



**German Chemical Society  
Gesellschaft Deutscher Chemiker**

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

**o-Chloroaniline,  
m-Chloroaniline**  
(1-Amino-2-chlorobenzene,  
1-Amino-3-chlorobenzene)

BUA Report 57  
(February 1991)



S. Hirzel

Wissenschaftliche Verlagsgesellschaft 1994

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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 o-Chloroaniline and m-Chloroaniline**

(1-Amino-2-chlorobenzene,  
1-Amino-3-chlorobenzene)

## **Summary and conclusions**

### **Ecological aspects**

#### **1. Manufacture, use, distribution in the compartments (entry into the environment, occurrence)**

##### **Manufacture, use**

In the Federal Republic of Germany annual production in 1988/89 totalled 3,600 - 4,000 t o- and 1,000 - 2,000 t m-chloroaniline, of which 50 % was exported (2,000 - 2,200 t/a o- and 500 - 1,000 t/a m-chloroaniline).

o- and m-chloroaniline are used exclusively as intermediates. In 1988/89 more than 99 % of the o-chloroaniline and 95 % of the m-chloroaniline which remained in the FRG was processed by the two West German producers.

In 1988/89 81 % of the o-chloroaniline was used to produce crop protection agents such as anilazine, 14 % was processed into azo dyestuffs, 4.5 % into photographic chemicals and 0.1 % was sold as dyeing salt. 91 % of the m-chloroaniline produced in the FRG and not exported was processed into m-chlorophenylisocyanate, a precursor for crop protection agents such as chloroprotham, and 4 % was used as a precursor for an antimalarial quinoline derivative used in human medicine.

It is not known whether o- and m-chloroaniline are imported into the FRG for processing by companies other than the West German producers.

##### **Entry into the environment**

For 1988/89 the amount entering the atmosphere from production and processing by the two West German producers was

estimated at considerably less than 76 kg/a o-chloroaniline and considerably less than 50 kg/a m-chloroaniline.

Approximately 2.5 - 3 t/a o-chloroaniline and approx. 0.2 - 0.3 t/a m-chloroaniline enter the hydrosphere from production and processing by the two West German producers and from other production processes carried out at one of these companies.

Production and processing waste containing o- and m-chloroaniline and some of the sewage sludge is incinerated by the two West German producers in their own combustion plants approved for controlled waste. The remaining sewage sludge is deposited.

An upper limit of 1.4 t/a has been calculated under "worst case conditions for the emission of o-chloroaniline into the geosphere and possibly the biosphere from the residue of o-chloroaniline in the crop protection agent anilazine following production. This figure was based on the amounts used in West Germany in 1989. o-Chloroaniline released into the geosphere, biosphere and hydrosphere during anilazine transformation can play only a minor role, if indeed the substance is emitted at all. Soil was treated for 5 years with twice the usual application rate of radioactively labelled anilazine; no free o-chloroaniline was detected with a limit of determination of 0.1 % total radioactivity.

The crop protection agent chloroprotham, a m-chloroaniline derivative, is registered for use in the FRG as a potato sprout inhibitor for potatoes in storage. In a Canadian study, m-chloroaniline was detected in potato skins. It is not known whether potatoes are treated with chloroprotham in the FRG, or whether potatoes treated with chloroprotham are imported. 100 % of the chloroprotham produced by the sole West German producer of m-chloroaniline is exported.

Dehalogenation of intermediate 3,4-dichloroaniline to form m- and p-chloroaniline has been observed during anaerobic

degradation of propanil; the possibility can therefore not be excluded that m-chloroaniline is released into the geosphere and perhaps the biosphere in the FRG under anaerobic conditions through transformation of 3,4- and 3,5-dichloro- and 3-chloro-4-fluoroaniline derivatives registered for use as crop protection agents in the FRG. Propanil is not registered for use in the FRG.

Input of o- and m-chloroaniline into the hydrosphere through microbial reduction of o- and m-chloronitrobenzenes cannot be quantified.

### **Occurrence**

No information is available on the occurrence of o- and m-chloroaniline in the atmosphere. In West Germany, annual input of o- and m-chloroaniline into the atmosphere is of an order of magnitude (see above) which is to be expected to produce concentrations beneath the present attainable limits of detection, particularly since rapid photooxidation of o- and m-chloroaniline is to be expected in the atmosphere (calculated  $t_{1/2} = 7$  and 4 hours).

The covalent binding of most of the o- and m-chloroaniline in soil, their low volatility from soil and their rapid photodegradation in the atmosphere make it likely that the concentration of these chemicals in the air over agricultural land treated with anilazine or with crop protection agents which release m-chloroaniline is below the limit of detection.

In the North Rhine-Westphalian section of the Rhine, the concentration of o-chloroaniline was below the limit of determination of 0.1 µg/l in all 21 samples taken in 1988 and in 38 out of 39 samples taken in 1989. The maximum value recorded in 1989 was 0.6 µg/l. The concentration of

m-chloroaniline was below the limit of determination of 0.1 µg/l in all 21 samples taken in 1988 and in all 39 taken in 1989.

In 1989, o-chloroaniline was not detected in 242 of the 256 samples taken from the Rhine at ten sampling points between Öhningen at its junction with Lake Constance and Lobith at the German border with the Netherlands (limit of determination 0.05 µg/l). In 12 samples the concentration of o-chloroaniline was between 0.05 and 0.09 µg/l, in the remaining two samples it was 0.14 and 0.34 µg/l. m-Chloroaniline was not detected in any of the 256 samples.

The concentration of o-chloroaniline in six tributaries of the Rhine in North Rhine-Westphalia (Sieg, Wupper, Erft, Ruhr, Emscher, Lippe) was determined at their confluence with the Rhine in 1988. The concentration in none out of 36 samples (six from each river) was above the limit of determination of 0.1 µg/l. In 1989 the concentration in 5 out of 49 samples (4 - 13 per river) was above the limit of determination of 0.1 µg/l with a maximum of 2.1 µg/l recorded in the mouth of the Emscher, the other three coming from the mouth of the Wupper (max. 1.3 µg/l). In 1988 the m-chloroaniline concentration was in one out of 36 samples above the limit of determination of 0.1 µg/l recorded in the mouth of the Wupper (0.3 µg/l). In 1989 the concentration was above the limit of determination of 0.1 µg/l in 2 out of 49 samples with a maximum of 0.2 µg/l recorded in the mouth of the Emscher.

In 1988 the concentrations of o- and m-chloroaniline in the Main were below the limit of determination of 0.1 µg/l. In 1989 o-chloroaniline was detected in 4 out of 26 samples, m-chloroaniline in none of the 26 samples (limit of determination 0.05 µg/l). The o-chloroaniline concentration in the 4 samples was between 0.08 and 0.16 µg/l.

In the USA 600 mg o-chloroaniline/kg dry weight were found in the sediment of a waste treatment lagoon of a company

processing o-chloroaniline; the concentration in fish collected near the outlet of the sewage treatment plant was 49 µg o-chloroaniline/kg wet weight. In oysters of an estuary close to an American city of more than 1.5 million inhabitants the mean value was 41 µg o-chloroaniline/kg wet weight. Very probably the first value encompasses free o-chloroaniline, the second one covalently bound o-chloroaniline which is releasable by hydrolysis and the third one free plus possibly covalently bound o-chloroaniline which is releasable by hydrolysis.

m-Chloroaniline was determined in µg/kg (wet weight), amounts in peels of potatoes obtained from a market in Canada. It can be assumed that m-chloroaniline was formed during chloroprotham metabolism. Microbes may form m-chloroaniline from propanil under anaerobic conditions when propanil is used on paddy fields. m-Chloroaniline was detected in fish and algae living in a paddy field treated with propanil. Low concentrations of m-chloroaniline could also occur in soil to which barban has been applied and subsequently hydrolyzed or metabolized by the *Penicillium* mould. Neither propanil nor barban is registered for use in the FRG.

## **2. Behaviour in the compartments**

### **Hydrosphere**

The UV spectra of o- and m-chloroaniline (> 295 nm) indicate that direct photodegradation of both substances is possible. A transformation half-life of 3 hours and a photomineralization half-life of 23 days have been determined for p-chloroaniline in a test system simulating field conditions with water from an estuary in daylight during winter 3 cm below the surface. The half-life for direct photodegradation of m-chloroaniline in water is 1.3 hours in light at 313 nm. There is no corresponding measurement for o-chloroaniline available.

The half-life of indirect photodegradation in water with carbonate radicals in concentrations which are found in the environment is 11 hours for aniline. The half-life of m-chloroaniline should be of the same order of magnitude.

o- and m-chloroaniline are potentially degradable in the hydrosphere under aerobic conditions.

In 7 out of 30 test series to investigate the aerobic degradation of o-chloroaniline by sewage microorganisms, in which BOD, CO<sub>2</sub> development or Cl<sup>-</sup> release were determined, between 1 and 89 % of the o-chloroaniline was degraded within up to 30 days. The BOD with unadapted sewage microorganisms from 4 activated sludge samples of various origins was between < 18 and 89 %. However, in the remaining 23 test series with adapted or unadapted sewage microorganisms there were no signs of degradation after up to 35 days.

In 18 test series DOC, COD or o-chloroaniline concentration under aerobic conditions were determined in filtrate, i.e. these tests recorded elimination both by degradation and by adsorption and chemical binding. In 14 of the 18 test series, elimination was between 14 % in 28 days and 98 % in 4.8 days. In the remaining 4 test series elimination was 0 % in 28 and 35 days respectively.

Overall, the results of the degradation studies with o-chloroaniline indicate that for this compound elimination by sorption plays a not insignificant role.

Adapted activated sludge degraded m-chloroaniline well in 13 - 20 days (69 % in 20 days, 97 % in 13 days). Unadapted activated sludge degraded ≤ 10 % of the m-chloroaniline in 20 days. Bacteria isolated from a river and adapted to aniline transformed > 80 % of the m-chloroaniline in 16 hours. The mean half-life for m-chloroaniline with mixed cultures from this river and two ponds without prior adaptation was

4.8 months. No transformation was observed after 14 days in the water of an eutrophic pond without adaptation.

The anaerobic degradation of o- and m-chloroaniline in water has not been investigated. m-chloroaniline is evidently not degraded under anaerobic conditions in sediment. m-Chloroaniline cleaved from 3,4-dichloroaniline accumulated during the two-month study period.

Elimination of o- and m-chloroaniline from water by volatilization plays a minor role as o- and m-chloroaniline do volatilize slowly from aqueous solutions.

Hydrolysis is unlikely at the temperatures and pH values (pH 5 - 9) encountered in the environment.

## **Geosphere**

Under aerobic conditions most of the o- and m-chloroaniline released into the soil is bound covalently to soil particles. After 16 weeks approx. 64 % of the o-chloroaniline was bound in gley with a very high humus content, and 60 - 82 % of the m-chloroaniline was bound in 8 different soil types.

o- and m-chloroaniline can be degraded aerobically by a number of soil bacteria once they have been adapted.

o-Chloroaniline was degraded not at all or slowly in soil under aerobic conditions without adaptation: 0 % ring cleavage in 9 weeks, 6.3 % mineralization in 16 weeks. Aerobic degradation of o-chloroaniline by bacterial pure cultures adapted to o-chloroaniline, p-chloroaniline or aniline was slow to rapid: 12.3 % mineralization in 7 days, up to 100 % ring cleavage in 18 hours.

m-Chloroaniline was degraded not at all or slowly in soil under aerobic conditions: 0 % ring cleavage in 9 weeks,

## XVIII

9 - 23 % mineralization in 16 weeks. Aerobic degradation of m-chloroaniline by bacterial pure cultures or mixed cultures isolated from soil and adapted to m-chloroaniline or to p-chloroaniline, aniline, o-toluidine or prophan was rapid:

40 % mineralization in 7 days, up to 100 % ring cleavage in 16 hours.

m-Chloroaniline underwent rapid aerobic degradation by an adapted and an unadapted culture of mould *Penicillium jensenii* which was isolated from soil treated with barban:

100 % reduction of the m-chloroaniline concentration in 2 and 5 hours respectively.

*Penicillium jensenii* occurs in large numbers in soil.

In anaerobic soil zones, o- and m-chloroaniline are neither bound chemically to a large extent nor degraded biologically. In eight months the concentration of free o- and m-chloroaniline decreased by less than 10 %. m-Chloroaniline cleaved from propanil and 3,4-dichloroaniline respectively accumulated under anaerobic conditions over periods of 3,3 and 8 months respectively.

o- and m-chloroaniline can be expected to have a pH-dependent and partly oxygen-dependent overall moderate tendency to sorption (physi- and chemisorption) in soil. The lower the pH and the higher the oxygen content, the stronger the sorption.

Concentration-dependent transport of o- and m-chloroaniline in soil via leachate into the ground water appears to be possible, particularly at high pH levels and under anaerobic conditions. It is not possible to estimate the extent to which this transport occurs, but it is presumably low.

The available study indicates that volatilization from soil is negligible: 0.5 - 1.8 % o-chloroaniline from gley with a very high humus content and not detectable - 3.2 % in chloroaniline in 16 weeks from 8 different soil types.

The results of studies on sorption, degradation in soil and volatilization from soils indicate on the whole that covalently bound o- and m-chloroaniline accumulate in soil under aerobic conditions and that free o- and m-chloroaniline accumulate in soil under anaerobic conditions, both forms of geoaccumulation being heavily dependent on the pH value. If geoaccumulation of free o- and m-chloroaniline not bound to soil particles were to occur under aerobic conditions, this geoaccumulation might be only transient because these compounds can potentially be biodegraded by a number of soil microorganisms.

### **Atmosphere**

It can be assumed that o- and m-chloroaniline released into the atmosphere undergo photochemical oxidative transformation. The calculated half-life for reaction with OH radicals is 7 hours for o-chloroaniline and 4 hours for m-chloroaniline.

### **Biosphere**

The log  $P_{OW}$  values of o- and m-chloroaniline indicate that free o- and m-chloroaniline have a weak bioaccumulation potential.

There is one indication that o-chloroaniline is bound covalently to macromolecules in the muscle tissue of carp.

### **3. Ecotoxicological effects**

In a reproduction inhibition test with *Pseudomonas putida* the 16 - 18 h toxic threshold concentration for reduction of cell density was 55 mg/l for o-chloroaniline and 19 mg/l for m-chloroaniline; the 18 h  $IC_{50}$  for m-chloroaniline was 179 mg/l. The reproduction rate  $IC_{50}$  for *Escherichia coli* was 281 mg/l with o-chloroaniline and 345 mg/l with m-chloroaniline. The 16 h  $IC_{50}$  for cell density of activated sludge was 91 and 300 mg o-chloroaniline/l respectively.

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In O<sub>2</sub> consumption tests with sewage microorganisms and o-chloroaniline, the following values were recorded: 0.5 - 3 h IC<sub>50</sub> values of 42 - 1,000 mg/l, 5-day IC<sub>50</sub> values of 55, > 100 and 367 mg/l and one 7-day IC<sub>50</sub> of > 27 mg/l. In tests to determine respiratory rate (O<sub>2</sub> consumption/time), the 3 h IC<sub>50</sub> values were 630 and 67,600 mg/l.

An IC<sub>50</sub> of 0.8 mg/l was recorded for o-chloroaniline in a nitrification inhibition test with a nitrifying bacterial culture; 5.6 mg/l was recorded with activated sludge (no information on length of exposure).

In studies to investigate the inhibitory effect on the bioluminescence of *Photobacterium phosphoreum* the 5 - 30 min IC<sub>50</sub> values were 9.3 - 18.8 mg/l for o-chloroaniline and 12.5 - 23.1 mg/l for m-chloroaniline.

The 24 h IC<sub>50</sub> value for reproduction (cell density) of the protozoa *Tetrahymena pyriformis* was 200 mg/l for o- and 100 mg/l for m-chloroaniline.

In reproduction inhibition tests with the unicellular green alga *Scenedesmus subspicatus*, the 48 h IC<sub>10</sub> and the 48 h IC<sub>50</sub> for reduction of cell density were 15 and 90 mg/l respectively for o-chloroaniline and 6.8 and 26 mg/l respectively for m-chloroaniline. The 48 h IC<sub>10</sub> and the 48 h IC<sub>50</sub> values for inhibition of the reproduction rate were 36 and 235 mg/l respectively for o-chloroaniline and 9.8 and 53 mg/l respectively for m-chloroaniline. The 72 h IC<sub>10</sub> and 72 h IC<sub>50</sub> values for reduction of cell density with o-chloroaniline were 6 and 40 mg/l respectively; the corresponding values for inhibition of the reproduction rate were 25 and 150 mg/l respectively. The 168 h IC<sub>10</sub> and 168 h IC<sub>50</sub> values for reduction of cell density were 3.9 and 58 mg/l respectively for o-chloroaniline and 4.1 and 31.8 mg/l respectively for m-chloroaniline.

In a fluorescence inhibition study with *Scenedesmus subspicatus* the following values were recorded after approx.

30 minutes exposure: IC<sub>10</sub> values of 1.68 mg/l for o-chloroaniline and approx. 1.7 mg/l for m-chloroaniline, IC<sub>50</sub> values of 53.2 mg/l for o-chloroaniline and 22.6 mg/l for m-chloroaniline.

In acute toxicity studies to investigate the mobility of *Daphnia magna*, the 24 h EC<sub>50</sub> and 24 h EC<sub>0</sub> values were 1.2 - 9.4 and 0.46 - 33 mg/l respectively for o-chloroaniline and 0.05 - 0.4 and 0.26 - 15 mg/l respectively for m-chloroaniline. The 48 h EC<sub>0</sub> and 48 h EC<sub>50</sub> values were 0.3 - 2.3 and 1.8 - 14 mg/l respectively for o-chloroaniline and 0.024 - 0.2 and 0.35 - 2.7 mg/l respectively for m-chloroaniline. The wide variations in these values are not explainable by the literature.

In 21-day reproduction studies with *Daphnia magna* a NOEC of approx. 0.03 mg/l for o-chloroaniline and 0.013 mg/l for m-chloroaniline was recorded. The reproduction rate EC<sub>50</sub> was approx. 0.1 mg/l for o-chloroaniline.

In a study to investigate the acute toxicity of o-chloroaniline in the rainbow trout (*Salmo gairdneri*), a 24 h LC<sub>0</sub> of 14.5 mg/l and a 24 h LC<sub>100</sub> of 121.5 mg/l were determined. The 24 h LC<sub>100</sub> was 1.66 ± 0.07 mg/l in a different study. This difference is not explainable on the basis of the literature.

The 48 h and 96 h LC<sub>50</sub> values for the golden orfe (*Leuciscus idus*), the rice fish *Oryzias latipes*, the zebrafish (*Brachydanio rerio*) and the fathead minnow (*Pimephales promelas*) were 3.1 - 6.7 mg/l for o-chloroaniline and 14 - 24 mg/l for m-chloroaniline. The 48 h and 96 h LC<sub>0</sub> was 2 mg/l for o-chloroaniline and 10 mg/l for m-chloroaniline.

The 14-day LC<sub>50</sub> for the guppy (*Poecilia reticulata*) was 6.3 mg/l for o-chloroaniline and 13.4 mg/l for m-chloroaniline.

Under aerobic conditions o- and m-chloroaniline initially inhibited biological activity in soil (microbial CO<sub>2</sub> formation) at the concentrations tested (2.5 % and 5 % of the nitrogen fertilizer added). However, inhibition lessened as the incubation time increased, and after 5 or more days the lower concentration of o-chloroaniline was stimulating soil activity.

Concentrations of 100 mg o- and m-chloroaniline/kg soil (based on 50 % of the maximum water-holding capacity) initially (up to two weeks) caused a reduction in the total count of bacteria. The compounds showed no negative effect on the number of soil bacteria at all subsequent testing times up to 12 weeks or at concentrations of 5, 10 and 50 mg/kg over the same period. At concentrations of 5, 10, 50 and 100 mg/kg o- and m-chloroaniline had a stimulating effect on the fungal count.

Reproduction of a bacterial strain of *Moraxella spec.* isolated from soil was inhibited by approx. 50 % during the exponential growth phase by 128 mg o- or m-chloroaniline/l.

After 8 weeks nitrification was inhibited by  $\geq 4$  or  $\geq 2$  mg/kg (based on 60 % of the maximum water-holding capacity) o-chloroaniline, depending on the soil type, and  $\geq 3$  or  $< 2$  mg/kg or above m-chloroaniline, again depending on the soil type. 50 % inhibition was observed with  $> 50$  mg/kg o-chloroaniline and 14 or  $< 2$  mg/kg m-chloroaniline. Slight stimulation of nitrification was observed at concentrations beneath the inhibitory threshold. Both o- and m-chloroaniline inhibited the reproduction of nitrifying bacteria.

o-chloroaniline (10.5 mg/kg soil) inhibited denitrification and, to a lesser extent, the proliferation of denitrifying bacteria in a soil sample under anaerobic conditions; however, neither o- nor m-chloroaniline inhibited denitrification in an isolated soil bacterium which reduces NO<sub>3</sub><sup>-</sup> only to N<sub>2</sub>O.

The 24 h  $IC_{50}$  values for reduction of the cell density of the yeast *Saccharomyces cerevisiae* and for the reproduction rate in the exponential growth phase were 689 - 702 mg o-chloroaniline/l and 459 - 536 mg m-chloroaniline/l. The short-term  $IC_{50}$  values for effects on the cell membrane were between 1,100 and 2,000 mg/l for o- and m-chloroaniline.

In a ribulose diphosphate carboxylase inhibition study with broad bean (*Vicia faba Major Harz*) protoplasts, the 36 h  $IC_{10}$  and the 36 h  $IC_{50}$  were 153 and 549 mg/l respectively for o-chloroaniline and 19.1 and 204 mg/l respectively for m-chloroaniline. The 15 - 20 min  $IC_{10}$  value for m-chloroaniline was 0.26 mg/l in an  $O_2$  development test.

### **Toxicological aspect**

m- and o-chloroaniline are absorbed well through the skin and also via the gastrointestinal tract and lung. The compounds are hydroxylated in the liver, kidney and lung; m-chloroaniline, at least, is N-acetylated, conjugated with glucuronic acid or sulphuric acid and excreted in the urine.

The  $LD_{50}$  values for oral and dermal administration range from 200 to over 1,000 mg/kg body weight. The  $LC_{50}$  values following four-hour inhalation are between 500 and 800 mg/m<sup>3</sup> for o-chloroaniline but between 4,300 and 6,000 mg/m for o-chloroaniline.

The predominant symptoms of intoxication in the rat, mouse and cat are those associated with methaemoglobinaemia (cyanosis, fatigue, dyspnoea, muscular weakness). A single oral dose of 191 mg m-chloroaniline/kg body weight or 127 mg o-chloroaniline/kg body weight caused kidney damage in rats. Lethal doses of m-chloroaniline administered to rats and of o-chloroaniline administered to cats additionally caused non-specific effects, predominantly in the liver.

m- and o-chloroaniline are both irritant on skin and mucous membrane. A maximization test provided no evidence for sensitization with o-chloroaniline; no experimental data are available for m-chloroaniline.

Like acute mammalian toxicity, toxicity following repeated administration of the two compounds to mammals is also characterized by methaemoglobinaemia. The potential of both compounds for damaging erythrocytes is reflected by an increase in Heinz bodies, anaemia and increased haematopoiesis. Changes in the spleen (enlargement, pigmentation) are presumably also due to increased erythrocyte depletion. These typical findings have been observed in barely evaluable experiments at low doses which produced no clinical symptoms (m-chloroaniline in the rat at 25 mg/kg body weight and above by the oral route and approx. 1.5 mg/m<sup>3</sup> by inhalation; o-chloroaniline in the female rat at 55 mg/m<sup>3</sup> by inhalation). Dystrophic liver and kidney damage has been observed macroscopically and microscopically following oral administration of 25 and 110 mg m-chloroaniline/kg body weight/day over an eight-month and three-month period. Inhalation of 55 mg/m<sup>3</sup> o-chloroaniline over a one-week period caused a reduction in liver weight with no abnormal histological findings. A reliable NOEL cannot be derived from the studies for either m- or o-chloroaniline.

The results of genetic toxicity testing are not uniform for either m- or o-chloroaniline but provide evidence for mutagenic potential. The results of gene mutation assays in bacteria with both compounds with and without metabolic activation are predominantly negative, but gene mutation assays in fungi and mammalian cells and studies of DNA damage and chromosome aberration have produced some positive results.

Information on long-term carcinogenicity is not available for either compound. o-Chloroaniline did not cause transformation in a short-term test on hamster embryo cells.

Apart from one study of the induction of sperm head abnormalities which produced negative results with both compounds, no data on reproductive toxicology are available.

No investigations have been carried out on immunotoxicity with either o- or m-chloroaniline.

Methaemoglobinaemia is the predominant feature of intoxication in man too. One publication reports positive patch test findings with m-chloroaniline-HCl in dyehouse workers.

## **Recommendations**

### **Ecological aspect**

The quantum yields for direct photochemical degradation of o- and m-chloroaniline in the aquatic medium need to be determined.

It should be noted that halogenated anilines may be released during metabolism of crop protection agents. It is not possible to assess the general relevance of this problem at present and further investigation is required.

### **Toxicological aspect**

The results of genetic toxicity studies and the chemical structure suggest that o- and m-chloroaniline may have carcinogenic potential. Both compounds are used exclusively as intermediates in industrial processing. Workplace measurements should be carried out; if they show that no relevant exposure occurs, then experimental investigation of carcinogenic potential is not an urgent consideration.

Experiments are currently in progress to elicit the subacute inhalation toxicity and reproductive toxicity of o-chloroaniline; the decision to pursue these endpoints with m-chloroaniline should be dependent on the results of this work. There is some evidence for a sensitizing effect of m-chloroaniline in man; this question should therefore be investigated in experimental animals.