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Some Halogenated Hydrocarbons and Pesticide Exposures

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Last updated: 13 April 1999

PENTACHLOROETHANE

VOL.: 41 (1986) (p. 99)

CAS No.: 76-01-7

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Pentachloroethane was produced commercially as a chemical intermediate, and occupational exposure may have occurred. Trace levels have been reported in ambient air and water.

5.2 Experimental data

Technical-grade pentachloroethane (containing 4.2% hexachloroethane) was tested for carcinogenicity by oral administration by gavage in one experiment in mice and one experiment in rats. Hepatocellular carcinomas were induced in mice of each sex and hepatocellular adenomas in female mice; a marginally increased incidence of kidney tubular-cell adenomas was observed in male rats but not in female rats.

No data were available to the Working Group on the carcinogenicity of pure pentachloroethane to experimental animals.

No data were available to evaluate the reproductive effects or prenatal toxicity of pentachloroethane to experimental animals.

Pentachloroethane is not mutagenic to *Salmonella typhimurium*.

5.3 Human data

No data were available to evaluate the reproductive effects or prenatal toxicity of pentachloroethane to humans.

No case report or epidemiological study of the carcinogenicity of pentachloroethane to humans was available to the Working Group.

5.4 Evaluation

There is *limited evidence* for the carcinogenicity of technical-grade pentachloroethane (containing hexachloroethane) to experimental animals.

No evaluation could be made of the carcinogenicity of pentachloroethane to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluation: [Vol. 71 \(1999\)](#)

Synonyms

- Ethane pentachloride
- Pentalin

Last updated: 13 April 1999

1,2-DICHLOROPROPANE

VOL.: 41 (1986) (p. 131)

CAS No.: 78-87-5

5. Summary of Data Reported and Evaluation

5.1 Exposure data

1,2-Dichloropropane has been used as an industrial solvent, as a chemical intermediate and in soil fumigants. Human exposure may occur during its production and industrial and domestic use, and due to the presence of low levels in ambient air and in water.

5.2 Experimental data

1,2-Dichloropropane was tested for carcinogenicity by oral administration by gavage in one experiment in mice and one experiment in rats. A dose-related increase in the incidence of hepatocellular tumours was observed in male and female mice. Inconclusive results were obtained with regard to female rats, and no effect was seen in male rats.

No data were available to evaluate the reproductive effects or prenatal toxicity of 1,2-dichloropropane to experimental animals.

1,2-Dichloropropane is mutagenic to *Salmonella typhimurium* but not to *Streptomyces coelicolor*. It induces mutations but not chromosomal effects in *Aspergillus nidulans*. It does not induce sex-linked recessive lethal mutations in *Drosophila melanogaster*.

5.3 Human data

No data were available to evaluate the reproductive effects or prenatal toxicity of 1,2-dichloropropane to humans.

No case report or epidemiological study on the carcinogenicity of 1,2-dichloropropane to humans was available to the Working Group.

5.4 Evaluation

There is *limited evidence* for the carcinogenicity of 1,2-dichloropropane to experimental animals.

No evaluation could be made of the carcinogenicity of 1,2-dichloropropane to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluation: [Vol.71 \(1999\)](#)

Synonyms

- ENT 15 406
- Propylene chloride

- Propylene dichloride

Last updated: 13 April 1999

BIS(2-CHLORO-1-METHYLETHYL)ETHER

VOL.: 41 (1986) (p. 149)

CAS No.: 108-60-1

Chem. Abstr. Name: 2,2'-Oxybis(1-chloropropane)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Bis(2-chloro-1-methylethyl)ether has been produced as a solvent and soil fumigant and is also formed in large quantities as a by-product in some propylene oxide/propylene glycol production processes. Low levels have been found in water. Thus, both occupational and environmental exposures may occur.

5.2 Experimental data

Bis(2-chloro-1-methylethyl)ether, containing 2-chloro-1-methylethyl(2-chloro-*n*-propyl)ether and bis(2-chloro-*n*-propyl)ether, was tested for carcinogenicity by oral administration by gavage in one experiment in mice and in one experiment in rats. In mice, increased incidences of lung adenomas in males and females and of hepatocellular carcinomas in males were observed. In rats, no increase in tumour incidence was observed.

No data were available to evaluate the reproductive or prenatal effects of bis(2-chloro-1-methylethyl)ether to experimental animals.

Bis(2-chloro-1-methylethyl)ether is mutagenic to *Salmonella typhimurium*. It does not induce sex-linked recessive lethal mutations in *Drosophila melanogaster*.

4.3 Human data

No data were available to evaluate the reproductive effects or prenatal toxicity of bis(2-chloro-1-methylethyl)ether to humans.

No case report or epidemiological study of the carcinogenicity of bis(2-chloro-1-methylethyl)ether to humans was available to the Working Group.

4.4 Evaluation

There is *limited evidence* for the carcinogenicity of bis(2-chloro-1-methylethyl)ether to experimental animals.

No evaluation could be made of the carcinogenicity of bis(2-chloro-1-methylethyl)ether to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluation: [Vol. 71 \(1999\)](#)

Synonyms

- BCMEE
- Bis(β -chloroisopropyl)ether

- Bis(2-chloroisopropyl)ether
- Bis(2-chloro-2-methylethyl)ether
- Bis(1-chloro-2-propyl) ether
- DCIP
- Dichlorodiisopropyl ether
- 2,2'-Dichlorodiisopropyl ether
- β,β' -Dichlorodiisopropyl ether
- Dichloroisopropylether
- 2,2'-Oxybis(2-chloropropane)

Last updated: 13 April 1999

METHYL IODIDE

VOL.: 41 (1986) (p. 213)

CAS No.: 74-88-4

Chem. Abstr. Name: Iodomethane

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Methyl iodide is formed principally in the oceans. Smaller amounts are produced industrially for use as a chemical intermediate. Exposures occur from occupational use and from ubiquitous low-level exposure in ambient air and in water.

5.2 Experimental data

Methyl iodide was tested for carcinogenicity in one experiment in rats by subcutaneous administration and in a screening test for lung adenomas in strain A mice by intraperitoneal injection. It induced local sarcomas in rats after single or repeated subcutaneous injections; a marginally increased incidence of lung tumours was observed in mice.

No data were available to evaluate the reproductive effects or prenatal toxicity of methyl iodide to experimental animals.

Methyl iodide induces DNA damage and is mutagenic to bacteria in the presence or absence of an exogenous metabolic system. It induces mitotic recombination in yeast and mutations in cultured mammalian cells. It induces transformation in Syrian hamster embryo cells but not in C3H 10T1/2 cells.

5.3 Human data

No data were available to evaluate the reproductive effects or prenatal toxicity of methyl iodide to humans.

No case report or epidemiological study of the carcinogenicity of methyl iodide to humans was available to the Working Group.

4.4 Evaluation

There is *limited evidence* for the carcinogenicity of methyl iodide to experimental animals.

No evaluation could be made of the carcinogenicity of methyl iodide to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Previous evaluation: [Vol. 15 \(1977\)](#)

Subsequent evaluation: [Vol. 71 \(1999\)](#)

CHLOROFLUOROMETHANE

VOL.: 41 (1986) (p. 229)

CAS No.: 593-70-4

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Chlorofluoromethane has been reported as an impurity in dichlorofluoromethane, and thus limited exposures may occur.

5.2 Experimental data

Chlorofluoromethane was tested for carcinogenicity in one study in rats by oral administration by gavage at one dose level. High incidences of squamous-cell carcinomas and of fibrosarcomas of the forestomach and stomach were induced in animals of each sex.

No evaluation of the effects of chlorofluoromethane on reproduction or on prenatal toxicity in experimental animals could be made on the basis of the available data.

Chlorofluoromethane was mutagenic to *Salmonella typhimurium* and to cultured mammalian cells in the presence and absence of an exogenous metabolic system.

5.3 Human data

No data were available to evaluate the reproductive effects or prenatal toxicity of chlorofluoromethane to humans.

No case report or epidemiological study of the carcinogenicity of chlorofluoromethane to humans was available to the Working Group.

5.4 Evaluation

There is *limited evidence* for the carcinogenicity of chlorofluoromethane to experimental animals.

No evaluation could be made of the carcinogenicity of chlorofluoromethane to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluation: [Vol. 71 \(1999\)](#)

Synonyms

- CFC 31
 - FC 31
 - R 31
-

Last updated: 13 April 1999

CHLORODIFLUOROMETHANE

VOL.: 41 (1986) (p. 237)

CAS No.: 75-45-6

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Chlorodifluoromethane is produced extensively for use in refrigeration and air conditioning; significant quantities are subsequently released into the atmosphere, resulting in widespread, low-level human exposure. Occupational exposure to chlorodifluoromethane occurs during its production and use.

5.2 Experimental data

Chlorodifluoromethane was tested for carcinogenicity in one experiment in rats by oral administration by gavage and in experiments in rats and mice by inhalation exposure. No increase in tumour incidence was observed in rats after oral administration. The inhalation study in mice was inconclusive for males, and negative results were obtained for females. In the inhalation study in rats, males receiving the high dose had increased incidences of fibrosarcomas and Zymbal-gland tumours; negative results were obtained for female rats.

Chlorodifluoromethane causes malformations of the eyes of fetal rats, but has no reproductive effect in male rats and does not cause prenatal toxicity in rabbits following exposure by inhalation.

Chlorodifluoromethane is mutagenic to *Salmonella typhimurium* in the presence and absence of an exogenous metabolic system. It does not induce mutation or gene conversion in yeast, or DNA damage or mutation in cultured mammalian cells. It does not induce chromosomal damage in bone marrow or dominant lethal mutations in mice or rats treated *in vivo*.

5.3 Human data

No data were available to evaluate the reproductive effects or prenatal toxicity of chlorodifluoromethane to humans.

A small study of workers exposed to a mixture of chlorofluorocarbons, including chlorodifluoromethane, was uninformative with regard to the carcinogenic hazard of this chemical.

5.4 Evaluation

There is *limited evidence* for the carcinogenicity of chlorodifluoromethane to experimental animals.

There is *inadequate evidence* for the carcinogenicity of chlorodifluoromethane to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluations: [Suppl. 7 \(1987\)](#); [Vol. 71 \(1999\)](#)

Synonyms

- Algeon 22
- Algofrene 22
- Algofrene Type 6
- Arcton 4
- Arcton 22
- CFC 22
- Daiflon 22
- Difluorochloromethane
- Difluoromonochloromethane
- Dymel 22
- Electro-CF 22
- F 22
- FC 22
- Flugene 22
- Forane 22
- Freon 22
- Frigen 22
- Genetron 22
- Haltron 22
- Isceon 22
- Isotron 22
- Khaladon 22
- Monochlorodifluoromethane
- R 22
- Ucon 22

Last updated: 13 April 1999

2-CHLORO-1,1,1-TRIFLUOROETHANE

VOL.: 41 (1986) (p. 253)

CAS No.: 75-88-7

5. Summary of Data Reported and Evaluation

5.1 Exposure data

2-Chloro-1,1,1-trifluoroethane is used as a chemical intermediate in the production of the anaesthetic halothane. Human exposure occurs due to its presence as a low-level impurity in, and at metabolite of, halothane.

5.2 Experimental data

2-Chloro-1,1,1-trifluoroethane was tested for carcinogenicity in one experiment in rats by oral administration by gavage at one dose level. Increased incidences of uterine carcinomas and benign testicular tumours were observed.

No data were available to evaluate the reproductive effects or prenatal toxicity of 2-chloro-1,1,1-trifluoroethane to experimental animals.

2-Chloro-1,1,1-trifluoroethane is not mutagenic to *Salmonella typhimurium* in the presence or absence of an exogenous metabolic system.

5.3 Human data

No data were available to evaluate the reproductive effects or prenatal toxicity of 2-chloro-1,1,1-trifluoroethane to humans.

No case report or epidemiological study of the carcinogenicity of 2-chloro-1,1,1-trifluoroethane to humans was available to the Working Group.

5.4 Evaluation

There is *limited evidence* for the carcinogenicity of 2-chloro-1,1,1-trifluoroethane to experimental animals.

No evaluation could be made of the carcinogenicity of 2-chloro-1,1,1-trifluoroethane to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluation: [Vol. 71 \(1999\)](#)

Synonyms

- 1-Chloro-2,2,2-trifluoroethane
- CFC 133a
- FC 133a
- R 133a

- 2,2,2-Trifluorochloroethane
- 1,1,1-Trifluoro-2-chloroethane
- 1,1,1-Trifluoroethyl chloride

Last updated: 13 April 1999

POLYBROMINATED BIPHENYLS

VOL.: 41 (1986) (p. 261)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Polybrominated biphenyls were produced primarily in the 1970s as flame retardants. Occupational exposure occurred during their production and use. The accidental addition of a hexabromobiphenyl product (FireMaster FF-1) to a large quantity of farm animal feed in Michigan (USA) in 1973 resulted in widespread population exposure.

5.2 Experimental data

The carcinogenicity of a commercial preparation of polybrominated biphenyls (FireMaster FF-1, various lots), composed primarily of hexabromobiphenyl with smaller amounts of penta- and heptabrominated isomers, was tested by oral administration by gavage in one strain of mice and two strains of rats and by perinatal exposure in one strain of rats. It produced malignant hepatic tumours in mice of each sex. In rats of each sex, it produced benign and malignant hepatic tumours, including cholangiocarcinomas, after single or multiple administrations.

Short-term exposures of rats to high doses of commercial preparations of polybrominated biphenyls induce embryonic death, growth retardation and malformation; malformations have not been observed following exposure to lower doses throughout gestation. Pre- and perinatal exposure of rats to polybrominated biphenyls reduces postnatal growth and viability.

Various commercial preparations of polybrominated biphenyls are not mutagenic to bacteria in the presence or absence of exogenous metabolic systems or in a host-mediated assay. Polybrominated biphenyls do not induce DNA damage, or mutation, in cultured mammalian cells or chromosomal aberrations in rat or mouse bone marrow, nor micronuclei in mouse bone marrow, but they do inhibit junctional intercellular communication in cultured mammalian cells.

5.3 Human data

No relevant data were available to evaluate the reproductive effects or prenatal toxicity of polybrominated biphenyls to humans.

A small cohort study of chemical workers potentially exposed to polybrominated biphenyls together with other chemicals was uninformative with regard to cancer.

5.4 Evaluation

There is *sufficient evidence* for the carcinogenicity of commercial mixtures of polybrominated biphenyls to experimental animals.

There is *inadequate evidence* for the carcinogenicity of polybrominated biphenyls to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Previous evaluation: [Vol. 18 \(1978\)](#)

Subsequent evaluation: [Suppl. 7 \(1987\)](#)

Last updated: 23 April 1998

AMITROLE

VOL.: 41 (1986) (p. 293)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Amitrole has been widely produced since the 1950s for use as a herbicide. Occupational exposures occur during production, formulation and application of this herbicide, and nonoccupational exposures may occur from residues in food.

5.2 Experimental data

Amitrole was tested in mice by oral administration, skin application and transplacental exposure, in rats by oral and subcutaneous administration, and in hamsters by oral administration. In mice, thyroid and liver tumours were produced after oral administration; no skin tumour was observed after topical application. The study by transplacental exposure yielded inconclusive results. In rats, amitrole induced thyroid and pituitary tumours after oral administration. No carcinogenic effect was observed in hamsters.

Dietary exposure of breeding pairs of rats to amitrole reduces growth and viability of offspring.

Amitrole does not induce DNA damage in bacteria but may have an effect in yeast. It is not mutagenic to *Salmonella typhimurium* or *Escherichia coli*. Amitrole induces aneuploidy in yeast, but not mutation in yeast or *Aspergillus nidulans*. However, conflicting results were obtained in assays for mitotic gene conversion and recombination. It is weakly mutagenic to *Streptomyces coelicolor*. It does not induce sex-linked recessive lethal mutations or nondisjunction in *Drosophila melanogaster*. Amitrole induced mutations at two loci in one mammalian cell line. Amitrole does not induce unscheduled DNA synthesis in hepatocytes of rats exposed *in vivo*. No aneuploidy or chromosomal aberration is found in cultured human lymphocytes. Micronuclei are not induced in mouse bone marrow. Cell transformation is induced in mammalian cells. A commercial preparation of amitrole induces chromosomal abnormalities in plants.

5.3 Human data

Two cytogenetic studies of occupational exposure to a number of herbicides, including amitrole, were available. A possible increase in the frequency of chromosomal aberrations was seen in one study, and an increased frequency of sister chromatid exchanges occurred in one group of workers in the other. The role of amitrole itself cannot be evaluated from these studies.

No data were available to evaluate the reproductive effects or prenatal toxicity of amitrole to humans.

In a small cohort study of Swedish railroad workers who had sprayed herbicides, there was a statistically significant excess of all cancers among those exposed to both amitrole and chlorophenoxy herbicides, but not among those exposed mainly to amitrole.

5.4 Evaluation

There is *sufficient evidence* for the carcinogenicity of amitrole to experimental animals.

There is *inadequate evidence* for the carcinogenicity of amitrole to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Previous evaluation: [Vol. 7 \(1974\)](#)

Subsequent evaluations: [Suppl. 7 \(1987\)](#); [Vol. 79 \(2001\)](#)

Last updated: 23 April 1998

OCCUPATIONAL EXPOSURES TO CHLOROPHENOLS

VOL.: 41 (1986) (p. 319)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Several chlorophenols and their salts have been widely produced since the 1950s and used as wood preservatives, fungicides, slimicides, weed-killers and as precursors for chlorophenoxy herbicides. Widespread occupational exposure to chlorophenols and their chlorinated dibenzodioxin and dibenzofuran impurities is known to have occurred, especially in manufacturing plants and in wood-treatment applications. Increased urinary levels of chlorophenols and increased concentrations in adipose tissue of some chlorinated dibenzodioxins and dibenzofurans have been measured in workers exposed in sawmills and tanneries and in the textile industry. Skin absorption is believed to be a major route of exposure in these occupations. Burning of chlorophenol-containing materials in industrial or municipal incinerators may lead to the formation of various dibenzodioxin and dibenzofuran congeners.

5.2 Experimental data

Previous IARC evaluations of the carcinogenicity to experimental animals of several individual chlorophenols and of their impurity, 2,3,7,8-tetrachloro-*para*-dibenzodioxin (TCDD), are summarized in section 3.1, in this volume.

5.3 Human data

Two studies among the wives of the workers at two chemical plants did not show an association between pregnancy outcomes and paternal exposure to 2,4,5-trichlorophenol, pentachlorophenol and TCDD and other dioxins.

Three studies have been published in which cytogenetic effects were investigated in workers exposed occupationally to chlorophenols. In two of the studies, no difference was seen between exposed and control subjects; but in one of these studies the persons were examined ten years after exposure. The other study showed increased incidences of dicentric and acentric chromosomal aberrations, but not of gaps, chromatid breaks or sister chromatid exchanges.

Several cohort studies have been conducted among chemical industry workers with potential exposure to 2,4,5-trichlorophenol, TCDD and other chemicals. Mortality rates for all cancers combined were not elevated. In a Danish cohort study, there may have been exposure to chlorophenols, present as intermediates in the production of chlorophenoxy herbicides. No increase in the incidence of cancers at all sites combined was observed, but there were statistically significantly increased risks of soft-tissue sarcoma and lung cancer in different subcohorts.

Two case-control studies conducted in different regions of Sweden showed a statistically significant association between exposure to chlorophenols and soft-tissue sarcoma; a study from New Zealand did not.

A statistically significant association between malignant lymphoma and exposure to chlorophenols was identified in a Swedish case-control study. A case-control study of non-Hodgkin's lymphoma in New Zealand suggested a possible association with fencing work, but not with other occupational exposures to chlorophenols.

A case-control study in Sweden detected a significant association between nasal and nasopharyngeal cancer and exposure to chlorophenols, independent of exposure to wood dust.

4.4 Evaluation

There is *limited evidence* for the carcinogenicity of occupational exposure to chlorophenols to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluation: [Vol. 71 \(1999\)](#)

Last updated: 20 January 2004

OCCUPATIONAL EXPOSURES TO CHLOROPHENOXY HERBICIDES

VOL.: 41 (1986) (p. 357)

5. Summary of Data Reported and Evaluation

5.1 Exposure data

Chlorophenoxy herbicides have been produced extensively since the 1950s for use in agriculture and as defoliants, although production and use are now decreasing in many countries. Widespread occupational exposure to chlorophenoxy herbicides and their chlorinated dibenzodioxin impurities is known to have occurred during their production, formulation, application and disposal. Increased urinary levels of chlorophenoxy compounds and increased concentrations of some chlorinated dibenzodioxins in adipose tissue have been measured in highly exposed persons. The presence of dibenzodioxins and dibenzofurans has been demonstrated in the adipose tissue of nonoccupationally exposed people in many countries.

During occupational exposure, such as ground spraying and other manual application of these herbicides, dermal absorption is a major route of entry into the body.

In manufacturing plants, exposures occur during the handling of raw materials, intermediates, finished products and process wastes. High-level short-term occupational exposures have also been caused by industrial accidents.

5.2 Experimental data

Previous IARC evaluations of the carcinogenicity to experimental animals of several individual chlorophenoxy herbicides and of 2,3,7,8-tetrachlorodibenzo-*para*-dioxin (TCDD), an impurity found in some of these herbicides, are summarized in section 3.1, in this volume.

5.3 Human data

Studies comparing the occurrence of congenital malformations in areas and periods characterized by different usage of chlorophenoxy herbicides were uninformative with regard to the teratogenicity of these agents. Two case-control studies on birth anomalies among the children of Australian and US veterans and of New Zealand pesticide sprayers showed no excess risk associated with paternal exposure to herbicides.

No study was available of pregnancy outcomes of women exposed occupationally to chlorophenoxy herbicides.

In one study of persons exposed to chlorophenoxy herbicides during military operations in Viet Nam, conducted ten years after exposure, no increase in the incidence of chromosomal aberrations or sister chromatid exchanges was observed.

Cytogenetic studies have been carried out on workers occupationally exposed to chlorophenoxy herbicides during spraying. In three of the studies, there was also exposure to other herbicides and the effect of chlorophenoxy herbicides could not be assessed. Studies in which occupational exposure was only to chlorophenoxy herbicides showed no increased incidence of chromosomal aberrations or sister chromatid exchanges.

In a large Danish cohort study of chemical workers exposed to chlorophenoxy herbicides [particularly (4-chloro-2-methylphenoxy)acetic acid (MCPA), 2-(4-chloro-2-methylphenoxy)propanoic acid (mecoprop), 2,4-dichlorophenoxyacetic acid (2,4-D) and 2-(2,4-dichlorophenoxy)propanoic acid (dichlorprop)], as well as other chemicals, no overall increase in cancer incidence rate was observed, but there were significantly increased

risks of soft-tissue sarcoma and lung cancer in different subcohorts, which were not necessarily those with the highest exposures to chlorophenoxy herbicide preparations. A Finnish cohort study of brush control workers with short follow-up time showed no increased risk. A small Swedish cohort study of railroad workers who sprayed herbicides showed an increased risk of cancers at all sites combined for those exposed to both chlorophenoxy herbicide preparations and other herbicides. An excess incidence of all cancers was also reported from a very small cohort of Swedish forestry foremen exposed to chlorophenoxy herbicide preparations and other herbicides. A study of long-term pesticide applicators in the German Democratic Republic, heavily exposed to a number of chemicals, including 2,4-D and MCPA, demonstrated an increased risk of bronchial carcinoma.

A population-based case-control study conducted in northern Sweden showed a statistically significant association between exposure to chlorophenoxy herbicides, especially in forestry, and the occurrence of soft-tissue sarcomas. A second study on this type of tumour was conducted in southern Sweden, where a significant increase in the risk of developing soft-tissue sarcomas was associated with previous exposures to chlorophenoxy herbicides, mainly in agriculture. An increased risk of soft-tissue sarcoma was described among highly exposed Italian rice weeders in a population-based case-control study. A case-control study from New Zealand did not demonstrate an increased risk of soft-tissue sarcoma in people exposed to chlorophenoxy herbicides.

A statistically significant association between malignant lymphoma and exposure to chlorophenoxy herbicides was found in a Swedish case-control study; however, no such association was seen in a case-control study of these tumours from New Zealand. In a Danish cohort of chemical workers exposed to chlorophenoxy herbicides, there was also no increased risk of malignant lymphoma.

Three Swedish case-control studies of colon, liver and nasal cancer, respectively, which used the same study design and methods as in the studies on soft-tissue sarcoma and malignant lymphoma, did not demonstrate significantly increased risks. Exposure recall bias of cancer patients thus does not seem to explain the differences between the results of the Swedish and the New Zealand case-control studies of soft-tissue tumours and lymphomas.

In summary, well-conducted case-control studies have provided the most information on the association between cancer and occupational exposure to chlorophenoxy herbicides. Statistically significant elevated odds ratios have been observed for cancers at some sites, but not consistently, independent studies. The results of one cohort study on the incidence of soft-tissue sarcoma support the finding in case-control studies of an increased relative risk for these tumours. Other cohort studies have added little information. No consistent exposure-response relationship emerged from the different studies, and, in the studies that found an association, exposures were shorter than those usually associated with occupation-related cancers.

5.4 Evaluation

There is *limited evidence* that occupational exposures to chlorophenoxy herbicides are carcinogenic to humans.

For definition of the italicized terms, see [Preamble Evaluation](#).

Subsequent evaluation: [Suppl. 7 \(1987\)](#)