packaging rooms was 3 mg/m^3, with an average value of 0.7 mg/m^3 (Menz *et al.*, 1974). The mean concentration of dichlorvos in air did not exceed 0.5 ppb (0.005 mg/m^3) in the office and insecticide storage rooms of commercial pest control buildings and 0.1 ppb (0.001 mg/m^3) in vehicles (Wright & Leidy, 1980).

Dichlorvos was sprayed at 8 ml active ingredient/100 m^3 in a unit used for mushroom cultures, and kept closed for 24 h. The air concentration decreased from 3.3 to 0.006 mg/m^3 in 24 h. The unit was also treated with paper strips drenched in 50% dichlorvos formulations (40 ml/100 m^3), which gave air concentrations of 0.38 and 0.024 mg/m^3 at 3 and 24 h, respectively (Grübner, 1972).

Following weekly 6-h applications, the maximum concentrations of dichlorvos observed in a large warehouse ranged from 2.4 to 7 mg/m^3. The amount of dichlorvos dispensed per application was 25-59 mg/m^3, which resulted in average air concentrations after eight applications of 4 mg/m^3 (Gillenwater *et al.*, 1971).

The work place concentration resulting from hot spraying of dichlorvos in six greenhouses at 0.4 ml/m^3 was 7-24 mg/m^3 (average, 16 mg/m^3) (Wagner & Hoyer, 1975). Spraying of 12 glass and plastic greenhouses gave concentrations between 0.7 and 2.7 mg/m^3 (average, 1.3 mg/m^3). Field application by spraying resulted in air concentrations of 0.01-0.26 mg/m^3 (average, 0.08 mg/m^3) (as reported by WHO, 1989). The air concentration of dichlorvos in greenhouses immediately after spraying with 0.2-0.3% dichlorvos solutions was 1.2 mg/m^3, which decreased to 0.01 mg/m^3 within 24 h. Disturbing the plants resulted in an increase of 10-26% in the dichlorvos concentration in air (Zotov *et al.*, 1977).

In a study designed to test the aeration period needed for safe reentry into a room following dichlorvos treatment with a pressurized home-fogger, the air levels after 30 min

Table 2. Indoor air concentrations of dichlorvos following various applications[a]

Location	Application	Dose[b]	Temperature (°)	RH[c] (%)	Ventilation	Time after application	Concentration (mg/m^3)
Food shops	Resin strips	1 strip/30 m^3			Normal	First week	0.03
						4 weeks	0.02
						10 weeks	0.01
Houses	Resin strips	1 strip/30 m^3	18–35	20–60	Normal	First week	0.06–0.17
						2–3 weeks	0.01
Hospital wards	Resin strips	1 strip/30 m^3	20–27	35–70	Varied	Several days	0.10–0.28
						20–30 days	0.02
Hospital wards	Strips of paper	0.2 ml ai/m^3	–	–	2 h	3 days	0.06
	drenched in 50%	0.2 ml ai/m^3	17	–	2 h	66 h	0.1–0.3
	dichlorvos solution	0.2 ml ai/m^3	17	–	2 h	90 h	0.3
	hanging in rooms for	0.8 ml ai/m^3	30	High	2 h	3 h	3.7
	24–36 h					46 h	0.6
Houses	0.5% solution according to typical pest control practice	225 or 1200 ml	26	47–60	None	0	0.4
						8 h	0.2
						24 h	< 0.1
Bathroom (sealed)	0.5% solution wall spray	25 ml	26	60	None	0	1.1
						4 h	0.3
						24 h	< 0.1
Living room (experimental)	Spray cans	2.3 mg ai/m^3	20–22		30 min	0	0.24
					1 h	0	0.13
	Fogging	240 mg ai/m^3	20–22		None	1 h	37
					None	24 h	5.5
					1 h	1 h	2.5
					120 h	1 h	< 0.2
Apartments[d]	0.5% solution	190 mg ai/m^3	26	82	–	0–2 h	0.5
						2–24 h	0.2

[a]Reviewed by WHO (1989)
[b]ai, active ingredient
[c]RH, relative humidity
[d]From Gold *et al.* (1984)
–, not stated

were below the industrial workplace permissible exposure level of 1 mg/m^3. Without ventilation, 18 h were required to reach an acceptable level. Because of concern for the health of infants and elderly persons, the acceptable level for homes was established at 1/40 of the permissible exposure level. Rooms treated with this type of applicator and ventilated after treatment were considered safe for reentry after 10 h (as reported by WHO, 1989).

Monitoring of mushroom-growing houses in the USA gave air concentrations of 0.1 mg/m^3; swabs of exposed surfaces revealed maximal residues of 0.026 μg/cm^2 (as reported by WHO, 1989).

In houses treated for pest control with 230-330 g dichlorvos as an aerosol and 40-50 g as emulsion spray, the mean dichlorvos residue on surfaces was 0.24 μg/cm^2 at the end of day 1 and decreased to 0.06 μg/cm^2 by day 5 (Das *et al.*, (1983).

1.3.2 *Water*

In water, dichlorvos is hydrolysed into dimethyl phosphoric acid and dichloroacetic acid (WHO, 1989).

1.3.3 *Soil*

Dichlorvos vaporized in a mushroom house to give 0.2-0.4 mg/m^3 degraded rapidly in the moist loam soil, with only 37% remaining after 3 days. The amount of free dichloroacetaldehyde at that time was 4% (Hussey & Hughes, 1964).

Dichlorvos is degraded by microorganisms. *Bacillus cereus* utilizes it as a single carbon source. In soil columns perfused with an aqueous solution containing dichlorvos at 1 kg/litre, 30% of the loss of the compound was attributed to microbial action (Lamoreaux & Newland, 1978). Species of *Pseudomonas* derived from sewage converted dichlorvos to dichloroethanol, dichloroacetic acid and ethyl dichloroacetate (Lieberman & Alexander, 1983). Fungi, such as *Trichoderma viride*, also degrade dichlorvos into water-soluble metabolites (Matsumura & Boush, *1968).*

1.3.4 *Plants*

Dichlorvos is rapidly lost from leaf surfaces by volatilization and hydrolysis, with a half-time of only a few hours. A small amount penetrates the waxy layers of plant tissues, where it may persist for longer (FAO/WHO, 1971).

In California, the estimated safe level of dislodgeable foliar dichlorvos from turf is 0.06 μg/cm^2 (WHO, 1989). Studies by Goh *et al.* (1986a,b) found that dislodgeable foliar dichlorvos residues decreased rapidly after 2-6 h and were not detectable after 24-48 h.

1.3.5 *Food*

Data on residues in food commodities resulting from pre- and post-harvest treatment and from use on animals were summarized by FAO/WHO (1967, 1968, 1971, 1975).

In Canada, of 262 bovine and porcine fat samples analysed between 1973 and 1981, only one was contaminated with dichlorvos (Frank *et al.*, 1983). In a national surveillence programme in Canada, 1984-85 to 1988-89, no residue was found in 898 samples of fruit, vegetables, meat or wine (Government of Canada, 1990).

Normally, dichlorvos residues present in food are destroyed by washing and cooking. Abbott *et al.* (1970) confirmed the absence of residues in a total-diet study in the United

Kingdom, 1966-67, finding no dichlorvos in 462 samples. A total-diet study carried out in the USA from 1975 to 1976 gave similar results (Johnson *et al.*, 1981).

Food, meals and unwrapped ready-to-eat foodstuffs exposed to dichlorvos from resin strips had mean residue levels of < 0.05 mg/kg (range, < 0.01-0.1 mg/kg) (Elgar *et al.*, 1972a,b) and < 0.02 mg/kg (Collins & deVries, 1973). No residue of dichloroacetaldehyde (< 0.03 mg/kg) was detected in the ready-to-eat foodstuffs (Elgar *et al.*, 1972b). Food and beverages exposed to air concentrations of 0.04-0.58 mg/m^3 for 30 min contained dichlorvos residues of 0.005-0.5 mg/kg, except for margarine which had up to 1.7 mg/kg (Dale *et al.*, 1973).

1.3.6 *Occupational exposure*

Mixed dermal and inhalation exposures were assessed for 13 professional pesticide applicators after a day's work spraying dichlorvos preparations. Absorbent pads recorded average exposures of 0.08 μg/cm^2 on the back and 0.04 μg/cm^2 on the chest. Levels found in respirator filters were 1.1 μg/cm^2, in contrast to surface residues of 0.04-0.5 μg/cm^2 measured at various sites around the treated houses. Although the men wore protective equipment, some absorption of dichlorvos occurred, as shown by the recovery of 0.32-1.4 μg dimethylphosphate from their urine (Das *et al.*, 1983).

1.4 Regulations and guidelines

The FAO/WHO Joint Meeting on Pesticide Residues evaluated dichlorvos at its meetings in 1965, 1966, 1967, 1969, 1970, 1974 and 1977 (FAO/WHO, 1965, 1967, 1968, 1970, 1971, 1975, 1978). In 1966, the Meeting established an acceptable daily intake for humans of 0.004 mg/kg bw (FAO/WHO, 1967).

Maximum residue levels have been established by the Codex Alimentarius Commission for dichlorvos in or on the following agricultural commodities (in mg/kg): fruit (e.g., apples, peaches, pears, strawberries), 0.1; mushrooms and vegetables (except lettuce), 0.5; head lettuce, 1; cereal grains, coffee beans, dried lentils, dried soya beans and peanuts, 2; and cacao beans, 5. As such residues decline rapidly during storage and shipment, these limits are based on residues likely to be found at harvest (Codex Committee on Pesticide Residues, 1990).

Maximum residue limits have also been established by the Codex Alimentarius Commission for dichlorvos in or on the following animal commodities (in mg/kg): milk, 0.02; eggs, goat meat, meat of cattle, pigs, sheep and poultry, 0.05, based on residues likely to be found at slaughter (Codex Committee on Pesticide Residues, 1990).

In the USSR, dichlorvos residues are not allowed in fishing areas; however, a level of 0.1 mg/l was established for other surface waters (Izmerov, 1984).

National and regional pesticide residue limits for dichlorvos in foods are presented in Table 3.

Table 3. National and regional pesticide residue limits for dichlorvos in foods[a]

Country or region	Residue limit (mg/kg)	Commodities
Argentina	2	Stored cereals in general
Australia	5	Cocoa beans
	2	Cereal grains, coffee beans (green), lentils, nuts, peanuts, soya beans
	1	Lettuce
	0.5	Mushrooms, tomatoes, vegetables (except lettuce)
	0.1	All foods for which no other maximum residue limit is specified (e.g., bread, cakes, cooked meats), fruit
	0.05	Eggs, meat, poultry
	0.02	Whole milk
Austria	2.0	Cereals
	0.1	Other foods of vegetable origin
	0.05	Eggs (without shell), meat, milk
Belgium	5	Cocoa beans
	2	Coffee beans, grains, leguminous vegetables (dried)
	0.5	Flour
	0.1	Fruit, vegetables
	0.05	Animal fats, fowl, game, hare, meat, meat products, poultry
	0.02	Milk and dairy products
	0 (0.02)[b]	Other foodstuffs of animal and vegetable origin
Brazil	5.0	Cocoa
	2.0	Barley, maize, coffee, cottonseed, peanuts, rice, rye, soya beans, wheat
	1.0	Lettuce, ornamental plants, tobacco
	0.5	Chick peas, eggs (without shell), field beans, onions, potatoes, vegetables (except lettuce)
	0.1	Apples, bran, Brazil nuts, cakes, citrus fruits, flour, mushrooms, piñon seed, strawberries, watermelon
	0.05	Meat and meat products, poultry
	0.02	Milk
Canada	2.0	Non-perishable packaged foods of high fat content (> 6%)
	0.5	Non-perishable packaged foods of low fat content (< 6%)
	0.25	Tomatoes
	Negligible	Beef and dairy cattle (meat and milk), foods exposed in food storage areas, homes and restaurants to dichlorvos generated from 20% resin strips
Chile	2.0	Lentils, raw cereals
	1.0	Lettuce
	0.5	Cereal products, garden vegetables (except lettuce)
	0.1	Fruits
	0.05	Eggs, carcasses, poultry
	0.02	Whole milk
China	0.2	Vegetables
	0.1	Grain
	None	Vegetable oils

Table 3 (contd)

Country or region	Residue limit (mg/kg)	Commodities
Czechoslovakia	2.0	Imported lentils, peanuts, raw cereals, soya beans, unroasted coffee
	1.0	Imported head lettuce
	0.5	Imported mill products, mushrooms, tomatoes
	0.2	Dried medicinal herbs (for preservation)
	0.1	Foodstuffs in general (for preservation), fruits, vegetables
	0.1	Imported fruits, various foodstuffs
	0.02	Imported eggs (without shell), milk
Denmark	2	Cereals
	1	Leafy vegetables
	0.5	Mushrooms
	0.1	Berries and small fruits, citrus fruits, other fruits, pome and stone fruits
European Community	2.0	Barley, buckwheat, grain sorghum, maize, millet, oats, other cereals, paddy rice, rye, triticale, wheat
	0.1	Other products
Finland	1.0	Cereal grains
	0.2	Flour
	0.1	Fruit, vegetables
France	2	Wheat
	0.1	Fruits, vegetables
Germany	2.0	Cereals
	0.5	Cereal products
	0.1	Other foods of plant origin
Hungary	2.0	Barley grain, maize, oat grain, rice (brown, polished), rye, sorghum, triticale, wheat grain
	1.0	Greenhouse lettuce, lettuce
	0.5	Beetroot, Brussels' sprouts, cabbage, carrots, cauliflower, celery, celery leaf, garlic, green beans, greenhouse cucumber, greenhouse green paprika, greenhouse tomatoes, horseradish, kohlrabi, mushrooms, paprika, peas, parsley, parsley root, radishes, red onion, savoy, sorrel, spinach
	0.2	Apples, apricots, cherries, grapes, greengages, peaches, pears, plums, quince, sour cherries, wine grapes
India	1.0	Food grains
	0.25	Milled food grains
	0.15	Vegetables
	0.1	Fruit
Ireland	1.0	Lettuce
	0.5	Mushrooms, other vegetables
	0.1	Other products

Table 3 (contd)

Country or region	Residue limit (mg/kg)	Commodities
Israel	5.0	Cocoa beans
	2.0	Coffee beans, raw cereals (e.g., barley, maize, oats, rice, sorghum, wheat), lentils, peanuts, soya beans
	1.0	Lettuce
	0.5	Milled products from raw grain, mushrooms, vegetables (except lettuce), tomatoes
	0.1	Fruit (e.g., apples, peaches, pears, strawberries), miscellaneous food items not otherwise specified that were treated with dichlorvos in warehouses, shops, etc. (e.g., bread, cakes, cheese, cooked meat)
	0.05	Eggs (without shell), meat of cattle, goats, sheep, pigs and poultry
	0.02	Milk
Italy	2.0	Cereals in bulk
	0.5	Milled products (from treated cereals)
	0.1	Fruits, garden vegetables, sugar beets
Japan	0.3[c]	Strawberries
	0.1	Asparagus, celery, eggplants, garden radishes, garden radish leaves, grapes, Japanese pears, Spanish paprika, spinach, stone leeks
	0.1[c]	Fruit (except strawberries); rice, oats and other minor cereals; potatoes, tea, vegetables
Kenya	5.0	Cocoa beans
	2.0	Coffee beans, lentils, peanuts, raw grain (e.g., barley, maize, oats, rice, rye, sorghum, wheat), soya beans
	1.0	Lettuce
	0.5	Fresh vegetables (except lettuce), milled products from raw grain, mushrooms, tomatoes
	0.1	Fresh fruit (e.g., apples, peaches, pears, strawberries), miscellaneous food items not otherwise specified
	0.05	Eggs (without shell), meat of cattle, goats, pigs, poultry and sheep
	0.02	Milk (whole)
Netherlands	5	Cocoa beans
	2	Buckwheat cereal, coffee beans, peanuts, pod vegetables, pulses
	0.5	Whole meal flour
	0.1	Fruit, other vegetables
	0.05	Eggs, meat, poultry meat
	0.02[d]	Milk
	0 (0.02)[e]	Other crops and foodstuffs
New Zealand	2.0	Cereals, fruit, vegetables
Peru	5.0	Cocoa beans
	2.0	Coffee beans, grain cereals, grain lentils, grain soya, peanuts
	1.0	Lettuce
	0.5	Edible mushrooms, tomatoes, vegetables (except lettuce)
	0.3	Cereal products (ground, for human consumption)
	0.1	Bread, cakes, cheese, cooked meat, fruits (except citrus)
	0.05	Eggs (without shell), meat of cattle, goats, hogs, poultry, sheep
	0.02	Whole milk
Romania	0.05	Eggs (without shell), meat
	0.02	Whole milk

Table 3 (contd)

Country or region	Residue limit (mg/kg)	Commodities
Singapore	0.5	Fruit, grains, vegetables
South Africa	0.1	Bananas, beans, cherries, cruciferae, grapes, lettuce, tomatoes, wheat
	0.05	Carcass meat (on the rendered or extracted carcass fat), eggs (without shell)
	0.02	Milk (on a fat basis)
Spain	2.0	Cereal grains
	0.1	Other plant products
Sweden	2.0	Cereals
	0.5[f]	Flakes and flour made from cereals, hulled grain
	0.1[f]	Fruit (fresh and dried, fresh and deep-frozen berries), vegetables (green and root)
	0.1	Butter, cheese
	0.05	Raw meat, eggs
	0.02	Milk
Switzerland	2.0	Cereals, cocoa beans
	0.3	Cereal products, vegetables (canned, fresh, frozen)
	0.1	Citrus fruit, fruit, other foodstuffs
	0.01	Milk
Taiwan	0.5	Fruit, vegetables, leafy vegetables with large wrapper leaves, leafy vegetables with small leaves, melon, mushrooms, peas, snap beans
	0.1	Root vegetables
United Kingdom	2	Barley, maize, oats, other cereals, paddy rice, rye, wheat
	1	Lettuce
	0.5	Beans, Brussels' sprouts, cabbage, carrots, cauliflower, celery, cucumbers, leeks, lettuce, mushrooms, onions, peas, potatoes, swedes, tomatoes, turnips
	0.1	Apples, bananas, blackcurrants, citrus, grapes, nectarines, peaches, pears, plums, raspberries, strawberries
	0.05	Eggs (birds' eggs in shell (other than eggs for hatching) and whole egg products and egg yolk products (whether fresh, dried or otherwise prepared)), meat, fat and preparations of meat, milk
	0.02	Milk (fresh raw cows' milk and fresh whole-cream cows' milk expressed as whole milk)
USA[g]	2.0	Raw agricutural commodities (nonperishable, packaged or bagged, containing more than 6% fat (post-harvest))
	1.0	Lettuce[h]
	0.5	Cucumbers[h], dried figs, mushrooms[h] and tomatoes (pre- and post-harvest)[h]; radishes, raw agricultural commodities (nonperishable, bulk stored regardless of fat content (post-harvest)); raw agricultural commodities (nonperishable, packaged or bagged, containing 6% fat or less (post-harvest))
	0.1	Figs
	0.1 (negligible)	Edible tissue of swine
	0.05 (negligible)	Eggs and poultry (fat, meat, and meat by-products)
	0.02 (negligible)	Cattle, goats, horses, sheep (fat, meat and meat by-products), milk

Table 3 (contd)

Country or region	Residue limit (mg/kg)	Commodities
USSR	0.3	Bran, grain
	0.05	Apples, grapes
	Not permitted	Flour, grouts
Yugoslavia	2.0	Cereals
	0.3	Processed cereals, vegetables
	0.1	Other foodstuffs

[a]From Health and Welfare Canada (1990)
[b]Residues should not be present; the value in parentheses indicates the lower limit for residue determination according to the standard method of analysis, this limit having been used to reach the no-residue conclusion.
[c]Standard for withholding registration of agricultural chemicals
[d]A pesticide may be used on an eating or drinking ware or raw material without a demonstrable residue remaining; the value listed is considered the highest concentration at which this requirement is deemed to have been met.
[e]Residues shall be absent; the value in parentheses is the highest concentration at which this requirement is still deemed to have been met.
[f]If analysis shows that two or more of certain substances are present in the same sample, in addition to the limit which applies for each substance, a maximum level of 1.0 mg/kg applies to the sum of the residues of these substances.
[g]From US Environmental Protection Agency (1989a,b)
[h]Residues expressed as naled

Occupational exposure limits and guidelines for dichlorvos in some countries and regions are given in Table 4.

Table 4. Occupational exposure limits and guidelines for dichlorvos[a]

Country or region	Year	Concentration[b] (mg/m^3)	Interpretation[c]
Austria	1987	1	TWA
Belgium	1987	1	TWA
China	1987	0.3	TWA
Denmark	1987	1	TWA
Finland	1987	1	TWA
		3	STEL
Germany	1989	1	TWA
Hungary	1987	0.2	TWA
		0.2	STEL
India	1987	1	TWA
		3	STEL
Indonesia	1987	1	TWA
Mexico	1987	1.5	TWA
Netherlands	1987	1	TWA

Table 4 (contd)

Country or region	Year	Concentration[b] (mg/m^3)	Interpretation[c]
Romania	1987	0.5	TWA
		1.5	STEL
Switzerland	1987	1	TWA
Taiwan	1987	1	TWA
United Kingdom	1987	1	TWA
		3	STEL
URSS	1987	0.2	TWA
USA			
ACGIH		0.9	Guideline
OSHA		1	TWA
Venezuela	1987	1	TWA
		3	Ceiling
Yugoslavia	1987	0.1	TWA

[a]From Izmerov (1984); Cook (1987); American Conference of Governmental Industrial Hygienists (ACGIH) (1989); Deutsche Forschungsgemeinschaft (1989); US Occupational Safety and Health Administration (OSHA) (1989)

[b]All values given are with skin notation

[c]TWA, time-weighted average; STEL, short-term exposure limit

2. Studies of Cancer in Humans

2.1 Case reports

In a case series, four children with aplastic anaemia and one with acute lymphoblastic leukaemia were reported by their parents to have been exposed at home to dichlorvos and propoxur (Reeves *et al.*, 1981).

2.2 Case-control studies

In a case-control study of leukaemia in the USA (Brown *et al.*, 1990), described in detail in the monograph on occupational exposure in spraying and application of insecticides (p. 68), significant excesses of leukaemia were noted among farmers who reported use of dichlorvos on animals (odds ratio, 2.0; 95% confidence interval [CI], 1.2-3.5). Risks were greater among those who had first used dichlorvos 20 or more years before diagnosis of leukaemia (odds ratio, 2.4; 95% CI, 1.1-5.4). The risks were greatest among farmers who used dichlorvos on animals on 10 or more days per year (odds ratio, 3.8; 95% CI, 1.0-14.8). The risk for leukaemia in this study was also associated with use of other agricultural pesticides, including crotoxyphos, famphur, pyrethrins, methoxychlor, nicotine and DDT, and it was not possible to evaluate exposure to dichlorvos in the absence of these other pesticides.

3. Studies of Cancer in Experimental Animals

The Working Group was aware of a study by Horn *et al.* (1987), which was of short duration and not considered informative for an evaluation.

3.1 Oral administration

3.1.1 *Mouse*

Groups of 50 male and 50 female B6C3F$_1$ hybrid mice, five to seven weeks of age, were fed technical-grade dichlorvos (minimum purity, 94%) in the diet at initial doses of 1000 and 2000 mg/kg. After two weeks, the doses were reduced to 300 and 600 mg/kg of diet, respectively, due to severe toxicity, and treated animals were maintained at these dietary levels for 78 weeks followed by 12-14 weeks on dichlorvos-free diets, after which time (92-94 weeks) the animals were killed and necropsied. The measured time-weighted average doses were 318 and 635 mg/kg of diet, respectively. Groups of 10 male and 10 female mice that served as matched controls were maintained on dichlorvos-free diets for 92 weeks; further control data were obtained from pooled control animals (100 males and 80 females). In females, 13/50 low-dose animals died before week 90; survival to 90 weeks was greater than 84% in all other groups. Average weights of high-dose males and females were generally lower than those of the low-dose and control groups, but the differences did not exceed 10%. The only findings of note were two squamous-cell carcinomas of the oesophagus (in one low-dose male and one high-dose female), one papilloma of the oesophagus (in a high-dose female) and three cases of focal hyperplasia of the oesophageal epithelium (in three low-dose males) (US National Cancer Institute, 1977). [The Working Group noted the short duration of treatment.]

Groups of 50 male and 50 female B6C3F$_1$ mice, eight weeks of age, were administered 0, 10 or 20 (males) and 0, 20 or 40 mg/kg bw (females) dichlorvos (99% pure) in corn oil by gavage per day on five days per week for 103 weeks. Survival was not affected by treatment. The incidence of squamous-cell papillomas of the forestomach was increased in males and females. A significant dose-response trend for the incidence of squamous-cell papillomas was seen in males (1/50 control, 1/50 low-dose, 5/50 high-dose; $p = 0.032$) and in females (5/49 control, 6/49 low-dose, 18/50 high-dose; $p = 0.002$). In females, the incidence in the high-dose group was significantly greater than that in controls ($p = 0.004$). Two of 50 high-dose females also had squamous-cell carcinomas (US National Toxicology Program, 1989).

3.1.2 *Rat*

Groups of 50 male and 50 female Osborne-Mendel rats, five to seven weeks of age, were fed diets containing 150 or 1000 mg/kg of diet technical-grade dichlorvos (minimum purity, 94%); due to severe toxicity, the high-dose was reduced to 300 mg/kg of diet after three weeks. Both groups were treated for 80 weeks and were maintained for a further 30 weeks on a dichlorvos-free diet. Time-weighted average doses were 150 and 326 mg/kg of diet, respectively. Groups of 10 males and 10 females served as matched controls and groups of 60 animals of each sex as pooled controls. Weight gain was consistently lower in high-dose groups than in low-dose and control groups. No significant difference in survival was

observed between treated and control groups at 105 weeks. The incidence of malignant fibrous histiocytomas in male rats showed a statistically significant trend (pooled control, 2/58; low-dose, 4/48; high-dose, 8/50; $p = 0.018$); a histiocytoma occurred in 1/10 matched male controls (US National Cancer Institute, 1977). [The Working Group noted the short duration of treatment].

Technical-grade dichlorvos (97% purity) was administered by gavage in water to 70 male and 70 female rats (inbred strain BD IX/Bln), six to eight weeks of age, at a dose of 0.1 mg per animal twice a week; or to 99 male and 99 female rats at a dose of 0.1 mg per animal three times a week for 60 weeks. Groups of 59 male and 60 female rats served as vehicle controls. Animals were killed 111 weeks after the beginning of treatment. There was no difference in median survival times between treated and control animals. Forestomach papillomas were observed in two males and in one female that received 0.3 mg dichlorvos. One male and one female rat receiving 0.3 mg had two and five papillomas of the urinary bladder, respectively (Horn *et al.*, 1988). [The Working Group noted the short duration of exposure.]

Groups of 50 male and 50 female Fischer 344/N rats, seven weeks of age, were administered 0, 4 or 8 mg/kg bw dichlorvos (99% pure) per day in corn oil by gavage on five days per week for 103 weeks. Survival was 31/50 control, 25/50 low-dose and 24/50 high-dose males and 31/50 control, 26/50 low-dose and 24/50 high-dose females; body weight gain was not affected by administration of dichlorvos. The incidence of acinar-cell adenomas of the pancreas was increased in treated males (16/50 control, 25/49 low-dose and 30/50 high-dose; $p < 0.001$ for trend). Further examination of horizontal sections of all pancreases revealed increases of reduced statistical significance (25/50, 30/50 and 33/50; [p for trend = < 0.05]). There were also more male rats with multiple adenomas in the treated groups than among controls (2/50, 7/49 and 13/50). Mononuclear-cell leukaemia occurred with a significant dose-response trend in male rats ($p = 0.011$), and the incidence in each of the treated groups was significantly greater than that in controls (11/50 control, 20/50 low-dose and 21/50 high-dose males). In females, fibroadenomas and adenomas of the mammary gland occurred with a significant dose-response trend ($p = 0.028$), and the incidence in both treated groups was significantly greater than that in controls (9/50 control, 19/50 low-dose and 17/50 high-dose females). Two female rats in the control group and two in the low-dose group had carcinomas of the mammary gland (US National Toxicology Program, 1989).

3.2 Inhalation and/or intratracheal administration

Rat: Groups of 50 male and 50 female Carworth Farm E strain rats, five weeks of age, were exposed continuously to atmospheres containing 0 (control), 0.05, 0.5 or 5 mg/m^3 technical-grade dichlorvos (purity, > 97%) for 104 weeks. The mean values for the entire test period were 0.05, 0.48 and 4.7 mg/m^3 [range ± 20%]. All treated groups showed decreased weight gain compared with controls, especially in the high-dose group. The numbers of males surviving at 99-102 weeks were 11/50 control, 21/50 low-dose, 15/50 mid-dose and 32/50 high-dose; survival in females at 104 weeks was 22/47 control, 27/47 low-dose, 26/47 mid-dose and 34/47 high-dose. Complete necropsy and histopathology were performed on 20-32% of males and 22-38% of females, reducing the effective numbers of animals per group to between 10 and 18. No significant increase in tumour incidence could

be attributed to treatment (Blair *et al.*, 1976). [The Working Group noted the small numbers of animals submitted for complete necropsy.]

Studies of cancer in experimental animals are summarized in Table 5.

4. Other Relevant Data

The toxicity of dichlorvos has been reviewed (FAO/WHO, 1965, 1967, 1968, 1971; Anon., 1974; FAO/WHO, 1978; WHO, 1989).

4.1 Absorption, distribution, metabolism and excretion

4.1.1 *Humans*

Dichlorvos is rapidly hydrolysed in human blood (half-time, 7-11 min), and no unchanged dichlorvos was found (detection limit, 0.1 μg/g) in blood samples taken 1 min after cessation of inhalation by two male volunteers exposed to 0.25 mg/m3 for 10 h or to 0.7 mg/m^3 for 20 h (Blair *et al.*, 1975).

A human volunteer who ingested 5 mg [^{14}C-vinyl]-dichlorvos excreted radiolabel at a rate similar to that seen after comparable oral dosing of rats, mice and hamsters, except that the output of $^{14}CO_2$ was somewhat greater. The urinary metabolites were tentatively identified as demethyldichlorvos, urea and hippuric acid (Hutson & Hoadley, 1972a).

More recently, it was established that dimethylphosphate is a metabolite in the urine of workers occupationally exposed to dichlorvos (Das *et al.*, 1983).

4.1.2 *Experimental systems*

The metabolism and disposition of dichlorvos have been reviewed (Wright *et al.*, 1979).

Metabolic disposition studies using radiolabelled dichlorvos have been reported in rats, mice, hamsters, pigs and humans. Labelling at different sites (e.g., ^{14}C-methyl, ^{14}C-vinyl, ^{36}Cl-chlorovinyl, ^{32}P-phosphate) has enabled specific pathways to be traced (Hutson *et al.*, 1971; Hutson & Hoadley, 1972a,b; Page *et al.*, 1972; Potter *et al.*,, 1973; Blair *et al.*, 1975). Furthermore, metabolic disposition has been determined after both inhalation exposure and oral administration (including slow-release polyvinyl chloride-pelleted dose forms).

There are two main metabolic pathways for dichlorvos: (1) ester hydrolysis of the *PO*-vinyl group to yield dimethylphosphate and dichloroacetaldehyde and (2) oxidative *O*-demethylation to demethyldichlorvos and formaldehyde. An alternative pathway for *O*-demethylation involves conjugation with glutathione (Dicowsky & Morello, 1971; Hutson *et al.*, 1971; Hutson & Hoadley, 1972a,b; Page *et al.*, 1972; Potter *et al.*,, 1973; Blair *et al.*, 1975). Hydrolysis of the *O*-demethylated metabolite yields methylphosphate and, eventually, phosphoric acid and methanol (WHO, 1989). Radiolabel from [^{14}C-methyl]- and [^{14}C-vinyl]-dichlorvos is ultimately incorporated into CO_2 (e.g., 39% of an oral dose of [^{14}C-vinyl]-dichlorvos over four days in rats) and enters the 1 and 2-carbon metabolic pools, resulting in the labelling of amino acids, proteins and purines. This labelling may confound the interpretation of studies of tissue disposition and urinary excretion if the chemical specificity and source of the radiolabel are not determined.

Patterns of urinary metabolites indicate that metabolic clearance varies very little by species or route. The hydrolysis pathway generally predominates over the *O*-demethylation pathway, although the latter is more prominent in mice.

Table 5. Studies of cancer in experimental animals

Reference	Species/strain	Sex	Dose schedule	Experimental parameter/ observation	Group				Statistical conclusion	Comment
					0	1	2	3		
US National Cancer Institute (1977)	Mouse $B6C3F_1$	M	In diet for 80 weeks	Dose (mg/kg of diet)[a] Oesophageal carcinoma	0	0	318 1/50	635		
		F	In diet for 80 weeks	Dose (mg/kg of diet) Oesophageal carcinoma Oesophageal papilloma	0	0	318	635 1/50 1/50		No significant increase in tumours
US National Toxicology Program (1989)	Mouse $B6C3F_1$	M	Gavage, 5 days/week for 103 weeks	Dose (mg/kg bw) Forestomach papilloma	0 1/50	10 1/50	20 5/50	-	$p = 0.032$ trend	
		F	Gavage, 5 days/week for 103 weeks	Dose (mg/kg bw) Forestomach papilloma Forestomach carcinoma	0 5/49 0/49	20 6/49 0/49	40 18/50 2/50	-	$p = 0.002$ trend	
US National Cancer Institute (1977)	Rat Osborne-Mendel	M	In diet for 80 weeks	Dose (mg/kg of diet)[a] Malignant fibrous histiocytomas	0 1/10	0 2/58	150 4/48	326 8/50	$p = 0.018$ trend	
		F	In diet for 80 weeks	Dose (mg/kg of diet)	0	0	150	326		No significant increase in tumours
Horn *et al.* (1988)	Rat BDIX/Bln	M	Gavage, 2 or 3 per week for 60 weeks	Dose (mg/animal) per week Forestomach papillomas Urinary bladder papillomas	0 0/10 0/55	0.1 × 2 0/13 0/65	0.1 × 3 2/26 1/95		NS NS	Number of animals with papillomas
		F	Gavage 2 or 3 per week for 60 weeks	Dose (mg/animal) per week Forestomach papillomas Urinary bladder papillomas	0 0/22 0/6	0.1 × 2 0/20 0/7	0.1 × 3 1/38 1/10		NS NS	Number of animals with papillomas
US National Toxicology Program (1989)	Rat Fischer 344/N	M	Gavage, 5 days/weeks for 103 weeks	Dose (mg/kg bw) Pancreatic acinar-cell adenomas Mononuclear-cell leukaemia	0 25/50 11/50	4 30/50 20/50	8 33/50 21/50		$p < 0.05$ trend $p = 0.011$ trend	
		F	Gavage, 5 days/weeks for 103 weeks	Dose (mg/kg bw) Pancreatic acinar-cell adenomas Mammary fibroadenomas/adenomas	0 2/50 9/50	4 3/50 19/50	8 6/50 17/50	-	NS $p = 0.028$ trend	

[a]Groups: 0, matched controls; 1, pooled controls

Hydrolytic metabolism of dichlorvos to dimethylphosphate and dichloroacetaldehyde, which in turn is rapidly reduced to dichloroethanol and conjugated with glucuronic acid, is so rapid that the half-time for the reaction *in vivo* has not been determined with any accuracy. *In vitro*, the half-time for blood-catalysed hydrolysis ranges from 2 min in rabbits to 30 min in rats. In human blood, the half-time is approximately 10 min, and the K_m for the reaction has been estimated to be approximately 3 μM. For this reason, unchanged dichlorvos is detected in blood only at relatively high dose rates (Blair *et al.*, 1975).

4.2 Toxic effects

4.2.1 *Humans*

The adverse effects of dichlorvos in humans have been reviewed (Cavagna & Vigliani, 1970; Gillett *et al.*, 1972a,b; Hayes, 1982). Depression of plasma cholinesterase is the most sensitive indicator of exposure to dichlorvos but is not necessarily an indicator of toxicity. At higher dose levels, red blood cell cholinesterase may also be affected.

Dichlorvos was administered in the form of slow-release polyvinyl resin formulation pellets as single doses (1-32 mg/kg bw) to 107 men and as repeated doses (1-32 mg/kg bw per day for 2-7 days; 1-16 mg/kg bw per day for up to three weeks) to 38 men. Maximal plasma cholinesterase depression occurred at approximately 6 mg/kg bw (single dose) and 1 mg/kg bw per day (repeated dose over three weeks). The single-dose threshold for plasma cholinesterase depression was approximately 1-3 mg/kg bw. Red blood cell cholinesterase activity was depressed at doses approximately four-fold higher. While the incidence of transient gastrointestinal and central nervous system-related subjective effects which accompanied the cholinesterase depression was relatively low at the lowest dose rates, they were sufficiently adverse to cause subjects given repeated doses of 8-32 mg/kg bw per day to withdraw from the study (Slomka & Hine, 1981).

Airborne levels of dichlorvos which cause slight to moderate cholinesterase depression have been reported to be 0.7 mg/m^3 average over one year in factory workers producing dichlorvos vaporizers (Menz *et al.*, 1974) and 0.1 mg/m^3 for 24 h per day in children and adults hospitalized for various periods in wards provided with dichlorvos-impregnated plastic strips. Plasma (but not red blood cell) cholinesterase levels were slightly depressed in 11 hospitalized babies exposed to air levels of over 0.1 mg/m^3 for 24 h per day, but children of 2-7 years were not affected at the same exposure level for 16 h per day (Cavagna *et al.*, 1969). As reported in an abstract, neither plasma nor red blood cell cholinesterase depression was found in 22 newborn babies when the average air levels of dichlorvos were reported to be up to 0.159 mg/m^3 (Vigliani, 1971).

Lethal exposures to dichlorvos have been reported in connection with accidental splashing of a concentrated formulation, coupled with failure to wash the material off (Hayes, 1982). A case of systemic poisoning resulted from an accident in which dichlorvos spray leaked down a man's back (Bisby & Simpson, 1975). Another accidental incident of skin contact resulted in symptomatic effects followed by the development of a persistent contact dermatitis (Mathias, 1983).

4.2.2 *Experimental systems*

The toxicology of dichlorvos in experimental animals has been reviewed (Attfield & Webster, 1966; Gillett *et al.*, 1972a,b; Anon., 1974; Wright *et al.*, 1979).

Dichlorvos is acutely neurotoxic by virtue of its ability to inhibit brain cholinesterase. The acute oral LD_{50} in rats was cited as 56-80 (Durham *et al.*, 1957) and 25-30 mg/kg bw (Ben-Dyke *et al.*, 1970) and that in mice as 140-275 mg/kg bw (Anon., 1974; Holmstedt *et al.*, 1978). The oral LD_{50} of dichlorvos in young pigs was 157 mg/kg bw; no death occurred in animals administered up to 100 mg/kg of a polyvinyl chloride formulation of dichlorvos (Stanton *et al.*, 1979). The large range cited for the dermal LD_{50} (75-900 mg/kg bw) in rats suggests that skin absorption is vehicle-dependent (Jones *et al.*, 1968).

Exposures after which cholinesterase depression was the only discernible toxic effect include two-year inhalation exposure of rats to 0.5-5 mg/m^3 (Blair *et al.*, 1976), 90-day feeding of 0.4-70 mg/kg bw per day to rats (effects observed at 3.5 mg/kg per day and above; Durham *et al.*, 1957), administration for 30 days of 1-16 mg/kg bw per day in polyvinyl chloride pellets to pigs (Stanton *et al.*, 1979) and administration for 10-21 days of 10-80 mg/kg bw per day in polyvinyl chloride pellets to rhesus monkeys (Hass *et al.*, 1972).

Dichlorvos has been ascribed only a slight risk of causing delayed neuropathy, because doses that inhibit neuropathy target esterase and result in ataxia in hens exceed the LD_{50} by several fold; protection with atropine is required if the test is to be completed (Johnson, 1978; Caroldi & Lotti, 1981; Johnson, 1981).

Both humoral immune response and cell-mediated immunity were inhibited in rabbits treated orally with dichlorvos for five days a week for up to five to six weeks at high dose rates (0.31-2.5 mg/kg bw: 2.5-20% of the LD_{50}; Dési *et al.*, 1978, 1980). Immunosuppression was also observed in mice given 120 mg/kg bw orally, but the authors commented that this phenomenon, seen with other organophosphonates and the cholinomimetic compound, arecoline, may be secondary to a profound cholinergic stimulation (Casale *et al.*, 1983).

The diurnal rhythm of the pituitary/adrenal axis was altered in rats given 2 ppm (mg/l) dichlorvos in the drinking-water for two weeks (approximate intake, 0.3 mg/kg bw per day), causing changes in plasma adrenocorticotrophic hormone levels and adrenal cholesterol ester concentrations. While adrenocorticotrophic hormone secretion is believed to be acetylcholine-sensitive, there was no detectable change in cholinesterase activity (Civen *et al.*, 1980).

Reactions with macromolecules: Dichlorvos is a phosphorylating and alkylating agent (Wright *et al.*, 1979). 4-Nitrobenzylpyridine is alkylated by dichlorvos (half-time, 28 min) more slowly than methyl methanesulfonate (half-time, 9.6 min). Metabolites of dichlorvos did not react with 4-nitrobenzylpyridine in this system (Bedford & Robinson, 1972). The relative reactivity of dichlorvos toward 4-nitrobenzylpyridine and acetylcholinesterase was greatly in favour of esterase phosphorylation (WHO, 1989), indicating that dichlorvos-associated methylation of DNA purines may not be as important *in vivo* as the esterase phosphorylation reaction (Wright *et al.*, 1979; Wooder *et al.*, 1977).

There may appear to be some conflict between this conclusion and the detection of radiolabelled *N*-7-methylated guanine in mouse urine following administration of [^{14}C-methyl]- or [^{3}H-methyl]-dichlorvos (24-90 μCi intraperitoneally or an estimated

8.5-11 μCi by inhalation) (Wennerberg & Löfroth, 1974). Since, however, methylated purines occur naturally in urine and [^{14}C-methyl]-dichlorvos metabolites enter the 1- and 2-carbon metabolic pool, it has been suggested that the mechanism of methylation may be indirect (Wooder & Wright, 1981). No *N*-7-guanine methylation was found in the DNA of lung, liver, heart, brain, testes or spleen of 20 rats exposed to [^{14}C-methyl]-dichlorvos by inhalation at 0.064 μg/l for 12 h (estimated total dose, 6 μg; specific activity, 113 μCi/mmol; resulting in a DNA detection limit of 0.000001% of the dose) (Wooder *et al.*, 1977).

Segerbäck and Ehrenberg (1981) also concluded that the likelihood of DNA methylation after dosing with dichlorvos *in vivo* is extremely small. Their estimate of the amount of DNA methylation in mice after intraperitoneal dosing with 1.9 μmol/kg bw [0.42 mg/kg] is of the order of 8×10^{-13} mol methyl per gram of DNA.

4.3 Reproductive and developmental effects

4.3.1 *Humans*

No data were available to the Working Group.

4.3.2 *Experimental systems*

Female Sherman rats were treated intraperitoneally with dichlorvos at 15 mg/kg bw in peanut oil on day 11 of gestation. No difference was noted in weight gain, number of fetuses per litter, number of resorptions per pregnant rat or weight of the fetuses or placentae on day 20 of gestation. Three omphalocoeles occurred among 41 offspring in the treated group, but no malformation was noted among controls (Kimbrough & Gaines, 1968).

No adverse developmental effect was observed in CF-1 mice administered the maximal tolerated dose by gavage on days 6-15 of gestation or in New Zealand rabbits administered 60 and 5 mg/kg bw per day on days 6-18 of gestation or by inhalation at 4 mg/m^3 for 7 h per day (Schwetz *et al.*, 1979).

Pregnant rabbits were treated [route not given] with dichlorvos at a dose of 6 mg/kg bw per day for the last 10 days of gestation. Light-microscopic examination of the brains of six pups from treated and six from untreated dams sacrificed at birth revealed no alteration in brain morphology; electron microscopic examination suggested 'immaturity' or delay in brain development in the treated animals. Synaptic junctions quantified in the motor cortex using electron microscopy were considered to be immature (Dambska *et al.*, 1979). [The Working Group noted the lack of adequate controls and the poor description of the study.]

Carworth E rats and Dutch rabbits were exposed to dichlorvos in air at concentrations of up to 6.25 mg/m^3 and 4 mg/m^3, respectively, for 23 h per day on seven days per week from the day of mating until the end of gestation. These treatments produced a dose-dependent decrease in plasma, red cell and brain cholinesterase activity in both species but had no effect on the number of pregnancies, the number of resorptions, the number of fetal deaths, litter size or fetal weight in rats or rabbits (Thorpe *et al.*, 1972).

In pregnant sows fed a polyvinyl chloride formulation of dichlorvos at doses of 5 or 25 mg/kg bw per day for the last 30 days of gestation, no alteration in reproductive performance was observed. Plasma and red cell cholinesterase activities and, at the high dose, myometrial acetylcholinesterase activity were decreased in the sows; the rhombencephalic acetylcholinesterase level was increased in fetuses (Stanton *et al.*, 1979).

A series of early studies reported in abstracts also examined reproductive and developmental effects. No effect on reproduction or development was seen in more than 6000 offspring of male and female rats treated for three generations with dichlorvos in feed at doses of up to 500 ppm [mg/kg] (Witherup *et al.*, 1971). In rabbits treated orally with a polyvinyl chloride formulation of dichlorvos, maternal toxicity was seen at 34 mg/kg; no alteration was observed in reproductive or developmental parameters at doses not associated with maternal toxicity (Vogin *et al.*, 1971). No effect on reproduction or development was seen over two generations in male and female swine treated for 37 months at doses in the feed of up to 500 ppm [mg/kg] (Collins *et al.*, 1971).

4.4 Genetic and related effects (see also Table 6 and Appendices 1 and 2)

4.4.1 *Humans*

No data were available to the Working Group.

4.4.2 *Experimental systems*

The genetic activity of dichlorvos has been reviewed (Ramel *et al.*, 1980).

In bacteria, dichlorvos bound covalently to DNA, RNA and protein and caused DNA damage and point mutations. Bacterial mutagenicity was reduced in the presence of liver preparations. Dichlorvos induced gene conversion, mutation and aneuploidy in yeast and fungi, and mutation, chromosomal aberrations and micronucleus formation in plants. In *Drosophila melanogaster*, chromosomal aberrations but not sex-linked recessive lethal mutation were induced. Autosomal lethal and polygenic viability mutations were induced in *D. melanogaster* by treatment over multiple generations. [The Working Group considered that these tests are not well validated.] In mammalian cells *in vitro*, dichlorvos caused DNA strand breaks, mutation, sister chromatid exchange, chromosomal aberrations and cell transformation. In human cells *in vitro*, it induced unscheduled DNA synthesis but neither chromosomal aberrations nor sister chromatid exchange.

No significant response was observed *in vivo* in any of the mammalian tests used for the induction of unscheduled DNA synthesis, sister chromatid exchange, micronucleus formation, chromosomal aberrations or dominant lethal mutation.

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Dichlorvos has been used widely as an insecticide since 1961 to control internal and external parasites in livestock and domestic animals, to control insects in houses, and in crop protection.

Dichlorvos has been formulated for use as dusts, granules, pellets/tablets, impregnated resin strips and concentrates.

Household and public health uses represent the main sources of human exposure to dichlorvos. Exposure may also occur during its production and application.

Table 6. Genetic and related effects of dichlorvos

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic sytem	With exogenous metabolic system		
PRB, Prophage induction	+	+	60.0000	Houk & DeMarini (1987)
ECB, *Escherichia coli* WP2, DNA strand breaks	+	0	2000.0000	Green *et al.* (1974)
ECB, *Escherichia coli* WP67, DNA strand breaks	+	0	500.0000	Green *et al.* (1974)
ECB, *Escherichia coli* ColE1 plasmid, DNA strand breaks	+	0	1000.0000	Griffin & Hill (1978)
ECD, *Escherichia coli pol A*, differential toxicity (spot test)	+	0	13.0000	Rosenkranz (1973)
ECD, *Escherichia coli pol A*, differential toxicity (liquid)	+	0	1400.0000	Rosenkranz (1973)
BSD, *Bacillus subtilis rec*, differential toxicity	+	0	2000.0000	Shirasu *et al.* (1976)
BSD, *Bacillus subtilis rec*, differential toxicity	+	0	0.0000	Kawachi *et al.* (1980)
BRD, Bacteria (other), differential toxicity	(+)	0	50000.0000	Adler *et al.* (1976)
BRD, Bacteria (other), differential toxicity	+	0	2.0000	Braun *et al.* (1982)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	300.0000	Byeon *et al.* (1976)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	275.0000	Löfroth (1978)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	0.0000	Kawachi *et al.* (1980)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	0	0.0000	Ishidate *et al.* (1981)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	(+)	1.0000	Braun *et al.* (1982)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	375.0000	Moriya *et al.* (1983)
SA0, *Salmonella typhimurium* TA100, reverse mutation	(+)	+	250.0000	Breau *et al.* (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	-	250.0000	Choi *et al.* (1985)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	167.0000	Zeiger *et al.* (1988)
SA0, *Salmonella typhimurium* TA100, reverse mutation	+	+	500.0000	US National Toxicology Program (1989)
SA2, *Salmonella typhimurium* TA102, reverse mutation	-	-	0.0000	Choi *et al.* (1985)
SA3, *Salmonella typhimurium* TA1530, reverse mutation	+	0	0.0000	Hanna & Dyer (1975)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	0	0.0000	Hanna & Dyer (1975)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	(+)	(+)	1500.0000	Byeon *et al.* (1976)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	0	2500.0000	Shirasu *et al.* (1976)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	0	1500.0000	Carere *et al.* (1978)
SA5, *Salmonella typhimurium* TA1535, reverse mutation	-	-	2500.0000	Moriya *et al.* (1978)

Table 6 (contd)

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic sytem	With exogenous metabolic system		
SA5, *Salmonella typhimurium* TA1535, reverse mutation	+	0	0.0000	Choi *et al.* (1985)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	-	0	0.0000	Hanna & Dyer (1975)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	-	0	2500.0000	Shirasu *et al.* (1976)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	-	0	2800.0000	Carere *et al.* (1978)
SA7, *Salmonella typhimurium* TA1537, reverse mutation	-	-	2500.0000	Moriya *et al.* (1983)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	-	0	0.0000	Hanna & Dyer (1975)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	-	0	2500.0000	Shirasu *et al.* (1976)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	-	-	1500.0000	Byeon *et al.* (1976)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	-	0	2800.0000	Carere *et al.* (1978)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	-	-	2500.0000	Moriya *et al.* (1983)
SA8, *Salmonella typhimurium* TA1538, reverse mutation	-	-	0.0000	Choi *et al.* (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	1500.0000	Byeon *et al.* (1976)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	0.0000	Kawachi *et al.* (1980)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	2500.0000	Moriya *et al.* (1983)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	0.0000	Breau *et al.* (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	0.0000	Choi *et al.* (1985)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	500.0000	Zeiger *et al.* (1988)
SA9, *Salmonella typhimurium* TA98, reverse mutation	-	-	500.0000	US National Toxicology Program (1989)
SAS, *Salmonella typhimurium* 64–320, reverse mutation	+	0	500.0000	Voogd *et al.* (1972)
SAS, *Salmonella typhimurium* C117, reverse mutation	(+)	0	6630.0000	Dyer & Hanna (1973)
SAS, *Salmonella typhimurium* C117, reverse mutation	-	0	0.0000	Hanna & Dyer (1975)
SAS, *Salmonella typhimurium* G46, reverse mutation	-	0	0.0000	Hanna & Dyer (1975)
SAS, *Salmonella typhimurium* TA1536, reverse mutation	-	0	2500.0000	Shirasu *et al.* (1976)
SAS, *Salmonella typhimurium* TA1536, reverse mutation	-	0	2800.0000	Carere *et al.* (1978)
ECF, *Escherichia coli* B, forward mutation	+	0	1100.0000	Wild (1973)
ECK, *Escherichia coli* K12, forward or reverse mutation	+	0	145.0000	Mohn (1973)
ECW, *Escherichia coli* WP2 *uvr*A, reverse mutation	+	0	2000.0000	Bridges *et al.* (1973)

Table 6 (contd)

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic sytem	With exogenous metabolic system		
ECW, *Escherichia coli* WP2 *uvr*A, reverse mutation	+	0	0.0000	Hanna & Dyer (1975)
ECW, *Escherichia coli* WP2 *uvr*A, reverse mutation	+	0	0.0000	Nagy *et al.* (1975)
ECW, *Escherichia coli* WP2 *uvr*A, reverse mutation	+	0	2000.0000	Bridges (1978)
EC2, *Escherichia coli* WP2, reverse mutation	-	0	0.0000	Dean (1972a)
EC2, *Escherichia coli* WP2, reverse mutation	+	0	2000.0000	Bridges *et al.* (1973)
EC2, *Escherichia coli* WP2, reverse mutation	+	0	0.0000	Hanna & Dyer (1975)
EC2, *Escherichia coli* WP2, reverse mutation	(+)	0	0.0000	Nagy *et al.* (1975)
EC2, *Escherichia coli* WP2, reverse mutation	+	0	5.0000	Green *et al.* (1976)
EC2, *Escherichia coli* WP2, reverse mutation	+	0	2500.0000	Shirasu *et al.* (1976)
EC2, *Escherichia coli* WP2, reverse mutation	+	0	5.0000	Bridges (1978)
EC2, *Escherichia coli* WP2, reverse mutation	+	0	2500.0000	Moriya *et al.* (1983)
ECR, *Escherichia coli* B(sd-4), reverse mutation	+	0	220.0000	Löfroth *et al.* (1969)
ECR, *Escherichia coli* K12 HfrH, reverse mutation	+	0	1000.0000	Voogd *et al.* (1972)
EC2, *Escherichia coli* WP67, reverse mutation	+	0	1000.0000	Bridges *et al.* (1973)
EC2, *Escherichia coli* WP67, reverse mutation	+	0	0.0000	Hanna & Dyer (1975)
EC2, *Escherichia coli* CM561, reverse mutation	-	0	2000.0000	Bridges *et al.* (1973)
EC2, *Escherichia coli* CM561, reverse mutation	-	0	0.0000	Hanna & Dyer (1975)
EC2, *Escherichia coli* CM571, reverse mutation	-	0	2000.0000	Bridges *et al.* (1973)
EC2, *Escherichia coli* CM571, reverse mutation	-	0	0.0000	Hanna & Dyer (1975)
EC2, *Escherichia coli* CM611, reverse mutation	-	0	2000.0000	Bridges *et al.* (1973)
EC2, *Escherichia coli* CM611, reverse mutation	-	0	0.0000	Hanna & Dyer (1975)
ECR, *Escherichia coli* CM881, reverse mutation	+	0	0.1000	Bridges (1978)
ECR, *Escherichia coli* B/r WP2, reverse mutation	+	+	2500.0000	Moriya *et al.* (1978)
KPF, *Klebsiella pneumoniae*, forward mutation	+	0	500.0000	Voogd *et al.* (1972)
SCG, *Saccharomyces cerevisiae*, gene conversion	+	0	4000.0000	Dean *et al.* (1972)
SCG, *Saccharomyces cerevisiae*, gene conversion	+	0	1326.0000	Fahrig (1973)
SCG, *Saccharomyces cerevisiae*, gene conversion	+	0	1770.0000	Fahrig (1976)
SCH, *Saccharomyces cerevisiae*, homozygosis by gene conversion	+	0	5000.0000	Choi *et al.* (1985)

Table 6 (contd)

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic sytem	With exogenous metabolic system		
ANG, *Aspergillus nidulans*, genetic crossing-over	+	.0	2800.0000	Morpurgo *et al.* (1977)
SZF, *Schizosaccharomyces pombe*, forward mutation	+	(+)	330.0000	Gilot-Delhalle *et al.* (1983)
ANR, *Aspergillus nidulans*, reverse mutation	+	0	14000.0000	Morpurgo *et al.* (1977)
ANN, *Aspergillus nidulans*, aneuploidy	+	0	800.0000	Morpurgo *et al.* (1979)
HSM, *Hordeum* species, mutation	-	0	166.0000	Bhan & Kaul (1975)
HSM, *Hordeum* species, mutation	+	0	1500.0000	Panda & Sharma (1979)
HSM, *Hordeum* species, mutation	+	0	5000.0000	Singh *et al.* (1980)
HSM, *Hordeum* species, mutation	+	0	0.0000	Sharma *et al.* (1983)
TSM, *Tradescantia paludosa*, mutation	-	0	0.0000	Schairer *et al.* (1978)
TSI, *Tradescantia paludosa*, micronuclei	+	0	0.0000	Ma *et al.* (1984)
ACC, *Allium cepa*, chromosomal aberrations	+	0	50.0000	Rao *et al.* (1987)
HSC, *Hordeum* species, chromosomal aberrations	+	0	55.0000	Bhan & Kaul (1975)
HSC, *Hordeum* species, chromosomal aberrations	+	0	100.0000	Panda & Sharma (1979)
HSC, *Hordeum* species, chromosomal aberrations	+	0	0.0000	Sharma *et al.* (1983)
VFC, *Vicia faba*, chromosomal aberrations	+	0	125.0000	Amer & Ali (1986)
PLC, *Capsicum annuum*, chromosomal aberrations	+	0	5000.0000	Devadas *et al.* (1986)
DMG, *Drosophila melanogaster*, crossing-over/recombination	-	0	350.0000	Jayasuriya & Ratnayake (1973)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	-	0	350.0000	Jayasuriya & Ratnayake (1973)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	-	0	0.0900	Kramers & Knaap (1978)
DMX, *Drosophila melanogaster*, sex-linked recessive lethal mutations	-	0	0.0700	Sobels & Todd (1979)
*, *Drosophila melanogaster*, polygenic viability mutations	+	0	4.0000	Marcos *et al.* (1989)
*, *Drosophila melanogaster*, autosomal recessive lethal mutations	+	0	0.7500	Hanna & Dyer (1975)

Table 6 (contd)

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic sytem	With exogenous metabolic system		
DMC, *Drosophila melanogaster*, chromosomal aberrations	+	0	1.0000	Gupta & Singh (1974)
DIA, DNA strand breaks, Chinese hamster V-79-4 cells *in vitro*	(+)	0	2000.0000	Green *et al.* (1974)
G9O, Gene mutation, Chinese hamster V79 lung cells (ouabain)	-	0	1100.0000	Aquilina *et al.* (1984)
G5T, Gene mutation, mouse lymphoma L5178Y cells *in vitro*, *tk* locus	+	0	25.0000	US National Toxicology Program (1989)
SIC, Sister chromatid exchange, Chinese hamster cells *in vitro*	+	0	20.0000	Tezuka *et al.* (1980)
SIC, Sister chromatid exchange, Chinese hamster cells *in vitro*	+	0	7.0000	Nishio & Uyeki (1981)
SIC, Sister chromatid exchange, Chinese hamster cells *in vitro*	+	0	22.0000	Shirasu *et al.* (1984)
SIC, Sister chromatid exchange, Chinese hamster cells *in vitro*	+	+	25.0000	US National Toxicology Program (1989)
SIR, Sister chromatid exchange, rat cells *in vitro*	+	0	10.0000	Lin *et al.* (1988)
CIC, Chromosomal aberrations, Chinese hamster cells *in vitro*	-	0	1000.0000	Sasaki *et al.* (1980)
CIC, Chromosomal aberrations, Chinese hamster cells *in vitro*	+	0	110.0000	Tezuka *et al.* (1980)
CIC, Chromosomal aberrations, Chinese hamster cells *in vitro*	+	0	130.0000	Ishidate *et al.* (1981)
CIR, Chromosomal aberrations, rat cells *in vitro*	+	0	80.0000	Lin *et al.* (1988)
TCS, Cell transformation, Syrian hamster embryo cells *in vitro*	+	0	0.0000	Tu *et al.* (1986)
TCL, Cell transformation, rat tracheal epithelial cells *in vitro*	+	0	40.0000	Lin *et al.* (1988)
UHL, Unscheduled DNA synthesis, human lymphocytes *in vitro*	+	0	5.0000	Perocco & Fini (1980)
UIH, Unscheduled DNA synthesis, EUE human cells *in vitro*	+	0	14365.0000	Aquilina *et al.* (1984)
SHF, Sister chromatid exchange, human fibroblasts *in vitro*	-	0	10.0000	Nicholas *et al.* (1978)
SHL, Sister chromatid exchange, human lymphocytes *in vitro*	-	0	10.0000	Nicholas *et al.* (1978)
CHL, Chromosomal aberrations, human lymphocytes *in vitro*	-	0	40.0000	Dean (1972b)
HMM, Host-mediated assay, *Salmonella typhimurium* in mice	-	0	25.000	Buselmaier *et al.* (1972)
HMM, Host-mediated assay, *Salmonella typhimurium* in mice	-	0	8.0000	Voogd *et al.* (1972)
HMM, Host-mediated assay, *Saccharomyces cerevisiae* in mice	-	0	100.0000	Dean *et al.* (1972)
UPR, Unscheduled DNA synthesis, rat hepatocytes *in vivo*	-	0	35.0000	Mirsalis *et al.* (1989)
SVA, Sister chromatid exchange, mouse lymphocytes *in vivo*	-	0	25.0000	Kligerman *t al.* (1985)

Table 6 (contd)

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic sytem	With exogenous metabolic system		
MVM, Micronucleus test, mouse bone-marrow cells *in vivo*	–	0	0.0150	Paik & Lee (1977)
CBA, Chromosomal aberrations, mouse bone-marrow cells *in vivo*	–	0	15.0000 (16-h inhal.)	Dean & Thorpe (1972a)
CBA, Chromosomal aberrations, Chinese hamster bone marrow *in vivo*	–	0	15.0000	Dean & Thorpe (1972a)
CBA, Chromosomal aberrations, mouse bone-marrow cells *in vivo*	–	0	100.0000	Kurinnyi (1975)
CBA, Chromosomal aberrations, mouse bone-marrow cells *in vivo*	–	0	10.0000	Moutschen-Dahmen *et al.* (1981)
CBA, Chromosomal aberrations, mouse bone-marrow cells *in vivo*	–	0	0.3300[c]	Degraeve *et al.* (1984a)
CBA, Chromosomal aberrations, Syrian hamster bone marrow *in vivo*	(+)	0	15.0000	Dzwonkowska & Hübner (1986)
CCC, Chromosomal aberrations, mouse spermatocytes *in vivo*	–	0	0.3300[c]	Degraeve *et al.* (1984a)
CCC, Chromosomal aberrations, mouse spermatocytes *in vivo*	–	0	10.0000	Degraeve *et al.* (1984b)
CGC, Chromosomal aberrations, mouse spermatogonia *in vivo*	–	0	0.3300[c]	Degraeve *et al.* (1984a)
CGC, Chromosomal aberrations, mouse spermatogonia *in vivo*	–	0	10.0000	Degraeve *et al.* (1984b)
DLM, Dominant lethal test, mice	–	0	53.0000 (16-h inhal.)	Dean & Thorpe (1972b)
DLM, Dominant lethal test, mice	–	0	16.5000	Epstein *et al.* (1972)
DLM, Dominant lethal test, mice	–	0	50.0000	Dean & Blair (1976)
DLM, Dominant lethal test, mice	–	0	10.0000	Moutschen-Dahmen *et al.* (1981)
DLM, Dominant lethal test, mice	–	0	0.3300[c]	Degraeve *et al.* (1984a)
BID, Binding to calf thymus DNA *in vitro*	+	0	20000.0000	Löfroth (1970)
BID, Binding to DNA, *Escherichia coli* WP2 *uvr*A *in vitro*	+	0	300.0000	Lawley *et al.* (1974)
BID, Binding to DNA, HeLa cells *in vitro*	+	0	215.0000	Lawley *et al.* (1974)
BID, Binding to DNA, *Escherichia coli* B *in vitro*	+	0	155.0000	Wennerberg & Löfroth (1974)
BID, Binding to calf thymus DNA *in vitro*	+	0	3.7500	Segerbäck (1981)

Table 6 (contd)

Test system	Result[a]		Dose[b] LED/HID	Reference
	Without exogenous metabolic sytem	With exogenous metabolic system		
BIP, Binding to RNA/protein, *Escherichia coli* WP2 *uvr*A *in vitro*	+	0	215.0000	Lawley *et al.* (1974)
BIP, Binding to RNA/protein, HeLa cells *in vitro*	+	0	215.0000	Lawley *et al.* (1974)
BIP, Binding to RNA/protein, *Escherichia coli* B *in vitro*	+	0	155.0000	Wennerberg & Löfroth (1974)
BVD, Binding to DNA, rats *in vivo*	–	0	0.0150 (12-h inhal.)	Wooder *et al.* (1977)
BVD, Binding to DNA, mice *in vivo*	–	0	0.4000	Segerbäck (1981)
BVP, Binding to RNA/protein, rats *in vivo*	–	0	0.0150 (12-h inhal.)	Wooder *et al.* (1977)
SPF, Sperm morphology, F1 mice *in vivo*	(+)	0	12.0000	Wyrobeck & Bruce (1975)

*Not displayed on profile

[a] +, positive; (+), weakly positive; –, negative; 0, not tested, ?, inconclusive (variable response in several experiments within an adequate study)

[b] In-vitro tests, μg/ml; in-vivo tests, mg/kg bw

[c] In drinking-water

5.2 Carcinogenicity in humans

One case-control study of leukaemia in the USA found an association with use of dichlorvos on animals; there were few exposed subjects, and they had potential exposure to many pesticides.

5.3 Carcinogenicity in experimental animals

Dichlorvos was tested for carcinogenicity by oral administration in two experiments in mice and in three experiments in rats. A few rare oesophageal squamous-cell tumours were found in mice treated with dichlorvos in the diet. A dose-related increase in the incidence of squamous-cell tumours (mainly papillomas) was noted in the forestomachs of mice that received dichlorvos in corn oil by gavage. In rats that received dichlorvos in water by gavage, a few squamous-cell papillomas of the forestomach were seen. In rats that received dichlorvos in corn oil by gavage, a dose-related increase in the incidence of mononuclear-cell leukaemia and an increased incidence of pancreatic acinar-cell adenomas were observed in males.

5.4 Other relevant data

A variety of studies in several species did not demonstrate developmental toxicity due to dichlorvos.

In vitro, dichlorvos phosphorylates esterases to a greater extent than it methylates nucleophiles; the likelihood of DNA methylation *in vivo* is extremely small.

Immunosuppression has been noted after short-term administration of high doses of dichlorvos which are associated with profound cholinergic hyperstimulation.

No data were available on the genetic and related effects of dichlorvos in humans.

Dichlorvos was not shown to have genetic activity in various assays in mammals *in vivo*. It induced gene mutation and chromosomal damage in cultured mammalian cells and in insects, plants, fungi, yeast and bacteria.

5.5 Evaluation[1]

There is *inadequate evidence* in humans for the carcinogenicity of dichlorvos.

There is *sufficient evidence* in experimental animals for the carcinogenicity of dichlorvos.

Overall evaluation

Dichlorvos *is possibly carcinogenic to humans (Group 2B).*

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[1]For definition of the italicized terms, see Preamble, pp. 26-28.

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