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**Gesellschaft Deutscher Chemiker**

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

**Chlorobenzene**  
BUA Report 54  
(November 1990)



S. Hirzel

Wissenschaftliche Verlagsgesellschaft 1993

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### **GDCh Office:**

Dr. H. Behret, GDCh, Frankfurt am Main

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BUA Report 54

(November 1990)

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

Beratergremium für  
Umweltrelevante Altstoffe (BUA)



S. Hirzel

Wissenschaftliche Verlagsgesellschaft 1993

Dr. H. Behret  
Gesellschaft Deutscher Chemiker  
Postfach 90 04 40  
D-60444 Frankfurt am Main

Translated by P. Karbe

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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 Chlorobenzene**

## **Summary and conclusions**

### **Ecological aspects**

#### **Occurrence and distribution in the compartments**

In 1989 a total of 60,000 to 70,000 t/a chlorobenzene were produced in the Federal Republic of Germany by two manufacturers. Approximately 76 % of this total was processed into nitrochlorobenzenes which are used as starting products for crop protection agents, dyestuffs and rubber chemicals; about 12 % was used as an intermediate for other compounds. A total of approx. 7 % was used as solvents, of which approx. 3 % went for process solvents used in chemical reactions, and approx. 4 % for formulating crop protection agents, of which between 94 and 95 % were exported. The proportion sold within the Federal Republic of Germany contained approx. 150 t chlorobenzene. There is no information on imports of crop protection agents containing chlorobenzene. 5 - 6 % of the 1989 production volume of chlorobenzene was exported. It is not possible to ascertain import data for chlorobenzene as the statistics do not distinguish between chlorobenzene and the isomeric dichlorobenzenes.

Chlorobenzene is released into the environment with exhaust air and waste water from industrial manufacture, processing and utilization as a process solvent. Some of the exhaust air is incinerated in thermal waste gas treatment plants. For 1989 the release into the atmosphere is estimated at about 46 t/a, while approx. 7.1 t/a are estimated to have been released into the hydrosphere with waste water. Some 150 t chlorobenzene were released into the environment in the Federal Republic of Germany in 1989 from known crop protection formulations. The manufacturing process produces 1,000 t of waste. This waste and the chlorobenzene-containing

waste caused during processing and utilization is incinerated in approved facilities.

In 1973  $0.9 \mu\text{g}/\text{m}^3$  chlorobenzene was detected in the ambient air in Frankfurt. A geometric mean of  $0.3 \mu\text{g}/\text{m}^3$  was detected in outdoor air in Hof, Bavaria in 1985, and an average level of  $1.5 \mu\text{g}/\text{m}^3$  was found in Leverkusen in 1986. In the Rhine-Ruhr region, the chlorobenzene concentration was below the stated limit of determination of  $0.4 \mu\text{g}/\text{m}^3$  in 1989. A range of  $0.1 - 4 \mu\text{g}/\text{m}^3$  and a geometric mean of  $0.5 \mu\text{g}/\text{m}^3$  were detected in air indoors in Hof, Bavaria. In the Netherlands, measurements taken in three locations with different levels of Industrialization produced mean values of  $0.28 - 0.47 \mu\text{g}/\text{m}^3$  with maximum values of  $3.41 - 11.68 \mu\text{g}/\text{m}^3$ . Analysis of ambient air carried out in various cities in the USA from 1977 to 1987 produced average values between not detectable and  $2.5 \mu\text{g}/\text{m}^3$  with maximum values between  $0.09$  and  $135 \mu\text{g}/\text{m}^3$ . The indoor air concentrations were between not detectable and  $72.22 \mu\text{g}/\text{m}^3$  with a mean of  $16.5 \mu\text{g}/\text{m}^3$ . Workplace values recorded in chlorobenzene and nitrochlorobenzene-producing plants in the USA in 1978/79 showed air concentrations ranging from not detectable to  $18.7 \text{ mg}/\text{m}^3$ .

A number of monitoring programmes have regularly investigated chlorobenzene in the River Rhine. The level of this substance has decreased steadily since 1977. In 1977 between  $1$  and  $20 \mu\text{g}/\text{l}$  were recorded in the part of the Rhine which runs through North Rhine-Westphalia. In the same year the concentrations measured in the Lower Main ranged from not detectable to  $259 \mu\text{g}/\text{l}$ . In 1981 - 1983 the mean levels detected in the Rhine between Basle and Lobith ranged from less than  $0.1$  to  $2.8 \mu\text{g}/\text{l}$ . Based on a geometric mean of  $0.06 \mu\text{g}/\text{l}$  and a mean water stream of  $2,400 \text{ m}^3/\text{sec}$  for 1984 at a measuring point in the Rhine near Düsseldorf a load of  $4.5 \text{ t/a}$  was calculated. Mean chlorobenzene concentrations recorded in 1987 in the Rhine between Karlsruhe-Maxau and

Lobith ranged from  $< 0.01$  to  $0.01 \mu\text{g/l}$ . In 1988 no chlorobenzene was detected in the section of the Rhine which runs through North Rhine-Westphalia (limit of determination  $0.01 \mu\text{g/l}$ ). In 1985 an annual mean of  $< 0.1 \mu\text{g/l}$  and a maximum value of  $0.6 \mu\text{g/l}$  were determined in the Dutch section of the Rhine at Lobith; in 1986 an annual mean of  $2.8 \mu\text{g/l}$  was recorded and a maximum value of  $262 \mu\text{g/l}$  was measured in the aftermath of hazardous incidents.

Between 70 and over 95 % of the chlorobenzene content of water from the Rhine was removed when it was treated for drinking by bank-filtering. In 1975 drinking-water prepared from bank-filtered water from the River Rhine in the Federal Republic of Germany contained  $< 0.05 \mu\text{g/l}$ . In 1983 chlorobenzene was not detectable (limit of determination  $0.01 \mu\text{g/l}$ ). Values ranging from  $0.01$  to  $< 5 \mu\text{g/l}$  were recorded in samples of drinking-water in the USA between 1975 and 1982.

In 1987/88 the chlorobenzene content of Rhine sediment was below the limit of determination of  $5 \mu\text{g/kg}$  in North Rhine-Westphalia. In the USA the sediment of a lake contained  $0.03 - 0.7$  chlorobenzene/kg wet weight, while river sediment near an industrial discharge point had a mean of  $3.15 \text{ mg/kg}$  dry weight.

Leachate from a German waste dump contained approx.  $8 \text{ mg/l}$  before and  $40 \mu\text{g/l}$  after conditioning. In the Federal Republic of Germany ground water contaminated by landfill leachate contained a maximum of  $300 \text{ g/l}$ . Measurements of contaminated ground water in the USA and Canada showed values between  $0.02$  and  $300 \mu\text{g/l}$ . Contaminated soil in the Netherlands contained  $2.2 \text{ mg/kg}$  chlorobenzene.

Blood and urine samples from people living near a former domestic and industrial waste dump in the USA were analyzed

## XIV

and concentrations of 0.05 - 17 µg/l for blood and 20 - 120 µg/l for urine were found.

Other studies in the USA recorded 0.04 - 0.6 µg/kg wet weight in mussels and 50 - 410 µg/kg lipid in crabs and fish. 290 µg/kg wet weight were recorded in mussels (*Mytilus edulis*) in Japan.

Concentrations of 5 mg/kg (stems) and < 1 mg/kg (leaves) were determined in lilies (fresh weight) growing at a pilot waste water treatment plant.

The physicochemical properties of chlorobenzene and the partition constants between water and air and soil and air indicate that chlorobenzene released into the various compartments largely passes into the atmosphere within a few days.

The soil sorption coefficients indicate low to moderate sorption of chlorobenzene in soils.

### **Degradability**

Chlorobenzene can be degraded aerobically by adapted micro organisms in water and in aerated soil layers. Non-adapted micro-organisms degrade the substance more slowly. Chlorobenzene is not degraded either in digested sludge or in sediment under anaerobic conditions.

Direct photodegradation in water is not possible because chlorobenzene absorbs sunlight extremely weakly. Hydrolysis is also not to be expected under environmental conditions. The half-life for photochemical oxidative degradation by OH radicals in the troposphere has been calculated at 18 - 24 days.

## Bioaccumulation

On the basis of chlorobenzene's n-octanol/water partition coefficient  $\log P_{OW}$  of 2.84, bioaccumulation is to be expected. The following bioconcentration factors have been determined experimentally for fish:  $\log BCF$  2.81 (dry weight) and  $\log BCF$  1.85 (wet weight). Bioconcentration factors up to  $\log BCF$  3.62 (dry weight) and  $\log$  2.36 (wet weight) have been determined for algae. Both accumulation and sorption occurred in algae.

## Ecotoxicological effects

Cell multiplication of *Pseudomonas putida* was inhibited at 17 mg/l. The  $EC_{50}$  in an  $O_2$  consumption test with activated sludge was 140 mg/l. 50 % inhibition of dehydrogenase activity was observed for *Bacillus sp.* (TL81) at  $447 \pm 28$  mg/l. The lowest minimum inhibitory concentration was 2.4 mg/l recorded for *Aeromonas hydrophila* and *Bacillus subtilis*. The  $EC_{50}$  values for reduction of luminescence in *Photobacterium phosphoreum* ranged from 9.4 to 20 mg/l after 5 - 30 minutes.

The effect of chlorobenzene on algae varied greatly in a number of experiments. No growth inhibition was observed for *Scenedesmus quadricauda* after 8 days at 390 mg/l (closed system). One growth inhibition test with *Selenastrum capricornutum* recorded a 96 h  $EC_{50}$  of 12.5 mg/l, while another experiment produced a 96 h  $EC_{50}$  of 232 and 224 mg/l (based on the chlorophyll-a content and on the cell count). In a photosynthesis inhibition test the 3 h  $EC_{50}$  ranged from 33 to 99 mg/l for various species.

In an immobilization test with *Daphnia magna* the 24 h  $EC_{50}$  ranged from 195 to 310 mg/l in an open system and from 4.3 to 16 mg/l in a closed system. One 48 h  $EC_{50}$  of 0.59 mg/l

was recorded. Acute toxicity tests on *Daphnia magna* produced 48 h LC<sub>50</sub> values ranging from 5.0 to 86 mg/l in closed test systems. EC<sub>50</sub> values from 1.1 to 2.5 mg/l were recorded in various reproduction tests lasting 14 or 16 days. The NOEC ranged from 0.32 to 1 mg/l. One 16-day LC<sub>50</sub> of 4 mg/l was recorded.

For fish (various species) the 48 h and 96 h LC<sub>50</sub> values for acute toxicity (in a closed and in a flow-through system) ranged from 4.1 to 19.12 mg/l. 24 h LC<sub>50</sub> values of 5.63 - > 20 mg/l, 48 h LC<sub>50</sub> values of 8.9 - 24 mg/l and 96 h LC<sub>50</sub> values of 4.5 - 45 mg/l were recorded in static test systems (open, or no details of whether they were open or closed). One 96 h LC<sub>50</sub> of 91 mg/l was recorded (open system). The LC<sub>50</sub> values for the embryo-larval stages of various species of fish in a closed flow-through system ranged from 0.05 to 3.48 mg/l depending on the species and length of exposure. A prolonged toxicity test with guppies (*Poecilia reticulata*) produced a 14-day LC<sub>50</sub> of 19.1 mg/l (closed, semistatic system). A 24 h LD<sub>50</sub> of 2 g/kg and a 96 h LD<sub>50</sub> of 1 g/kg were recorded following intraperitoneal administration of chlorobenzene to rainbow trout (*Salmo gairdneri*).

LC<sub>50</sub> values ranging from 0.9 to 1.65 mg/l were recorded for the embryo-larval stages of amphibians.

At concentrations of 10 - 100 mg/l chlorobenzene showed initial signs of a phytotoxic effect on terrestrial plants (chloroplasts from spinach leaves).

A 48 h LC<sub>50</sub> of 29 µg/cm<sup>3</sup> was determined for the earthworm (*Eisenia foetida*).#

## **Toxicological Aspect**

Chlorobenzene may be absorbed via the lungs or the gastrointestinal tract. It is likely that only very small amounts are absorbed via the skin. Chlorobenzene is distributed relatively rapidly in the body, depending on the organ fat content.

Chlorobenzene is oxidized to chlorobenzene-3,4-epoxide and chlorobenzene-2,3-epoxide by the microsomal cytochrome P 450 system and subsequently transformed to chlorophenylmercapturic acid, monohydroxychlorobenzenes and dihydroxychlorobenzenes. The hydroxychlorobenzenes are excreted mainly as glucuronides or sulphates. Chlorophenylmercapturic acid, glucuronid and sulphate conjugates are excreted predominantly in the urine. Unmetabolized chlorobenzene is excreted via the lungs. The half-life of inhaled chlorobenzene is given as a few hours for various species. The toxic effect of chlorobenzene is attributed to the covalent macromolecular binding of the reactive epoxides.

The acute toxicity of chlorobenzene in animal studies after ingestion or inhalation is moderate. At high doses chlorobenzene causes depression of the central nervous system and lesions of the liver and the kidney. The clinical symptoms of acute intoxication in animal studies are uncharacteristic. Initial excitation followed by drowsiness, incoordination and unconsciousness, cyanosis, areflexia and fibrillation of the mimetic muscles, transient irritation of the upper respiratory tract, vomiting and nausea have been described in man following accidental ingestion of chlorobenzene. Percutaneous toxicity is low in experimental animals.

Chlorobenzene is moderately irritant to the skin and eyes and does not cause sensitization.

In experimental animals the liver and kidney are the target organs following repeated administration of chlorobenzene. Dose-related liver lesions in the form of centrolobular degeneration and necrosis, lipid accumulation, increased organ weight and hepatic porphyria, and kidney lesions in the form of focal coagulative degeneration and necrosis of the proximal tubules and increased organ weight were observed. In addition, urine excretion and serum liver enzymes were increased.

Subchronic and chronic administration of chlorobenzene at lethal doses to experimental animals also led to lesions of the spleen, bone marrow, thymus and lungs, modified serum enzyme activity and increased reticulocytes. Lethal and non-lethal doses also led to a reduction in leukocytes, with a particular reduction in neutrophil granulocytes. In subchronic studies no or only very slight toxic effects were observed after oral administration of chlorobenzene to rats and mice in doses of 60 or 125 mg/kg body weight.

Two cases of anaemia following many years of occupational exposure to mixtures of chemicals containing chlorobenzene were reported in the literature.

Most of the gene mutation assays carried out with chlorobenzene have not provided any evidence for gene toxicity of the compound. There is some evidence that chlorobenzene may bind to DNA.

In long-term studies, oral administration of chlorobenzene to rats and mice did not increase the incidence of malignant tumors. There was an increase in the incidence of benign liver nodules in male rats in the highest dose group. These changes were not considered to provide clear evidence of carcinogenicity of chlorobenzene in male rats. Chlorobenzene did not act as tumor promotor in one initiation-promotion test; however, the methodology used in this test was inadequate.

Chlorobenzene did not impair fertility in experimental animals and was neither embryotoxic nor teratogenic. Questionable signs of retardation observed in one rabbit study were not confirmed in a subsequent experiment.

## **Recommendations**

### **Ecology**

Extensive ecological data are available, and no further studies are required.

### **Toxicology**

The mammalian toxicity of chlorobenzene is well documented. The only remaining uncertainty concerns its DNA binding. It is questionable whether the observed low level of DNA binding is due to protein contamination. A DNA binding study in which the test methods exclude the measurement of protein binding should therefore be carried out to ascertain whether DNA binding actually occurs.