HEXACHLOROBENZENE

1. Chemical and Physical Data

1.1 Synonyms and trade names

*Chem. Abstr. Services Reg. No.:* 118-74-1

*Chem. Abstr. Name:* Hexachlorobenzene

*Synonyms:* HCB; pentachlorophenyl chloride; perchlorobenzene

*Trade names:* Amatin; Anticarie; Bunt-cure; Bunt-no-more; Co-op Hexa; Granox NM; Julin’s carbon chloride; No Bunt; No Bunt 40; No Bunt 80; No Bunt Liquid; Sanocide; Snieciotox

1.2 Structural and molecular formula and molecular weight

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\begin{array}{c}
\text{Cl} \\
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C\textsubscript{6}Cl\textsubscript{6} \hspace{1cm} \text{Mol. wt: 284.8}

1.3 Chemical and physical properties of the pure substance

From Weast (1976), unless otherwise specified

(a) *Description:* White needles (Hawley, 1977)

(b) *Boiling-point:* Sublimes at 322°C

(c) *Melting-point:* 230°C

(d) *Spectroscopy data:* \( \lambda_{\text{max}} 291, 301 \text{ nm (E}_1^1 = 7.7, 7.9 \) in isooctane; infrared, ultraviolet and mass spectral data have been tabulated (Grasselli & Ritchey, 1975).

(e) *Solubility:* Insoluble in water, sparingly soluble in cold ethanol and soluble in ether, benzene, chloroform and boiling ethanol (Hawley, 1977)
(f) **Volatile**: Vapour pressure is $1.089 \times 10^{-5}$ mm at 20°C (Mumma & Lawless, 1975).

(g) **Stability**: Very stable; nonreactive; inflammable, with a flash-point at 242°C (Hawley, 1977).

(h) **Reactivity**: Not broken down by physical or chemical processes in the environment (Mumma & Lawless, 1975); photolysis in methanol or hexane ($\lambda_{\text{max}} > 260$ or 220 nm) is rapid, giving penta- and tetrachlorobenzenes (Plimmer & Klingebiel, 1976).

### 1.4 Technical products and impurities

Hexachlorobenzene is available in the USA as a technical grade, containing 98% hexachlorobenzene, 1.8% pentachlorobenzene and 0.2% 1,2,4,5-tetrachlorobenzene. Some commercial hexachlorobenzene is derived from residual tar obtained as a byproduct in the production of tetrachloroethylene. Since this tar also contains hexachlorobutadiene, it is a potential impurity in commercial hexachlorobenzene derived from this source.

Hepta- and octachlorodibenzofurans and octachlorodibenzo-para-dioxin have been found in commercial hexachlorobenzene (Villanueva et al., 1974).

Formulations include wettable powders containing 40 or 80%, liquids containing 12.4–33% and a flowable product containing 35.1% of the chemical (US Environmental Protection Agency, 1972). Other commercial dust formulations for fungicidal use contain 10–40% hexachlorobenzene.

### 2. Production, Use, Occurrence and Analysis

#### 2.1 Production and use

(a) **Production**

Hexachlorobenzene was prepared by Lorentz in 1893 by heating carbon with chlorine in the presence of boric oxide (Prager et al., 1922). It can be produced commercially by reacting benzene with excess chlorine in the presence of ferric chloride at 150–200°C. However, at least one US producer isolates hexachlorobenzene from the distillation residues obtained as a byproduct in the manufacture of tetrachloroethylene.

Commercial production of hexachlorobenzene in the USA was first reported in 1933 (US Tariff Commission, 1934). Three US producers made it up to the end of 1973 (with an
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estimated total production of 300 thousand kg in 1973); but there was only one US producer in 1974, and only one company reported commercial production of an undisclosed amount in 1975 (US International Trade Commission, 1977a). That company is believed to have discontinued production in early 1978.

Hexachlorobenzene is a byproduct or waste material in the production of many chemicals. The quantities produced in 1972 have been estimated in relation to various end-products: tetrachloroethylene, 0.8–1.6 million kg; trichloroethylene, 104–203 thousand kg; carbon tetrachloride, 90–181 thousand kg; chlorine, 90–176 thousand kg; dimethyl tetrachloroterephthalate, 36–45 thousand kg; vinyl chloride, 0–12 thousand kg; atrazine, propazine and simazine, as a group, 2–4 thousand kg; pentachloronitrobenzene, 1–3 thousand kg; and mirex, 0.5–0.9 thousand kg.

In 1975, imports through the principal US customs districts of Grannox NM Seed Treatment, a formulation of hexachlorobenzene in combination with maneb, were 100 thousand kg (US International Trade Commission, 1977b).

One company in Spain produces an estimated 150 thousand kg hexachlorobenzene annually. In Japan, about 300 thousand kg were obtained in 1977 as a byproduct in the production of tetrachloroethylene; almost all was incinerated.

(b) Use

In 1972, the principal use of hexachlorobenzene in the USA was as a fungicide to control wheat bunt and smut fungi on other grains. Other applications in 1972 were as an additive for pyrotechnic compositions for military uses, as a porosity controller in the manufacture of electrodes, as a chemical intermediate in dye manufacture and organic synthesis and use as a wood preservative.

Minor amounts have been used as an additive for polymers and as a raw material for synthetic rubber. It has been used as a plasticizer for polyvinyl chloride (Plimmer & Klingebiel, 1976). In 1974, the largest US producer reported that all of its production for several years had been committed for use as a rubber peptizing agent in the manufacture of nitroso and styrene-type rubbers.

Hexachlorobenzene is registered by the US Environmental Protection Agency as a treatment for control of fungi which infect the seeds of onions, sorghum and wheat. It is also used in combination with captan or maneb for the treatment of seeds of barley, beans, corn, flax, oats, peanuts, rye and soya beans (US Environmental Protection Agency, 1972). It is reported to be a candidate for the issuance of a notice of a rebuttable presumption against
renewal of registration (RPAR) (see General Remarks on the Substances Considered,) because of possible carcinogenicity, teratogenicity and mutagenicity (Anon., 1978).

From 1 August 1974, the use on lettuce and on seed-potatoes of pentachloronitrobenzene containing more than 0.1% hexachlorobenzene was prohibited in The Netherlands. From 1 May 1975, the same restriction was applied to its use on flower bulbs and to all other uses (WHO, 1975).

In December 1974, the Joint Meeting of the FAO Working Party of Experts on Pesticide Residues and the WHO Expert Committee on Pesticide Residues established a value of 0–0.0006 mg/kg bw as a conditional acceptable daily intake in man (WHO, 1975).

2.2 Occurrence

Hexachlorobenzene is not known to occur as a natural product. It is a contaminant of various pesticides, including dimethyl tetrachloroterephthalate (Dacthal) and pentachloronitrobenzene (Cabral et al., 1977).

The distribution of hexachlorobenzene as a byproduct of the petrochemical industry has been reviewed (Laska et al., 1976). Reviews have been published on the occurrence of hexachlorobenzene residues in the environment in Italy (Leoni & D’Arca, 1976) and in Czechoslovakia (Mahelova et al., 1977).

(a) Water

Hexachlorobenzene has been found in four river-water samples, eight finished drinking-water samples, one sample from a sewage treatment plant and in the effluent water from seven chemical plants in various US and European locations (Shackelford & Keith, 1976). It has also been detected in urban rainwater runoff in the USA, at levels of 0–339 ng/L (Dapper, 1974); in the Rhine River (Greve, 1972); in 108 samples of surface waters in Italy, at average levels of 2.5 ng/L (Leoni & D’Arca, 1976); and in most river-water residues in an industrialized region of the USA, at levels of less than 2 μg/L, but as high as 90 μg/L in one sample (Laska et al., 1976).

(b) Soil and sediments

Hexachlorobenzene has been detected in: (1) greenhouse soil in the USA, 19 months after application, at levels of 0.19 mg/kg in the top 2 cm of soft and of 0.11 mg/kg in the 2–4-cm layer (Beall, 1976); (2) soil in Belgium, at average levels of 0.44 and 0.85 mg/kg (Dejonck-heere et al., 1976); (3) untreated and treated greenhouse and field soil in the Federal Republic of Germany, at levels of 0.002–1.03 mg/kg (Haefner, 1975, 1977); (4) the soil in farming areas in Italy, at levels of 40 pa/kg (Leon) & D’Arca, 1976); and (5) levee
and ditch soil in an industrialized region of the USA, at levels ranging from 0 to nearly 900 μg/kg (wet-weight basis) and 1677 μg/kg (dry-weight basis) (Laska et al., 1976).

(c) Food and drink

In the Total Diet Program of the US Food and Drug Administration, hexachlorobenzene was detected in food composites in 30 US cities, at levels of 0.006–0.041 mg/kg (Johnson & Manske, 1976). As part of the same study, the average daily intake of hexachlorobenzene was calculated to be 0.3978 μg/day in fiscal year 1973 and 0.0725 μg/day in fiscal year 1974 (US Food & Drug Administration, 1977).

The average intake of hexachlorobenzene from cooked food samples taken from an Italian Navy mess was reported to be 4.11 μg/man per day (Leoni et al., 1975). In Japan, hexachlorobenzene residues were detected at low levels in 16 foods, e.g., beef, 12 μg/kg; pike, 11 μg/kg; salmon, 9 μg/kg; carp, 8 μg/kg; and pork, 7 μg/kg (Morita et al., 1975a,b). Residues of pesticides, including hexachlorobenzene, have been detected in foods representing an average Canadian diet, at levels of 0.001–0.085 mg/kg (Smith et al., 1975).

The contamination of milk and dairy products by organochlorine pesticides, including hexachlorobenzene, in The Netherlands between 1967 and 1973 has been reviewed (Tuinstra, 1974). Hexachlorobenzene residues have been detected in: (1) milk and milk products in the Federal Republic of Germany, at levels of up to 0.5 mg/kg (Heeschen et al., 1976) and 0–2 mg/L (Knöppler, 1976) on a fat basis; (2) whole cow’s milk in Italy, at an average level of 4.2 μg/L (Leoni & D’Arca, 1976); (3) some Italian grating cheeses (Corvi et al., 1976); (4) milk in Spain, at a mean level of 0.654 mg/L (Pozo Lora et al., 1977); (5) butter from five Spanish regions, with a mean level of 0.15 mg/kg on a fat basis (Polo Villar et al., 1977); and (6) dairy products in France (Richou-Bac et al., 1974).

Hexachlorobenzene has also been detected in tinned vegetables and fruits (Biston et al., 1975) and in meat at mean levels of 0.08–0.064 mg/kg (Knöppler, 1976).

(d) Animals

Hexachlorobenzene has been detected in: (1) starlings from 126 US sites, at levels of 0–9.11 mg/kg (White, 1976); (2) wild ducks, at levels of 0–0.24 mg/kg (White & Kaiser, 1976); (3) eggs of common terns, at a level of 7.67 mg/kg (dry weight) (Gilbertson & Reynolds, 1972); (4) captive and free pheasants, at levels of 1.2–3.8 and 2.3–2.8 μg/kg, respectively (Mikulik et al., 1977); (5) the livers of birds, at levels of up to 7.2 mg/kg (Leoni & D’Arca, 1976); (6) wild foxes, boars and does, at levels of 0.02–3.11 mg/kg (Koss & Manz, 1976); and (7) swine, at an average level of 0.616 mg/kg, with 67% of the samples containing residues of more than 0.5 mg/kg (Lohse, 1975).
It has also been detected in: (1) fish in Lake Superior, at concentrations of < 0.1 mg/kg (Veith et al., 1977); (2) aquatic animals in Australia, at levels of 1–2 μg/kg (Thomson & Davie, 1974); (3) 8 species of fish, at mean levels of < 1 μg/kg to 16 mg/kg (Johnson et al., 1974); and (4) mosquito fish, at levels of 71.8–379.8 μg/kg, and commercial fish, at a level of 88 μg/kg, from an industrialized region of the USA (Laska et al., 1976).

(e) Humans

Hexachlorobenzene residues have been detected in human milk in: (1) Ghana, at a level of 0.086 mg/L (Polishuk et al., 1977); (2) Australia, at levels of 0.012–0.034 mg/L (Stacey & Thomas, 1975); (3) Norway (Bakken & Seip, 1977); (4) Austria, at a mean concentration of 1.24 mg/L (Pesendorfer, 1975); (5) France, at average levels of 0.98 mg/L (Luquet et al., 1975); and (6) Spain, at levels of up to 0.08 mg/L (Trigo Lorenzo & Fernandez Garcia, 1976).

It has also been detected in human adipose tissue in: (1) Japan, at levels of < 0.003–0.77 μg/g (Curley et al., 1973) and at a level of 0.21 μg/g (Morita et al., 1975a,b); (2) New Zealand, at a mean level of 0.31 μg/g (Solly & Shanks, 1974); (3) Canada, at levels of 0.001–0.520 μg/g (Mes et al., 1977); and (4) Italy, at an average level of 491 ng/g (Leoni & D’Arca, 1976).

Hexachlorobenzene has been detected in the blood of the umbilical cord in newborn infants and of their mothers in Argentina, at levels of up to 19 ng/L (Astolfi et al., 1974), and in the blood of children 1–18 years old in the Federal Republic of Germany at a maximum of 22 ng/L in boys and 17 ng/L in girls (Richter & Schmid, 1976).

(f) Occupational exposure

Hexachlorobenzene has been detected in: workplace air during the production of pentachlorophenol (Mel’nikova et al., 1975); the blood of workers in a factory making chlorinated solvents, at levels of 14–233 μg/L (Burns & Miller, 1975); and the blood of vegetable spraymen, at levels of 0–310 μg/L (Burns et al., 1974).

(g) Other

Hexachlorobenzene has been detected in: animal feeds (Richou-Bac et al., 1975); various grain samples, at mean levels of 0.27 mg/kg or less (Arrifai & Acker, 1975); and laboratory plastic wash bottles, at levels of 0.16–2.7 μg/bottle (Rourke et al., 1977).
2.3 Analysis

A review of methods of analysis for hexachlorobenzene is available (Li et al., 1976).

Determination and confirmation of low levels of hexachlorobenzene residues is hampered by the presence of other organochlorine pesticides and polychlorinated biphenyls. Methods for analysing residual hexachlorobenzene include separation and clean-up procedures, specific gas chromatographic columns and formation of chemical derivatives. Methods used for the analysis of hexachlorobenzene in environmental samples are listed in Table 1.

Other analytical methods to isolate and identify hexachlorobenzene include: gel-permeation chromatography (Johnson et al., 1976), gas chromatography/electron capture detection on various columns (Di Muccio et al., 1972; Szokolay et al., 1975) and gas chromatography/mass spectrometry (Lunde & Baumann Ofstad, 1976).

Recovery of hexachlorobenzene from a magnesium silicate (Florisil) column, eluted with methylene chloride-hexane-acetonitrile, has been investigated for use with fatty and non-fatty foods (US Food & Drug Administration, 1975).

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

3.1 Carcinogenicity studies in animals¹

(a) Oral administration

Mouse: Groups of 30–50 male and 30–50 female six- to seven-week-old Swiss mice were fed diets containing 0, 50, 100 or 200 mg/kg diet hexachlorobenzene (> 99.5% pure) until the animals were 120 weeks old, at which time all survivors were killed. Another group of 30 male and 30 female mice were fed 300 mg/kg diet hexachlorobenzene for 15 weeks. At 90 weeks of age, the percentage survival rates in males and females in the five different groups were: 50 and 48, 30 and 40, 27 and 30, 4 and 0, 13 and 57, respectively. The incidence of lymphomas and lung tumours was not increased in treated animals; no liver-cell tumours were found in the controls or in the group receiving 50 mg/kg diet. In the groups receiving 100, 200 and 300 mg/kg diet, the incidences of liver-cell tumours in the survivors (males and females) at the time the first liver-cell tumour was observed were: 3/12 and 3/12, 7/29 and 14/26, 1/3 and 1/10. The effective intake of hexachlorobenzene that induced liver-cell tumours was 12–24 mg/kg bw per day (Cabral et al., 1978, 1979¹).

¹ The Working Group was aware of studies in progress to assess the carcinogenicity of hexachlorobenzene in mice and rats by oral administration (IARC, 1978).

¹It was also reported in this article that an increased incidence of liver-cell tumours was observed in a small group of MRC rats fed 100 mg/kg diet hexachlorobenzene (5 mg/kg bw per day) for 75 weeks.
This page is occupied by Table 1
Table 1 (contd)
Hamster: A total of 159 female and 157 male Syrian golden hamsters, six weeks of age, were administered dietary concentrations of 0, 50, 100 and 200 mg/kg diet hexachlorobenzene (> 99.5% pure) for lifespan, equivalent to 0, 4, 8 and 16 mg/kg bw/day. The incidences of hepatomas, liver haemangioendotheliomas and thyroid adenomas were increased by exposure to hexachlorobenzene. In females and males given 0, 50, 100 and 200 mg/kg diet hexachlorobenzene, hepatomas occurred in 0/39 and 0/40, 14/30 and 14/30, 17/30 and 26/30 and 51/60 and 49/57 animals, respectively; the first hepatoma (with multiple nodules, largest diameter 7 mm) was found in one female hamster after 18 weeks of treatment. The incidences of liver haemangioendotheliomas in males and females receiving the highest dose were 20/57 and 7/60; three of these gave metastases; no liver haemangioendotheliomas were found in the controls. Alveolar thyroid adenomas were found in treated animals, and a significant increase ($p < 0.05$) was found in males treated with 200 mg/kg diet (8/57 versus 0/40 controls); these tumours also occurred in 2/30 females given 50 mg, in 1/30 males and 1/30 females given 100 mg and in 3/60 females given 200 mg (Cabral et al., 1977).

(b) Intraperitoneal administration

Mouse: Groups of 20 male A/St mice, six to eight weeks old, were given thrice weekly i.p. injections of 8, 20 or 40 mg/kg bw hexachlorobenzene in tricaprylin for eight weeks. All survivors were killed 24 weeks after the first injection. The average numbers of lung tumours per mouse were 0.68, 0.28 and 0.75 in the treated groups, which were not significantly different from that in controls injected with tricaprylin (Theiss et al., 1977) [The Working Group noted the limitations of a negative result obtained with this test system; see General Remarks on the Substances Considered.].
3.2 Other relevant biological data

(a) Experimental systems

The toxicity and metabolism of hexachlorobenzene have been reviewed (Cooper, 1976, 1978).

Toxic effects

The oral LD$_{50}$ of hexachlorobenzene in rats varies from 3500–10 000 mg/kg bw; death is due to neurotoxic effects (Booth & McDowell, 1975).

The LD$_{50}$ of technical hexachlorobenzene (93–95% pure) in female rats given repeated administrations in the diet over four months was about 500 mg/kg diet, which was lower than for males. Effects of such chronic feeding included hepatocellular hypertrophy and necrosis, spleen enlargement and porphyria (Kimbrough & Linder, 1974). Porphyrins accumulate in urine liver kidney and spleen suggesting an effect on the activity of uroporphyrinogen decarboxylase (Doss et al., 1976; Goerz et al., 1978; Kuiper-Goodman et al., 1977). Mice given 167 mg/kg diet hexachlorobenzene for six weeks became immunosuppressed, as indicated by decreased serum globulin levels and a decreased response of spleen lymphocytes to sheep red blood cells (Loose et al., 1977). In rats fed hexachlorobenzene for 4 weeks, subsequent food deprivation appeared to enhance the toxic response, implying decreased mobilization of hexachlorobenzene residues into fat and resulting in a higher plasma, liver, brain and adrenal accumulation of hexachlorobenzene (Villanueva et al., 1977).

Doses ranging from 0.05–50 mg/kg bw per day hexachlorobenzene were administered to pigs for 90 days. Porphyria and death occurred in animals given the highest dose level. Increased urinary excretion of coproporphyrin was observed in groups receiving 0.5 and 5 mg/kg bw per day after eight weeks; in those receiving 5 mg/kg bw, induction of microsomal liver enzymes, accompanied by increased liver weight, was also observed (den Tonkelaar et al., 1978).

Low dietary doses of hexachlorobenzene induced various hepatic mixed-function oxidases in rats (Grant et al., 1974; Mehendale et al., 1975; Stonard, 1975).

Hexachlorobenzene enhanced the hepatocarcinogenicity of polychlorinated terphenyls (PCT) in ICR mice: 0/28 animals had hepatocellular carcinomas with 250 mg/kg diet PCT, while 8/26 had these tumours with the same dose of PCT plus 50 mg/kg diet hexachlorobenzene (Shirai et al., 1978).
**Embryotoxicity and teratogenicity**

Placental transfer of hexachlorobenzene has been reported in mice and rats (Andrews & Courtney, 1976; Villeneuve & Hierlihy, 1975). A minimal teratogenic effect of hexachlorobenzene observed in Wistar rats could not be reproduced in the same laboratory with doses up to 120 mg/kg bw administered during organogenesis (Khera, 1974). In other studies with 100 mg/kg bw hexachlorobenzene and with pentachloronitrobenzene (PCNB) contaminated by hexachlorobenzene, cleft palate and some kidney malformations were found in mice (Courtney et al., 1976).

In a four-generation test, groups of 10 male and 20 female Sprague-Dawley rats were treated with 0, 10, 20, 40, 80, 160, 320 or 640 mg/kg diet hexachlorobenzene from weaning. Suckling pups in the F₁ generation were particularly sensitive, and many died prior to weaning when the mothers were fed concentrations of 320 or 640 mg/kg diet. No gross abnormalities were found (Grant et al., 1977).

Hexachlorobenzene decreased survival of chicks of Japanese quail treated with 20 mg/kg diet for 90 days (Schwetz et al., 1974). These results confirmed those of another study in which administration of 80 mg/kg diet for 90 days reduced egg production and hatchability (Vos et al., 1971).

**Absorption, distribution, excretion and metabolism**

Hexachlorobenzene administered orally to rats was absorbed slowly from the gut, mainly via the lymphatic system, and was stored extensively in the fat after 48 h (Iatropoulos et al., 1975). The quantitative recovery of intraperitoneally and orally administered ¹⁴C-hexachlorobenzene in rats was dose-dependent, but more ¹⁴C was recovered from faeces than from the urine. The major urinary metabolites were pentachlorophenol, tetrachlorohydroquinone and pentachlorothiophenol. The other urinary metabolites were tetrachlorobenzene, pentachlorobenzene, 2,4,5- and 2,4,6-trichlorophenols and 2,3,4,6- and 2,3,5-6-tetrachlorophenols; 2,3,4-trichlorophenol and other tetrachlorophenols were present in traces. These metabolites were excreted as conjugates or in free form in the urine. Unchanged hexachlorobenzene was found in the faeces and in fat (Engst et al., 1976; Koss et al., 1976; Mehendale et al., 1975; Renner & Schuster, 1977).

When 110 µg/day ¹⁴C-hexachlorobenzene were given orally to Macaca mulatta monkeys for 11–15 months, 50% of the radioactivity found in the urine was in pentachlorophenol and 25% in pentachlorobenzene, the remainder being in unidentified metabolites and unchanged hexachlorobenzene. In the faeces, 99% of the radioactivity was in unchanged hexachlorobenzene. During the last 10 days of the experiment, males excreted 7.2% of the administered dose in the urine and 52% in the faeces; females excreted 4.6 and 42.2%, respectively (Rozman et al., 1977).
Hexachlorobenzene was found in the milk of cows administered hexachlorobenzene (Fries & Marrow, 1976), and in organs of 18-day-old rats whose mothers were fed a diet containing hexachlorobenzene (Mendoza et al., 1975).

**Mutagenicity and other related short-term tests**

Hexachlorobenzene did not significantly increase the frequency of reversions to histidine and methionine auxotrophy in Saccharomyces cerevisiae (strain 632/4) in the absence of a metabolic activation system (Guerzoni et al., 1976).

In a dominant lethal test, male rats that received 20, 40 or 60 mg/kg bw hexachlorobenzene orally for 10 days were mated sequentially with untreated females (one male with two females; 14 mating periods, each of five days’ duration). There were no significant differences between the test and control groups with regard to the incidence of pregnancies, corpora lutea, live implants or decidualmas, at any dose level or in any of the mating periods (Khera, 1974).

**(b) Humans**

The occurrence of hexachlorobenzene in human tissues is described in section 2.2 (e).

An epidemic of 4000 cases of porphyria cutanea tarda occurred in Turkey between 1955 and 1959 as a result of human consumption of grain that had been treated with hexachlorobenzene. The estimated daily intake was 50–200 mg/day hexachlorobenzene over a relatively long period before the disease became apparent (Mazzei & Mazzei, 1973; Peters, 1976; Peters et al., 1966, 1978). The majority of the patients were children, mostly boys, aged 4–14 years (Cam & Nigogosyan, 1963). A mortality rate of 14% was reported within several years (Peters et al., 1966, 1978). Children under the age of four rarely developed porphyria, but in breast-fed infants a condition known as ‘pink-sore’ was reported, with a mortality rate greater than 95% (Cam, 1960; Peters, 1976). Samples of breast milk from the mothers of these infant were shown to contain hexachlorobenzene (Peters et al., 1966). Follow-up studies of 32 of the patients have shown that abnormal porphyrin metabolism and active symptomatology persist 20 years after hexachlorobenzene ingestion (Peters et al., 1978).

Hexachlorobenzene levels in plasma of people living near a hexachlorobenzene manufacturing plant but not exposed occupationally averaged 3.6 μg/L; there was no evidence of porphyria, but plasma coproporphyrin levels were abnormally high (Burns & Miller, 1975).
Farm workers exposed occupationally to hexachlorobenzene-contaminated Dacthal (dimethyl-tetrachloroterephthalate) had average blood hexachlorobenzene concentrations of 0.040 mg/L, but no evidence of porphyria was found in this group (Burns et al., 1974).

### 3.3 Case reports and epidemiological studies

No data were available to the Working Group.

### 4. Summary of Data Reported and Evaluation

#### 4.1 Experimental data

Hexachlorobenzene was tested by oral administration in one experiment in mice and in one in hamsters. In mice, it produced liver-cell tumours in animals of both sexes. In hamsters of both sexes, it produced hepatomas, liver haemangiotheliomas and thyroid adenomas. An experiment involving intraperitoneal administration in mice was considered to be inadequate.

Hexachlorobenzene is fetotoxic and produces some teratogenic effects. It was not mutagenic in yeast and did not induce dominant lethal effects in male rats.

#### 4.2 Human data

No case reports or epidemiological studies were available to the Working Group.

The production and use of hexachlorobenzene as a fungicide over the past several decades and its occurrence as a byproduct in the manufacture of other chemicals indicate that widespread human exposure occurs in both the general and working environments. This is confirmed by many reports of its occurrence in the general environment and in human body fluids.

A group of people who were accidentally exposed over a period of time is known to exist; many of these showed toxic manifestations, some lasting for as long as 20 years. No data on carcinogenic effects have been reported.

#### 4.3 Evaluation

There is *sufficient evidence* that hexachlorobenzene is carcinogenic in mice and hamsters. In the absence of adequate data in humans, it is reasonable, for practical purposes, to regard hexachlorobenzene as if it presented a carcinogenic risk to humans.
5. References


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Richter, E. & Schmid, A. (1976) [Hexachlorobenzene content in the whole blood of children.] *Arch. Toxikol.*, 35, 141–147 (in German)


