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Dicyclopentadiene
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THE ECETOC PROGRAMME FOR THE

JOINT ASSESSMENT OF COMMODITY CHEMICALS (JACC)

This report has been prepared as part of the ECETOC programme for preparing critical reviews of the toxicology and ecotoxicology of selected existing existing industrial chemicals.

In the programme, commodity chemicals, that is those produced in large tonnage by several companies and having widespread and multiple uses, are jointly reviewed by experts from a number of companies with knowledge of the chemical. It should be noted that in a JACC review only the chemical itself is considered; products in which it appears as an impurity are not normally taken into account.

ECETOC is not alone in producing such reviews. There are a number of organisations that have produced and are continuing to write reviews with the aim of ensuring that toxicological knowledge and other information are evaluated. Thus a Producer, Government Official or Consumer can be informed on the up-to-date position with regard to safety, information and standards. Within ECETOC we do not aim to duplicate the activities of others. When it is considered that a review is needed every effort is made to discover whether an adequate review exists already; if this is the case the review is checked, its conclusions summarised and the literature published subsequent to the review assessed. To assist ourselves and others working in this field we publish annually a summary of international activities incorporating work planned, in hand, or completed on the review of safety data for commodity chemicals. Interested readers should refer to our Technical Report No 30 entitled "Existing Chemicals; Literature Reviews and Evaluations".

This document presents a critical assessment of the toxicology and ecotoxicology of dicyclopentadiene (CAS No 77-73-6).

CONTENTS

1. SUMMARY AND CONCLUSIONS

Dicyclopentadiene (DCPD) is a chemical intermediate, used in the manufacture of a wide range of organic chemicals.

The results of biodegradation studies suggest dicyclopentadiene is poorly degraded in soil and water, with estimated half-lives of 1-2 years and 4-7 years respectively. The rate of photolysis in water is slow. In the event of release into top soil or water, concentrations will decrease largely as a result of volatilisation into the atmosphere; the rate of degradation of dicyclopentadiene in air is rapid, the estimated half-life being one day.

Acute and subacute studies indicate that dicyclopentadiene is slightly toxic to fish, algae and a variety of other aquatic species. Although detected in the tissues of fish immediately following exposure, concentrations declined during the period of exposure and rapid decontamination occurred following transfer to clean water. No significant bioaccumulation was seen in duck, quail or plants and a low potential to accumulate was supported by the results of absorption/ excretion studies in mice, rats, dogs and cows.

Distribution studies using ^{14}C-dicyclopentadiene in mice, rats and dogs have shown that up to 85% of orally administered radioactivity appears in the urine or faeces within 24 hours. Tissues containing the highest concentration 1-2 hours after administration were the urinary bladder, gall bladder and body fat; metabolites were found in the urine. In the lactating cow, most dicyclopentadiene was eliminated within 24 hours as glucuronide conjugates in urine; only trace amounts were detected in milk.

Animal studies indicate that the predominant acute systemic effect is on the central nervous system; stimulation is followed by prolonged depression. There is some inter-species variation in susceptibility to the lethal effect of dicyclopentadiene. Percutaneous LD_{50} values indicate that dicyclopentadiene is poorly absorbed through the skin. Prolonged skin exposure under occlusion caused slight redness, a 4-hour exposure under semi-occluded conditions

resulted in well-defined irritation and swelling, whilst non-occluded application to bare skin caused moderate irritation. Direct application of the liquid to the eye caused only slight irritation. Studies in guinea pigs revealed no potential to induce allergic skin reactions.

Studies on the effects of repeated dietary exposure to dicyclopentadiene for up to 90 days in mice and rats revealed no treatment-related effects at nominal concentrations up to 273 ppm or 750 ppm respectively. In a study of similar duration in dogs there was some evidence of gastro-intestinal disturbance at the highest dietary concentration (1,000 ppm nominal). Repeated exposure of mice, rats and dogs to dicyclopentadiene vapour produced reversible kidney lesions in male rats only; the lesions were similar to those of hyaline droplet degeneration produced by certain hydrocarbon solvents. The role of alpha-2μ-globulin accumulation in the aetiology of such lesions and the fact that they are of no relevance to man is widely accepted. The reason for the absence of renal effects in the diet studies has not been investigated.

Dicyclopentadiene does not induce gene mutation in bacterial or yeast assays. Studies in animals indicated there is no selective toxicity to the embryo or foetus or any teratogenic potential. No long-term or carcinogenicity studies have been reported.

The odour of dicyclopentadiene has been reported to be detectable at concentrations as low as 0.003 ppm. Headache was reported in workers following prolonged exposure to low vapour concentrations.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

Common Name : Dicyclopentadiene

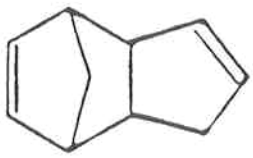
Synonyms: 4,7-Methano-1H-indene, 3a,4,7,7a-tetrahydro-
Bicyclopentadiene
Biscyclopentadiene
3a,4,7,7a-Tetrahydro-4,7-methanoindene
4,7-Methanoindene, 3a,4,7,7a-tetrahydro-
Cyclopentadiene dimer
Tricyclo[5.2.1.02,6]deca-3,8-diene

CAS No: 77-73-6

EINECS No: 201-052-9

Molecular formula: $C_{10}H_{12}$

Structural formula:



Molecular weight: 132.21

2.2 Physical and Chemical Properties

Dicyclopentadiene (DCPD) is a colourless, waxy, flammable solid with a camphor-like odour. Generally, the endo-configuration is present at higher concentrations than the exo-configuration under normal conditions. It is soluble in ethyl alcohol, diethyl ether and acetic acid and sparingly soluble in water. Its physical and chemical data are summarised in Table 1.

2.3 Conversion Factors

1 ppm = 5.40 mg/m^3
1 mg/l = 185 ppm

2.4 Analytical Methods

Methods to determine DCPD are generally based on gas chromatography. Typical conditions for the gas chromatographic analysis of hydrocarbon mixtures like DCPD are given in Table 2.

DCPD has been assayed in air at concentrations in the range of 0.1 - 10 mg/m^3 after absorption on active charcoal and desorption with carbon disulfide. The conditions for gas chromatographic determination were similar to those described in Table 2 (Shell, 1990).

DCPD has been analysed in ground water by gas chromatography/mass spectroscopy following extraction with methylene chloride (Van Breemen et al, 1987) or by gas chromatography, following extraction with carbon disulfide. The latter method is capable of determining DCPD at concentrations of 10 µg/l (Shell, 1990).

2.5 Purity of Commercial DCPD

Commercial samples of DCPD are of different degrees of purity. Typical commercial specifications are:

DCPD 94% - Impurities :

- Acylic dienes <2%
- Cyclopentadiene monomer <3%
- Methylcyclopentadienes <1%
- Inhibitor 100-200ppm

DCPD 92% -	Impurities:	Codimers of cyclopentadiene with isoprene, piperylene, butadiene - total approximately 8% Benzene <0.1% Inhibitor - approx. 100ppm
DCPD 75% -	Impurities:	Codimers of cyclopentadiene with isoprene, piperylene, butadiene - total approximately 23% Benzene approximately 0.05% Inhibitor - approx. 100ppm

More than 50% of DCPD produced is of the 92% and 94% purity grades. Unless otherwise stated in the text, data presented refers to the higher purity grades.

3. PRODUCTION, STORAGE, TRANSPORT AND USE

DCPD is produced commercially by recovery from hydrocarbon streams originating from high temperature cracking of petroleum fractions and as a by-product of the coke-oven industry. It is formed by the spontaneous dimerization of cyclopentadiene in a Diels-Alder addition reaction. Cyclopentadiene and its dimer may be readily inter-converted and the proportion of each present depends on the physical conditions: cyclopentadiene is favoured in the vapour state, particularly at elevated temperatures (above 130^{o}C) and DCPD in the liquid or solid phases. World production in 1989 was estimated to be of the order of 185,000 tonnes (Exxon, 1990a).

DCDP is unstable when stored at temperatures above 50^{o}C at atmospheric pressure; partial polymerisation can occur (Exxon, 1990b). Commercial grades contain small quantities of anti-oxidant inhibitor to prevent peroxide formation.

DCDP is produced as a chemical intermediate for use in the manufacture of alkyd resins, synthetic rubbers, perfume ingredients, plasticizers, flame retardants

pharmaceuticals, paints, lubricants, antioxidants, pesticides and a variety of other organic chemicals (Griesbaum and Hoenicke, 1987; OECD, 1977).

4. ENVIRONMENTAL DISTRIBUTION, BIOTRANSFORMATION AND ENVIRONMENTAL FATE

4.1 Environmental Distribution

The environmental distribution of DCPD at equilibrium has been estimated using the computer programme QSAR, developed and maintained by the Institute for Process Analysis, Montana State University on behalf of the EPA (1989). Taking the solubility in water to be 300 mg/l, the distribution was estimated as 72% in water, 15% in air and 12% in soil and sediment. When taking the solubility in water as 100 mg/l, the distribution was estimated as 55% in water, 35% in air and 10% in soil and sediment.

These results suggest that in the environment a major part of DCPD will be present in water, but also a substantial amount in air. However, uncertainty exists concerning the solubility of DCPD in water (Table 1) which is reported as less than 300 mg/l and probably less than 100 mg/l. If the solubility in water was much below the latter value, then DCPD is expected to partition mainly in air.

Smith et al (1980) calculated the rate of volatilisation of DCPD from water. From the experimentally determined volatilisation rate constant and reported values for oxygen reaeration rate constants in representative water bodies (lake, pond, river), a range of volatilisation rate constants for DCPD in the environment could be estimated. The half-life in water was estimated to range from 1.3-9.9 days. Spanggord et al (1979) estimated a half-life of DCPD in still surface water (marshland) of 5.3 days using a similar experimental method and calculations. Dow (1989) showed 77% removal of DCPD from water with aeration in a 4-hour laboratory test.

Volatilisation thus appears to be rapid when taking the concentration in air to be zero.

4.2 Biotransformation and Environmental Fate

4.2.1 Atmospheric Fate

DCPD will be transformed in air by reaction with hydroxyl radicals and ozone. Its half-life in the troposphere is estimated as less than 0.1 day (Hendry and Kenly, 1979; Atkinson, 1985; OECD, 1990).

4.2.2 Aquatic Fate

Spanggord et al (1979) studied the rate of phototransformation of DCPD in water. The results suggested that DCPD was transformed indirectly, by reaction with reactive species such as hydroxyl radicals and singlet oxygen. Spanggord concluded that the half-life of DCPD through indirect phototransformation in natural water would be about 76 days.

4.2.3 Terrestrial Fate

DCPD is expected to degrade slowly in soil. While the absorption coefficient of 2.9 suggests that only moderate soil adsorption would occur (EPA, 1989), a ^{14}C-DCPD tracer study (O'Donovan and Woodward, 1977) showed that the major portions of the 20 ppm DCPD test samples remained fixed in the soil under experimental conditions. The experiment was designed to observe the stability of DCPD in soil under a moving airstream. After 250 hours, moist soil samples had retained 62% and dry soil samples 95% of their activity.

4.2.4 Biodegradation

DCPD appears not to be readily biodegraded in water or in soil. Spanggord et al (1979) studied the biodegradation of DCPD by micro-organisms. The half-life for microbial decomposition in water was estimated to be 1 to 2 years. Decomposition by micro-organisms in the

soil takes place still more slowly than in water. At a soil temperature of 25°C, the estimated half-life was 4 to 7 years. The growth of water and soil micro-organisms in culture medium was not inhibited when DCPD was added at 10 mg/l or less; higher concentrations slowed growth.

In a 5 day biological oxygen demand test (BOD5) oxygen consumption of less than 4% of the theoretical oxygen demand (ThOD) was observed (Kaczmarek and Palis, 1981). On the basis of these results DCPD can be classified as not readily biodegradable.

4.2.5 Bioaccumulation

Bluegill sunfish (Lepomis macrochirus) were exposed to ^{14}C-DCPD at a concentration in water of approximately 1 mg/l for 14 days. During the first 96 hours the concentration of DCPD in fish muscle tissue increased to 51 mg/kg. Subsequently this concentration decreased rapidly to a constant level of 11 mg/kg during the next 10 days. When placed in pure water the concentration in fish muscle tissue declined to a level of less than 5 mg/kg within 24 hours (Bentley et al, 1976). These results suggest that, after a short adaptation period, DCPD may be metabolised by fish. On the basis of the experimental results during the first 96 hours, the bioaccumulation factor is calculated to be 53. This is in close agreement with calculated values of 37 (Mackay, 1982) and 76 (EPA, 1989). However, the bioaccumulation factor subsequently fell to around 11, possibly due to metabolism.

DCPD did not bioaccumulate in the plasma, liver, adipose tissue, skin, red blood cells, kidney, brain or muscle of Mallard duck (Anas platyrhynchos) or Bobwhite quail (Colinus virginianus) fed diet containing 100 mg DCPD/kg for 3 or 5 days, or dosed once by gavage at 100 mg DCPD in corn oil/kg body weight. In the dietary studies the average DCPD tissue residues were less than 1 ppm, and declined to less than the detection limit (average 0.04 ppm) in most tissues by the 3rd day following withdrawal. All tissues, except quail skin and duck kidney, were clear of DCPD residues by day 5 after withdrawal from radiolabelled diet. In the dosing experiments, the maximum residue of

50 ppm was in quail adipose tissue two hours after dosing. As was seen in the feeding study, DCPD tissue residues decreased rapidly, with a biological half-life of 12.7 hours, so that concentrations in most tissues were near the detection limit after 48 hours (Aulerich et al, 1979). Taking into consideration the rapid elimination of DCPD (see Section 7.2), it is probable that this compound will not significantly bioaccumulate despite its low or negligible water solubility.

O'Donovan and Woodward (1977) observed no uptake of DCPD above a level of 100 ppm in 10 plant species after treatment with DCPD in a water culture system (hydroponic) at concentrations up to level of 1,000 ppm.

On the basis of the above result it is concluded that DCPD has a low potential for bioaccumulation.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

DCPD does not occur naturally and few data on environmental concentration are available. It has been detected in ground water near chemical disposal sites and identified in river water contaminated by industrial and agricultural activities. Drinking water standards and occupational exposure limits have been established.

5.1 Environmental Levels

5.1.1 Air

No data on environmental concentrations could be found, possibly because of short atmospheric half-life (see Section 4.2.1).

5.1.2 Water

DCPD was detected in certain groundwater supplies in Colorado, USA (Burrows, 1977). It arose from the disposal of pesticide wastes in unlined ponds or from deep-well injection at the Rocky Mountain Arsenal.

Although the disposal of these wastes ended no later than 1966, DCPD continued to be detectable in the sub- to low- ppm range in some well-water supplies (quantities not specified). Van Breemen et al (1987) reported that extensive transformation of DCPD occurs in the environment, as evidenced by the many derivatives of the compound still detected in ground water extracts near the Rocky Mountain Arsenal.

DCPD was also detected in drinking water in a survey of water from 13 U.S. cities (Keith et al, 1976). In particular, three drinking water sources on the Mississippi River at New Orleans were investigated because of consumer complaints of "oily" and "chemical" flavours; DCPD was identified (not quantified) in these three samples. It was not found in the water supplies of the other cities studied.

During an evaluation of water treatment methods, DCPD was also identified, at a low concentration, in a sample of water from the River Rhine in the Netherlands (Zoeteman et al, 1982).

In a study of water samples from an aquifer beneath an alkyd resin plant in Italy (Mantica et al, 1986) DCPD and its oxidation products were detected but not quantified.

5.1.3 Soil and Plants

No data on environmental concentrations could be found.

5.2 Hygiene Standards

5.2.1 Occupational Exposure Levels

In the USA (ACGIH, 1989-1990) and The Netherlands (Arbeidsinspectie, 1989), an occupational exposure limit (8 hour TWA) of 5 ppm (27 mg/m^3) has been adopted for DCPD, based largely on the data from animal and human studies published by Kinkead et al (1971). An occupational exposure limit of 0.185 ppm (1 mg/m^3) is reported in the USSR (Shashikina, 1965).

5.2.2 Water Standards

Based on the Rocky Mountain Arsenal investigations the USA Army Medical Bioengineering Research and Development Laboratory (BRDL) suggested temporary maximum levels of DCPD of 1.3 mg/l in drinking water, 13 mg/l in recreational water, 0.5 mg/l to protect aquatic life and 20 mg/l in irrigation water (Burrows, 1977).

More recently (Dacre, 1984) the BRDL has recommended interim criteria for DCPD of 2.84 mg/l for water quality (protection of aquatic organisms) and 3.32 mg/l for drinking water (protection of human health). In the USSR a limit of 0.001 mg/l has been suggested (Taradin et al, 1972).

6. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

6.1 Microorganisms

DCPD caused moderate growth inhibition of the protozoan Tetrahymena pyriformis; the 24 hour I_{50} value for growth inhibition was 5.3 mg/l (Yoshioka et al, 1985). Growth of microorganisms isolated from water and soil samples and subsequently cultured in water with nutrients was not inhibited at DCPD concentrations below 10 mg/l (Spanggord et al, 1979).

6.2 Toxicity to Aquatic Organisms

6.2.1 Fish

The acute toxicity of DCPD to fish is summarised in Table 3. DCPD has a low order of acute toxicity (Rainbow trout, Salmo gairdnery, 96 hour LC_{50} value 16 mg/l) and is practically harmless to fish eggs (Fathead minnow, Pimephales promelas, 144 hour LC_{50} value 2,400 mg/l; DCPD was added as a 1% solution in acetone) (Bentley et al, 1976).

No toxic effects were observed during continuous exposure of Bluegill sunfish (Lepomis macrochirus) for 14 days to approximately 1 mg/l ^{14}C-dicyclopentadiene (Bentley et al, 1976).

6.2.2 Invertebrates

The acute toxicity of DCPD to invertebrate species is summarised in Table 4. DCPD has a low order of toxicity to invertebrates. The 48 hour LC_{50} value for Daphnia magna was 11 mg/l (Bentley et al, 1976) and for Moina macrocopa was 40 mg/l (Yoshioka et al, 1986).

6.2.3 Algae

Toxicity data for DCPD to algae are summarised in Table 5. DCPD has a low order of toxicity to algae. The 96h LC_{50} value for DCPD to Anabeana flos-aquae (blue-green algae) was 22 mg/l and to Selenastrum capricornutum (green algae) >100 mg/l (Bentley et al, 1976).

6.3 Toxicity to Terrestrial Organisms

6.3.1 Mammals

6.3.1.1 Acute Toxicity

No deaths occurred in mink administered 1,000 mg DCPD/kg by gavage (Aulerich et al, 1979). Signs of intoxication were similar to those seen in laboratory rodents (see Section 8.1) and consisted of convulsions, incoordination and other central nervous system effects. Recovery was generally rapid and complete within 90 minutes. Mink administered an intraperitoneal dose of 960 mg DCPD/kg or more died within minutes.

6.3.1.2 Short-term Toxicity

Groups of 5 male and 5 female juvenile mink were administered DCPD at nominal dietary levels of 0, 1, 10, 100, 1,000 or 10,000 ppm for 21

days, after which a recovery period of 7 days on control diet was allowed. At 10,000 ppm, 4 of 5 male and 2 of 5 female mink died; this dietary concentration also reduced the rate of weight gain. Feed consumption was reduced by approximately 20% at a dietary concentration of 1,000 ppm and by approximately 60% at 10,000 ppm. Necropsy revealed severe depletion of body fat and reduced heart, spleen and liver weight in animals receiving 10,000 ppm. The only haemotological effect at this dose was a decreased haematocrit value (Aulerich et al, 1979).

6.3.1.3 Subchronic Toxicity and Reproduction

Groups of 6 male and 24 female 3 month old mink were administered DCPD at nominal dietary levels of 0, 100, 200, 400 or 800 ppm for 12 months. After 9 months the animals were allowed to mate for a period of 20 days. There was a trend towards reduced feed consumption and concomitant lower body weight gain in the top dose animals but the differences did not attain statistical significance. No effects were observed on clinical chemical or haematological indices. Fertility and viability indices were not affected by treatment. Body weight gain of pups during lactation was significantly reduced in a dose related fashion at 200, 400 and 800 ppm. The testes weight of male parents at 800 ppm was significantly less than in controls but no histopathological abnormalities were seen (Aulerich et al, 1979).

The results of this study are consistent with the effects being a consequence of a reduced feed consumption.

6.3.2 Birds

6.3.2.1 Acute Toxicity

Groups of ten male and ten female Mallard duck (Anas platyrhynchos) were administered DCPD by gavage at doses from 0 to 40,000 mg/kg.

The 40,000 mg/kg was administered as 5,000 mg aliquots over a period of 2.5 hours. After 20,000 to 30,000 mg/kg had been given, moderate tremors of the head and body were noted in 10% of the birds. All of the birds recovered within 2 hours after dosing. The LD_{50} was concluded to be greater than 40,000 mg/kg (Aulerich et al, 1979).

Groups of 5 male and 5 female Bobwhite quail (Colinus virginianus) were administered single doses of DCPD, by gavage, ranging from 0 to 1,600 mg/kg body weight. Decreased activity and incoordination were noted after 24 hours. The LD_{50} value for DCPD in quail was 1,010 mg/kg, most deaths occurring within 4 days after dosing; recovery was generally complete after 96 hours (Aulerich et al, 1979).

6.3.2.2 Short-term Toxicity

Ten groups of ten 14 day old Bobwhite quail (Colinus virginianus) were fed on diets containing DCPD at nominal levels of 0, 2,000, 4,000, 6,000, 8,000, 10,000, 12,000, 14,000, 16,000 or 18,000 ppm for 5 days after which the birds received control diet for three days. No significant changes were observed in feed consumption, body weights, mortality or gross pathology. There was no consistent trend in mortality but 20% mortality occurred at 2,000 and 10,000 ppm, while 10% mortality occurred with the top concentration (18,000 ppm). The daily dose of DCPD ingested by Bobwhite quail on diets containing 6,000 ppm or more was in excess of the LD_{50}. The absence of deaths was probably due to the fact that lower blood levels would have occurred than those produced by the gavage administration used in determining the LD_{50} value (Aulerich et al, 1979).

Groups of ten, 12 day old Mallard ducklings (Anas platyrhynchos) were fed diets containing nominally 10,000, 20,000, 30,000, 40,000, 50,000, 60,000, 70,000, 80,000 or 90,000 ppm of DCPD. The reduced food intake was such that the three highest dose groups took hardly any feed; there was a dose related decrease in consumption and the ducklings in the high dose groups ingested less DCPD than those in the lower dose groups. The experiment was terminated after 5 days.

In a subsequent experiment, 23 week old adult Mallard ducks were fed diets containing nominally 0, 10, 100, 1,000, 5,000 or 10,000 ppm DCPD for 32 days. Feed consumption was not affected at any of these levels. Body weight loss occurred in a dose related fashion in birds given diet containing 1,000 ppm DCPD or more. Necropsies showed no evidence of gross pathological change (Aulerich et al, 1979).

6.3.2.3 Subchronic Toxicity and Reproduction

Groups of 15 male and 15 female Bobwhite quail (Colinus virginianus) were administered diets containing nominal DCPD levels of 0, 400, 1,250 or 4,000 ppm for 28 weeks. No dose related differences were found in feed consumption, body weight gain, mortality, egg production, hatchability or egg shell thickness. The liver weight of males at the highest dietary concentration was significantly less than in the control group. No other gross or histopathological abnormalities were found in twelve major organs examined. In addition, no haematological effects were found. Examination of offspring did not reveal any malformations or changes in survival or behaviour. The no-observed-effect levels in this combined subchronic and reproduction study was 1,250 ppm (Aulerich et al, 1979).

In a 22 week subchronic/reproduction feeding study, groups of 15 female and 6 male Mallard duck (Anas platyrynchos) were fed DCPD at nominal dietary levels of 0, 32, 100 or 320 ppm. Dicyclopentadiene did not affect body weight, feed consumption, mortality, egg production, hatchability or egg shell thickness. Gross and histological examination of 12 major organs and haematological examination did not reveal any adverse effect from the test chemical. In addition, no malformations or behavioural effects were seen in offspring. The no observed effect level in this study was > 320 ppm (Aulerich et al, 1979).

6.3.3 Higher Plants

DCPD was included for 5 months at 0, 1, 10, 100 or 1,000 ppm in the nutrient solutions used in hydroponic cultures of 10 plant species. Morphological changes, such as discoloration of foliage, stunted or enhanced growth and biomass were studied. Substantial stunting at the 1,000 ppm treatment was observed, while tissue damage occurred above 100 ppm in most plants (O'Donovan and Woodward, 1977).

Seeds of 5 plant species were treated with irrigation solutions containing 0, 1, 8 or 20 ppm DCPD. After 201 days, entire plants were removed and examined for appearance and weight. No inhibition of seed germination or signs of phytotoxicity were observed at any of the test concentrations (O'Donovan and Woodward, 1977).

7. KINETICS AND METABOLISM

7.1 Human

There are no data available on toxicokinetics or metabolism of DCPD in man.

7.2 Experimental

Hart (1976) studied the toxicokinetics and metabolism of DCPD in mice, rats and dogs. A single oral administration of 40 mg/kgbw of uniformly labelled ^{14}C-DCPD to mice or of 100 mg/kgbw to rats and dogs was rapidly absorbed.

Blood plasma concentrations of DCPD reached a maximum at 2 hours after administration in mice and dogs and at 6 hours in rats. The author considered that graphs of plasma concentration of DCPD against time showed a biphasic decrease of DCPD in all three species. In the rapid phase the half-lives were 4 hours in mice and 10 hours in dogs. The rat data obtained were insufficient to make a precise estimation of the first half-life. For the slow phase, half-lives of 18, 27 and 18 hours for mice, rats and dogs, respectively, were calculated. The results indicated that

absorption and metabolism of ^{14}C-DCPD are similar in mice and dogs while absorption and metabolism in rats appears to be slow and complex. DCPD was widely distributed in all three species after 1 to 2 hours with the highest concentrations occurring in the urinary bladder, gall bladder and body fat of mice, in the gall bladder and bile of dogs and in body fat, adrenals and urinary bladder of rats. Excretion was rapid, 68.5% to 85% of administered radioactivity being excreted in urine and faeces within the first 24 hours in all three species - see below:

Excretion of labelled DCPD in urine and faeces

	Urine	Faeces
Mouse	75%	10%
Rat	53.7%	15%
Dog	64.5%	4%

More than 97% of the radioactivity detected in urine represented metabolized ^{14}C-DCPD. Thin layer chromatography showed three metabolites in rat urine and two in the urine of mice and dogs; enzymatic hydrolysis revealed conjugates in the urine samples. None of these metabolites were identified (Hart, 1976).

A similar pattern of absorption and excretion of DCPD was observed in a lactating cow. The animal, weighing 293 kg, was given 10 mg/kgbw/d of unlabelled DCPD for 5 days and a single oral dose of ^{14}C-DCPD (equivalent to 10 mg/kgbw) on day 6. Administered radiocarbon was rapidly excreted after oral administration of the ^{14}C-DCPD (mostly within 24 hours), about 81% in the urine and about 4% in the faeces; only a trace amount (<0.1%) was secreted into the milk during the 24 hour period after treatment. Analysis of the urine indicated a number of metabolites, present mainly as glucuronide conjugates. Based on the structure of DCPD, it was suggested that these metabolites arose, at least in some cases, through epoxidation of one or both of the DCPD double bonds, followed by hydrolysis of the epoxides to diols (or possibly epoxy diols or tetraols) and conjugation with glucuronic acid (Ivie and Oehler, 1980; Palmer et al, 1981).

Oral dosing and feeding experiments with fowl (Bobwhite quail and Mallard duck) similarly showed that DCPD does not persist for long within the animal's body. Ducks and quail consumed food containing 100 ppm ^{14}C-DCPD for 5 days followed by 5 days on control diet; ^{14}C residues declined to less than detection limits, averaging 0.04 ppm in most tissues by the 3rd day after withdrawal. All tissues except quail skin and duck kidney were clear of residues within 5 days when taken off radioactive diet. In dosing experiments, the rate of elimination of ^{14}C residues from ducks and quail receiving 100 mg/kgbw ^{14}C-DCPD could be calculated for most tissues:

Half-lives (hours) of ^{14}C-DCPD residues in quail and duck tissues

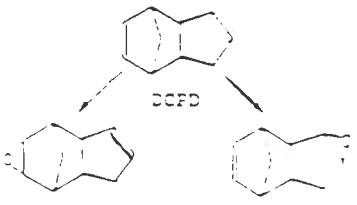
	Plasma	Liver	Adipose	Skin	RBC	Kidney	Brain	Muscle
Quail	11.1	14.7	10.4	11.9	*	14.5	12.5	14.4
Duck	*	13.6	14.8	15.1	*	10.9	13.5	8.3

* Could not be calculated

The average half-life for DCPD in quail and duck tissues was 12.7 hours. Maximum residues at 2 hours were 5.6 to 50.1 ppm, depending on tissue and species. These values declined rapidly; most tissues were at or close to the detection limit at 48 hours (Aulerich et al, 1979).

7.3 Enzymatic Metabolism in Vitro

DCPD was incubated with immobilised, unpurified, rabbit liver cytochrome P-450 and NADPH cofactor overnight at 37°. This resulted in the formation of two major metabolites which were identified as monoepoxides of DCPD by comparison with compounds synthesised in the laboratory.



Monoepoxides of DCPD

These epoxides could be precursors of ketone and hydroxyl-containing derivatives and also of the possible glucuronide metabolites of DCPD detected in cow urine by Ivie and Oehler (1980) (Van Breemen et al, 1987).

8. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS

8.1 Acute toxicity

8.1.1 Oral

LD_{50} values for DCPD indicate a moderate order of acute oral toxicity. Values ranging from 190 (mouse) to 820 (rats) mg/kg body weight have been reported (Table 6).

In the only acute oral toxicity test conducted according to OECD guidelines, the LD_{50} was found to be 590 mg/kg in rats. The purity of the sample (75%) used in this study, was low in relation to samples tested in other studies. Deaths occurred on the day of dosing. Immediately after dosing hunched posture, lethargy, pilo-erection, decreased respiratory rate and red/brown staining of the snout was observed. Survivors appeared normal from the second day after treatment. Necropsy findings consisted of haemorrhagic lungs, dark liver and sloughing of non-glandular gastric epithelium (Blackwell, 1989).

Similar signs have been reported by other authors for both rats and mice dosed with DCPD. Necropsy findings also included hyperaemia of the lungs (Hart, 1976).

8.1.2 Dermal

DCPD has a low order of acute dermal toxicity. LD_{50} values reported in rats and rabbits were greater than 2,000 mg/kg (Table 7).

In the only study conducted according to OECD test guideline 402, none of the rats exposed for 24 hours under occluded conditions to 2,000 mg/kg DCPD died. Signs of systemic toxicity included hunched posture, lethargy, piloerection and ptosis with isolated cases of red/brown staining around the snout. No signs of toxicity were seen after two days. Signs of dermal irritation (erythema, oedema) at the site of application were recorded one day after dosing and eschar was seen up to 12 days after dosing (Jones, 1989a).

8.1.3 Inhalation

Data on the acute inhalation toxicity of DCPD (LC_{50} values) are presented in Table 8.

In studies in rats and mice, wet nares or nasal discharge and loss of coordination, tonic and clonic convulsions and other signs of central nervous system toxicity were observed. The 6 hour LC_{50} values for male and female rats were 284 and 353 ppm and for male and female mice were 143 and 126 ppm respectively (Snellings and Weil, 1981).

Exposure to air saturated with vapour of DCPD (the concentration was not quantified) killed all six male rats within two hours (Smyth et al, 1954) and 50% of an unspecified number of rats in one hour (Kinkead et al, 1971). In a further study, in which rats were exposed to a saturated atmosphere for 30 minutes, no deaths occurred. When exposed for four hours at 1,000 ppm, all six rats died but only one of six rats died when exposed for four hours to 500 ppm (Smyth et al, 1962).

In an experiment on Beagle dogs, the only reaction seen on exposure to 68 ppm DCPD vapour for four hours was urination immediately after exposure in one female. Exposure to 272 ppm caused tremors within three hours, whilst exposure to 458 ppm caused tremors within 15 minutes with signs of eye and nose irritation followed by lacrimation within 50 minutes. Similar signs were seen in a dog exposed to 773 ppm; these were followed by tonic and clonic convulsions within 30 minutes and death after 60 minutes (Kinkead et al, 1971).

Following inhalation exposure, mice died sooner and at lower exposure concentrations than did rats (Snellings and Weil, 1981). This is in agreement with the findings of Kinkead et al (1971) who showed that the order of sensitivity of the species tested was mouse> rat> dog> guinea pig> rabbit.

8.1.4 Intraperitoneal

An LD_{50} value of 0.31 ml DCPD/kg in the rat has been reported without experimental details (Kinkead et al, 1971).

8.2 Skin and Eye Irritation, Sensitisation

8.2.1 Skin Irritation

Smyth et al (1954, 1962) reported moderate irritation of the skin of five albino rabbits after non-occluded exposure to undiluted DCPD. Following 24h occluded application of DCPD, slight erythema persisting for up to 7 to 9 days was reported (Hart, 1976). The skin irritancy of a sample of 75% pure DCPD was tested according to OECD test guideline 404 (Jones, 1989b). A single application of 0.5 ml of undiluted DCPD under a semi-occlusive patch for 4 hours produced well-defined erythema and slight or moderate oedema. (Mean scores for erythema and oedema after 24, 48 and 72 hours were 2 and 2.3 respectively). DCPD was concluded to be moderately irritant to rabbit skin.

8.2.2 Eye Irritation

Smyth et al (1954, 1962) reported only slight corneal damage to the rabbit eye after instillation of 0.5 ml of undiluted DCPD. Some conjunctival irritation was reported following instillation of 0.1 ml DCPD into the rabbit eye (Hart, 1976). The eye irritation potential of 75% pure DCPD was examined according to OECD test guideline 405 (Jones, 1989c). Instillation of 0.1 ml of the undiluted material into the eye caused only slight conjunctival redness in two rabbits after 24 hours. Within one hour a slight dulling of the cornea was seen together with

minor effects on the iris but these effects had disappeared within 24 hours. (Mean of scores after 24, 48, 72 hours for corneal damage and iritis were 0, for conjunctival redness was 0.4 and for conjunctival chemosis was 0.1). It was concluded that DCPD was only slightly irritant to the rabbit eye.

8.2.3 Skin Sensitisation

The skin sensitising potential of DCPD was evaluated in guinea pigs using the Draize technique. Intradermal induction was with a 0.1% solution of DCPD in physiological saline three times a week for a total of ten injections. The dose-volume of the first injection was 0.05 ml, and was 0.1 ml for the other nine injections. Two weeks after the last induction an intradermal challenge dose of 0.05 ml of the same concentration was given. No evidence of sensitisation was seen in the DCPD treated guinea pigs 24 or 48 hours after challenge (Hart, 1976).

A modified Buehler study on 75% pure DCPD in guinea pigs (Dunkin-Hartley) has been reported. The test was carried out in accordance with OECD test guideline 406. Induction was with 0.5 ml of undiluted DCPD on days 0, 2, 4, 7, 9, 11, 14, 16 and 18. Challenge on day 28 was done on day 28 with 0.2 ml of undiluted DCPD. During induction mild erythema was seen, occasionally accompanied by fissuring, superficial cracking and skin thickening. On challenge, no skin responses were seen. It was concluded that DCPD showed no skin sensitising potential (Guest, 1989).

8.3 Subchronic Toxicity

8.3.1 Oral

Groups of 32 male and 32 female young Swiss albino mice were given diets (prepared weekly) containing DCPD at nominal concentrations of 0, 28, 91 or 273 ppm for 90 days. No evidence of toxicity was found at any of the levels administered (Hart, 1976; Hart and Dacre, 1978).

Groups of 30 male and 30 female young Sprague Dawley rats were given diets containing DCPD at nominal concentrations of 0, 80, 250 or 750 ppm for 90 days. Clinical observations and food consumption, body and organ weight, haematology and clinical chemistry studies and gross and microscopic examination of 25 different tissues revealed no signs of toxicity (Hart, 1976; Hart and Dacre, 1978).

Groups of one male and one female Beagle dog were fed diets containing DCPD at nominal concentrations of 0, 40, 125 or 375 ppm for 14 days. Clinical behaviour and food consumption, body and organ weight, haematology and clinical chemistry studies and gross and microscopic examination of 27 different tissues revealed no signs of toxicity (Hart, 1976; Hart and Dacre, 1978).

Groups of 4 male and 4 female Beagle dogs were fed diets containing DCPD at nominal concentrations of 0, 100, 300 or 1,000 ppm for 13 weeks. Clinical behaviour and food consumption, body and organ weight, haematology and clinical chemistry studies and full gross and microscopic examinations were carried out. Treatment produced no significant toxicity; some evidence of gastro-intestinal disturbance (slightly increased frequency of vomiting and soft stools) was recorded in the top dose group (Hart, 1980). Thus the dietary levels having no adverse effects were greater than 270 ppm in mice, 750 ppm in rats and 300 ppm in dogs.

8.3.2 Inhalation

The results of inhalation toxicity studies in mice and rats are summarised in Table 9.

Groups of eight or nine male and ten female B6C3F_1 mice were exposed 6 hours/per day, for 9 days to DCPD vapour at measured concentrations of 0, 5, 33 or 100 ppm. Mice at 100 ppm demonstrated decreased response to stimuli, incoordination and tremors; all had died by the end of the fifth exposure. Some mice at 5 or 33 ppm also showed decreased response

to stimuli but to a lesser extent. No other signs were seen in these dose groups (Snellings and Weil, 1981).

Groups of 6 male and 6 female albino mice were exposed to DCPD vapour at measured concentrations of 0, 47, 72 or 146 ppm 7 hours/day, 5 days/week for 2 weeks. Mice at the top dose had convulsions and died on the first day of exposure. Five mice of each sex died during exposure to 72 ppm. These deaths were not preceded by convulsions and no gross lesions were observed. No deaths occurred at 47 ppm and no adverse signs were observed (Kinkead et al, 1971).

Groups of 45 male and 45 female $B6C3F_1$ mice were exposed to DCPD vapour at measured concentrations of 0, 1.0, 5.1 or 51 ppm 6 hours/day, 5 days/week for 13 weeks (64 exposures). No signs of toxicity were observed (Dodd et al, 1982).

Groups of ten male and ten female Fischer 344 rats were exposed 6 hours/day, for 9 days to measured DCPD vapour concentrations of 0, 5, 33 or 100 ppm. Rats at 100 ppm displayed nasal discharge and body weight gain was significantly lower than in control rats. Kidney/body weight ratio in male rats of all three test groups were slightly increased in a non dose-related fashion. No histopathological examination of the kidneys was undertaken. Rats exposed to 5 ppm or 33 ppm demonstrated no treatment-related effects (Snellings and Weil, 1981).

A group of 2 male and 2 female Wistar rats were exposed 6 hours/day, 5 days per week to DCPD vapour at 250 ppm for a total of 10 exposures and a group of 4 male and 4 female rats to a concentration of 100 ppm for a total of 15 exposures. One rat died after the second exposure to 250 ppm, while survivors exhibited weight loss, irritation of the nares, breathing difficulties, lethargy and tremors. At 100 ppm no signs of toxicity were observed (Gage, 1970).

Groups of 6 male and 6 young female Wistar rats were exposed to DCPD vapour at concentrations of 0, 72, 146 or 332 ppm for 7 hours/day, 5 days/week for 2 weeks. At the top concentration all rats had died

within 4 days. Convulsions occurred from the second exposure and all rats had haemorrhages in lungs and intestines; females also had haemorrhages in the thymus. None of the rats of the two lower exposure groups exhibited adverse clinical signs and no gross lesions were found in these groups (Kinkead et al, 1971).

Groups of 12 male and 12 female Wistar rats were exposed to DCPD vapour at concentrations of 0, 19.7, 35.2 or 73.8 ppm 7 hours/day, 5 days/week for 89 days. Mean body weight gain, kidney and liver weights were slightly increased in a non dose-related fashion in males of all dose groups but not in females. At a concentration of 35.2 ppm, microscopic examination of male animals revealed round cell accumulations, dilated tubules, casts, and tubular degeneration of the kidneys; similar but more severe changes were recorded following exposure at 73.8 ppm. Such lesions were not found in female rats at any dose. No treatment related changes were found in other organs (Kinkead et al, 1971).

Groups of 51 male and 51 female Fischer 344 rats were exposed by inhalation to DCPD vapour at concentrations of 0, 1.0, 5.1 or 51 ppm 6 hours/day, 5 days/week for 13 weeks (64 exposures). No signs of toxicity were seen in the female rats but in male rats the kidneys were affected. Increased kidney weights were observed in male rats from the highest exposure group killed after only 10 exposures. Results of urinalysis indicated renal dysfunction within four weeks and histopathological examination of the kidneys revealed dose-related protein accumulation in the proximal tubules, tubular compensatory hyperplasia, interstitial nephritis and glomerular basement membrane thickening after 2 or more weeks of treatment. All male test groups had kidney effects, the extent of which was dose related. The effects subsided with termination of exposure. In the recovery period the relationship of the severity of renal effects to DCPD exposure was compromised because of the occurrence of spontaneous chronic glomerulonephrosis which is normal for ageing male Fischer 344 rats (Dodd et al, 1982).

Single male beagle dogs were exposed to DCPD vapour at concentrations of 0, 20, 47 or 72 ppm, 7 hours/day, 5 days/week for 2 weeks. Following exposure at 72 ppm, the dog was inactive; at 47 ppm, the dog had diarrhoea and excessive salivation on day 2 and lacked control of hind legs on day 9 of exposure. All dogs gained weight normally during exposure and no dose-related gross lesions were observed at necropsy (Kinkead et al, 1971). Thus the atmospheric concentrations having no adverse effects, other than of the kidney (see 8.3.2.1), over a 3 month exposure period were 50 ppm in mice, 70 ppm in rats and 30 ppm in dogs.

Groups of 3 male Beagles were exposed to DCPD vapour at levels confirmed by gas-chromatography of 0, 8.9, 23.5 or 32.4 ppm 7 hours/day, 5 days/week for 89 days. No significant signs of toxicity were seen during or after the exposure period (Kinkead et al, 1971).

Thus the atmospheric concentrations having no adverse effects, other than of the kidney (see Section 8.3.2.1), over a 3 month exposure period were 50 ppm in mice, 70 ppm in rats and 30 ppm in dogs.

8.3.2.1 Dicyclopentadiene - Effects on the Kidney

The results of inhalation studies in rats in which histopathological examination of the kidneys has been undertaken (Kinkead et al, 1971 and Dodd et al, 1982) indicate the kidney as target organ in male rats. No such changes were seen in female rats or in mice (Dodd et al, 1982) or dogs of either sex (Kinkead et al, 1971). Taken together, these observations suggest that DCPD belongs to the group of chemicals which produce kidney damage in male rats by a mechanism involving alpha-2μ-globulin.

Alpha-2μ-globulin, a protein found in male rats (but not in female rats or in either sex of mouse, dog or man), is synthesised by the liver and subsequently transported to the kidney. It is normally present in the cytoplasm of the proximal convoluted tubules of untreated animals in the form of hyaline droplets, visible by light microscopy. Some xenobiotics or their metabolites become bound to

the alpha-2μ-globulin in the liver of animals; this conjugate is more difficult to hydrolyse than alpha-2μ-globulin and induces the formation of excess hyaline droplets which accumulate in the kidney tubules (Swenberg et al, 1989). Accumulation of the chemical/alpha-2μ-globulin complex causes lysosomal protein overload and necrosis of the cells, with subsequent cellular regeneration.

A small increase of nephropathy in male rats (tubular mineralisation and epithelial hyperplasia of the renal pelvis) and tubular neoplasia has resulted from lifetime exposure of experimental animals to a number of such substances. The compounds tested did not produce any such changes in female rats or in mice of either sex. To explain this species- and sex-specific phenomenon, special investigations have been carried out (Olson et al, 1986; Lock et al, 1987; Charbonneau and Swenberg, 1988; Goldsworthy et al, 1988; Lehmann-McKeeman and Cladhill, 1988) on d-limonene, decalin, trimethylpentane (TMP), p-dichlorobenzene and chlorinated hydrocarbons. Berghoff and Swenberg (1989) have suggested that in view of the absence of alpha-2μ-globulin in humans, such effects are of no relevance for man.

No effects on the kidneys of rats were reported following exposure to DCPD in the diet for up to 90 days (Hart, 1976; Hart and Dacre, 1978) at nominal concentrations up to 750 ppm. This apparent divergence from the results of the inhalation studies reported for rats may be due to volatilisation of DCPD from the test diets since no data on diet analysis were presented to confirm the reported exposure concentrations. However other causes such as differences in the rates of absorption following exposure by different routes or variations in metabolism following absorption at different sites, could also contribute to the lack of kidney effect following ingestion.

8.4 Mutagenesis

The results of mutagenicity tests on dicyclopentadiene are summarised in Table 10.

8.4.1 Gene Mutation in Bacteria; Ames Salmonella Test

DCPD did not increase the number of reverse mutations in plate incorporation assays using Salmonella typhimurium strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538. All strains were tested both in the presence or absence of metabolic activation (Arochlor 1254 - induced rat liver microsomal fraction), at doses from 0 to 5,000 µg/plate (Simmon and Kauhanen, 1978). Negative results were also reported in a later study using the same strains of bacteria exposed to DCPD at doses from 0.001 to 5µl per plate. The top dose was reported to be cytotoxic to all strains (Hart, 1980).

DCPD was also found to give negative results in an assay on Salmonella typhimurium strains TA 98, TA 100, TA 1535 and TA 1537 with or without metabolic activation by Arochlor 1254 induced microsomal liver preparations from male Sprague Dawley rats or male Syrian hamsters. Concentrations used were from 0 to 333 µg/plate. The highest dose was always cytotoxic to the bacteria, indicating that the chosen doses were adequate (Zeiger et al, 1987).

8.4.2 Yeast Assays

DCPD did not cause mitotic gene conversion in the yeast Saccharomyces cerevisiae strain D4. This test was done both with and without metabolic activation (Arochlor 1254 induced rat liver microsomal fraction). Test doses varied from 0.001 to 10µl per plate, the top dose being cytotoxic to the yeast (Hart, 1980).

Similar negative results were obtained in a study using Saccharomyces cerevisiae strain D3, both in the presence or absence of a rat liver metabolic activating system; DCPD was included at a range of

concentrations between 0 and 0.09%. Concentrations greater than 0.015% were toxic to the test system (Simmon and Kauhanen, 1978).

8.4.3 Mammalian Cells In Vitro

No test have been reported on the clastogenic or mutagenic effect of DCPD in mammalian cells in vitro.

8.5 Chronic Toxicity and Carcinogenicity

No studies have been reported. However, Rosenblatt et al (1975) cite a carcinogenicity study by intramuscular injection sponsored by the US National Cancer Institute at the Institute of Chemical Biology, University of San Francisco. No details were provided but DCPD was not considered to be carcinogenic under the conditions of the experiment.

Evidence from long-term inhalation studies on gasoline (Short and Swenberg, 1988) and isophorone (NTP, 1986) in which the kidney lesions described in 8.3.2.1 were shown to progress to formation of kidney cancers, suggest that long-term exposure to DCPD will also lead to development of kidney cancers in male rats one via a non-genotoxic mechanism. This is not considered to indicate a hazard to man.

8.6 Developmental and Reproductive Toxicity

8.6.1 Teratology

Groups of 20 female pregnant Sprague Dawley rats were given diets containing DCPD at nominal concentrations of 0, 80, 250 or 750 mg/kg of feed from days 6-15 of gestation. On day 19, the dams were sacrificed and examined; each uterus was examined for implantation sites, placement in uterine horns, number of live and dead foetuses and resorptions. Foetuses were examined for soft tissue changes and skeletal abnormalities. No compound-related gross pathological effects or changes in reproductive performance were seen in the dams. There were no visceral or skeletal malformations or changes in sex ratio in the

foetuses. Only normal variations were observed (Hart, 1980). The highest nominal dietary concentration, 750 ppm, represents an intake of approximately 150 mg/kg body weight/day, assuming a pregnant rat eats 200 g of feed per kg body weight per day.

8.6.2 Reproduction

In a three generation reproduction study, groups of 10 male and 20 female Sprague Dawley rats were given diets containing DCPD at nominal concentrations of 0, 69.3 or 693 ppm. Examination of litter data, fertility-, survival- and lactation indices, body weights, food consumption and gross pathology findings on parental, F_1, F_2 and F_3 generations revealed no compound related effects on reproductive performance (Hart, 1980). The highest nominal dietary concentration, 693 mg/kg diet, represents a daily intake of 50 mg/kg body weight assuming a rat eats 70 g of feed per kg body weight per day; during pregnancy it represents an intake of 140 mg/kg body weight, assuming a pregnant rat eats 200 g of feed per kg body weight per day.

8.7 Toxicity to Domestic Animals

Groups of 2 male and 2 female 8-10 week old calves of mixed breed were administered single oral doses by gastric intubation of 250, 500, 1,000 or 2,000 mg DCPD/kg body weight. No control group was employed. Blood and urine was collected 1 and 12 days before and 1, 3, 7 and 14 days after dosing. Following necropsy, 21 different tissues were examined by histopathology. All four calves receiving 2,000 mg DCPD/kg died within 6 days. One calf receiving 1,000 mg DCPD/kg died on day 3. Signs of intoxication included excessive salivation, anorexia and ataxia at 250 mg/kg; more severe clinical signs were seen at a dose of 500 mg/kg including prostration, tonic and clonic spasms and incoordination. At a dose of 1,000 mg/kg, the same signs occurred sooner and were more intense.

Slight dose-related increases were seen in erythrocyte counts, haemoglobin and haematocrit values in all dose groups, returning to pretreatment levels within 3 days. The morphology of the various types of leucocytes appeared

normal, although the total leucocyte count was increased at doses of 500 mg/kg or greater. Neutrophilia and lymphocytopenia were also reported. Increases in serum creatine phosphokinase (CPK), glutamic oxalacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) enzyme activities occurred at doses of 1,000 and 2,000 mg DCPD/kg; these returned to normal by day 14.

Gross lesions observed at autopsy of animals given DCPD at 1,000 mg/kg consisted of congestion of the lungs, small intestine, rumen and abomasum. These effects were also seen in animals given 2,000 mg DCPD/kg but in addition there was meningeal and renal congestion and epicardial bleeding. One calf given 250 mg/kg developed severe pneumonia. On microscopic examination, congestion of meningeal and cerebral vessels was confirmed at 2,000 mg/kg. Small haemorrhages were seen in brains of some but not all calves given 1,000 mg DCPD/kg (Cysewski et al, 1981).

9. EFFECTS ON MAN

During the first 2 months of a 5 month period of inadvertent exposure to DCPD vapour (concentrations not reported), 3 workers experienced transitory headaches. No symptoms were observed during the subsequent three months. The authors concluded "that man can become hardened to DCPD vapour". Two volunteers inhaled DCPD vapour at concentrations of 1 ppm or 5.5 ppm for 30 minutes. Sporadic eye and throat irritation was reported after exposure (Kinkead et al, 1971).

To determine the odour threshold for DCPD vapour, three volunteers were exposed to a series of DCPD concentrations for approximately 10 seconds. The odour threshold appeared to be slightly below 0.003 ppm (Kinkead et al, 1971). In a more recent study, Amoore and Hautala (1983), reported an air odour threshold of 0.0057 ppm.

10. FIRST AID AND SAFE HANDLING ADVICE

10.1 First Aid and Medical Treatment

Eye contact: Irrigate immediately with water for at least 15 minutes. Obtain medical advice.

Skin contact: Contaminated clothing, including shoes, should be removed and the affected skin area should be washed in flowing water or shower. Use of soap may help to remove the product.

Inhalation: Remove to fresh air. If not breathing, give mouth-to-mouth resuscitation; if breathing is difficult, give oxygen and obtain medical assistance.

Ingestion: Do not induce vomiting. Call a physician and/or transport to emergency facility immediately.

10.2 Safe Handling

Personal protection: Adopt engineering practices which eliminate exposure. Where not possible, ventilation may be required. General and/or local exhaust ventilation should control airborne levels below the appropriate occupational exposure limit.

Respiratory protection: Atmospheric levels should be maintained below appropriate occupational exposure limit. When respiratory protection is required for certain operations (eg. maintenance), use an approved air-purifying respirator. For emergency and other conditions where exposure guidelines may be

greatly exceeded, use an approved positive pressure self-contained breathing apparatus.

Eye and skin protection: Use safety glasses with side shields, long sleeves and chemical resistant gloves.

Storage: Store in properly designed and approved containers. Suitable: inorganic, zinc, epoxy resins, phenolic resins, carbon steel, stainless steel, cast iron, Monel, coating resins.
Unsuitable: amine epoxy, rubber.

10.3 Management of Spillage and Waste

Leaks of vapour or spills of liquid can readily form flammable mixtures at temperatures at or above the flash point. The product can accumulate static charges which can cause an incendiary electrical discharge. Remove all sources of ignition. Ventilate enclosed areas. Prevent liquid or vapour entering sewers.

Small spill or leak: absorb with suitable agent such as sand or vermiculite; after removal of loaded absorbent, wash the area with soap and water.

Large spill: contain with bunds, cover with foam, pump water into the area, recover DCPD to be burnt or purified for re-use.

Disposal: Incinerate in properly designed furnaces; comply with relevant regulations on such disposal.

Fire: Extinguishing media are water fog, foam, alcohol foam, CO_2 or dry chemical.

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Table 1

Physical and Chemical Data for Dicylopentadiene *

		Reference
Molecular weight	132.21	
Physical form	waxy solid	
Relative density at 35°C	0.9770	1
Boiling point °C at 1013hPa	172.8	1
Melting point °C	32.5	1
Refractive index at 35°C n_D	1.5050	1
Vapour pressure hPa at 20°C	1.86	9
hPa at 37,8°C	6.3	8
hPa at 47,6°C	13.3	5
hPa at 77,9°C	53.3	6
hPa at 101,7°C	101.3	6
Concentration (ppm) in saturated air at 20°C and 1013hPa	1842	9
Vapour density (air = 1)	4.57	2
Critical pressure MPa	3.04	1
Critical temperature °C	383	1
Surface tension at 37°C mN/m	3.17×10^{-2}	8
Flashpoint °C	41	1
Flashpoint °C	32.2	3
Auto ignition temp °C	503	8
Heat of combustion kJ/kg	41,870	1
Heat of vapourization at B.p. kJ/kg	321.8	1
Heat of fusion at m.p. kJ/kg	95,385	1
Solubility : water	<0.03%	7
	<0.01% (estimated)	4
soluble in ethanol, diethylether and other organic solvents		
Octanol/water part. coeff (Log Kow)	2.89 (calculated)	7
Henry's constant (Log H) atm m^3/mole	-3.36	7

* purity > 90 %

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1 Griesbaum and Hoenicke (1987)
2 Veschueuren (1983)
3 Sax (1979)
4 Rippen (1990)
5 Weast (1975-1976)
6 Weast (1988-1989)
7 EPA (1989)
8 SHELL (1984)
9 Kinkead et al (1971)

Table 2. Gas Chromatographic Conditions for the Analysis of DCPD

Column	Fused silica capillary	Fused silica capillary
Dimensions	50 m / 0.25 mm	60 m / 0.32 mm
Coating	OV-101 or CP Sil 5 CB	Durabond-1
Injection temp	200°C	175°C
Temp. Program	Injection at 80°C Isotherm 8 min. at 80°C 80°C-200°C rate 4°C/min. Isotherm at 200°C	Injection at 50°C Isotherm 6 min. at 50°C 50°C-275°C rate 5°C/min. Isotherm at 275°C
Detector	Flame ionisation	Flame ionisation
Carrier gas	Helium or nitrogen	Hydrogen
Injection	0.3 ul liquid	0.3 ul liquid
Reference	Dow, 1990	Shell, 1990

Table 3. Acute Toxicity of Dicyclopentadiene to Fish

Species	Exposure Time (hr)	LC50 (mg/l)	Reference
Red killifish (Orizias Latipes)	48	25	Yoshioka et al, 1986
Rainbow trout (Salmo gairdneri)	96	16	Bentley et al, 1976
Channel catfish (Ictalurus punctatus)	96	16	idem
Bluegill sunfish (Lepomis macrochirus)	96	23	idem
Fathead minnow (Pimephales promelas)			
- Eggs	144	2400	idem
- 1h post-hatching	96	23	idem
- 7-day post-hatching	96	12	idem
- 30-day post-hatching	96	86	idem
- 60-day post-hatching	96	100	idem

Table 4. Acute Toxicity of Dicyclopentadiene to Invertebrates

Species	48 h LC50 (mg/l)	Reference
Daphnia magna (water flea) <24 h old	11	Bentley et al, 1976
Moina macrocopa (water flea)	40	Yoshioka et al, 1986
Asellus militaris (sowbug)	15	Bentley et al, 1976
Gammarus fasciatus (scud)	21	idem
Chironomus tentans (midge) 2nd-3rd instar	120	idem
Dugesia japonica (flatworm)	50	Yoshioka et al, 1986

Table 5. Acute Toxicity of Dicyclopentadiene to Algae

Species	96 h LC50 (mg/l)	Reference
Blue - green algae		
Anabeana flos-aquae	22	Bentley et al, 1976
Microcystis aeruginosa	31	idem
Green algae		
Selenastrum capricornutum	> 100	idem
Diatomae		
Navicula pelliculosa	53	idem

Table 6.

Acute Oral LC50 values for Dicyclopentadiene

Species	Strain	Number of animals/dose	LD50 value (mg/kg body wt)	Reference
Rat	Wistar	-	346.5	Kinkead et al, 1971
Rat	Wistar	5M	820	Smyth et al, 1954
Rat	Carworth	5M	400	Smyth et al, 1962
Rat	Sprague-Dawley	10M	520	Hart, 1976; Hart and Dacre, 1978
Rat	Sprague-Dawley	10F	378	Hart, 1978; Hart and Dacre, 1978
Rat	Sprague-Dawley	5M+5F	590*	Blackwell, 1989
Mouse	Swiss Webster	10M	190	Hart, 1976; Hart and Dacre, 1978
Mouse	Swiss Webster	10F	250	Hart, 1976; Hart and Dacre, 1978

* Material tested had a purity of 75%, for composition see Section 2.5

Table 7.

Acute Dermal LC50 values for Dicyclopentadiene

Species	Strain	Number of animals/dose	LD50 value (mg/kg body wt)	Reference
Rat	Sprague - Dawley	5M + 5F	> 2000*	Jones, 1989a
Rabbit	New Zealand	4M	6600	Smyth et al, 1954
Rabbit	New Zealand	4M	4380	Smyth et al, 1962
Rabbit	Not specified	Not specified	4990	Kinkead et al, 1971

* Material tested had a purity of 75%; for composition see Section 2.5

Table 8.

Acute Inhalation LC50 values for Dicyclopentadiene

Species	Strain	Number of animals/dose	LD50 value (4h exposure)	Reference
Rat	Fischer 344	6M	284 ppm*	Snellings and Weil, 1981
Rat	Fischer 344	6F	353 ppm*	idem
Rat	albino	6M	<2000 ppm	Smyth et al, 1954
Rat	Wistar	2M + 2F	<1000 ppm	Gage, 1970
Rat	albino	6M or 6F	500-1000 ppm	Smyth et al, 1962
Rat	Not specified	6M	359 ppm	Kinkead et al, 1971
Rat	Not specified	6F	385 ppm	idem
Mouse	B6C3F1	6M	143 ppm*	Snellings and Weil, 1981
Mouse	B6C3F1	6F	126 ppm*	idem
Mouse	Not specified	6F	145 ppm	Kinkead et al, 1971
Guinea pig	Not specified	6M	771 ppm	idem
Rabbit	Not specified	4M	771 ppm	idem
Dog	beagle	1F	458-773 ppm	idem

* 6 hour exposure

Table 9. Subacute and Subchronic Inhalation Toxicity of Dicyclopentadiene

SPECIES AND STRAIN (Group size)	EXPOSURE CONCENTRATION (ppm)	DURATION OF EXPERIMENT (Exposure Period)	OBSERVATION AND REMARKS	REFERENCE
Mouse - B6C3F1 (8-9 M/10 F)	5 33 100	9 d (6 h/d)	Decreased response to stimuli. Decreased response to stimuli. Decreased response to stimuli; incoordination and tremors. All died after 5th exposure.	Snellings and Weil, 1981
Mouse Albino (6 M/6 F)	47 72 146	2W, 5 d/w (7 h/d)	No deaths; no adverse signs. Convulsions; 5 of each sex died. Convulsions; all died first day of exposure.	Kinkead et al, 1971
Mouse - B6C3F1 (45 M/45 F)	1 5.1 51	13W, 5 d/w (6 h/d)	)) No signs of toxicity observed in any group.)	Dodd et al, 1982
Rat-F-344 (10 M/10 F)	5 33 100	9 d (6h/d)	No treatment related effects. No treatment related effects. Wet nares and red-black crusty nasal discharge. Significantly lower body wt. gain. Non dose-related increase in kidney/wt. ratio in male rats	Snellings and Weil, 1981
Rat - Wistar (4 M/4 F) (2 M/2 F)	100 250	3W, 5 d/w (6 h/d) 2W, 5 d/w (6 h/d)	No signs of toxicity observed. Wt. loss, nose irritation, breathing difficulties lethargy and tremors (1 death)	Gage, 1970

Table 9. Subacute and Subchronic Inhalation Toxicity of Dicyclopentadiene (cont.)

SPECIES AND STRAIN (Group Size)	EXPOSURE CONCENTRATION (ppm)	DURATION OF EXPERIMENT (Exposure Period)	OBSERVATION AND REMARKS	REFERENCE
Rat - Wistar (6 M/6 F)	72 146 332	2W, 5 d/w (7 h/d)	No adverse clinical signs. No gross lesions No adverse clinical signs. No gross lesions. All rats died by day 4; Convulsions, haemorrhages in lungs and intestines, and thymus (females only)	Kinkead et al, 1971
Rat - Wistar (12 M/12 F)	19.7 35.2 73.8	13W, 5 d/w (7 h/d)	No treatment related effects. Round cell accumulations, dilated tubules, casts, and tubular degeneration of the kidneys; greater frequency and severity in males. Non dose-related increase in liver and kidney weight in male rats.	Kinkead et al, 1971
Rat-F-344 (51 M/51 F)	1 5.1 51	13W, 5 d/w (6 h/d)	All male groups had dose-related kidney effects, including : increased wt., protein accumulation in the proximal tubules. Recovery groups indicated reversibility of effects. No signs of toxicity in females.	Dodd et al, 1982
Dog - Beagle (1 M)	20 47 72	2W, 5 d/w (7 h/d)	No effects reported. Diarrhoea, excessive salivation, lack of control hind limbs. Inactive without other signs.	Kinkead et al, 1971
Dogs - Beagle (3 M)	8.9 23.5 32.4	13W, 5 d/w (7 h/d)	No significant signs of toxicity were seen during or after the exposure period	Kinkead et al, 1971

Table 10.

Mutagenicity Tests on Dicyclopentadiene

Mutation Type	Test System	Metabolic Activation	Results	Reference
Gene mutation	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538	+/- S9	(-)ve	Simmon and Kauhanen, 1978
	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538	+/- S9	(-)ve	Hart, 1980
	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537	+/- S9	(-)ve	Zeiger et al, 1987
	Saccharomyces cerevisiae strain D3	+/- S9	(-)ve	Simmon and Kauhanen, 1978
	Saccharomyces cerevisiae strain D4	+/- S9	(-)ve	Hart, 1980

APPENDIX 1

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No.19	Joint Assessment of Commodity Chemicals, Dicyclopentadiene

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