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**Gesellschaft Deutscher Chemiker**

GDCh-Advisory Committee  
on Existing Chemicals of  
Environmental Relevance (BUA)

**Tetrachlorobenzene**  
BUA Report 86  
(December 1991)



S. Hirzel

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# Tetrachlorobenzene

BUA Report 86  
(December 1991)

edited by the GDCh-Advisory  
Committee on Existing Chemicals  
of Environmental Relevance

Beratergremium für  
Umweltrelevante Altstoffe (BUA)



S. Hirzel

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## Foreword

The German Chemicals Act (Chemikaliengesetz - ChemG) of 1980 stipulates that certain existing chemicals must be reported to the competent authority, if they exhibit properties which indicate that they may be hazardous, either alone or in combination with other substances.

In the summer of 1982, an Advisory Committee on Existing Chemicals of Environmental Relevance (BUA) was set up by the German Chemical Society (Gesellschaft Deutscher Chemiker - GDCh). It brings together representatives from the scientific community, the chemical industry and the governmental authorities. This Advisory Committee is responsible for elaborating appropriate solutions for substances of relevance for health and the environment on the basis of voluntary measures. It selects and examines existing chemicals from the aforementioned angles. The testing and evaluation are based on scientific criteria alone.

It was, therefore, necessary to develop priority setting procedures. In a first phase reports were only prepared for priority chemicals. Within the framework of a first priority setting procedure, chemicals were compiled from several priority lists and 135 chemicals were selected for detailed substance reports.

In a second priority setting procedure the survey of the German Chemical Industry Association (VCI) on all substances with a production volume of more than 10 tons per year was used as a starting list. Since this survey covered 4,600 chemicals, BUA decided to process the corresponding list in several stages. The first stage included approx. 1,050 substances with a production volume of more than 1,000 tons per year.

Detailed reports are drawn up on chemicals suspected of having a hazard potential and abridged reports on those presenting only a minor hazard potential, according to the current state of knowledge.

The detailed BUA reports take in both the published literature and data from industry. If data for the evaluation of the chemicals are not available, additional studies are recommended and the results are published as updates to the reports. The reports serve as a basis for the instigation of administrative measures, when there are indications of risks to health or the environment.

Tübingen, May 1993

Ernst Bayer  
Chairman of the Advisory Committee  
on Existing Chemicals  
of Environmental Relevance

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# **BUA Report on 1,2,4,5-Tetrachlorobenzene**

## **Summary and conclusions**

### **Ecological aspects**

#### **Manufacture, use and distribution in the compartments (release, occurrence)**

##### **Manufacture and use**

From 1985 to the end of 1986 1,2,4,5-tetrachlorobenzene (1,2,4,5-TeCB) was specifically manufactured and isolated by just one company in the Federal Republic of Germany. Today 1,2,4,5-tetrachlorobenzene occurs exclusively as a by-product in association with other chlorinated benzenes in the trichlorobenzene production of a single manufacturer. After the trichlorobenzenes have been distilled off, part of the residue mixture, which accounts for approx. 200 t 1,2,4,5-TeCB/a, is further chlorinated to hexachlorobenzene. The remainder is disposed of in an incineration plant specially designed to handle hazardous waste.

Until 1983 1,2,4,5-tetrachlorobenzene was important in the Federal Republic of Germany as a starting product for 2,4,5-trichlorophenol, a compound used predominantly to manufacture crop protection agents. Between 1963 and 1977 an estimated 1000 t 1,2,4,5-tetrachlorobenzene were added to transformer oils containing PCB. It is impossible to estimate the amount of these 1,2,4,5-tetrachlorobenzene containing oils still present in transformers because no figures are available on the number of transformers being exported, imported or disposed of. During the 1970s and early 1980s a possible use of 1,2,4,5-tetrachlorobenzene was also to process dyestuffs, optical brighteners, flame retardants, and water-repellent products.

## Release

In 1990 approx. 11 kg of a mixture of tetrachlorobenzene isomers were released into the atmosphere during manufacture, and approx. 1240 kg 1,2,4,5-tetrachlorobenzene were emitted during further processing.

It is not possible to estimate the amount of 1,2,4,5-tetrachlorobenzene being formed and released along with other compounds, when waste containing chlorine is incinerated at temperatures between 400 and 900 °C.

Less than 560 kg 1,2,4,5-TeCB/a is released into the hydrosphere from manufacturing and processing.

It is not possible to estimate an entry into the geosphere through 1,2,4,5-TeCB containing wastes in dumps, particularly through wastes deposited from the 1960s to the mid 1980s.

1,2,4,5-Tetrachlorobenzene has been identified in a number of organisms as an intermediate metabolite in a subsidiary route of biotransformation of gamma-hexachlorocyclohexane. It is, however, not possible to quantify this as a release into the bio- and geosphere.

## Occurrence

In 1986/87 a mean concentration of 0.73 ng 1,2,3,5- and/or 1,2,4,5-TeCB/m<sup>3</sup> was measured in the air at different places of Hamburg City while at the vicinity of a lindane production facility closed in 1984 an average peak value of 20.9 ng 1,2,3,5- and/or 1,2,4,5-TeCB/m<sup>3</sup> was found.

In 1984/85 an average of 0.01 - 0.06 µg/l and peak values of 0.1 - 0.2 µg/l were recorded for the sum of the tetrachlorobenzene isomers in the Upper Rhine. In the middle course of the Rhine (Hesse; 1986/87), the Lower Rhine (North Rhine-Westphalia; 1984 - 1989) and at the mouths of

the tributaries, concentrations of 1,2,4,5-tetrachlorobenzene were below the limits of determination of 0.5 µg/l resp. 0.1 µg/l.

Analysis of concentrated suspended solids from the Rhine at Kleve-Bimmen in 1989 gave a mean of 5.2 µg TeCB/kg dry weight, with a minimum of < 2 µg TeCB/kg dry weight and a maximum of 8.0 µg TeCB/kg dry weight. In 1990 an observation trip recorded concentrations of the isomer mixture 1,2,3,5- + 1,2,4,5-tetrachlorobenzene between 0.006 µg/l and 0.209 µg/l in the middle course of the River Elbe and < 0.001 µg/l at the Havel mouth. In 1989 concentrations of 1,2,3,5- + 1,2,4,5-tetrachlorobenzene between 0.002 and 0.019 µg/l were recorded in the Lower Elbe between Schnackenburg and Wedel; between Brunsbüttel and Scharhörn concentrations were below the limit of determination of 0.001 µg/l with the exception of one value with 0.002 µg/l.

Sediment samples taken in Hesse from the Rhine, the Main and its tributaries (one sample/year and location; particle size < 63 µm) contained less than 0.3 µg 1,2,4,5-TeCB/kg dry weight in 1987 and less than 0.02 µg/kg dry weight in 1988. From 1987 to 1989 concentrations of 1,2,4,5-tetrachlorobenzene in sediment from the Rhine between Oberwinter and Bimmen ranged from < 1 resp. < 2 µg/kg dry weight to 6.7 µg/kg dry weight in an old branch of the Rhine near Binnen. In April 1989 a peak concentration of 23 µg TeCB/kg dry weight was recorded in a gravel pit at the Rhine near Lohrwardt following high water. In 1989 no 1,2,4,5-tetrachlorobenzene was detected in sediment from the River Lippe at kilometre marker 46.9 (near Marl) with a limit of determination of 2 µg/kg dry weight; a concentration of 16 µg/kg dry weight was recorded at kilometre marker 37.1. In sediment of the River Aa between Ibbenbüren and Hörstel at the Hörstel depth gauge a 1,2,4,5-tetrachlorobenzene concentration of about 2 µg/kg dry weight was analysed in 1989.

1,2,4,5-Tetrachlorobenzene was accumulated to 3.1 µg/kg in the innards of rainbow trouts (aged 3 months at the start of study) after keeping them for 11 months in Rhine water (1,2,4,5-TeCB concentration < 0.1 µg/l sediment separated). No 1,2,4,5-tetrachlorobenzene was determined in the muscle of these fish nor in the muscle or innards of trout kept in drinking water (limit of determination 1 µg/kg). As the source of the 1,2,4,5-tetrachlorobenzene pollution the water with its dissolved substances, e.g. 1,2,4,5-TeCB in an analytically not identified concentration or pesticides like gamma-hexachlorocyclohexane being metabolised in the fish, is discussed.

1,2,4,5-Tetrachlorobenzene was also identified in seagull liver (USA) at a concentration of 60 µg/kg wet weight, in human tissue (Japan) at a concentration of 6 - 39 µg/kg lipid and in benthic organisms (USA) at up to 210 µg/kg dry weight.

### **Distribution and degradation in the environment**

Biological degradation of 1,2,4,5-tetrachlorobenzene by sewage sludge is classified as "difficult to degrade", degradation by soil micro-organisms usually rarely occurs. Elimination from waste water treatment plants is due primarily to chemico-physical processes. However, microorganisms capable of a primary degradation of 1,2,4,5-tetrachlorobenzene have been isolated from soils. Other authors have shown that microorganisms which contain a special plasmid are capable of dehalogenating 1,2,4,5-tetrachlorobenzene.

An experimental half-life of 48.9 days has been determined for hydrolytic degradation at pH 7. Phototransformation of 1,2,4,5-tetrachlorobenzene in water barely occurs because of the weak UV adsorption from sunlight. The "environmental

half-life“ is estimated to be about 450 years on the basis of comparisons with 1,2,4-trichlorobenzene.

The UV absorption at 294 nm being observed in the gaseous phase, at least does not preclude the possibility of photolysis. Calculations by Atkinson suggest a half-life for 1,2,4,5-tetrachlorobenzene of 155 days due to photochemical oxidative degradation by reactions with OH radicals in the troposphere.

A BCF of 50,300 in fat tissue of fish and an elimination half-life of 2 days add up to very high short-term bioaccumulation. This bioaccumulation factor for lipid corresponds to a log BCF of 4.7 and thus agrees with the high log  $K_{OW}$  of about 4.6.

On the basis of its Henry constant 1,2,4,5-tetrachlorobenzene is considered to be highly volatile from aqueous solution. At the same time, the available data on its log  $K_{OC}$  (3.2 to 6.4) let expect strong to very strong binding to organic matter. The very high soil sorption (cf. section 6.3.3) and the limited degradation indicate that geoaccumulation is likely. Further evidence is provided by a concentration profile of a sediment core.

### **Ecotoxicological effects**

Investigation of the ecotoxicological effect of 1,2,4,5-tetrachlorobenzene is rendered difficult because of its very high volatility and poor solubility of only about 0.3 mg/l at room temperature. Two authors report undissolved 1,2,4,5-tetrachlorobenzene in the test series even when solubilizers were used.

Table 43 summarizes the values obtained with 1,2,4,5-tetrachlorobenzene for various organisms in studies.

**Tab. 43: Concentrations of 1,2,4,5-TeCB toxic to various organisms**

<u>Organism</u>	<u>Test-criterion</u>	<u>Conz.</u> <u>[mg/l]</u>	<u>Notes</u>
Photobacterium phosphoreum	30 min-EC <sub>50</sub>	4.51 N	Parameter: Light reduction
Ankistrodesmus falcatus var.	4 h-EC <sub>50</sub>	4.97 N	Parameter: Uptake of Na <sub>2</sub> CO <sub>3</sub>
Daphnia magna (F)	28 h-LC <sub>0</sub>	≥ 0.3 E	No solubilizer used
Mysidopsis bahia (S)	96 h-LC <sub>50</sub>	1.48 N	
Salmo gairdneri (F)	96 h-LC <sub>0</sub>	10.0 N	5 different stages of development (egg-larva, 42 d)
	96 h-LC <sub>50</sub>	1.2 N	Larva, 77 d
Lepomis macrochirus (F)	96 h-LC <sub>50</sub>	1.6 N	TeCB Sediment
Cyprinodon variegatus (S)	96 h-LC <sub>50</sub>	0.33 N	Juveniles
	96 h-LC <sub>50</sub>	0.8 N	Juveniles
	96 h-NOEC	0.3 N	Juveniles
Poecilia reticulata (F)	14 d-LC <sub>50</sub>	0.31 N	
Jordanella floridae (F)	NOEC	0.24 E	No. of hatched + development up to day 10
	10 d-LC <sub>0</sub>	> 0.3 E	Juveniles
	28 d-NOEC	0.14 E	Juveniles
	28 d-LOEC	0.085 E	Growth of juven.
Cyprinodon variegatus (S)	NOEC	0.3 E	No. of hatched
	28 d MATC	>0.09 to < 0.18 E	Embryos and juveniles

F: fresh water                      S: sea water

E: effective concentration                      N: nominal concentration

Unless otherwise stated, the test series were carried out with solubilizers.

In germination and growth studies with barley and oats in soil contaminated with 1,2,4,5-tetrachlorobenzene, both types of plant failed to germinate in sandy soils at concentrations of approx. 2 - 150 mg/kg soil. They did, however, germinate in clayey soil. An  $EC_{50}$  of 11 resp. 4 mg TeCB/kg soil after 18 days of growth was estimated graphically for barley and oats regarding the seedling heights.

### **Toxicological aspects**

1,2,4,5-Tetrachlorobenzene is absorbed from the gastrointestinal tract in the rat, mouse, monkey and dog, and, because of its lipophilicity, is stored in fat tissue. It is metabolized to 2,3,5,6-tetrachlorophenol and eliminated with the urine and faeces at a low rate, so that accumulation occurs following repeated administration. Elimination in the rat is mainly by the renal route, in the monkey mainly in the faeces. There appears to be no predominant elimination route in the dog, while exhalation seems to play a role in the rabbit. Percutaneous absorption was not observed in the rabbit. There are no studies available on absorption via the respiratory tract.

The  $LD_{50}$  values following oral intake in the rat, mouse and rabbit are between 1035 and 3105 mg/kg body weight. The symptoms observed following acute intoxication are uncharacteristic. Liver and kidney changes were observed in the male rat following administration of a single non-lethal dose (300 mg/kg body weight).

1,2,4,5-Tetrachlorobenzene is not irritant to the skin or mucous membranes. In a study carried out in 1963 1,2,4,5-tetrachlorobenzene did not cause dermal sensitization in the guinea pig.

From approx. 30 mg/kg body weight 1,2,4,5-tetrachlorobenzene caused characteristic induction of the microsomal liver enzymes in subacute and subchronic rat studies. Effects on the liver which were also visible under the microscope were observed in subacute and subchronic studies following administration of feed containing  $\geq 100$  ppm 1,2,4,5-tetrachlorobenzene (approx. 7 mg/kg body weight). In a ten-week study the first evidence for hepatotoxicity appeared after administration of doses of 300 ppm and above in feed. The  $\alpha_2\mu$  nephropathy typically observed in male rats occurred at 1,2,4,5-tetrachlorobenzene concentrations of  $\geq 50$  ppm (approx. 3.4  $\mu\text{g}/\text{kg}$  body weight) in subacute studies and at 30 ppm and above in subchronic studies. The first evidence for hepato-toxicity of 1,2,4,5-tetrachlorobenzene in the mouse appeared in the 1000 ppm group (approx. 150 mg/kg body weight) in a 13-week study. Microscopic liver-cell degeneration was observed at 2000 ppm, a dose lethal in the female mouse. The NOEL in this study was 300 ppm. Daily ingestion of doses  $\leq 5$  mg/kg body weight over a period of up to two years produced no clinical symptoms in the dog. Doses  $\geq 10$  mg/kg body weight over a 144-day period caused liver lesions.

The Ames test for 1,2,4,5-tetrachlorobenzene is negative both with and without metabolic activation. In mouse lymphoma cells L51178Y 1,2,4,5-tetrachlorobenzene did not lead to an increased point mutation rate. Neither an increased rate of chromosome aberrations nor an increased rate of sister chromatid exchange was observed in CHO cells following incubation with 1,2,4,5-tetrachlorobenzene. 1,2,4,5-tetrachlorobenzene had no mutagenic effect in a sex-linked recessive lethal test in *Drosophila melanogaster*. A slight increase in the number of erythrocytes with micronuclei was observed in the bone marrow of mice treated with 1,2,4,5-tetrachlorobenzene.

No information is available on long-term carcinogenicity. 1,2,4,5-Tetrachlorobenzene had a promoting effect in a liver foci test initiated by diethylnitrosamine.

A fetotoxic effect was observed in the rat at maternotoxic doses, but there was no teratogenic effect. Rat fertility was not affected even at paternotoxic doses.

Investigation of the enzyme-inducing effect of 1,2,4,5-tetrachlorobenzene showed that the induction pattern is of the phenobarbital type. 1,2,4,5-Tetrachlorobenzene did not affect porphyrin metabolism either *in vivo* or *in vitro*.

The conclusiveness of the only epidemiological study to describe chromosomal changes in workers exposed to 1,2,4,5-tetrachlorobenzene is limited because no estimated exposure is given.

## **Recommendations**

### **Ecological aspects**

The available data on the occurrence of 1,2,4,5-tetrachlorobenzene in the environment and on its ecotoxicology can be considered sufficient for evaluation of its environmental relevance.

### **Toxicological aspects**

The toxicologically relevant properties of 1,2,4,5-tetrachlorobenzene have been largely clarified.

The conclusiveness of the sensitization studies which produced negative results is limited. However, a new study of this type does not need to be carried out because in the past there have been no reports of sensitization even though the substance was handled at the workplace over a period of many years.

The result of the micronucleus test should be reviewed by repeating the test in accordance with current standards; this will clarify the vague evidence for a mutagenic effect.

The ongoing carcinogenicity study listed in the National Toxicology Program 1990 did not feature in the October 1991 Chemical Status Report of the NTP. The reason why this study has (possibly) been cancelled should be established.