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IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

Volume 53
Occupational Exposures in Insecticide Application, and Some Pesticides

Summary of Data Reported and Evaluation

Insecticides

Fungicides

Herbicides

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OCCUPATIONAL EXPOSURES IN SPRAYING AND APPLICATION OF INSECTICIDES (Group 2A)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 45)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Chemicals have been used to control insects for centuries but have come into widespread use only within the past century, with the development of a variety of synthetic insecticides. Of the several hundred chemicals that have been applied for insecticidal purposes, fewer than one hundred have been used extensively.

The principal classes of compounds that have been used as insecticides are organochlorine, organophosphorus, carbamate and pyrethroid compounds and various inorganic compounds. Insecticides comprise a higher proportion of the total pesticide usage in developing countries than in developed countries.

Insecticides are applied by aerial spraying and by various ground-based techniques, ranging from hand-held sprayers and dusters to vehicle-mounted hydraulic sprayers, air sprayers, foggers and power dusters.

Occupational exposures occur in the mixing and loading of equipment and in the spraying and application of insecticides. Absorption resulting from dermal exposure is the most important route of uptake for exposed workers.

5.2 Carcinogenicity in humans

5.2.1 *Descriptive and ecological studies*

Several death certificate case-control studies in the USA evaluated cancer risks in association with ecological measures of insecticide exposure. The risk for multiple myeloma tended to be greater for farmers residing in counties where insecticides were more heavily used, but that for leukaemia did not.

5.2.2 *Cohort studies*

A cohort of workers from a large pest control company in the USA had an excess lung cancer risk. Similarly, in a cohort of licensed pest control workers from Florida, there was significantly increased mortality from lung cancer, which was particularly high among workers licensed for 20 years or more; a nonsignificant excess risk for brain cancer was also seen. A follow-up of deaths among plant protection workers and agronomists in eastern Germany showed an increased risk of lung cancer which also increased with length of exposure; survey data indicated that the smoking habits of these pesticide workers were similar to those of the general population.

Among farmers licensed for pesticide use in the Piedmont region of Italy, increased risks for skin cancer and malignant lymphomas were reported; lung cancer incidence was not studied.

A cohort of licensed pesticide applicators in Sweden showed excess risks for cancers of the lip and testis, a slight excess risk for Hodgkin's disease, and risks similar to those of the general population for non-Hodgkin's lymphoma and soft-tissue sarcoma. Overall, there was a deficit of lung cancer risk that was probably related to the lower smoking rates of the applicators.

In a study of a large cohort of grain millers in the USA, flour-mill workers had excess risks for non-Hodgkin's lymphoma and pancreatic cancer; the risk for lung cancer was not increased.

5.2.3 *Case-control studies*

The risk for non-Hodgkin's lymphoma rose with frequency of use of organophosphorus insecticides among farmers in Nebraska, an association that could not be accounted for by use of phenoxyacetic acid herbicides. In Kansas, the risk increased slightly with frequency of use of insecticides as a group. In a study in Washington State, non-Hodgkin's lymphoma was associated with potential contact with chlordane and DDT. DDT use was also associated with non-Hodgkin's lymphoma in one of two studies in Sweden.

Multiple myeloma was associated with use of pesticides (particularly organochlorine insecticides) in a study in the USA. The risk for multiple myeloma was also elevated among farmers in the USA exposed to unspecified herbicides and pesticides.

The results of six studies in Sweden and the USA on soft-tissue sarcoma in association with exposure to insecticides were inconsistent.

Chronic lymphocytic leukaemia has been associated with use of insecticides in the USA and with use of DDT in Sweden.

The risk for brain cancer was associated with exposure to insecticides and fungicides in farmers in Italy.

Overall, the strongest evidence that exposure to nonarsenical insecticides causes cancer in humans comes from the cohort studies of applicators. Two of these studies showed significant excesses of lung cancer. Two showed rising risks with duration of exposure, whereas the third showed an inverse association. These findings were based on small numbers in the subgroups with the longest exposure, and applicators in some of these studies had potential contact with arsenical insecticides. Some case-control studies of multiple myeloma and other tumours of B-cell origin show small excesses among people exposed to insecticides. In most studies, however, potential confounding by other agricultural exposures had not been fully explored.

5.3 Other relevant data

In a study in India, an excess of spontaneous abortions was reported among couples exposed to several pesticides in grape gardens. In a population in Colombia, where exposure to many different pesticides occurred, increased risks for spontaneous abortion and decreased birth weight were reported.

Several studies on the cytogenetic effects of work with pesticide formulations are described. Only in the case of ethylene dibromide and phosphine was exposure to a single, identified insecticide. No cytogenetic effect was observed with exposure to ethylene dibromide, while a significant excess of chromosomal aberrations was observed among the phosphine fumigators. All other studies were of workers handling not only a mixture of insecticide formulations but also other pesticide formulations. The majority of these studies reported increases in the frequency of chromosomal aberrations and/or sister chromatid exchange among the exposed workers. With the exceptions noted above, in no instance, however, could the involvement of non-insecticides be eliminated.

5.4 Evaluation

There is *limited evidence* that occupational exposures in spraying and application of nonarsenical insecticides entail a carcinogenic risk.

Overall evaluation

Spraying and application of nonarsenical insecticides entail exposures that are *probably carcinogenic to humans (Group 2A)*.

For definition of the italicized terms, see Preamble Evaluation.

N.B.: Arsenic and arsenic compounds are carcinogenic to humans (IARC,1987). This evaluation applies to the group of chemicals as a whole and not necessarily to all individual chemicals within the group.

Last updated: 20 November 1997

ALDICARB
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 93)

CAS No.: 116-06-3
Chem. Abstr. Name: 2-Methyl-2-(methylthio)propanal, *O*-[(methylamino)carbonyl]oxime

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Aldicarb is a moderately persistent systemic insecticide, acaricide and nematicide formulated as granules. It was first used in 1970 and is applied mainly on cotton and potatoes.

Exposure to aldicarb may occur during its production and application and, at lower levels, *via* contamination of groundwater and consumption of food containing residues.

5.2 Carcinogenicity in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Aldicarb has not been tested adequately for carcinogenicity in experimental animals.

5.4 Other relevant data

Aldicarb is highly acutely toxic: it is one of the most potent cholinesterase-inhibiting carbamate insecticides.

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

Aldicarb induced chromosomal aberrations in rat bone-marrow cells *in vivo*. It induced various kinds of chromosomal damage and gene mutation in cultured human cells and induced gene mutation in rodent cells. It did not cause mutation in bacteria.

5.5 Evaluation

No data were available from studies in humans.

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

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- AI3-27 093
- ENT 27 093
- 2-Methyl-2-(methylthio)propionaldehyde, *O*-methylcarbamoyloxime
- OMS 771
- Temik
- UC 21149

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CHLORDANE AND HEPTACHLOR
Chlordane (Group 2B)
Heptachlor (Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 115)

Chlordane
CAS No.: 57-74-9

Chlordane [technical grade]
CAS No.: 12789-03-6

***cis*-Chlordane**
CAS No.: 5103-71-9

***trans*-Chlordane**
CAS No.: 5103-74-2

γ-Chlordane
CAS No.: 5566-34-7

Heptachlor
CAS No.: 76-44-8

Heptachlor epoxide
CAS No.: 1024-57-3

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Chlordane has been used since the 1950s as a broad-spectrum contact insecticide, mainly for nonagricultural purposes and to a lesser extent on crops and on livestock. Since the mid-1970s, its use has generally been restricted to underground control of termites.

Heptachlor has been used since the 1950s as an insecticide in agriculture and in the control of termites and soil insects. Like chlordane, its use is now largely restricted to subsoil treatment for termites.

Chlordane and heptachlor have been formulated as granules, emulsifiable concentrates and solutions.

Both compounds can persist in soil for many years. Human exposure to chlordane and heptachlor occurs mainly during their application and in the air of buildings where they have been applied for termite control. When these compounds were used on crops, exposure may have occurred at much lower levels as a result of consumption of foods containing residues.

5.2 Carcinogenicity in humans

Case reports of leukaemia and other blood dyscrasias have been associated with exposure to chlordane/heptachlor, primarily in domestic situations.

Mortality from lung cancer was slightly elevated in two cohort studies of pesticide applicators and one of chlordane/heptachlor manufacturers. Termite control operators probably have greater exposure to chlordane than other pesticide applicators; however, in one study of applicators, the excess occurred only among workers who were not engaged in termite control. In the other study of applicators, the relative risk for lung cancer among workers engaged in termite control was similar to that of workers engaged in other pest control. Inconsistencies in these findings make it difficult to ascribe the excesses to exposure to chlordane.

Small excess risks for other cancers, including leukaemia, non-Hodgkin's lymphoma and soft-tissue sarcoma and cancers of the brain, skin, bladder and stomach were observed, with little consistency among studies.

5.3 Carcinogenicity in experimental animals

Chlordane, technical-grade chlordane, heptachlor, technical-grade heptachlor, heptachlor epoxide and a mixture of heptachlor and heptachlor epoxide have been tested for carcinogenicity by oral administration in several strains of mice and rats. These studies uniformly demonstrate increases in the incidence of hepatocellular neoplasms in mice of each sex. Increases in the incidence of thyroid follicular-cell neoplasms were observed in rats treated with chlordane and technical-grade heptachlor. An increased incidence of malignant fibrous histiocytomas was observed in one study in male rats treated with chlordane. A small increase in the incidence of liver adenomas was seen in one study in male rats treated with technical-grade chlordane.

5.4 Other relevant data

Metabolites of chlordane and heptachlor, like those of other chlorinated hydrocarbons, accumulate in human fat. Chlordane and heptachlor induce liver microsomal enzymes. The liver is the target organ for chronic toxicity.

No data were available on the genetic and related effects of chlordane or heptachlor in humans.

Chlordane and heptachlor did not cause dominant lethal effects in mice. Both compounds inhibited gap-junctional intercellular communication and induced gene mutations in rodent cells but did not induce unscheduled DNA synthesis. In plants, heptachlor induced mutations and chromosomal aberrations. Neither chlordane nor heptachlor was mutagenic to bacteria and neither damaged bacterial or plasmid DNA.

5.5 Evaluation

There is *inadequate evidence* in humans for the carcinogenicity of chlordane and of heptachlor.

There is *sufficient evidence* in experimental animals for the carcinogenicity of chlordane and of heptachlor.

Overall evaluation

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

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

Subsequent evaluation: Vol. 79 (2001)

Previous evaluations: Vol. 20 (1979) (p. 45); Suppl. 7 (1987) (p. 146)

Synonyms for Chlordane

- Aspon
- Belt
- CD 68
- Chlordan
- Chlorindan
- Chlor Kil
- Chlorotox
- Corodane
- Cortilan-neu
- Dowchlor
- ENT 9932
- Gold crest
- HCS 3260
- Intox
- Kypchlor
- M 140
- M 410
- Niran
- Octachlor
- 1,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene
- 1,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-indene
- Octachloro-4,7-methanotetrahydroindane
- 1,2,4,5,6,7,8,8-Octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindan
- Octa-Klor
- Oktaterr
- OMS 1437
- Ortho-Klor
- Starchlor
- Sydane
- Synklor
- Tat Chlor 4
- Termex
- Topiclor
- Toxichlor
- Unexan-Koeder
- Velsicol 1068

Synonyms for *cis*-Chlordane

- α-Chlordan
- α-Chlordane
- *cis*-Chlordan
- 1α,2α,3α,4β,7β,7aα)-1,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-indene
- 1α,2α,4β,5,6,7β,8,8-Octachloro-3aα,4,7,7aα-tetrahydro-4,7-methanoindan

Synonyms for *trans*-Chlordane

- β-Chlordan
- β-Chlordane
- *trans*-Chlordan
- 1α,2β,3aα,4β,7β,7aα)-1,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-indene
- 1β,2α,4α,5,6,7α,8,8-Octachloro-3aβ,4,7,7a,7aβ-tetrahydro-4,7-methanoindan

Synonyms for γ-Chlordane

- γ-Chlordan
- 2,2,4,5,6,7,8,8-Octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-indene
- 2,2,4,5,6,7,8,8-Octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindan stereoisomer

Synonyms for Heptachlor

- Aahepta
- Agroceres
- Arbinex 30TN
- Basaklor
- 3-Chlorochlordene
- Drinox
- E 3314
- ENT 15,152
- GPKh
- Hepta
- 1,4,5,6,7,8,8-Heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene
- 1,4,5,6,7,8,8-Heptachloro-3a,4,7,7a-tetrahydro-4,7-methano-1*H*-indene
- Heptagranox
- Heptamak
- Heptasol
- Heptox
- Heptachlorane
- Heptagran
- Heptamul
- OMS 193
- Rhodiachlor
- Soleptax
- Velsicol 104

Synonyms for Heptachlor epoxide

- ENT 25584
- Epoxyheptachlor
- GPKh epoxide
- HCE
- Hepox
- Heptachlor *cis*-oxide
- 1aα,1bβ,2α,5α,5aβ,6β,6aα)-2,3,4,5,6,7,7-Heptachloro-1a,1b,5,5a,6,6a-hexahydro-2,5-methano-2*H*-indeno(1,2-b)-oxirene
- 1,4,5,6,7,8,8-Heptachloro-2,3-epoxy-3a,4,7,7a-tetrahydro-4,7-methanoindan
- Heptepoxide
- Velsicol 53-CS-17

For definition of the italicized terms, see Preamble Evaluation.

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DDT AND ASSOCIATED COMPOUNDS
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 179)

***para*,*para*'-DDT**
CAS No.: 50-29-3

***ortho*,*para*'-DDT**
CAS No.: 789-02-6

***para*,*para*'-TDE**
CAS No.: 72-54-8

***ortho*,*para*'-TDE**
CAS No.: 53-19-0

***para*,*para*'-DDE**
CAS No.: 72-55-9

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Technical-grade DDT is a complex mixture of *para*,*para'*-DDT, its isomers and related compounds. It has been used since 1943 as a nonsystemic insecticide with a broad spectrum of activities. DDT has been used extensively for the control of vectors of malaria, typhus, yellow fever and sleeping sickness, and also on food crops. Its use is banned in some countries and has been restricted since the 1970s in many others to the control of vector-borne diseases.

DDT has been formulated in almost every conceivable form, including granules and powders, solutions, concentrates, aerosols and others, alone and in combination with other insecticides.

DDT is ubiquitous in the environment. It is highly persistent and has been found extensively in foods, soils and sediments. Residual levels in human tissues have been declining slowly with the decreasing use of DDT worldwide.

Exposure may occur during its production and application and as a result of persistent residual levels in surface water and sediments, and in foods.

5.2 Carcinogenicity in humans

Slight excess risks for lung cancer were observed among workers at two DDT producing facilities in the USA. A nested case-control study in one of these investigations found a slight deficit of respiratory cancer. No other cancer occurred in sufficient numbers for analysis. In a prospective cohort study in which exposures were estimated on the basis of serum levels of DDT, the risk for lung cancer rose with increasing concentration but was based on small numbers.

Several investigators have compared serum or tissue levels of DDT and/or DDE among individuals with and without cancer, with inconsistent results.

Results from case-control studies of soft-tissue sarcoma do not point to an association.

An elevated risk for non-Hodgkin's lymphoma in relation to potential exposure to DDT was found in a study from Washington State in the USA, but not for other agricultural exposures. An elevated risk for malignant lymphomas was also found in a case-control study in northern Sweden, with adjustment for exposure to herbicides. The only study available found no association between exposure to DDT and primary liver cancer. In the USA, a slight increase in the risk for leukaemia occurred among farmers who reported use of DDT and many other agricultural exposures. The relative risks for leukaemia rose with frequency of use of DDT on animals.

Epidemiological data on cancer risks associated with exposure to DDT are suggestive, but limitations in the assessments of exposure in the studies and the finding of small and inconsistent excesses complicate an evaluation. The slight excesses of respiratory cancer seen among cohorts exposed to DDT are based on differences of five or fewer cases between exposed and unexposed groups. In case-control studies of lymphatic and haematopoietic cancers, exposure to agricultural pesticides other than DDT resulted in excesses as large as or larger than those associated with exposure to DDT. In most of the case-control studies, adjustment was not made for the potential influence of other exposures.

The cohort and case-control studies that have become available since the last evaluation was made in 1987 (see IARC, 1987) add to some extent to the concern about DDT. Most of these investigations were not specifically designed to evaluate the effects of DDT; consequently, the findings for DDT were not reported as fully as would have been desirable.

5.3 Carcinogenicity in experimental animals

DDT has been tested adequately for carcinogenicity by oral administration in mice, rats and hamsters, and by subcutaneous administration in mice. Following oral administration to mice, it caused liver-cell tumours, including carcinomas, in animals of each sex and hepatoblastomas in males. In one study, the incidence of lung carcinomas was increased, and in three studies the incidence of malignant lymphomas was increased; the incidence of lymphoma was decreased in two studies. The incidence of liver tumours was increased in mice following subcutaneous injection of DDT. Oral administration of DDT to rats increased the incidence of liver tumours in female rats in one study and in male rats in two studies. In two studies in which DDT was administered orally to hamsters at concentrations similar to or higher than those found to cause liver tumours in mice and rats, some increase in the incidence of adrenocortical adenomas was observed.

A metabolite of DDT, *para*,*para*'-DDE, has been tested for carcinogenicity by oral administration in mice and hamsters. A second metabolite, TDE, was tested by oral administration in mice and rats. TDE increased the incidence of liver tumours in male mice and of lung tumours in animals of each sex in one of the two studies in mice. An increase in the number of thyroid tumours was observed in one study in male rats. DDE produced a high incidence of liver tumours in male and female mice in two studies. An increased incidence of neoplastic liver nodules was observed in one study in male and female hamsters.

5.4 Other relevant data

The liver is the target organ for the chronic toxicity of DDT. This compound induced liver microsomal enzymes in rodents and primates and increased the frequency of enzyme-positive foci in rat liver.

DDT impaired reproduction and/or development in mice, rats, rabbits, dogs and avian species.

In one study, higher DDT levels were noted in the serum of women who had delivered prematurely than in those who had had a normal delivery. Studies of spontaneous abortion, gestational period and newborn status showed no clear association with body levels of DDT.

In one study, increased frequencies of chromatid-type but not chromosome-type aberrations were observed in peripheral lymphocytes of workers with increased plasma levels of DDT. No data were available on the genetic and related effects of metabolites of DDT in humans.

DDT reduced gap-junctional areas in rat liver cells *in vivo* and inhibited gap-junctional intercellular communication in rodent and human cell systems. Conflicting data were obtained with regard to some genetic endpoints. In most studies, DDT did not induce genotoxic effects in rodent or human cell systems nor was it mutagenic to fungi or bacteria.

para,*para*'-DDE weakly induced chromosomal aberrations in cultured rodent cells and caused mutation in mammalian cells and insects, but not bacteria. *para*,*para*'-DDE inhibited gap-junctional intercellular communication in cultured rodent cells.

In most studies, *para*,*para*'-TDE did not induce genetic effects in short-term tests *in vitro*. It inhibited gap-junctional intercellular communication in cultured rodent cells.

There is no evidence that *ortho*,*para*'-TDE induced genetic effects in short-term tests *in vitro* on the basis of the few studies available.

5.5 Evaluation

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

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

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluations: Vol. 5 (1974) (p. 83); Suppl. 7 (1987) (p. 186)

Synonyms for *para*,*para*'-DDT

- Aavero-extra
- Agritan
- Anofex
- Arkotine
- Azotox M 33
- Benzochloryl
- 2,2-Bis(*para*-chlorophenyl)-1,1,1-trichloroethane
- 1,1-Bis(*para*-chlorophenyl)-2,2,2-trichloroethane
- 1,1-Bis(4-chlorophenyl)-2,2,2-trichloroethane
- Bosan supra
- Bovidermol
- Chlorophenothane
- Chlorphenotoxum
- α,α-Bis(*para*-chlorophenyl)- β,β,β-trichlorethane
- Citox
- Clofenotane
- DDT

- 4,4'-DDT
- Deoval
- Detox
- Detoxan
- Dibovin
- *para*,*para*'-Dichlorodiphenyltrichloroethane
- 4,4'-Dichlorodiphenyltrichloroethane
- *para*,*para*'-Dichlorodiphenyltrichloromethylmethane
- Dicophane
- Dinocide
- Dodat
- Dykol
- ENT 1506
- Estonate
- Gesarol
- Guesarol
- Genitox
- Gesafid
- Guesapon
- Gyron
- Hildit
- Ivoran
- Ixodex
- Mutoxan
- Neocid
- Neocidol
- OMS 0016
- Parachlorocidum
- PEB 1
- Pentachlorin
- Penticidum
- Trichlorobis(4'-chlorophenyl)ethane
- 2,2,2-Trichloro-1,1-bis(4-chlorophenyl)ethane
- 1,1,1-Trichloro-2,2-bis(4-chlorophenyl)ethane
- 1,1,1-Trichloro-2,2-bis(*para*-chlorophenyl)ethane
- 1,1,1-Trichloro-2,2-bis(4,4'-dichlorodiphenyl)ethane
- 1,1'-(2,2,2-Trichloro-ethylidene)bis(4-chlorobenzene)
- Zerdane

Synonyms for *ortho*,*para*'-DDT

- 2-(2-Chlorophenyl)-2-(4-chlorophenyl)-1,1,1-trichloroethane
- 1-Chloro-2-(2,2,2-trichloro-1-(4-chlorophenyl)ethyl)-benzene
- 2,4'-DDT
- 1,1,1-Trichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl)ethane
- 1,1,1-Trichloro-2-(*ortho*-chlorophenyl)-2-(*para*-chlorophenyl)ethane

Synonyms for *para*,*para*'-TDE

- 1,1-Bis(*para*-chlorophenyl)-2,2-dichloroethane
- 1,1-Bis(4-chlorophenyl)-2,2-dichloroethane
- 2,2-Bis(*para*-chlorophenyl)-1,1-dichloroethane
- 2,2-Bis(4-chlorophenyl)-1,1-dichloroethane
- DDD
- *para*,*para*'-DDD
- 4,4'-DDD
- 1,1-Dichloro-2,2-bis(*para*-chlorophenyl)ethane

- 1,1'-(2,2-Dichloroethylidene)-bis(4-chlorobenzene)
- 1,1-Dichloro-2,2-bis(4-chlorophenyl)ethane, dichlorodiphenyl dichloroethane
- *para*,*para*'-Dichlorodiphenyldichloroethane
- *para*,*para*'-Dichlorodiphenyl-2,2-dichloroethylene
- Dilene
- ME 1700
- Rothane
- TDE

Synonyms for *ortho*,*para*'-TDE

- CB 313
- Chloditan
- 1-Chloro-2-[2,2-dichloro-1-(4-chlorophenyl)ethyl]benzene
- 2-(2-Chlorophenyl)-2-(4-chlorophenyl)-1,1-dichloroethane
- *ortho*,*para*'-DDD
- 1,1-Dichloro-2-(*ortho*-chlorophenyl)-2-(*para*-chlorophenyl)ethane
- 2,4'-Dichlorodiphenyldichloroethane
- Lysodren
- Mitotan

Synonyms for *para*,*para*'-DDE

- 2,2-Bis(4-chlorophenyl)-1,1-dichloroethene
- 1,1-Bis(*para*-chlorophenyl)-2,2-dichloroethylene
- 2,2-Bis(4-chlorophenyl)-1,1-dichloroethylene
- 1,1'-(Dichloroethenylidene)-bis-(4-chlorobenzene)
- 1,1-Dichloro-2,2-bis(*para*-chlorophenyl)ethylene
- 1,1-Dichloro-2,2-di(4-chlorophenyl)ethylene
- *para*,*para*'-Dichlorodiphenyldichloroethylene

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DELTAMETHRIN
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 251)

Deltamethrin

CAS No.: 52918-63-5

***trans*-Deltamethrin**

CAS No.: 64363-96-8

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Deltamethrin is a highly active contact insecticide. It was first marketed in 1977 and is used mostly on cotton and on crops such as coffee, maize, cereals, fruit, vegetables and hops. It is also used in public health programmes and for the protection of stored crops.

Deltamethrin has been formulated as solutions, concentrates, granules, powders and aerosols, alone and in combination with other pesticides.

Exposure can occur during its production and application and, at much lower levels, from the consumption of food containing residues.

5.2 Carcinogenicity in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Deltamethrin was tested for carcinogenicity in one experiment in mice and in one experiment in rats by oral administration. In mice, no increase in tumour incidence was seen. In rats, a statistically significant increase in the incidence of unspecified thyroid adenomas was observed in low-dose males and high-dose females.

5.4 Other relevant data

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

Deltamethrin induced micronuclei and chromosomal aberrations in bone marrow and abnormal sperm morphology in mice treated *in vivo*. The only other indication of genotoxic potential was induction of chromosomal aberrations in plants.

5.5 Evaluation

No data were available from studies in humans.

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

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Synonyms for Deltamethrin

- Butox
- Butoflin
- Cislin
- Crackdown
- (S)-α-Cyano-3-phenoxybenzyl, (1R,3R)-3-(2,2-dibromovinyl)-2,2-dimethylcyclo-propanecarboxylate
- Decamethrin
- Decamethrine
- Decis
- *cis*-Deltamethrin
- (1R-(1α(S*),3α))-(2,2-Dibromoethenyl)-2,2-dimethylcyclopropanecarboxylic acid, cyano(3-phenoxyphenyl)methyl ester
- FMC 45498
- K-Othrine
- NRDC 161
- OMS 1998
- RU 22974
- RUP 987

Synonyms for *trans*-Deltamethrin

- (S)-α-Cyano-3-phenoxybenzyl, (1R,3SR)-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate
- 1R-(1α(S*),3β))-(2,2-Dibromoethenyl)-2,2-dimethylcyclopropanecarboxylic acid, cyano(3-phenoxyphenyl)methyl ester
- RU 26979

Last updated: 20 November 1997

DICHLORVOS
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 267)

CAS No.: 62-73-7
Chem. Abstr. Name: Phosphoric acid, 2,2-Dichloroethenyl dimethyl ester

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.

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

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)*.

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluations: Vol. 20 (1979) (p. 97); Suppl. 7 (1987) (p. 62)

Synonyms for Dichlorvos

- Atgard
- Atgard V
- Bibesol
- Brevinyl
- Brevinyl E50
- Canogard
- Chlorvinphos
- DDVP
- Dedevap
- Des
- Dichlofos
- Dichlorman
- 2,2-Dichloroethenyl dimethyl phosphate
- 2,2-Dichloroethenol, dimethyl phosphate
- Dichlorovos
- Dimethyl 2,2-dichloroethenyl phosphate
- Dimethyl dichlorovinyl phosphate
- Dimethyl 2,2-dichlorovinyl phosphate
- *O*,*O*-Dimethyl 2,2-dichlorovinyl phosphate
- Divipan
- ENT 20738
- Equigard
- Equigel
- Estrosel
- Estrosol
- Fecama
- Fekama
- Herkol
- Insectigas D
- Mafu Strip
- Mopari
- Nefrafos
- Nerkol
- Nogos
- Nogos 50

- Nogos G
- Novotox
- No-Pest Strip
- Nuan
- Nuvan
- Nuvan 100 EC
- OKO
- OMS 14
- Panaplate
- Phosphoric acid, 2,2-dichlorovinyl dimethyl ester
- Phosvit
- Prima U
- SD 1750
- Szklarniak
- TAP 9VP
- Task
- Unitox
- Unifos
- Unifos 50 EC
- Vapona
- Vapona insecticide
- Vaponite
- Vinylofos
- Vinylophos
- Winylophos

Last updated: 21 November 1997

FENVALERATE
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 309)

Fenvalerate
CAS No.: 51630-58-1

Fenvalerate β
CAS No.: 66267-77-4

Esfenvalerate
CAS No.: 66230-04-4

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Fenvalerate is a highly active contact insecticide. It has been used since 1976, mostly in agriculture but also in public health programmes, in homes and gardens and on cattle, alone or in combination with other insecticides. It has been formulated as concentrates, dusts and wettable powders.

Exposure to fenvalerate can occur during its production and application and, at much lower levels, from consumption of foods containing residues.

5.2 Carcinogenicity data in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Fenvalerate was tested for carcinogenicity in two experiments in mice and in two experiments in rats by oral administration. There was no increase in the incidence of tumours in mice. In rats, there was an increased incidence of benign mammary tumours in females in one study. In another study at a higher dose, no increase in tumour incidence was seen in animals of either sex.

5.4 Other relevant data

In one study, fenvalerate increased the frequency of enzyme-positive foci in rat liver.

Administration of fenvalerate to mice *in vivo* induced chromosomal aberrations and micronucleus in bone marrow and morphological abnormalities in sperm. Induction of chromosomal aberrations and sister-chromatid exchange was observed in cultured human cells, and aneuploidy was seen in insects. Fenvalerate inhibited gap-junctional intercellular communication in cultured mammalian cells. It did not induce mutation in insects or bacteria.

5.5 Evaluation

No data were available from studies in humans.

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

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Synonyms for Fenvalerate

- Aqmatrine
- Belmark
- 4-Chloro-α-(1-methylethyl)benzeneacetic acid, cyano(3-phenoxyphenyl)methyl ester
- α-Cyano-3-phenoxybenzyl 2-(4-chlorophenyl)isovalerate
- α-Cyano-3-phenoxybenzyl α-(4-chlorophenyl)isovalerate
- α-Cyano-3-phenoxybenzyl isopropyl-4-chlorophenylaetate
- (RS)-α-Cyano-3-phenoxybenzyl (RS)-2-(4-chlorophenyl)-3-methylbutyrate
- Cyano(3-phenoxyphenyl)methyl 4-chloro-α-(1-methylethyl)benzene acetate
- Ectrin
- Evercide 2362
- Fenkill
- Fenval
- OMS 2000
- Phenvalerate
- Pydrin^R
- S-5602
- Sanmarton
- SD 43775
- Sumibac
- Sumicidin
- Sumifleece
- Sumifly
- Sumipower
- Sumitik
- Sumitox
- WL 43775

Synonyms for Fenvalerate β

- (R-(R*,S*))-4-Chloro-α-(1-methylethyl) benzeneacetic acid, cyano(3-phenoxyphenyl)methyl ester
- (R)-α-Cyano-3-phenoxybenzyl (S)-2-(4-chlorophenyl)-3-methylbutyrate
- Fenvalerate Aβ
- S 5602Aβ

Synonyms for Esfenvalerate

- Asana
- (S-(R*,R*))-4-Chloro-α-(1-methylethyl) benzeneacetic acid, cyano(3-phenoxyphenyl)methyl ester
- (S)-α-Cyano-3-phenoxybenzyl (S)-2-(4-chlorophenyl)-3-methylbutyrate
- Fenvalerate α
- Fenvalerate Aα

- Halmark
- S-1844
- S 5602 Aα
- Sumi-alfa
- Sumi-alpha
- Sumicidin Aα

Last updated: 20 November 1997

PERMETHRIN
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 329)

Permethrin
CAS No.: 52645-53-1

***trans*-Permethrin**
CAS No.: 61949-77-7

***cis*-Permethrin**
CAS No.: 61949-76-6

(-)-*trans*-Permethrin
CAS No.: 54774-47-9

(-)-*cis*-Permethrin
CAS No.: 54774-46-8

(+)-*cis*-Permethrin
CAS No.: 54774-45-7

(±)-*cis*-Permethrin
CAS No.: 52341-33-0

(±)-*trans*-Permethrin
CAS No.: 52341-32-9

(+)-*trans*-Permethrin
CAS No.: 51877-74-8

5. Summary of Data Reported and Evaluation

5.1 Exposure

Permethrin is a highly active contact insecticide, which was first marketed in 1977. It is used mainly on cotton and food crops. Other uses are in forestry and for public health purposes, in public buildings, residences and aircraft.

Permethrin has been formulated as granules, powders, emulsifiable concentrates, aerosols and other forms.

Exposure can occur during its production and application and, at much lower levels, from consumption of food containing residues.

5.2 Carcinogenicity data in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

One preparation of permethrin (*cis*:*trans*, 40:60) was tested for carcinogenicity in one study in mice and in one study in rats by oral administration in the diet.In mice, a marginal increase in the incidence of pulmonary adenomas was observed in males.No increased tumour incidence was observed in treated rats.

5.4 Other relevant data

Permethrin has caused dermal irritation after topical exposure.It induced microsomal enzymes in rats and mice.

No data were available on the genetic and related effects of permethrin in humans. No effect was observed in the limited number of short-term tests available.

5.5 Evaluation

No data were available from studies in humans.

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

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Synonyms for Permethrin

- Adion
- Ambush
- Ambushfog
- Anomethrin N
- Antiborer 3768
- Atroban
- BW-21-Z
- Cellutec
- Chinetrin
- Coopex
- Corsair
- 3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- Diffusil H
- Dragon
- Ecsumin
- Ectiban
- Efmethrin
- Eksmin
- Exmin
- FMC 33297
- FMC 41655
- ICI-PP 557
- Imperator
- Indothrin
- Ipitox

- Kafil
- Kavil
- Kestrel
- LE 79-519
- MP 79
- NIA 33297
- NRDC 153
- OMS 1821
- Outflank
- Perigen
- Permanone
- Permasect
- Permit
- Perthrine
- *meta*-Phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
- 3-Phenoxybenzyl(1RS)-*cis-trans*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate
- 3-Phenoxybenzyl(1RS,3RS;1RS,3SR)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclo-3-(2,2-dichlorovinyl)cyclopropanecarboxylate
- 3-Phenoxybenzyl-2,2-dimethyl-3-(2,2-dichlorovinyl)cyclopropanecarboxylate
- Picket
- Pounce
- PP 557
- Pramex
- Pynosect
- Qamlin
- S 3151
- SBP 1513
- SBP 15131TEC
- Spartan
- Stockade
- Stomoxin
- Talcord
- Torpedo
- WL 43479

Synonyms for *trans*-Permethrin

- *trans*-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- *trans-meta*-Phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

Synonyms for *cis*-Permethrin

- *cis*-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- *cis-meta*-Phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate

Synonyms for (-)-*trans*-Permethrin

- (1S-*trans*)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- 1S-*trans*-Permethrin

Synonyms for (-)-cis-Permethrin

- (1S-*cis*)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- 1S-*cis*-Permethrin

Synonyms for (+)-cis-Permethrin

- (1R-*cis*)-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- NRDC 167
- 1R-*cis*-Permethrin

Synonyms for (±)-*cis*-Permethrin

- *cis*-(±)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- (±)-cis-FMC 33297
- FMC 35171
- NRDC 148
- 1RS-*cis*-Permethrin

Synonyms for (±)-trans-Permethrin

- trans-**(±)**-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- NRDC 146
- 1RS-*trans*-Permethrin

Synonyms for (+)-*trans*-Permethrin

- (1R-*trans*)-3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid, (3-phenoxyphenyl)methyl ester
- Biopermethrin
- NRDC 147
- 1R-*trans*-Permethrin
- RU 22090

Last updated: 21 November 1997

CAPTAFOL
(Group 2A)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 353)

CAS No.: 2425-06-1

Chem. Abstr. Name: 3α,4,7,7α-Tetrahydro-2-[(1,1,2,2-tetrachloroethyl)thiol]-1*H*-isoindole-1,3-(2*H*)dione

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Captafol is a fungicide that has been widely used since 1961 for the control of fungal diseases in fruits, vegetables and some other plants.

It has been formulated for use as dusts, emulsifiable concentrates, flowable suspensions and water-dispersible granules, and also in combination with other pesticides.

Exposure can occur during its production and application and, at much lower levels, from consumption of foods containing residues.

5.2 Carcinogenicity in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Captafol was tested for carcinogenicity in one study in mice and in two studies in rats by oral administration. In mice, it produced a high incidence of adenocarcinomas of the small intestine and of vascular tumours of the heart and spleen; the increase in tumours of the heart was dose-related for animals of each sex. Increases in the incidence of hepatocellular carcinomas were also observed in animals of each sex. In two studies in rats, captafol produced a dose-related increase in the incidence of renal carcinomas in males; in one of these, it also induced dose-related increases in the incidence of benign renal tumours in females and of liver tumours in males and females.

5.4 Other relevant data

In one study, captafol increased the frequency of enzyme-positive foci in rat liver.

Captafol did not affect embryonic development in rabbits or monkeys but was embryolethal and teratogenic at high doses in hamsters.

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

Administration of captafol induced dominant lethal effects in rats. Captafol induced positive results in various short-term tests in human and mammalian cells *in vitro*, including gene mutation and chromosomal aberrations. It induced DNA damage and gene mutation in fungi and bacteria.

5.5 Evaluation

No data were available from studies in humans.

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

In making the overall evaluation, the Working Group took into consideration the following supporting evidence: Captafol is active in a wide range of tests for genetic and related effects, including the generally insensitive in-vivo assay for dominant lethal mutation.

Overall evaluation

Captafol is *probably carcinogenic to humans (Group 2A)*.

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- Alfloc
- Arborseal
- CS 5623
- Difolatan
- Folcid
- Foltaf
- Haipen 50
- Merpafol
- Nalco 7046
- Ortho 5865
- Proxel EF
- Santar SM
- Terrazol
- *N*-[(1,1,2,2-Tetrachloroethyl)thio]cyclohex-4-ene-1,2-dicarboximide
- *N*-[(1,1,2,2-Tetrachloroethyl)thio]-4-cyclohexene-1,2-dicarboximide
- *N*-(Tetrachloroethylthio)tetrahydrophthalimide
- *N*-(1,1,2,2-Tetrachloroethylthio)-*delta*4-tetrahydrophthalimide
- 3α,4,7,7α-Tetrahydro-*N*-(1,1,2,2-tetrachloroethanesulfenyl)phthalimide

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PENTACHLOROPHENOL
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 371)

CAS No.: 87-86-5

Chem. Abstr. Name: Pentachlorophenol

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Since its introduction in the 1930s, pentachlorophenol has been used in large quantities, mainly as a wood preservative. It has also found minor use as a herbicide, defoliant, bactericide and molluscicide. In recent years, its use in agriculture has been restricted in many countries.

Pentachlorophenol is usually formulated and applied to wood with a hydrocarbon diluant. Technical-grade pentachlorophenol has been shown to contain a large number of impurities, including tetrachlorophenols and, to a much lesser extent, polychloro-dibenzodioxins, polychlorodibenzofurans, polychlorodiphenyl ethers, polychlorophenoxy phenols and chlorinated hydrocarbons.

Pentachlorophenol has been detected in fruits, vegetables, meats, water and soils. It has been detected in the urine of the general population in several countries and at higher levels in the urine of workers in wood treatment plants.

Exposure to pentachlorophenol can occur during its production and use; from contact with pentachlorophenol-treated wood; at lower levels, from consumption of foods and water containing residues; and as a result of its ubiquitous presence as an environmental contaminant.

5.2 Carcinogenicity in humans

Two population-based case-control studies of soft-tissue sarcoma and non-Hodgkin’s lymphoma in New Zealand found no increased risk associated with potential exposure to sodium pentachlorophenate through work in a sawmill or timber company. A similar study of multiple myeloma showed a slightly increased risk. A Swedish population-based case-control study found an increased risk for soft-tissue sarcoma associated with self-reported exposure to pentachlorophenol.

Excess incidences of cancers of the skin and of the lip, mouth and pharynx and of leukaemia were found in a cohort study of sawmill workers in Finland. Pentachlorophenol constituted only a minor proportion of the chlorophenols to which the workers were exposed.

5.3 Carcinogenicity in experimental animals

Two different pentachlorophenol formulations were tested for carcinogenicity by oral administration in two separate experiments in mice. A dose-related increase in the incidence of hepatocellular adenomas and carcinomas was observed in males exposed to either formulation and of hepatocellular adenomas in females exposed to one of the formulations. A dose-related increase in the incidence of adrenal phaeochromocytomas was observed in male mice exposed to either formulation, and an increase was also seen in females exposed to one of the formulations at the highest dose. A dose-related increase in the incidence of malignant vascular tumours of the liver and spleen was seen in female mice exposed to either formulation.

5.4 Other relevant data

Pentachlorophenol was embryotoxic and embryolethal and caused a slight increase in the number of malformations in rats.

Significant increases in the incidence of dicentric chromosomes and acentric fragments were detected in the peripheral lymphocytes of workers exposed occupationally to penta-chlorophenol in one study, but no increase in the frequency of sister chromatid exchange was observed.

Pentachlorophenol gave negative results in most tests for genetic and related effects. It gave weakly positive results for somatic gene mutation in a mouse spot test. It induced chromosomal aberrations in cultured rodent cells but not in human cells and caused gene conversion in yeast.

5.5 Evaluation

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

There is *sufficient evidence* in experimental animals for the carcinogenicity of penta-chlorophenol.

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- Chlorophen
- 1-Hydroxypentachlorobenzene
- PCP
- Penchlorol
- Penta
- 2,3,4,5,6-Pentachlorophenol

THIRAM
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 403)

CAS No.: 137-26-8
Chem. Abstr. Name: Tetramethylthioperoxydicarbonic diamide

5. Summary of Data Reported and Evaluation

5.1 Exposure data

The major use of thiram is as an accelerator and vulcanization agent in the rubber industry. It is also used as a fungicide on seeds and as a foliar fungicide on turf, fruit and vegetables. It has been in commercial use since 1925.

Thiram has been formulated for use as dusts, wettable powders and flowable suspensions and also in combination with other pesticides.

Exposure may occur during its production, its use in the rubber industry and its application as a fungicide, and, at much lower levels, from consumption of foods containing residues. Thiram is also an environmental degradation product of the two fungicides, ferbam and ziram.

5.2 Carcinogenicity in humans

No adequate data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Thiram was tested adequately for carcinogenicity by oral administration in one study in rats. No increase in incidence was seen for tumours at any site.

When thiram was administered orally to rats in combination with nitrite, a high incidence of tumours of the nasal cavity was observed in males and females.

5.4 Other relevant data

Thyroid abnormalities were observed in a group of subjects exposed occupationally to thiram.

Thiram marginally increased the frequency of enzyme-positive foci in rat liver. It decreased fertility in rats and caused embryolethality and embryotoxicity in rats and hamsters and malformations in mice and hamsters.

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

Thiram induced various kinds of chromosomal damage and altered sperm morphology in rodents *in vivo*. It induced unscheduled DNA synthesis and sister chromatid exchange in cultured human cells. It was genotoxic to insects, plants, fungi and bacteria.

5.5 Evaluation

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

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

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluations: Vol. 12 (1976) (p. 225); Suppl. 7 (1987) (p. 72)

Synonyms

- Aapirol
- Aatiram
- Accel TMT
- Accelerator T
- Accelerator thiuram
- Aceto TETD
- Apirol
- Atiram
- Arasan
- Aules
- Basultra
- Betoxin
- Bis(dimethylthiocarbamoyl) disulphide
- Bis(dimethylthiocarbamyl) disulfide
- Delsan
- Ekagom TB
- Falitiram
- Ferna-Col
- Fernasan
- Fernide
- Formalsol
- Hermal
- Hermat TMT
- Heryl
- Hexathir
- Kregasan
- Mercuram
- Methyl thiram
- Methyl tuads
- Metiurac
- Nobecutan
- Normersan
- Nocceler TT
- Panoram 75
- Pol-Thiuram
- Polyram ultra
- Pomarsol
- Pomasol
- Puralin
- Radothiram

- Radotiram
- Rezifilm
- Rhenogran TMTD
- Rhodiauram
- Robac TMT
- Royal TMTD
- Sadoplon
- Sadoplon 75
- Soxinol TT
- Spotrete
- SQ 1489
- Tersan
- Tetramethylthiuram bisulfide
- Tetramethyl thiuram disulphide
- *N*,*N*,*N*',*N*'-Tetramethylthiuram disulfide
- Tetrasipton
- Thillate
- Thiosan
- Thioscabin
- Thiotox
- Thirasan
- Thiride
- Thiulin
- Thiurad
- Thiuram disulfide, tetramethyl-
- Thiuram
- Thiuram TMTD
- Thiuramyl
- Thylate
- Tigam
- Tiradin
- Tiuramyl
- TMTD
- TMTDS
- TMT
- Trametan
- Tridipam
- Tripomol
- Tuads
- TUEX
- Tulisan
- Tutan
- Tyradin
- VUAgT-I-4
- Vucafor
- Vulcacit thiuram
- Vulkacit Th
- Zaprawa Nasienna T
- Zupa S 80

Last updated: 21 November 1997

ZIRAM
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 423)

CAS No.: 137-30-4
Chem. Abstr. Name: (T-4)-Bis(dimethylcarbamodithioato-S,S')-zinc

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Ziram is used primarily as a rubber vulcanization accelerator but is also used as a foliar fungicide, mainly on fruit and nuts. It has been in commercial use since the 1930s.

Ziram has been formulated for use as a wettable powder, a paste and water-dispersible granules and also in combination with other pesticides.

Exposure can occur during its production, its use in the rubber industry and its application as a fungicide, and, at much lower levels, from consumption of foods containing residues.

5.2 Carcinogenicity in humans

No data were available in the Working Group.

5.3 Carcinogenicity in experimental animals

Ziram was tested adequately for carcinogenicity by oral administration in one study in mice and one study in rats. In mice, the incidence of benign lung tumours was increased in females. In rats, a dose-related increase in the incidence of C-cell thyroid carcinomas was observed in males.

5.4 Other relevant data

In single studies, ziram caused embryotoxicity and minor malformations in rats and embryolethality in chicks hatched from injected ova.

An increased frequency of chromatid and chromosomal aberrations was seen in peripheral blood lymphocytes of workers who handled and packaged ziram.

Ziram was clastogenic in mammalian cells *in vivo* and *in vitro* and induced mutations in cultured rodent cells and in insects and bacteria.

5.5 Evaluation

No data were available from studies in humans.

There is limited evidence in experimental animals for the carcinogenicity of ziram.

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluations: Vol. 12 (1976) (p. 259); Suppl. 7 (1987) (p. 74)

Synonyms

- Aaprotect
- Aavolex
- Aazira
- Accelerator L
- Aceto ZDED
- Aceto ZDMD
- Alcobam ZM
- Bis(dimethyldithiocarbamato)zinc
- Carbazinc
- Corozate
- Crittam
- Cuman
- Cymate
- Dimethylcarbamodithioic acid, zinc complex
- Dimethylcarbamodithioic acid, zinc salt
- Eptac 1
- Fuclasin
- Fuklasin
- Hermat ZDM
- Hexazir
- Karbam white
- Methasan
- Methazate
- Methyl zimate
- Methyl zineb
- Methyl ziram
- Mezene
- Milbam
- Molurame
- Mycronil
- Nocceler PZ
- Orchard brand ziram
- Pomarzol Z-forte
- Rhodiacid
- Rodisan
- Soxinal PZ
- Soxinol PZ
- Trikagol
- Tricarbamix Z
- Vancide
- Vancide MZ-96
- Vulcacure ZM
- Vulkacite L
- Z 75
- Z-C Spray
- Zerlate
- Zarlate

- Zinc bis(dimethyldithiocarbamate)
- Zinc, bis(dimethyldithiocarbamate)
- Zinc dimethyldithiocarbamate
- Zirberk
- Ziride
- Zirthane

Last updated: 20 November 1997

ATRAZINE
(Group 2B)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 441)

CAS No.: 1912-24-9
Chem. Abstr. Name: 6-Chloro-*N*-ethyl-*N*'-(1-methylethyl)-1,3,5-triazine-2,4-diamine

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Atrazine was introduced in 1957. It is now one of the most extensively used herbicides worldwide, with US production of at least 50 000 tonnes per annum since 1980. It is widely used on maize and to a lesser extent on a variety of other crops.

Atrazine has been formulated as wettable powders, granules and liquid formulations.

Exposure can occur during production and application of atrazine and *via* contaminated ground- and surface water. Exposure could also occur from consumption of foods containing residues. Atrazine residues were not detected in large-scale surveys of foods products in Canada and the USA.

5.2 Carcinogenicity in humans

One population-based case-control study in northern Italy found an elevated risk for ovarian cancer in women considered to have been exposed to triazine herbicides. A hospital-based case-control study in the same area found an elevated risk for ovarian tumours among women exposed to herbicides, including triazine herbicides.

A case-control study from Kansas, USA, indicated an association between self-reported use of triazine herbicides and risk for non-Hodgkin's lymphoma. A nonsignificant doubling of the risk was found in the absence of exposure to phenoxyacetic acid herbicides and uracils. In another study in Kansas, USA, in which apparently the same controls were used, self-reported use of triazine herbicides was associated with a slight excess risk of colon cancer, as was employment on a farm in general.

In two case-control studies from Iowa and Minnesota, USA, there was no association between self-reported use of atrazine and leukaemia, whereas a slightly increased risk was suggested for a subgroup of lymphomas.

In a case-control study in Nebraska, USA, a nonsignificant elevation in risk for non-Hodgkin's lymphoma was associated with self-reported use of atrazine. Risks were greater among men with 16 or more years of use than among those with a shorter duration.

These seven studies were considered to provide some evidence for the carcinogenicity of exposure to triazine herbicides. Complex exposures and insufficient reporting made it difficult to evaluate the carcinogenicity of individual triazine herbicides, including atrazine.

5.3 Carcinogenicity in experimental animals

Atrazine was tested for carcinogenicity in one experiment by oral administrationm to rats, producing increased incidences of mammary tumours (mainly benign) in males and of uterine adenocarcinomas and tumours of the haematopoietic system in females. It was also tested by intraperitoneal administration to mice; it was stated in a preliminary report to have produced an increase in the incidence of lymphomas.

5.4 Other relevant data

Atrazine was embryotoxic and embryolethal but not teratogenic in rats and rabbits when administered at maternally toxic doses.

Atrazine and its de-ethylated metabolite have been shown to alter the activity of some testosterone-metabolizing enzymes in the rat pituitary and hypothalamus, and to decrease hormone-receptor binding in the prostate.

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

Atrazine induced DNA strand breaks in stomach, liver and kidney cells but not lung cells of rats treated orally. Chromosomal aberrations were induced in plants and insects, but not in cultured rodent cells. Aneuploidy was induced in *Drosophila melanogaster* and fungi. Atrazine induced gene mutation in plants, but not in bacteria or cultured rodent cells.

5.5 Evaluation

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

There is *limited evidence* in experimental animals for the carcinogenicity of atrazine.

In making the overall evaluation, the Working Group took into consideration the following supporting evidence. The increased risks for tumours that are known to be associated with hormonal factors, which were observed in studies of both animals and human beings, are consistent with the known effects of atrazine on the hypothalamic-pituitary-gonadal axis.

Overall evaluation

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

Subsequent evaluation: Vol. 73 (1999)

Synonyms

For definition of the italicized terms, see Preamble Evaluation.

- A 361
- Aatrex
- Akticon
- Aktikon
- Aktinit A
- Argezin
- Atrataf
- Atrazin
- ATZ
- CET
- 6-Chloro-N^2-ethyl-N^4-isopropyl-1,3,5-triazine-2,4-diamine
- 2-Chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine

- 2-Chloro-4-(ethylamino)-6-(isopropylamino)triazine
- 2-Chloro-4-(ethylamino)-6-(isopropylamino)-*s*-triazine
- Chromozin
- Cyazin
- G 30027
- Gesaprin
- Herbatoxol
- Hungazin
- Oleogesaprim
- Primatol A
- Radazin
- Triazine A 1294
- Wonuk
- Zeapos
- Zeazin
- Zeazine
- Zeopos

Last updated: 30 September 1999

MONURON
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 467)

CAS No.: 150-68-5
Chem. Abstr. Name: *N*'-(4-Chlorophenyl)-*N*,*N*-dimethylurea

5. Summary of Data and Evaluation

5.1 Exposure data

Monuron is a nonselective systemic herbicide which inhibits photosynthesis. It was introduced in 1952 and has been used for the control of grasses and weeds in non-cropland areas, such as rights-of-way, industrial sites and drainage ditch banks. It has been used at lower application rates in agricultural areas in some countries as a pre- or post-emergence herbicide.

Monuron has been formulated for use as wettable powder and granules.

Exposure may occur during its production and use and, at much lower levels, from consumption of foods containing residues.

5.2 Carcinogenicity in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Monuron was tested adequately for carcinogenicity in one study in mice and in one study in rats by oral administration. No increase in tumour incidence was found in mice. In rats, dose-related increased incidences of renal and liver-cell tumours were observed in males.

5.4 Other relevant data

Monuron forms chloroaniline-haemoglobin adducts in rats. In one study, it increased the number and volume fraction of enzyme-positive foci in rat liver.

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

Monuron induced micronucleus formation, chromosomal aberrations and abnormal sperm in mice *in vivo*. It induced chromosomal aberrations in cultured mammalian cells, insects and plants, sister chromatid exchange and cell transformation in cultured mammalian cells and mutation in plants.

5.5 Evaluation

No data were available from studies in humans.

There is *limited evidence* in experimental animals for the carcinogenicity of monuron.

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Previous evaluations: Vol. 12 (1976) (p. 167); Suppl. 7 (1987) (p. 67)

Synonyms

- Chlorfenidim
- 3-(4-Chlorophenyl)-1,1-dimethylurea
- 1-*para*-Chlorophenyl-3,3-dimethylurea
- 1-(4-Chlorophenyl)-3,3-dimethylurea
- 3'-(4'-Chlorophenyl)-1,1-dimethylurea
- 3-*para*-Chlorophenyl-1,1-dimethylurea
- *N*-(4-Chlorophenyl)-*N*',*N*'-dimethylurea
- *N*-*para*-Chlorophenyl-*N*',*N*'-dimethylurea
- 3-(4-Chlorophenyl)-1,1-dimethyluronium trichloroacetate
- CMU
- 1,1-Dimethyl-3-(*para*-chlorophenyl)urea
- 1,1-Dimethyl-3-(4-chlorophenyl)urea
- *N*,*N*-Dimethyl-*N*'-(4-chlorophenyl)urea
- Karmex Monuron Herbicide
- Karmex W. Monuron Herbicide
- Telvar
- Telvar Monuron Weedkiller
- Telvar W. Monuron Weedkiller

Last updated: 21 November 1997

PICLORAM
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 481)

CAS No.: 1918-02-1
Chem. Abstr. Name: 2-Pyridinecarboxylic acid, 4-amino-3,5,6-trichloro-

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Picloram is a systemic herbicide used to control broad-leaved weeds on pasture, rangeland, rights-of-way, forestland and some grains. It was first registered for use in 1963.

Picloram has been formulated as granules and soluble concentrates in the form of amine and potassium salts and esters.

Exposure to picloram may occur during its production and application and, at much lower levels, from consumption of foods containing residues.

5.2 Carcinogenicity in humans

No data were available to the Working Group.

5.3 Carcinogenicity in experimental animals

Technical-grade picloram was tested for carcinogenicity in one experiment in mice and in two experiments in rats by administration in the diet. No increase in tumour incidence was observed in mice. In rats, it increased the incidence of liver-cell tumours (mainly benign) in males in one study and in males and females in another, and of C-cell adenomas of the thyroid in female rats in one study.

5.4 Other relevant data

The liver is the primary organ for picloram toxicity following chronic administration to rats.

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

Picloram did not induce chromosomal aberrations in mouse bone-marrow cells *in vivo* nor in cultured human cells. With the exception of a single report in which forward mutation was induced in *Streptomyces coelicolor*, picloram gave negative results in all short-term tests for mutation. It induced mitotic recombination in yeast but not in fungi.

5.5 Evaluation

No data were available from studies in humans.

There is *limited evidence* for the carcinogenicity of picloram of technical grades in experimental animals.

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- 4-Amino-3,5,6-trichloropyridine-2-carboxylic acid
- 4-Aminotrichloropicolinic acid
- 4-Amino-3,5,6-trichloropicolinic acid
- ATCP
- Picolinic acid, 4-amino-3,5,6-trichloro-
- 3,5,6-Trichloro-4-aminopicolinic acid
- Tordon

Last updated: 21 November 1997

SIMAZINE
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 495)

CAS No.: 122-34-9
Chem. Abstr. Name: 6-Chloro-*N*,*N*'-diethyl-1,3,5-triazine-2,4-diamine

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Simazine was introduced in 1957 as a systemic herbicide for use on grasses and weeds in food crops, especially maize, and for general weed control. It is available in many types of formulation, including wettable powders, granules, concentrates, suspensions and liquids. Exposure can occur during its production and application and *via* contamination of ground- and surface water.

Exposure could also occur through consumption of foods containing residues. Simazine residues were not detected in large-scale surveys of food products in Canada and the USA.

5.2 Carcinogenicity in humans

No adequate data were available to the Working Group.

5.3 Experimental carcinogenicity data

No adequate data were available to the Working Group.

5.4 Other relevant data

No data on the genetic and related effects of simazine in humans were available to the Working Group.

Simazine did not induce micronucleus formation in mice. It induced a small increase in the frequency of sister chromatid exchange in human cells *in vitro* but not in rodent cells. Simazine did not induce genetic damage in any other tests, except in plants where chromosomal aberrations were induced and in *Drosophila melanogaster* where dominant lethal effects and gene mutation were induced.

5.5 Evaluation

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

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

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Subsequent evaluation: Vol. 73 (1999)

Synonyms

- Aktinit S
- Aquazine
- Azotop
- 4,6-Bis(ethylamino)-2-chlorotriazine
- 2,4-Bis(ethylamino)-6-chloro-*s*-triazine
- Bitemol S 50
- CAT
- CDT
- CET
- 6-Chloro-N^2,N^4-diethyl-1,3,5-triazine-2,4-diamine
- 2-Chloro-4,6-bis(ethylamino)-*s*-triazine
- Geigy 27,692
- Gesatop
- H 1803
- Herbazin
- Herbex
- Herbatoxol S
- Herboxy
- Hungazin DT
- Premazine
- Princep
- Radocon
- Radokor
- Simanex
- Simatsin-neste
- Simazin
- Symazine
- Tafazine
- Taphazine
- Triazine A 384
- W 6658
- Yrodazin

Last updated: 30 September 1999

TRIFLURALIN
(Group 3)

For definition of Groups, see Preamble Evaluation.

VOL.: 53 (1991) (p. 515)

CAS No.: 1582-09-8
Chem. Abstr. Name: 2,6-Dinitro-*N*,*N*-dipropyl-4-(trifluoromethyl)benzenamine

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Trifluralin is a selective pre-emergence herbicide used for the control of annual grasses and certain broadleaf weeds. It was first registered for use in 1963.

Trifluralin has been formulated as emulsifiable concentrates, granules and liquids.

Exposure to trifluralin may occur during its production and application and, at much lower levels, from consumption of residues in food and water.

N-Nitrosodi-*n*-propylamine has been detected in technical trifluralin, and levels of nitrosamines in trifluralin have been restricted in some countries.

5.2 Carcinogenicity in humans

Use of trifluralin was associated with an increased risk for non-Hodgkin's lymphoma in a study in the USA. A study of ovarian cancer in Italy did not suggest an association with exposure to trifluralin. Both results were based on small numbers of exposed subjects. A larger US study showed no association with the occurrence of leukaemia.

5.3 Carcinogenicity in experimental animals

One technical grade of trifluralin (possibly contaminated with *N*-nitrosodi-*n*-propylamine) was tested for carcinogenicity in mice and rats by administration in the diet. In female mice, it induced an increased incidence of hepatocellular carcinomas; in the same study, an increase in the incidence of lung adenomas or carcinomas was observed in females. An increased incidence of squamous-cell carcinomas of the forestomach was noted in female mice at the lower but not at the higher dose. In rats, an increase in the combined incidence of follicular-cell adenomas and carcinomas of the thyroid was noted at the lower but not at the higher dose in females.

Another preparation of trifluralin was tested for carcinogenicity in mice by administration in the diet. No increase in tumour incidence was observed.

5.4 Other relevant data

In a single study, trifluralin was embryolethal and increased the incidence of skeletal variants in mice at doses that caused some maternal toxicity.

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

A commercial trifluralin formulation induced chromosomal aberrations in bone marrow, embryonal cells and the male germ line in mice. Chromosomal aberrations were also induced in plants. Aneuploidy was induced in several lower eukaryotes. There was little evidence for the induction of gene mutation in any test system.

5.5. Evaluation

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

There is *limited evidence* in experimental animals for the carcinogenicity of technical-grade trifluralin.

Overall evaluation

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

For definition of the italicized terms, see Preamble Evaluation.

Synonyms

- Agreflan
- Agriflan 24
- 2,6-Dinitro-*N*,*N*-dipropyl-4-trifluoromethylaniline
- Elancolan
- L 36352
- Lilly 36352
- Nitran K
- Nitran
- Olitref
- Super-Treflan
- Synfloran
- Trefanocide
- Treflan
- Trifloran
- α,α,α-Trifluoro-2,6-dinitro-*N*,*N*-dipropyl-*para*-toluidine
- 4-(Trifluoromethyl)-2,6-dinitro-*N*,*N*-dipropylaniline
- Trifluraline
- Trikepin
- Tristar

Last updated: 21 November 1997