GDCh-Advisory Committee
on Existing Chemicals (BUA)

4-Chloro-2-nitroaniline

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S. Hirzel

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für Altstoffe (BUA)

S. Hirzel
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Preface

The Advisory Committee on Existing Chemicals, BUA for short, was established in May 1982 to help the German federal government cope with the large task of dealing with existing chemicals. In an agreement between federal government, scientific community, and the chemical industry, it was associated with the German Chemical Society (GDCh, Gesellschaft Deutscher Chemiker) to ensure objective work, carried out in accordance with scientific principles. Since the beginning of 2001 the BUA has been composed of a new constellation of cooperating scientists from the research areas of chemistry, chemical analysis, monitoring, toxicology, primary and secondary exposition, aquatic and terrestrial toxicology as well as the fate and behaviour of compounds in water, soil, air. In addition the BUA is supported by experts within the national government agencies and the German Chemical Industry Association (VCI, Verband der Chemischen Industrie).

No other national or international body has dealt with the ecological and health-related effects of so many existing chemicals as the BUA. Upon the recommendation of the national government, since 2000, the BUA has participated as Peer-Review-Group in the pilot phase of the evaluation of ICCA-compounds (ICCA, International Council of Chemical Associations) and, in addition, acts as the national 'Contact Point' in this OECD existing chemicals program. The goal of the initiative is, on the one hand to create a more expansive database to evaluate the HPV chemicals and on the other to screen these chemicals for potential hazards.

In 1997 BUA began an additional national project, which also selects and assesses existing chemicals with a lower production volume in the range of 100 - 1000 tonnes/year. Comprehensive reports are published on chemicals suspected of having a hazardous potential. If the data available for substance assessment are insufficient, the gaps in knowledge are documented and, if necessary, investigations recommended. On the national level, the BUA has produced comprehensive reports on about 300 substances and carried out preliminary evaluation and classification (priority setting) for approximately 200 more. Publication of the process leading to priority setting, in addition to the BUA reports, lends transparency to the Committee's work.

Moreover, BUA is increasingly addressing scientific questions and problems such as "Endocrine Disruptors", selection criteria for "Persistent Organic Pollutants" (POPs), "Risk Assessment of Substances in Soils", "Evaluation Criteria for the Marine Sector" and "Safety Factors Within the Framework of Toxicological Risk Assessment". The aim of BUA is to develop assessment concepts, determine data gaps, point out the need for further research and, last but not least, also to reduce information deficits in the general population.

Weihenstephan, April 2001

Helmut Greim
BUA Chairman

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BUA report on 4-chloro-2-nitroaniline

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Ecological Aspect

Clariant GmbH, the sole producer of 4-chloro-2-nitroaniline, produced 1000 - 5000 tonnes of the substance in 1997 and 1998, respectively. 35 % of this amount were further processed within the company. The remainder was mostly exported. The end products were also pigments in this case. Clariant GmbH terminated production in 1999 but currently processes imported goods (< 1000 t in 2000).

Maximum atmospheric emissions of about 165 kg/yr can be calculated for the period of 1997 - 1998 as the result of production in Germany.

There are minimal atmospheric emissions resulting from internal and external processing and the use of pigments as industrial varnishes, building paints and printing dyes.

From production in Germany about 17 kg 4-chloro-2-nitroaniline were released in the receiving canals in 1997 and 1998, respectively. A total of < 140 kg were released into the rivers Main and Rhine as the result of processing at the company.

The measurements of the research ship Argus taken below the lock at Eddersheim were below the detection limit of 0.05 µg/l. A concentration of 0.05 µg/l in the Main at a flow rate of 60 m^3/s and an emission over 365 d corresponds to a load of 94.5 kg/yr.

Resulting from the processing of 4-chloro-2-nitroaniline and based on measurement values (Bischofsheim/Main), an emission of 400 and 273 kg 4-chloro-2-nitroaniline into the Main River can be calculated for 1999 and 2000, respectively.

According to the Technical Guidance Documents (TGD), maximum emissions of 13.2 tonnes into wastewater can be calculated for the other sources of external processing of 4-chloro-2-nitroaniline in Germany and abroad.

The emissions into the hydrosphere are negligible. In the hydrosphere 4-chloroaniline can be converted to 4-chloro-2-nitroaniline by biological nitration. This entry route, however, is not very important.

The geospheric emissions are minimal.

From 1999 to 2001 < 0.5 µg 4-chloro-2-nitroaniline/l was found in the Main River at Bischofsheim. 4-Chloro-2-nitroaniline concentrations of 4.7, 2.5 and 1.2 µg/l were determined respectively in 1999, 2000 and 2001 in the discharge tailings in the Main from the Höchst industrial park. Concentrations of < 0.05 µg/l were found in the rivers Werra and Fulda. Moreover, < 1.5 µg 4-chloro-2-nitroaniline/l was detected in the rivers Niers (at Goch), Rhine (Kleve-Bimmen), Wupper, Erft, Ruhr, Emscher, Lippe (Wesel), Rur (End), Weser (Peterhagen) and Ems.

An abiotic elimination takes place in the atmosphere by direct and indirect photodegradation. There are indications that a hydrospheric degradation is likely from photochemical-oxidative reactions with OH- and peroxy radicals. A hydrolytic degradation is not expected. There is a slight to low adsorption of 4-chloro-2-nitroaniline to organic matter of soil. A significant bioaccumulation potential of 4-chloro-2-nitroaniline in fish is unlikely.

4-Chloro-2-nitroaniline is poorly volatile from aqueous solution. 4-Chloro-2-nitroaniline was not degradable in the test on ready biodegradability according to OECD 301 C.

A 24h EC_{50} value of 34 mg 4-chloro-2-nitroaniline/l was determined for its toxicity to the bacterium *Escherichia coli.* For the green alga *Scenedesmus subspicatus*, E_bC_{10} and E_bC_{50} values of 0.15 and 2.6 mg 4-chloro-2-nitroaniline/l were determined in the 8-day cell-multiplication inhibition test, respectively. Furthermore, a 72h E_bC_{10} value of 1.6 mg/l was found for this endpoint. After an exposure of 2 hours, the EC_{10} and EC_{50} values in the fluorescence test were 2.1 and 10.2 mg 4-chloro-2-nitroaniline/l, respectively.

A NOEC of 0.63 mg 4-chloro-2-nitroaniline/l was determined in the 21d reproduction test on the water flea *Daphnia magna*; in the same test, the LOEC was 1.3 mg/l. The 48h EC_{50} value according to DIN 38412 Part II was 3.2 mg 4-chloro-2-nitroaniline/l. A 96h LC_{50} value of 6.5 and a NOEC of 0.56 mg 4-chloro-2-nitroaniline/l were established for the crustacean *Chaetogammarus marinus.*

In the available vertebrate study, a 48h LC_{50} value of 17.4 mg 4-chloro-2-nitroaniline/l was determined for the killifish (*Oryzias latipes*).

An EC_{10} value of 1.3 mg 4-chloro-2-nitroaniline/l was found in an *in vitro* plant study on the oxygen development of protoplasts.

Toxicological Aspect

4-Chloro-2-nitroaniline is completely absorbed after oral administration. It is excreted mainly as a sulfate conjugate in the urine. An accumulation of 4-chloro-2-nitroaniline was not observed. The values for the acute toxicity (LD_{50}) to the rat exceed 5000 mg/kg b.w.

According to the available data, 4-chloro-2-nitroaniline does not cause any skin or mucous membrane irrititation.

The target organs of the toxic effect after subacute and subchronic application are the spleen, kidney and liver. Following a 13-week study with oral administration, a NOEL of 150 mg/kg b.w. was specified for male mice and that of 50 mg/kg b.w. for male rats. The kidneys of the treated male rats showed eosinophilic hyaline drops and regeneration in the proximal tubule from doses of 100 mg/kg b.w. onwards; this effect is species- and sex-specific and is supposedly irrelevant for humans. A NOEL was not ascertained for female rats and mice; the LOEL is 50 mg/kg b.w. for rats and 75 mg/kg b.w. for mice. There are no studies available on the dermal and inhalative toxicity.

4-Chloro-2-nitroaniline was proven to be mutagenic in the Ames test as well as clastogenic in an *in vitro* chromosome aberration test. An *in vivo* micronucleus test was negative after oral application. A study on carcinogenicity was planned by the NTP for 1982 but was not performed because of the structural analogy of 4-chloro-2-nitroaniline to other carcinogens (4-chloro-*o*-phenylenediamine, 2,6-dichloro-p-phenylenediamine) and the existing genotoxicity data which suggest a carcinogenic potential.

There are no studies available on fertility impairment. In a subchronic study after oral application, mice showed decreased sperm motility, and rats exhibited increased relative weights of the testes and decreased absolute weights of the epididymis with simultaneous body weight loss. Studies are missing on the developmental toxicity potential.

There are no conclusive studies available on sensitization. Based on the structure of the substance, a possible sensitizing effect cannot be completely excluded (so-called para-group allergy, e.g. p-phenylenediamine, 2,4-dinitrochlorobenzene).