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November 21, 2001

Via US Mail and e-mail

Christine Todd Whitman, Administrator
U.S. Environmental Protection Agency (EPA)
P.O. Box 1473
Merrifield, VA 22116

Re: Monocyclic Aromatic Amines and Nitroaromatics (MAANA) Panel, Consortium No.
HPV Chemical Challenge Program Submission
Monocyclic Aromatic Amines Category
Category Justification and Testing Rationale

Dear Governor Whitman:

The MAANA Panel of the American Chemistry Council is pleased to submit the subject documentation for the Monocyclic Aromatic Amines category to EPA's HPV Chemical Challenge Program (Program). This submission covers four of the five chemicals MAANA has committed to sponsor in the program. Documentation for the fifth chemical (m-nitrotoluene) was submitted on November 12, 2001. MAANA Panel member companies are Albemarle Corporation, Bayer Corporation, Buffalo Color Corporation, and First Chemical Corporation.

In this submission, please find the *Category Justification and Testing Rationale* for the *Monocyclic Aromatic Amines category*. The four chemicals in this category are listed in the following table:

Monocyclic Aromatic Amines Category Chemicals Sponsored in the US HPV Chemical Challenge Program	
CAS Number	Compound Name
91-66-7	N, N-Diethyl Aniline
99-97-8	N,N-dimethyl-p-toluidine
102-27-2	N-ethyl-m-toluidine
103-69-5	N-ethylaniline

Data for five additional chemicals (listed in the table below) are used to support the conclusions reached for this category. The five additional chemicals have either undergone review in the Organization for Economic Co-operation and Development (OECD) Screening Information Data Sets (SIDS) program or are scheduled for SIDS review under the International Council of Chemical Associations' (ICCA) HPV program.

Monocyclic Aromatic Amines Category Additional Chemicals in the Category	
CAS Number	Compound Name
62-53-3	Aniline
95-53-4	o-Toluidine
106-49-0	p-Toluidine
108-44-1	m-Toluidine
121-69-7	N,N-Dimethyl aniline

In addition to the *Category Justification and Testing Rationale*, please also find attached robust summaries contained in IUCLID format for each of the four sponsored chemicals and the five additional supporting chemicals in the category.

This submission is also being sent electronically to the following e-mail addresses:

Oppt.ncic@epa.gov
Chem.rtk@epa.gov

If you require additional information, please contact the MAANA Panel's technical contact, Dr. Anne P. LeHuray at (703) 741-5630 or *anne_lehuray@americanchemistry.com*.

Sincerely yours,

Courtney M. Price
Vice President, CHEMSTAR

Attachments

cc: C. Auer, EPA/OPPT
B. Leczynski, EPA/OPPT
MAANA Panel (without attachments)
Steve Russell, ACC (without attachments)

AR201-13310A

MONOCYCLIC AROMATIC AMINES
Category Justification and Testing Rationale

CAS Nos. 91-66-7, 102-27-2, 99-97-8, and 103-69-5

(Plus SIDS/ICCA chemicals 62-53-3, 121-69-7, 95-53-4, 108-44-1, and 106-49-0 for data purposes).

Monocyclic Aromatic Amines and Nitroaromatics Panel
American Chemistry Council
November 2001

Member companies in the Monocyclic Aromatic Amines and Nitroaromatics Panel are Albemarle Corporation, Bayer Corporation, Buffalo Color Corporation, and First Chemical Corporation.

I. INTRODUCTION

The Monocyclic Aromatic Amines and Nitroaromatics Panel and its member companies submit for review and public comment their test plan for monocyclic aromatic amines in the Environmental Protection Agency's High Production Volume (HPV) Challenge Program (the HPV program). The member companies are committed to making existing test data publicly available for products in this category and developing any additional screening level data needed on health and environmental effects, fate, and physiochemical properties.

In order to minimize the use of animals in the testing of chemicals, the Panel has conducted a thorough literature search for all available data, published and unpublished. It also has performed an analysis of the adequacy of the existing data. Further, it developed a scientifically supportable category of related chemicals and used structure-activity relationship information as appropriate. No testing of whole animals is proposed; only *in vitro* genetic toxicity testing is included to develop needed screening data.

This document describes the monocyclic aromatic amines included in the HPV program and notes the related chemicals that are being sponsored through the International Council of Chemical Associations' (ICCA) testing program and the OECD SIDS program. Data on all these chemicals are included to provide justification for the proposed categories. IUCLID documents have been prepared and are included for each of these chemicals. Finally, the rationale for proposed testing is described.

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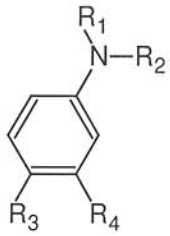
II. DEVELOPMENT OF THE MONOCYCLIC AROMATIC AMINES CATEGORY

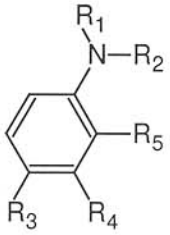
All chemicals included in the program are monocyclic aromatic amine compounds. The aromatic amines all have a single amino group and are secondary or tertiary amines with methyl or ethyl substituents on the nitrogen atom. Some of these aromatic amines also have a methyl substituent on the aromatic ring. Figure 1 gives the names, CAS numbers, and structures of the compounds in the HPV program. Other chemicals in this category are scheduled for review under the ICCA program and are undergoing or have undergone review in the OECD SIDS program. The data from these chemicals provides a more complete understanding of this category, and they are listed in Figure 2.

Figure 1. Monocyclic Aromatic Amines Included in the HPV Program



Chemical Name	CAS Number	R1	R2	R3	R4
N,N-Diethyl aniline	91-66-7	C_2H_5	C_2H_5	H	H
N,N-Dimethyl-p-toluidine	99-97-8	CH_3	CH_3	CH_3	H
N-Ethyl m-toluidine	102-27-2	C_2H_5	H	H	CH_3
N-Ethyl aniline	103-69-5	C_2H_5	H	H	H

Figure 2. Related Monocyclic Aromatic Amines



Chemical Name	CAS Number	R1	R2	R3	R4	R5	Program
o-Toluidine	95-53-4	H	H	H	H	CH_3	ICCA
p-Toluidine	106-49-0	H	H	CH_3	H	H	ICCA
m-Toluidine	108-44-1	H	H	H	CH_3	H	OECD SIDS
Aniline	62-53-3	H	H	H	H	H	OECD SIDS
N,N-Dimethyl aniline	121-69-7	CH_3	CH_3	H	H	H	OECD SIDS

Manufacturing, Use, and Exposure Information on Monocyclic Aromatic Amines

The N-alkyl substituted aromatic amines (N,N-diethyl aniline, N,N-dimethyl-p-toluidine, N-ethyl-m-toluidine, and N-ethyl aniline) are typically manufactured by reaction of aniline or a toluidine isomer with either ethanol or acetaldehyde for N-ethyl derivatives, or methanol or formaldehyde for the N-methyl compounds. The largest category of use for these chemicals is as chemical intermediates in the synthesis of a variety of organic chemicals. Because the majority of the production volume is converted to other chemicals (i.e., is used as a chemical intermediate), human and environmental exposure is limited. N,N-Diethyl aniline is used as a chemical intermediate to make dyes, pesticides, polyester resins, and pharmaceuticals. N-Ethyl-m-toluidine is an intermediate in the production of dyes and color developers for photographic films, while N-ethyl aniline is an intermediate in the production of dyes and pharmaceuticals. N-Ethyl aniline is also used as a promoter in the production of polyester resins. Two products, N,N-dimethyl-p-toluidine and N,N-diethyl aniline, are also used as cure accelerators in unsaturated polyester and epoxy vinyl resins and cyanoacrylate adhesives. In this application, they chemically reduce peroxides used as initiators of polymerization at room temperature.

Because of their use as chemical intermediates, the potential for exposure exists primarily in the workplaces of the manufacturers and their customers. The manufacturers use and recommend both personal protective equipment and engineering controls. Splash-proof chemical safety goggles, full-faceshields, or full-face respirators are recommended to protect against eye contact. Local exhaust ventilation is recommended to minimize inhalation exposure. Organic vapor cartridge respirators are recommended for use if there is a potential for exposure to vapors or mists. In case of a spill or leak, appropriate protection, which may include a respirator with supplied air, is required. Appropriate gloves, aprons, and chemical resistant clothing are used to prevent dermal contact.

Test Plan Rationale

There is a large amount of test data available for the four sponsored HPV aromatic amines and the five other related aromatic amines. These data allow the use of categories and estimation to predict effects where data are missing. The IUCLID documents enclosed for each chemical summarize the available studies. The critical studies to fulfill required HPV Challenge endpoints were chosen according to several factors, including documentation and detail, when the study was conducted, and access to a detailed publication or report. Overall, existing data has been identified for all of the HPV Challenge endpoints, however, as explained in detail below, the Panel proposes to perform low pH cell transformation assays on N-ethyl aniline and N-ethyl-m-toluidine.

Physical and Chemical Properties

The physical and chemical properties of all the chemicals in the category are summarized in Table 1 below. All 4 HPV compounds are liquids at room temperature, with relative densities ranging from 0.9625 (N-ethyl aniline) to 0.9307 (N,N-diethyl aniline). The boiling points all range from 184°C (aniline) to 221°C (N,N-dimethyl-p-toluidine). The vapor pressure range at 25°C is from 0.70 mm Hg for N,N-dimethyl aniline to an estimated value of 0.125 mm Hg for N-ethyl-m-toluidine. Water solubility data are available for 8 of the 9 compounds, and range from 36 g/l (aniline) to 0.13 g/l (N,N-diethyl aniline). The water solubility of N,N-dimethyl-p-toluidine is estimated at 0.46 g/l. The range of the log of the octanol-water partition coefficients is from 0.91 (aniline) to 3.2 (N,N-diethyl aniline). These data are sufficient to describe the properties of this category, and no further testing is proposed.

Table 1. Physical and Chemical Properties

	Aniline 62-53-3	o-Toluidine 95-53-4	p-Toluidine 106-49-0	m-Toluidine 108-44-1	N,N-Dimethyl aniline 121-69-7	N-Ethyl aniline 103-69-5	N,N-Dimethyl-p-toluidine 99-97-8	N-Ethyl-m-toluidine 102-27-2	N,N-Diethyl aniline 91-66-7
Molecular weight	93.13	107.16	107.16	107.16	121.18	121.18	135.21	135.21	149.24
Melting point (ºC)	-6.2	-16.3	43.7	-50.5	2.4	-63.5	-6.6	8.7	-38.8
Boiling point (ºC)	184.0	200.3	200.4	203.3	194.1	203.0	211	221	216.3
Density g/cc at 20º C	1.0213	0.9984	0.9619	0.9889	0.9557	0.9625	0.9366	0.9450	0.9307
Vapor pressure, mm Hg at 25º C	0.49	0.26	0.286	0.303 (Chao et al, 1990)	0.70	0.31	0.178	0.125 (est);1.00 mm at 54º C	0.136
Log P	0.91	1.4	1.39	1.4	2.28	1.92	2.81	2.66	3.17
Water solubility, g/l	36	8	11	12	1.2	2.7	0.46	1.1	0.13

= ICCA and OECD SIDS chemicals

Metabolism

Metabolism of arylamines generally proceeds through N-oxidation, hydroxylation of aromatic ring carbons, and formation of conjugates such as glucuronides, sulfates, and acetates (Kharchevnikova and Zholdakova, 1997; Cheever et al, 1980; Son et al, 1980). Ring alkyl substituents may also be oxidized to alcohols and further metabolized to acids (Son et al, 1980). N-Oxidation is an important step that can lead to the formation of metabolites that will react with cellular macromolecules (Kiese, 1963; Burstyn et al, 1991; Garner et al, 1984). The N-phenylhydroxylamines and nitrosobenzenes produced by N-oxidation are capable of binding to the heme ion in hemoglobin and causing oxidation. This reaction can produce the methemoglobinemia that is the most typical toxicity associated with aromatic amines. Aniline itself is oxidized primarily to o- and p-aminophenol. These metabolites are subsequently conjugated with glutathione to form o- and p-aminophenylmercapturic acids for urinary excretion (Radomski, 1979; Baranowska-Dutkiewicz, B, 1982; Irons et al, 1980; Williams, 1959; Parke, 1960). For three of these arylamines, the rates of both N-oxidation and N-dealkylation *in vitro* were found to occur in the order N,N-dimethyl-p-toluidine >N,N-dimethyl aniline > N,N-diethyl aniline (Seto and Guengerich, 1993). N-ethyl aniline has also been found to be metabolized *in vitro* by N-oxidation, N-dealkylation, and ring hydroxylation (Appel et al, 1965; Seto and Guengerich, 1993). N-Dealkylation of methyl groups proceeds more rapidly than that of ethyl groups (Seto and Guengerich, 1993; Gorrod and Patterson, 1983). The most common metabolic reaction for the toluidines is ring hydroxylation. o-Toluidine undergoes hydroxylation in the para position, as well as a lesser amount of N-acetylation, and conjugation with sulfates and glucuronides (Cheever et al, 1980; Son et al, 1980). p-Toluidine is hydroxylated in the ortho position, while m-toluidine is converted to a mixture of the ortho and para-hydroxylated metabolites; these derivatives are also subsequently conjugated. (Cheever et al, 1980). While metabolism studies of N-ethyl-m-toluidine are not available, N-dealkylation and ring hydroxylation are expected based on these related chemicals. The metabolism of the eight compounds that have been studied is typical of monocyclic aromatic amines. Typical metabolic reactions are diagrammed in Figure 3.

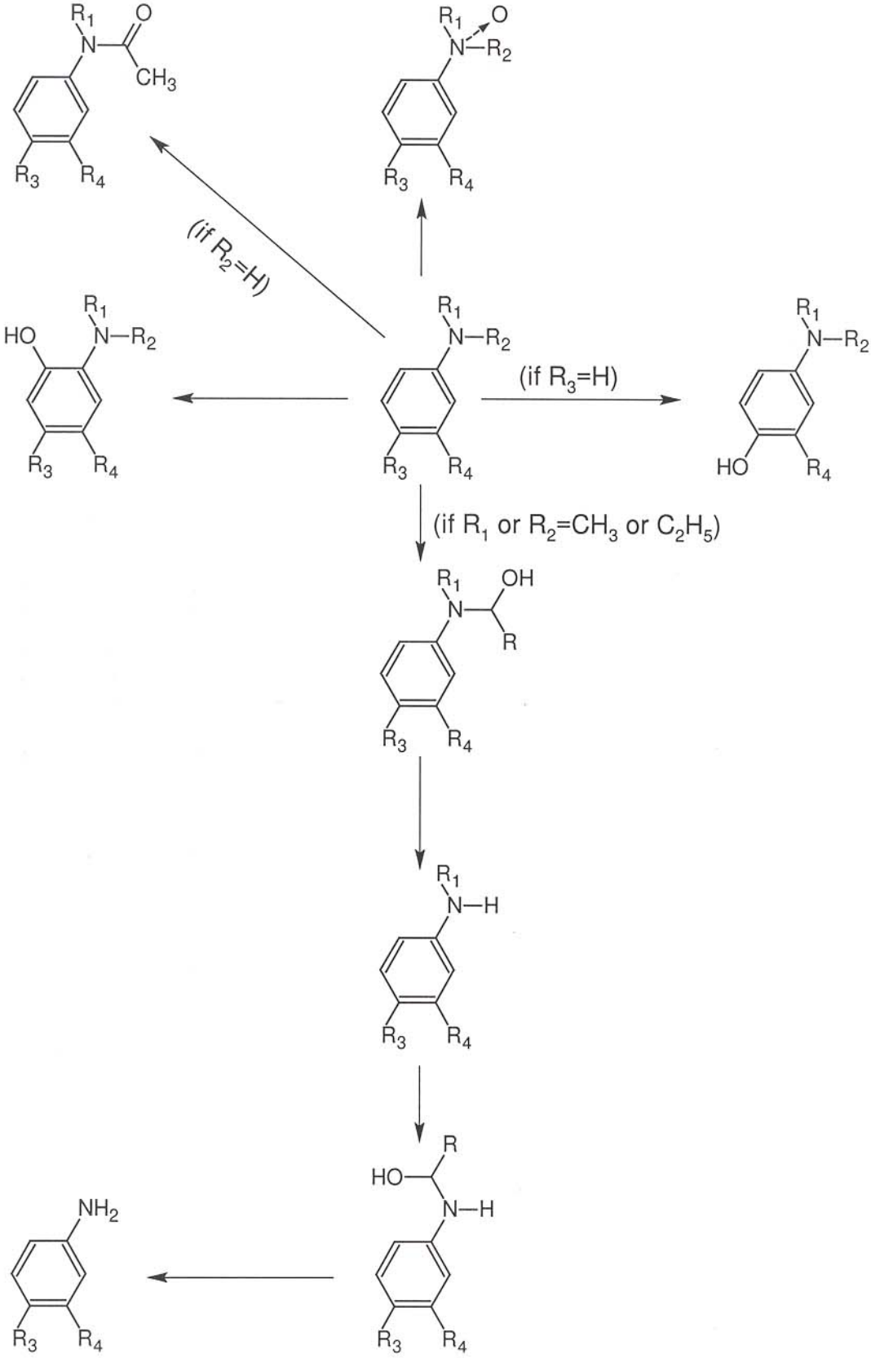
Fate

If released into water, biodegradation will be a major removal process. A short acclimation period generally enhances biodegradation of monocyclic aromatic amines. Biodegradation has been studied for three of the four HPV compounds and for five other chemicals in the category. Conflicting results have been published regarding the ready biodegradability of N-ethyl aniline. However, this chemical is inherently biodegradable. Likewise, N,N-diethylaniline was readily biodegradable by one test protocol and not readily biodegradable by another. N-Ethyl-m-toluidine was not readily biodegradable. Based on the other members of the category, N-ethyl-m-toluidine is expected to be ultimately biodegradable. Aniline, N,N-dimethyl aniline, m-toluidine, p-toluidine, and o-toluidine have all been found to be readily biodegradable, although N,N-dimethyl aniline and m-toluidine had mixed results for this endpoint. N,N-Dimethyl-p-toluidine has not been tested for biodegradation. Based on biodegradation results for these chemicals, N,N-dimethyl-p-toluidine is expected to biodegrade after acclimation. Adsorption to sediments is predicted to be low for all these aromatic amines, but the protonated forms of these bases will bind more strongly. In surface waters, photodegradation is expected to occur at a moderate to rapid rate for all four compounds. Aniline photodegradation was measured and found to occur at a moderate rate; photodegradation of N,N-dimethyl aniline occurred at a moderate to slow rate. Evaporation may also contribute to loss from water, and will be followed by photodegradation in the atmosphere. N-Ethyl aniline, aniline, o-toluidine, and p-toluidine degrade slowly in pure water in the absence of sunlight. Many aromatic amines will readily react with organic constituents in natural waters. None of the four HPV compounds is likely to bioaccumulate in aquatic organisms, based on their octanol-water partition coefficients. Lack of bioaccumulation has been demonstrated for N,N-dimethyl aniline, N,N-diethyl aniline, aniline and o-toluidine. If released into soil, leaching and reaction with organic constituents are expected to be major removal processes. Binding to soil is predicted to be low to moderate, and as for sediments, binding will vary with pH. Evaporation from dry soil is expected to be low. There are sufficient data for monocyclic aromatic amines to characterize the fate of these chemicals, and no further testing is proposed.

Aquatic Toxicity

In most acute toxicity tests, the four compounds were harmful to fish (96-hr LC_{50}>10≤100 mg/L). N-ethyl aniline was toxic (96-hr LC_{50}>1≤10 mg/L) to one species, however. N-ethyl aniline was harmful to algae, but N,N-diethyl aniline was toxic. Related chemicals in the category were not harmful to algae (N,N-dimethyl aniline), harmful (aniline, o-toluidine, and m-toluidine), or toxic (o-toluidine and p-toluidine). N,N-dimethyl-p-toluidine and N-ethyl-m-toluidine have not been tested for algal toxicity, and their algal toxicity was calculated using EPIWIN v. 3.05. Both of these compounds are predicted to be harmful to algae. N-ethyl aniline was harmful to Daphnia, as was o-toluidine in several studies, while N,N-dimethyl aniline and N,N-diethyl aniline were toxic. Aniline and m-toluidine were very toxic to Daphnia (48-hr LC_{50}≤1 mg/L); o-toluidine was also very toxic in one study. p-Toluidine was toxic to a salt water invertebrate, Mysid shrimp. The toxicity to Daphnia of N,N-dimethyl-p-toluidine and N-ethyl-m-toluidine was calculated, and both compounds were predicted to be harmful. There is a large amount of data available on chemicals in this category, and no further testing is proposed.

Figure 3. Some Typical Metabolic Reactions of the Category



Mammalian Acute Toxicity

All four of the HPV aromatic amines have been tested for acute toxicity. Three of the four compounds are considered harmful by single oral doses, as the rat oral LD_{50}'s are >500 and ≤2000 mg/kg. The N-ethyl substituted chemicals appear to be slightly more toxic than the N-methyl substituted group in acute oral studies, and N-ethyl aniline is considered toxic by the oral route (LD_{50}>50 and ≤500 mg/kg). The rabbit dermal LD_{50}'s for three compounds are all >2000 mg/kg, which is not considered harmful by single dermal applications. N,N-Diethyl aniline is considered toxic by the dermal route, with a rabbit LD_{50} of >468<935 mg/kg. Systemic toxicity was not evident after dermal application of the toluidines, N,N-dimethyl-p-toluidine and N-ethyl-m-toluidine. N-ethyl aniline, N,N-diethyl aniline, N-ethyl-m-toluidine, and N,N-dimethyl-p-toluidine are all classified as toxic by single inhalation exposures (rat 4 hr LC_{50} >0.5≤5.0 mg/l). Where systemic toxicity was found, all these compounds caused cyanosis and increased respiratory rate from methemoglobinemia. No further testing is proposed on acute toxicity.

Mammalian Repeated Dose Toxicity

Oral or inhalation repeated exposure studies have been completed on two of the four compounds, N,N-diethyl aniline and N-ethyl-m-toluidine. Repeated exposure studies have also been completed on related aromatic amines: aniline, N,N-dimethyl aniline, o-toluidine, m-toluidine, and p-toluidine. Regardless of exposure route or length, all of these aromatic amines affected the blood as the primary target organ. The blood effects included methemoglobinemia, hemolytic anemia, splenomegaly, extramedullary hematopoiesis, reticulocytosis, Heinz bodies, and hemosiderosis. In a direct comparison, aniline and o-toluidine were given orally to rats for 5, 10, or 20 days at ¼ of the LD_{50}. Histopathology examinations found splenic congestion, increased hematopoiesis, hemosiderosis, and bone marrow hyperplasia from both chemicals (Short et al, 1983). Rats were exposed to aniline by inhalation for 10 days over a 14 day period, followed by a two week recovery period. Hematological parameters were affected, and the organ to body weight ratios for the liver, spleen, and thymus were increased (O'Neal et al, 1982). A directly comparable inhalation study of N-ethyl-m-toluidine found similar hematological effects. Changes in the liver, spleen, bone marrow, and kidneys were secondary to effects on the blood (Stephens et al, 1999). A 30 day gavage study of m-toluidine and a 28 day gavage study of N,N-diethyl aniline in rats also found hematological effects and no other target organs. A 14 day gavage study in rats and a 15 day study in mice of N,N-dimethyl aniline found similar effects on the blood. A 28 day dietary study of p-toluidine in rats at rather low doses found decreased body weight gains and increased liver weight; no hematology data were given. Thus, in all eight of these screening studies of four weeks of exposure or less where hematology results were reported, pathological changes were found only in the blood and in other organs affected by the blood changes. Based on the consistency of these effects, as well as the acute results for all the compounds, N-ethyl aniline, N,N-dimethyl-p-toluidine, and N-ethyl-m-toluidine are proposed to be covered by the results of the other monocyclic aromatic amines, and no further repeated exposure testing is proposed.

Genetic Toxicity

Standard bacterial mutagenicity assays with and without metabolic activation have been conducted for all four HPV compounds. Only N-ethyl-m-toluidine was positive, with metabolic activation.

Two of the four compounds have been tested for clastogenicity, and there is information on related aromatic amines. N,N-Dimethyl-p-toluidine induced chromosome aberrations *in vitro* in Chinese hamster V79 (fibroblast) cells without activation, while N,N-diethylaniline did not induce micronuclei in the mouse micronucleus assay. N-Ethyl aniline and N-ethyl-m-toluidine have not been tested for clastogenicity. A number of assays have been done on related aromatic amines in this category. N,N-dimethyl aniline induced chromosome aberrations *in vitro* in Chinese hamster ovary and V79 cells. Aniline caused chromosome aberrations *in vitro* in Chinese hamster ovary and lung cells with activation, and in Chinese hamster V79 cells both with and without activation. Positive and negative results occurred in mouse and rat micronucleus assays with aniline, but most were positive. However, aniline did not cause a dominant lethal effect in rats. p-Toluidine also induced chromosome aberrations in Chinese hamster lung cells with activation, but it did not increase micronuclei in the mouse micronucleus assay. o-Toluidine caused chromosome aberrations in most assays *in vitro,* including in rat liver and Chinese hamster liver, lung, and ovary cells, but not *in vivo* in most of the micronucleus assays (Danford, 1991). A long treatment time was needed *in vitro* for a positive result.

The low pH SHE cell transformation assay has been found to be a useful short-term test for the identification of rodent carcinogens. The use of a lower pH has resulted in demonstration of a dose-response relationship for carcinogens, which was difficult to do with the earlier protocol in SHE cells (Yamasaki, 1996). A recent study found that there was excellent correlation between this assay and long-term rodent studies for a group of 10 aromatic amines and nitroaromatics (Kerckaert et al, 1998). The assay outperformed the Ames test in specificity, correctly identifying chemicals that were positive in the Ames test but not rodent carcinogens. o-Toluidine was one of the chemicals tested in this study, and it was found to cause cell transformation. o-Toluidine was also positive in SHE cells and many other cell lines at neutral pH.

Aniline has not been tested using the low pH protocol, but it was also tested in several cell lines at neutral pH. While most of these older assays were negative, a few were reported to be positive. Based on the usefulness of this assay for aromatic amines, the Panel proposes to do low pH cell transformation assays on N-ethyl aniline and N-ethyl-m-toluidine.

Developmental and Reproductive Toxicity

Screening developmental toxicity studies in mice for N,N-diethylaniline categorized this compound as a low priority for further study. A full developmental toxicity study in rats for N,N-diethyl aniline found fetotoxicity at maternally toxic doses, but no evidence of teratogenicity or embryotoxicity. Other compounds in the category have also been tested for developmental toxicity. A mouse screening developmental toxicity study of N,N-dimethyl aniline also placed it as a low priority for additional studies. A full developmental toxicity study of aniline failed to find evidence of a teratogenic effect. When methemoglobinemia is induced in the gravid female by these aromatic amines, the fetus is also adversely affected by lack of oxygen. There is no evidence of increased susceptibility of the fetus in these developmental studies, however. The repeated dosing studies discussed above for this category show that studies in rodents with exposure duration similar to that of a developmental toxicity study will cause the adverse effects described on the blood. Based on these results, N-ethyl aniline, N-ethyl-m-toluidine, and N,N-dimethyl-p-toluidine are covered by the testing of the related compounds, and no developmental toxicity testing is proposed.

Consideration is given to effects on reproductive organs in repeated exposure studies to determine whether reproductive toxicity studies are needed. The four week oral study of N,N-diethyl aniline in rats did not find any evidence of pathology in the reproductive organs, nor did the two week inhalation study of N-ethyl-m-toluidine in rats. All of the related chemicals in this category have undergone long-term animal studies. Subchronic and chronic studies of N,N-dimethyl aniline, o-toluidine, and aniline in rats and mice found no evidence that reproductive function would be affected, nor did 78 week studies of m-toluidine and p-toluidine in rats. A dominant lethal study of aniline in rats was also completed to address the possibility of heritable effects being transmitted to the offspring from parental males. No dominant lethal effect was found in the rat. In keeping with the lack of heritable genetic damage from aniline exposure, o-toluidine did not cause sperm-head abnormalities in mice. o-Toluidine was also tested for reproductive effects in a dermal screen in which mice were treated for four months before mating and offspring were maintained up to two months of age. While there was evidence of systemic toxicity, there were no effects on fertility or signs of embryotoxicity, and no evidence of greater sensitivity of the reproductive system as compared to general toxicity. No reproductive toxicity testing has been completed for N,N-diethyl aniline, N-ethyl-m-toluidine, N-ethyl aniline, and N,N-dimethyl-p-toluidine. These chemicals are covered by the subchronic, chronic, and developmental data discussed above for these and related aromatic amines, and no further testing for reproductive toxicity is proposed.

The existing data and proposed test plan are summarized in Table 2 below.

head abnormalities in mice. o-Toluidine was also tested for reproductive effects in a dermal screen in which mice were treated for four months before mating and offspring were maintained up to two months of age. While there was evidence of systemic toxicity, there were no effects on fertility or signs of embryotoxicity, and no evidence of greater sensitivity of the reproductive system as compared to general toxicity. No reproductive toxicity testing has been completed for N,N-diethyl aniline, N-ethyl-m-toluidine, N-ethyl aniline, and N,N-dimethyl-p-toluidine. These chemicals are covered by the subchronic, chronic, and developmental data discussed above for these and related aromatic amines, and no further testing for reproductive toxicity is proposed.

The existing data and proposed test plan are summarized in Table 2 below.

Table 2. Summary of Data Gaps and Method of Completion

	Aniline 62-53-3	o-Toluidine 95-53-4	p-Toluidine 106-49-0	m-Toluidine 108-44-1	N,N-Dimethyl aniline 121-69-7	N-ethyl aniline 103-69-5	N,N-dimethyl-p-toluidine 99-97-8	N-Ethyl-m-Toluidine 102-27-2	N,N-Diethyl aniline 91-66-7
Environmental Fate									
Photodegradation	A	S	S	S	A	S	S	S	S
Hydrolysis	A	A	A		A	C	C	C	C
Fugacity	S	S	S	S	S	S	S	S	A
Biodegradation	A	A	A	A	A	A	C	A	A
Eco Toxicity									
Acute fish	A	A	A	A	A	A	A	A	A
Acute invertebrate	A	A	A	A	A	A	A	S	A
Acute algal	A	A	A	A	A	A	S	S	A
Mammalian Toxicity									
Acute toxicity	A	A	A	A	A	A	A	A	A
Repeated dose toxicity	A	A	A	A	A	C	C	C; NG	A
Genetic toxicity									
in vitro: gene mutation	A	A	A	A	A	A	A	A	A
in vitro: chromosome aberrations	A	A	A		A		A		
in vitro: cell transformation (SHE cells)	A	A				T		T	
in vivo: chromosome aberrations	A	A	A						A
Reproductive toxicity	P	P; NG	P	P	P	C	C	C	C
Developmental toxicity	A	NG			NG	C	C	C	A; NG

= ICCA and OECD SIDS chemicals (testing will be addressed under ICCA HPV Program)

A = Adequate data available
NG=Non-guideline data available
C = Use of Category Approach

T = Testing to be done
S = Structure-activity relationship (modeling program used)
P = ≥90 Day study found no pathology of reproductive organs

References

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AR201-13310B

I U C L I D

D a t a S e t

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OPPT NCIC
2001 NOV 23 PM 12: 46

Existing Chemical	ID: 102-27-2
CAS No.	102-27-2
EINECS Name	N-ethyl-m-toluidine
EINECS No.	203-019-4
Molecular Weight	135.2
Molecular Formula	C9H13N

Producer Related Part
Company:
Creation date: 15-JUL-1999

Substance Related Part
Company:
Creation date: 15-JUL-1999

Memo: Bayer Corporation

Printing date: 29-OCT-2001
Revision date:
Date of last Update: 29-OCT-2001

Number of Pages: 21

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association), Monocyclic Aromatic Amines and Nitro Aromatics (MAANA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States

17-AUG-2001

Type: cooperating company
Name: Albemarle Corporation
Country: United States

24-SEP-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

Flag: Critical study for SIDS endpoint
24-SEP-2001

Type: cooperating company
Name: Buffalo Color
Country: United States

24-SEP-2001

Type: cooperating company
Name: ChemFirst
Country: United States

24-SEP-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information

Substance type: organic
Physical status: liquid
Purity: >= 99.3 % w/w
21-OCT-1999

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms

ANILINE, N,N-DIETHYL-
09-SEP-1999

BENZENAMINE, N,N-DIETHYL-
09-SEP-1999

DIETHYLANILINE
09-SEP-1999

DIETHYLPHENYLAMINE
09-SEP-1999

N,N-DIETHYLAMINOBENZENE
09-SEP-1999

N,N-DIETHYLAMINOBENZOL
09-SEP-1999

N,N-DIETHYLBENZENAMINE
09-SEP-1999

1.3 Impurities

CAS-No:
EINECS-No:
EINECS-Name: Basic nitrogen
Contents: ca. 9.3 % w/w
21-OCT-1999

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern

Type: type
Category: Use in closed system
20-JAN-2000

Type: industrial
Category: Chemical industry: used in synthesis
20-JAN-2000

Type: use
Category: Intermediates
20-JAN-2000

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: -38.8 degree C
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
17-AUG-2001 (1) (2) (3)

2.2 Boiling Point

Value: 216.3 degree C at 1013 hPa
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
17-AUG-2001 (2)

Value: 215.5 degree C
Decomposition: no
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
17-AUG-2001 (4) (3)

Value: 217.1 degree C at 1013 hPa
17-AUG-2001 (1)

Value: 92.4 degree C at 13.333 hPa
Decomposition: no
Method: other: no data
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not stated
17-AUG-2001 (5)

2.3 Density

Type: relative density
Value: .9307 g/cm3 at 20 degree C
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
17-AUG-2001 (2) (3)

Type: density
Value: .94 g/cm3 at 20 degree C
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
16-APR-2001 (1)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: .2 hPa at 20 degree C
Method: other (measured): Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
24-SEP-2001 (1) (3)

Value: .18 hPa at 25 degree C
Method: other (measured)
GLP: no
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
24-SEP-2001 (6)

Value: .4 hPa at 30 degree C
Method: other (measured): Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
24-SEP-2001 (1) (3)

Value: 1 hPa at 44.3 degree C
Method: other (measured): Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
24-SEP-2001 (7)

Value: 1.4 hPa at 50 degree C
Method: other (measured): Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Flag: Critical study for SIDS endpoint
17-AUG-2001 (1)

2.5 Partition Coefficient

log Pow: 3.17 at 25 degree C
Method: OECD Guide-line 107 "Partition Coefficient (n-octanol/water), Flask-shaking Method"
Year: 1979
GLP: no
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Result: n-octanol-water Partition coefficient = 1491.54
log Pow = 3.17
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (8)

log Pow: 3.153
Method: other (calculated): KOWWIN Program (v1.65)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
17-AUG-2001 (9)

log Pow: 3.2
Method: other (calculated): A. Leo, CLOGP-3.63 (1991) Daylight, Chemical Information Systems, Inc. Irvine, CA USA
Year:
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
17-AUG-2001 (10) (11) (3)

log Pow: 3.31 - 4
Method: other (measured): see references
Year:
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not stated
17-AUG-2001 (12) (13) (14) (3)

2.6.1 Water Solubility

Value: 130 mg/l at 20 degree C
Qualitative: moderately soluble (100-1000 mg/L)
Method: other
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not stated
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
17-AUG-2001 (10) (3)

Value: = 14400 mg/l at 12 degree C
Qualitative: very soluble (> 10000 mg/L)
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
17-AUG-2001 (15) (3)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: 79 degree C
Type: closed cup
Method: other: DIN 51758
Year:
16-APR-2001 (10)

2.8 Auto Flammability
-

2.9 Flammability

Result:
Remark: Ignition temperature: approx. 500 degree C
16-APR-2001 (10)

2.10 Explosive Properties

-

2.11 Oxidizing Properties

-

2.12 Additional Remarks

Remark: The BUA-report No. 40 includes further information
16-APR-2001

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: = .0000000001642617 cm3/(molecule * sec)
Degradation: 50 % after .8 hour(s)
Method: other (calculated): AOP v1.89
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
17-AUG-2001 (9)

3.1.2 Stability in Water

Type: abiotic
Method: other: (calculated): Hydrowin v1.67
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Result: Hydrowin v1.67 cannot estimate a hydrolysis rate constant for this structure.
Reliability: (2) valid with restrictions
24-SEP-2001 (9)

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 121-69-7.

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air water soil sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: BCF v2.13 Level III Fugacity Model
Year: 1999
Result:

Media	Distribution (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.2	1.56	1000	5.19e-012
Water	22.3	900	1000	2.27e-009
Soil	76.8	900	1000	4.26e-009
Sediment	0.718	3.6e+003	0	1.73e-009

Persistence Time: 528 hr
Reaction Time: 605 hr
Advection Time: 4.11e+003 hr
Percent Reacted: 87.2
Percent Advected: 12.8
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
17-AUG-2001 (9)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l
Degradation: 0 % after 28 day
Result: under test conditions no biodegradation observed
Method: OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year: 1983 GLP: yes
Test substance: other TS: N,N-diethylaniline; purity = 99.5 %
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (16)

Type: aerobic
Inoculum: predominantly domestic sewage, adapted
Concentration: .8 mg/l related to Test substance
Degradation: > 90 % after 20 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: 1977 GLP: no
Test substance: other TS: N,N-diethylaniline; purity not noted
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (10)

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Degradation: after 14 day
Result: under test conditions no biodegradation observed
Method: OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year: 1981 GLP: no
Test substance: other TS: N,N-diethylaniline; purity not noted
Remark: Method: "Biodegradation test of chemical substance by microorganisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test I" stipulated in the OECD Guideline for Testing of Chemicals (May 12, 1981).
Sludge conc.: 30 mg/l
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (17)

3.6 BOD5, COD or BOD5/COD Ratio

C O D

COD: 2346 mg/g substance

16-APR-2001 (10)

Year: 1983 GLP: yes
Concentration: 4 mg/l related to Test substance

Remark: BOD5 < 0.1 g/g
COD 1.28 g/g
16-APR-2001 (16)

3.7 Bioaccumulation

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 56 day
Concentration: .02 mg/l
BCF: 17 - 125
Elimination:
Method: OECD Guide-line 305 C
Year: 1981 GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not stated
Remark: Method: "Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "305C, Bioaccumulation: Degree of Bioconcentration in Fish" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
17-AUG-2001 (17)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 56 day
Concentration: .2 mg/l
BCF: 44 - 161
Elimination:
Method: OECD Guide-line 305 C
Year: 1981 GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not stated
Remark: Method: "Bioaccumulation test of chemical substance in fish and shellfish" stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, the Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "305C, Bioaccumulation: Degree of Bioconcentration in Fish" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
17-AUG-2001 (17)

Species:
Exposure period:
Concentration:
BCF: 70.58
Elimination:
Method: other: BCF Program (v2.13)
Year: GLP: no
Test substance: other TS: molecular structure
Result: Log Kow (estimated) : 3.15
Log Kow (experimental): 3.31
Log Kow used by BCF estimates: 3.31

Equation Used to Make BCF estimate:
Log BCF = 0.77 log Kow - 0.70

Estimated Log BCF = 1.849 (BCF = 70.58)
Reliability: (2) valid with restrictions

Accepted calculation method
17-AUG-2001 (9)

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: 16.4
Method: EPA OPP 72-1
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline purchased from Aldrich Chemical Co., Milwaukee, WI; purity = 99%
Method: pH was adjusted to approximate that of Lake Superior water (pH 7.8) with NaOH or HCL.
Compound analyses were done by GLC: all exposure chambers at 0,24,48,72, and 96 hr.

Fathead minnows used in this experiment were 34 days old and were cultured at USEPA Environmental Research Laboratory, Duluth, MN and University of Wisconsin - Superior campus.

10 fish/concentration and control. Behavior and toxic signs were noted at 4,24,48,72 and 96 hours.
Test condition: Temperature = 25.1 degree C (+/-0.57); Dissolved oxygen = 7.0 mg/l; pH =7.74; hardness = 39.5 mg/l CaCO3; Tank volume = 1 liter; Concentrations (measured)= 6.15, 13.1, 20.6, 27.9, 33.9 mg/l.
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (18)

Type: static
Species: Oncorhynchus mykiss (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 38.5
Method: other
Year: 1983 GLP: yes
Test substance: other TS: N,N-diethylaniline; purity = 99.5 %
Test condition: Temperature: 15 degree C, pH 6.8-8.0,
Oxygen conc.: 6.0-10.6 mg/l
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
17-AUG-2001 (16)

Type:
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 25
Method: other: according to Japan Industrial Standards
Year: 1971 GLP:
Test substance: other TS: N,N-diethylaniline; purity not noted
Result: LC50 (24 hours) = 40.0 mg/l
Reliability: (2) valid with restrictions
19-JUN-2001 (8)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: 20
LC100: 50
Method: other: Bestimmung der akuten Wirkung von Stoffen auf Fische. Arbeitskreis "Fischtest" im Hauptausschuss "Detergentien" (15.10.73)
Year: 1973 GLP: no
Test substance: other TS: N,N-diethylaniline; purity not stated
17-AUG-2001 (10)

Type:
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 7.63
Method:
Year: GLP: no
Test substance: other TS: molecular structure
Remark: QSAR calculation
24-SEP-2001 (19)

Type: other: calculation
Species: other: Fish
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 9.181
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
24-APR-2001 (9)

Type:
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 16.8
Method: other: Japanese Industrial Standard (JIS K 0102-1986-71) "Testing methods for industrial waste water"
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not stated
17-AUG-2001 (17)

Type:
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mol/l Analytical monitoring: no data
LC50: 3.959
Method: other: no data
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not stated
17-AUG-2001 (20)

Type:
Species: Salmo gairdneri (Fish, estuary, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 6.14
Method:
Year: GLP: no
Test substance: other TS: molecular structure
Remark: QSAR calculation
17-AUG-2001 (19)

Type: other: calculation
Species: other: Fish
Exposure period: 14 day
Unit: mg/l Analytical monitoring: no
LC50: 19.963
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
24-APR-2001 (9)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 35.4
EC50: 70.7
EC100: 141
Method: OECD Guide-line 202, part 1 "Daphnia sp., Acute Immobilisation Test"
Year: 1984 GLP: no
Test substance: other TS: N,N-diethylaniline; purity not noted
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (10) (21)

Type: static
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: yes
EC50: 1 - 1.6
Method: EPA OTS 797.1300
Year: 1992 GLP: yes
Test substance: other TS: N,N-diethylaniline; purity >99%; supplied by Merck
Result:

	Nominal	Measured
EC50 -24hr	18mg/l(2.8-116)	3.5mg/l (0.25-25)
EC50 -48hr	7.7 mg/l (6.5-9.1)	1.3mg/l (1.0-1.6)

Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
24-SEP-2001 (22)

Type: static
Species: other: Tetrahymena pyriformis
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
EC50: 35.1
Method: other: according to Schultz, T. et al. (1991)
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity >95%
Result: Log of the inverse of 48hr 50% Inhibitory Growth Concentration (IGC50) = 3.629 mol/l
28-SEP-2001 (23)

Type: other: calculation
Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 10.651
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
19-JUN-2001 (9)

Type: other: calculation
Species: Mysidopsis bahia (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50 : 1.165
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
24-APR-2001 (9)

Type: other: calculation
Species: Daphnia sp. (Crustacea)
Exposure period: 16 day
Unit: mg/l Analytical monitoring: no
EC50: .903
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
19-JUN-2001 (9)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus subspicatus (Algae)
Endpoint: other: cell count
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring: no
EC10: 2.8
EC50: 5.6
Method: other: Bestimmungbder Hemmwirkung von Wasserinhaltsstoffen auf Grunalgen Scenedesmus-Zellvrmehrungs-Hemmtest L 9 Stand 1987g
Year: 1987 GLP: no
Test substance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
17-AUG-2001 (10) (24)

Species: other algae: green algae
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC50: 7.114
ChV : 1.383
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
17-AUG-2001 (9)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring:
EC50: > 100
Method: other: ETAD 103: A Screening Test for the Assessment of the Possible Inhibitory Effect of a Chemical Substance on Aerobic Waste Water Bacteria (26.07.1979)
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity = 99.5 %
17-AUG-2001 (16)

Type: aquatic
Species: Pseudomonas fluorescens (Bacteria)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 1000
Method: other: Bestimmung der biologischen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L 8 (1968) modifiziert
Year: 1973 GLP: no
Test substance: other TS: N,N-diethylaniline; purity not stated
17-AUG-2001 (10)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species: other
Endpoint: other
Exposure period: 30 day
Unit: mg/l Analytical monitoring: no
ChV : 1.424
Method: other: ECOSAR v0.99e
Year: GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
17-AUG-2001 (9)

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia magna (Crustacea)
Endpoint:
Exposure period: 21 day
Unit: mg/l Analytical monitoring: no
Method: other: UBA-Verfahrensvorschlag (vorlaeufiger) "Verlaengerter Toxizitaetstest bei Daphnia magna" (Bestimmung der NOEC fuer Reproduktionsrate, Mortalitaet und den Zeitpunkt des ersten Auftretens von Nachkommen, 21 d)(01.02.1984)
Year: GLP: no
Test substance:
Remark: R 21: 82.1 % at 0.3 mg/l
16-APR-2001 (10)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type: other: calculation
Species: Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint: other
Exposure period: 14 day
Unit: other: ppm
LC50: 406.143
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Remark: Chemical may not be soluble enough to measure this predicted effect.
Reliability: (2) valid with restrictions
Accepted calculation method
17-AUG-2001 (9)

4.6.2 Toxicity to Terrestrial Plants

-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks

Remark: BUA Report No. 40 includes further ecotoxicological data.
16-APR-2001

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: Wistar
Sex: male
Number of Animals: 10
Vehicle: other: undiluted
Value: ca. 606 mg/kg bw
Method: Directive 84/449/EEC, B.1 "Acute toxicity (oral)"
Year: 1978 GLP: no
Test substance: other TS: undiluted N,N-diethylaniline; purity not noted
Method: single oral application by gavage of undiluted TS, 0.1, 0.5, 0.7, 0.8 ml/kg, 14 d observation period
Remark: LD50 = 0.65 ml/kg bw
Result: signs of toxicity: cyanosis, palmospasms, disorders of balance, increased diuresis, impaired general condition

Doses ml/kg	toxicological result no.of rats with toxic signs	no of deaths	time of death
0.1	0	0	
0.5	10	1/10	d 2
0.6	10	2/10	d 4-6
0.7	10	6/10	d 2-4
0.8	10	10/10	d 2-5

Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (25)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 720 mg/kg bw
Method:
Year: GLP: no
Test substance: other TS: undiluted N,N-diethylaniline
16-APR-2001 (26)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 720 - 1159 mg/kg bw
Method: other: no data
Year: GLP: no data
Test substance: no data
10-AUG-2000 (27)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 782 mg/kg bw
Method:
Year: GLP: no data
Test substance:
16-APR-2001 (28)

Type: LDLo
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 486 - 1870 mg/kg bw
Method: other: no data
Year: GLP: no data
Test substance: no data
10-AUG-2000 (27)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: = 1.92 mg/l
Method: other: according to: OECD Acute Toxicity Screening Program, Protocol for Acute Inhalation Toxicity Studies (modified)
Year: GLP: yes
Test substance: other TS: N,N-diethylaniline; purity not noted

Remark: LC50 value expressed as actual exposure concentration (analytically determined)
Particle size ~ 3.5 - 5.0 microns; 75-89% <10 microns
Result: signs of toxicity (among others): ataxia and tremors in animals exposed to an actual concentration of 1.97 mg/l or greater
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (29)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rat
Strain: no data
Sex: no data
Number of Animals:
Vehicle: other: undiluted
Value: > 5000 mg/kg bw
Method: other: undiluted TS, observation time: 14 d, no further information
Year: GLP: no
Test substance: other TS: undiluted N,N-diethylaniline; purity not noted
Remark: no signs of intoxication, no local irritancy
Flag: Critical study for SIDS endpoint
17-AUG-2001 (30)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 468 - 935 mg/kg bw
Method: other: no data
Year: GLP: no data
Test substance: no data
Remark: Mortality 0/4 at 468 mg/kg; 4/4 at 935 mg/kg.
16-APR-2001 (31)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value: = 870 mg/kg bw
Method:
Year: GLP: no
Test substance: other TS: undiluted N,N-diethylaniline
16-APR-2001 (32)

Type: LD50
Species: mammal
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: other: unreported
Value: = 2570 mg/kg bw
Method:
Year: GLP: no data
Test substance:
16-APR-2001 (33)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: slightly irritating
EC classificat.:
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1981 GLP: no data
Test substance: other TS: undiluted N,N-diethylaniline
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (34)

Species: rat
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: according to: Draize, J.P. et al.: J. of Pharmacol. 82, 377 (1944)
Year: GLP: no
Test substance:
Reliability: (2) valid with restrictions
16-APR-2001 (35)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: moderately irritating
EC classificat.:
Method: other: site of application: back or ear; exposure time: 1 min., 5 min., 15 min. (back) and 20 hours (back or ear); observation period: 8 days
Year: GLP: no
Test substance: other TS: undiluted N,N-diethylaniline
16-APR-2001 (30)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result:
EC classificat.:
Method: other: exposure time: 24 hours, site of application: ear, dose: 500 ul/animal, semiocclusive, observation period: 7 days
Year: GLP: no
Test substance:
Remark: result: highly irritating, corrosive
16-APR-2001 (36)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.:
Method: OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year: 1987 GLP: no data
Test substance: other TS: undiluted N,N-diethylaniline; purity not noted
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (37)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.:
Method: other: dose: 50 mg/animal, observation period: 8 days
Year: GLP: no
Test substance: other TS: undiluted N,N-diethylaniline
16-APR-2001 (30)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method: other: dose: 0.1 ml/animal (according to: Draize, J.P. et al.: J. of Pharmacol. 82, 377 (1944))
Year: GLP: no
Test substance: other TS: undiluted N,N-diethylaniline
Remark: result: little irritative effects (maximal effects 1 hour after application); effects completely reversible after 48-96 hours
16-APR-2001 (35)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method: other: dose: 100 ul/animal, observation period: 7 days
Year: GLP: no
Test substance:
16-APR-2001 (36)

5.3 Sensitization

Type: other
Species: guinea pig
Number of Animals:
Vehicle:
Result: not sensitizing
Classification:
Method: other: induction exposure by dermal application of a 10 % solution of N,N-diethylaniline; challenge exposure by dermal application of 1 or 2 % solutions of the test substance
Year: GLP: no
Test substance: other TS: N,N-diethylaniline was dissolved in acetone
Flag: Critical study for SIDS endpoint
16-APR-2001 (35)

Type: other
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method:
Year: GLP:
Test substance: other TS: N,N-diethylaniline; commercial grade
Remark: No cases of allergic sensitization have been reported as a result of exposures at Buffalo Color Corporation.
Flag: Critical study for SIDS endpoint
16-APR-2001 (38)

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain: Wistar
Route of admin.: gavage
Exposure period: 28 d
Frequency of treatment: daily, 7 d/w
Post. obs. period: no
Doses: 10, 50 or 250 mg/kg bw/d
Control Group: yes, concurrent vehicle
LOAEL: 10 mg/kg bw
Method: OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year: 1981 GLP: no data
Test substance: other TS: N,N-diethylaniline; purity: 99.73 %
Result: all dose groups: mortality and growth of the animals not significantly altered; food intake and water intake comparable to control values; haematology: decreased red cell counts, decreased haemoglobin contents, decreased packed cell volume (PCV) values in males and females, increased MCV- and MCH-values in the females; black colouration of the spleen; absolute and relative spleen weights increased; histological evidence of the spleen: haemosiderosis, extramedullary haematopoiesis, splenic hyperaemia; histological evidence of the liver: haemosiderosis in the Kupffers cells
10 mg/kg bw/d: no clinical signs of toxicity
10 and 50 mg/kg bw/d: no indications of nephrotoxic effects
50 mg/kg bw/d: increased frequency of respiratory sounds in the males
50 and 250 mg/kg bw/d: haematology: increased MCV- and MCH-values in the males, decreased MCHC-values in males and females, hyperbilirubinaemia; polychromasia; swollen spleens; histological evidence of the liver: increase in the extramedullary haematopoiesis
250 mg/kg bw/d: increased frequency of respiratory sounds in the females; increased salivation in the females; black colouration of the kidneys in the females; histopathological findings in the kidneys of males and females: ferriferous pigment detectable in the epithelia of the pars contorta; clinical chemistry of the peripheral blood: increased albumin levels in the males, decreased potassium levels in males and females
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (39)

Species: dog Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 3 d
Frequency of treatment: no data
Post. obs. period: no
Doses: 5 g/animal (total dose given to the animal in the course of the experimental period)
Control Group: no data specified
Method:
Year: GLP: no
Test substance: other TS: N,N-diethylaniline was dissolved in olive oil
Remark: one animal was used in the study
Result: signs of toxicity (no details) on the second experimental day, death of the animal on the third day; p-diethylaminophenol identifiable as urinary metabolite; neither N,N-diethylaniline nor N,N-diethylaniline-N-oxide detectable in the urine
16-APR-2001 (40)

Species: rabbit Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 5 d
Frequency of treatment: no data
Post. obs. period: no
Doses: 2.9 g/animal (total dose given to the animals during the experimental period)
Control Group: no data specified
Method:
Year: GLP: no
Test substance: other TS: N,N-diethylaniline was dissolved in olive oil
Remark: 2 animals were used in the study
Result: signs of toxicity (no details) on the fourth experimental day, death of the animals 2 days later; p-diethylaminophenol identifiable as urinary metabolite; neither N,N-diethylaniline nor N,N-diethylaniline-N-oxide detectable in the urine
16-APR-2001 (40)

Species: guinea pig Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 5 h
Frequency of treatment: 4 s.c. injections within 5 h
Post. obs. period: no
Doses: total dose: 3000 mg/kg bw
Control Group: no
Method:
Year: GLP: no
Test substance:
Remark: 1 animal was used
Result: signs of toxicity: tremor, convulsions, paralysis of the pelvic extremities, nystagmus, accelerated respiration; death of the animal 4 hours after the final application
16-APR-2001 (41)

Species: guinea pig Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 33 h
Frequency of treatment: 9 s.c. injections within 33 h
Post. obs. period: no
Doses: total dose: 11000 mg/kg bw
Control Group: no
Method:
Year: GLP: no
Test substance:
Remark: 1 animal was used
Result: signs of toxicity: tremor, convulsions, paralysis of the pelvic extremities, decelerated and laboured respiration, blood not black-coloured
16-APR-2001 (41)

Species: rabbit Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 41.5 h
Frequency of treatment: 3 s.c. injections within 41.5 h
Post. obs. period: no
Doses: total dose: 1400 mg/kg bw
Control Group: no
Method:
Year: GLP: no
Test substance:
Remark: 1 animal was used
Result: no signs of toxicity following the first and the second application (administration of 300 and 500 mg/kg bw, respectively, at an interval of 17.5 hours); signs of toxicity following the third injection after further 24 hours: brownish discoloration of the pupils and of the blood, no central nervous effects; death occurred 26 hours after the third application due to a subacute feverish nephritis
16-APR-2001 (41)

Species: mouse Sex:
Strain:
Route of admin.: other: injection
Exposure period: 4 days
Frequency of treatment: 12 injections/day
Post. obs. period: No Data
Doses: 450 mg/kg/day
Control Group: no data specified
Method:
Year: GLP: no data
Test substance: no data
Remark: 10 out of 10 tumor-bearing mice failed to survive more than four days at 450 mg/kg/day. All of 10 tumor-bearing mice survived 12 daily injections of 225 mg/kg. May cause kidney and/or liver damage.
10-AUG-2000 (42)

Species: mouse Sex: no data
Strain: no data
Route of admin.: i.p.
Exposure period: 3 d
Frequency of treatment: daily
Post. obs. period: no data
Doses: 0.5 mM/kg bw/d (= 75 mg/kg bw/d)
Control Group: yes
Method:
Year: GLP: no
Test substance:
Result: forty-eight hours after the final administration, no significant methaemoglobin or sulphhaemoglobin formation was observed (no further data)
16-APR-2001 (43)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 100, TA 1535, TA 1537, TA 1538, TA 2637
Concentration: 1-5000 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: modified preincubation method of the Ames assay
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not noted
Reliability: (2) valid with restrictions
Guideline study with acceptable restrictions
Flag: Critical study for SIDS endpoint
17-AUG-2001 (44)

Type: Unscheduled DNA synthesis
System of testing: primary cultured rat hepatocytes
Concentration: 1 uM - 1 mM (= 0.15 - 150 ug/ml)
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method: OECD Guide-line 482 "Genetic Toxicology: DNA Damage and Repair/Unscheduled DNA Synthesis in Mammalian Cells in vitro"
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not stated
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (45)

Type: Escherichia coli reverse mutation assay
System of testing: Escherichia coli WP2 uvrA, WP2 uvrA/pKM
Concentration: 1-5000 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: modified preincubation method of the Ames assay
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not noted
Flag: Critical study for SIDS endpoint
17-AUG-2001 (44)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 1535
Concentration: 1-333 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: preincubation assay
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; label purity: 99 %
17-AUG-2001 (46)

Type: Bacterial gene mutation assay
System of testing: bacterial test system (no further data)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance:
17-AUG-2001 (47)

Type: Ames test
System of testing: Salmonella typhimurium (no further data)
Concentration: no data
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance:
17-AUG-2001 (48)

Type: Ames test
System of testing: Salmonella typhimurium TA 98
Concentration: 1-5000 ug/plate
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other: modified preincubation method of the Ames assay
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not noted
Remark: the test was performed in the presence of norharman
24-SEP-2001 (44)

Type: Ames test
System of testing: Salmonella typhimurium TA 98
Concentration: 1-5000 ug/plate
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other: modified preincubation method of the Ames assay
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity not noted
Remark: the test was performed in the presence of norharman
24-SEP-2001 (44)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species: mouse Sex: male/female
Strain: other: Bor: NMRI (SPF Han)
Route of admin.: i.p.
Exposure period: single administration
Doses: 600 mg/kg bw
Result: negative
Method: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year: GLP: yes
Test substance: other TS: N,N-diethylaniline; purity: 99.73 %
Result: no indications of a clastogenic effect of N,N-diethyl-aniline were found; there was an altered ratio between polychromatic and normochromatic erythrocytes
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (49)

5.7 Carcinogenicity
-

5.8 Toxicity to Reproduction

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 108-44-1; 121-69-7.

5.9 Developmental Toxicity/Teratogenicity

Species: rat Sex: female
Strain: other: CD (Sprague-Dawley derived)
Route of admin.: gavage
Exposure period: days 6-15 of gestation
Frequency of treatment: daily
Duration of test: sacrifice of the females on day 20 of gestation
Doses: 50, 250 or 500 mg/kg bw/d
Control Group: yes, concurrent vehicle
NOAEL Maternalt.: 250 ml/kg bw
NOAEL Teratogen.: 250 ml/kg bw
Method: EPA OTS 798.4900
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; purity: 98.4 - 98.5 %
Remark: the low- and mid-dose groups contained 24 females each; the high-dose group contained a total of 29 females
Result: all dose groups: maternal effects: mean food consumption statistically lower than control; excessive salivation; no adverse effect of treatment evident from uterine implantation data; evaluation of fetuses recovered from treated group females for external, visceral and skeletal malformations indicated no adverse effect of treatment (no teratogenic or embryotoxic effects)
50 and 250 mg/kg bw/d: no maternal mortality; mean fetal weight and fetal sex distribution unaffected
250 and 500 mg/kg bw/d: maternal effects: excessive lacrimation; staining of the skin/fur in the ano-genital area
500 mg/kg bw/d: maternal toxicity: two females died and three females were killed in a moribund condition (mortality rate = 17.2 %); fetotoxicity: mean fetal weight statistically lower than control, increase in the incidence of fetuses with unossified sternebral elements (suggestive of a retardation in ossification)
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (50)

Species: rat Sex: female
Strain: other: CD (Sprague-Dawley derived)
Route of admin.: gavage
Exposure period: days 6-15 of gestation
Frequency of treatment: daily
Duration of test: sacrifice of all surviving females on day 20 of gestation
Doses: 100, 250, 500, 750, 1000, 1500 or 2000 mg/kg bw/d
Control Group: yes, concurrent vehicle
Method: EPA OTS 798.4900
Year: GLP: no data
Test substance: other TS: N,N-diethylaniline; 98.4 % active ingredient
Remark: five females/group were used
type: range-finding study
Result: all dose groups: no external malformations were seen in fetuses
100, 250 or 500 mg/kg bw/d: maternal data: no mortality; reduced body weight gain during the day 6-15 treatment period; decrease in food consumption during the day 6-10 interval of the treatment period
250 and 500 mg/kg bw/d: maternal effects: staining of the fur in the anogenital area
500 and 750 mg/kg bw/d: mean fetal body weight data lower than control
750 mg/kg bw/d: three females were killed in a moribund condition after one to three days of treatment; only one female survived to day 20 sacrifice
1000 mg/kg bw/d: all five females were sacrificed in a moribund condition on day 7 of gestation; maternal toxicity: ataxia, labored/shallow breathing, prostrate posture, cooler body temperature
1500 and 2000 mg/kg bw/d: the first two females in each group died or were killed in a moribund condition on day 7 of gestation following a single treatment day; due to this mortality, the dose groups were terminated
Reliability: (2) valid with restrictions
17-AUG-2001 (51)

5.10 Other Relevant Information

Type: Biochemical or cellular interactions
Remark: in vitro assay: N,N-diethylaniline revealed no inhibitory effect on mouse cytosolic aldehyde dehydrogenase activity; test system: L1210/CPA cells (= murine leukemia cell lines resistant to cyclophosphamide)
07-MAY-1993 (52)

Type: Metabolism
Remark: dogs received a single intravenous injection of 108 mg/kg bw of N,N-diethylaniline hydrochloride; 2 hours after the application the N,N-diethylaniline-N-oxide concentration attained a maximum of ca. 5.5 ug N-oxide/ml blood (no further data)
16-APR-1993 (53)

Type: Metabolism
Remark: in an in vitro assay, the metabolism of N,N-diethylaniline (concentration: 5 umol) by rabbit liver microsomal preparations was studied; after 20 min. incubation, 7.8 % of the initial substrate concentration was mono-N-demethylated (formation of N-ethylaniline), 4.2 % was N-oxidated (formation of N,N-diethylaniline-N-oxide) and 8.6 % of the initial concentration of N,N-diethylaniline was metabolized otherwise (unidentified metabolites)
19-APR-1993 (54)

Type: Metabolism
Remark: in vitro assays: the oxidative dealkylation of N,N-diethylaniline by synthetic iron(III) porphyrin systems (as a model of cytochrome P-450) was studied; N-ethylaniline was found to be formed by oxidation of N,N-diethylaniline
19-APR-1993 (55) (56)

Type: Metabolism
Remark: in vitro assay: microsomes from pork liver homogenates were incubated with N,N-diethylaniline (concentration: 5.0 umoles/ml = ca. 750 ug/ml): the N-oxide of N,N-diethylaniline was formed only when the reaction medium was supplemented with flavin adenine dinucleotide (FAD)
27-APR-1993 (57)

Type: other
Remark: the effectiveness of various antidotes in the treatment of oral intoxication with N,N-diethylaniline was investigated in male rats; N,N-diethylaniline and the antidotes were given orally by gavage, the administration of the antidote following immediately the treatment with N,N-diethylaniline: the administration of cows milk, caster oil or liquid paraffin did not affect significantly the mean survival time of the animals; the application of activated charcoal as a 10 % aqueous suspension induced a significant prolongation of the mean survival time
05-MAY-1993 (58) (59) (60) (61) (62) (63)

Type: other: acute inhalation risk
Remark: rats were exposed to an atmosphere saturated with vapours of N,N-diethylaniline at 20 degrees Centigrade for 8 h; no signs of toxicity were observable, no deaths occurred; no pathological findings were detectable in the animals killed after the 14 d-observation period (the test substance exhibited only little volatility)
21-APR-1993 (64)

Type: other: acute inhalation toxicity
Remark: rats (number of animals unspecified) were exposed to N,N-diethylaniline at a concentration of 0.8 mg/l for 6 hours (whole-body exposure; test concentration analytically determined); no signs of toxicity were observable during the exposure period; during the observation period (14 days) no deaths occurred and no significant changes of body weights

were detectable
16-APR-2001 (35)

Type: other: haemotoxicity
Remark: dogs were injected i.v. with 108 mg/kg bw of N,N-diethylaniline hydrochloride (single administration); ca. 3 hours after application, the methaemoglobin concentration attained a maximum of ca. 40 % of the total blood pigment; in an additional experiment, N,N-diethylaniline-N-oxide was found to display only minimal methaemoglobin-forming activity; thus the authors conclude that N,N-diethylaniline-N-oxide can be ruled out almost completely as the factor in the methaemoglobin formation following the injection of N,N-diethylaniline; the authors suppose that another metabolite of N,N-diethylaniline, namely p-diethylaminophenol, plays an important role in the methaemoglobin formation following the absorption of N,N-diethylaniline (this assumption has not yet been experimentally verified)
19-APR-1993 (53)

Type: other: haemotoxicity
Remark: after administration of lethal doses of N,N-diethylaniline to cats, methaemoglobin was detectable in blood samples (no further data)
16-APR-2001 (40)

Type: other: haemotoxicity
Remark: cats (1 male, 1 female) received a single oral administration of 50 ul/kg bw (= ca. 47 mg/kg bw) of N,N-diethylaniline; cyanosis was detectable and 4 h after application the maximal methaemoglobin level of blood was found to be 77.8 %; after 48 hours the methaemoglobin levels had returned to normal; the following further signs of toxicity were observed: abdominal position, apathy, vomiting, salivation (the effects had disappeared after 1 day); in this study, the methaemoglobinaemic activity of N,N-diethylaniline was comparable to that of aniline
26-APR-1993 (65)

Type: other: haemotoxicity
Remark: after a single i.p. administration of 0.5 mM/kg bw (= 75 mg/kg bw) of N,N-diethylaniline to mice, methaemoglobin formation was induced; a maximum concentration of ca. 15 % methaemoglobin was reached 10 min. after application; 24 hours after the administration the concentration of methaemoglobin was comparable to control values; a significant sulphhaemoglobin formation was not observable at any time
16-APR-2001 (43)

Type:
Remark: N,N-diethylaniline was administered to rats orally (doses: 180 - 2100 mg/kg bw) or i.p. (doses: 280 - 2100 mg/kg bw) or percutaneously (doses: 7100 - 16000 mg/kg bw) (single administrations; 1 animal/dose used); the lowest lethal dose was found to be 620 mg/kg bw given orally and 420 mg/kg bw given i.p.; even the highest dose given percutaneously (16000 mg/kg bw) did not induce deaths (the authors suppose that in the case of percutaneous application the relatively volatile test substance was not completely absorbed); the following signs of toxicity were observable in the experiments: cyanosis, clonic spasms, uraemia; at higher doses: unconsciousness, lateral position, small enlargement of the liver; histological findings (at higher doses): degeneration and necrosis of the renal tubular epithelium; granular degeneration of the liver cells
16-APR-2001 (35)

Type:
Remark: N,N-diethylaniline given orally to rats (single administration) revealed almost no methaemoglobinaemic activity, in comparison with aniline (no further data)
16-APR-2001 (66)

5.11 Experience with Human Exposure

Remark: Due to the considered adequacy of the engineering controls, routine atmospheric monitoring sufficient to result in statistically significant statements on exposure control has not been carried out. Raised methaemoglobin levels have not been observed in personnel operating the plant, thus the confidence in the controls in place has been confirmed by the lack of observed effects.
16-APR-2001

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7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 102-27-2
CAS No.	102-27-2
EINECS Name	N-ethyl-m-toluidine
EINECS No.	203-019-4
Molecular Weight	135.2
Molecular Formula	C9H13N

Producer Related Part
  Company:
  Creation date: 15-JUL-1999

Substance Related Part
  Company:
  Creation date: 15-JUL-1999

Memo: Bayer Corporation

Printing date: 29-OCT-2001
Revision date:
Date of last Update: 29-OCT-2001

Number of Pages: 21

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association), Monocyclic Aromatic Amines and Nitro Aromatics (MAANA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States

21-AUG-2001

Type: cooperating company
Name: Albemarle Corporation
Country: United States

25-SEP-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

25-SEP-2001

Type: cooperating company
Name: Buffalo Color
Country: United States

25-SEP-2001

Type: cooperating company
Name: ChemFirst, Inc.
Country: United States

25-SEP-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information
-

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms
-

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

```
Value:            8.7 degree C
Method:           other: (calculated) MPBPWIN (v1.31)
  Year:           1999
Testsubstance:    other TS: molecular structure
Result:           Melting Point:    9.63 deg C (Adapted Joback Method)
                  Melting Point:    7.84 deg C (Gold and Ogle Method)
                  Mean Melt Pt :    8.74 deg C (Joback; Gold, Ogle Methods)
                    Selected MP:    8.74 deg C (Mean Value)
Reliability:      (2)  valid with restrictions
                  Accepted calculation method
Flag:             Critical study for SIDS endpoint
19-JUN-2001                                                              (1)
```

2.2 Boiling Point

```
Value:            221 degree C
Method:           other: Handbook value
Testsubstance:    other TS: N-ethyl-m-toluidine; purity not stated
Reliability:      (2)  valid with restrictions
                  Data from Handbook or collection of data
Flag:             Critical study for SIDS endpoint
19-JUN-2001                                                              (2)
```

2.3 Density

```
Type:             density
Value:            ca. .945 g/cm3 at 20 degree C
Testsubstance:    other TS: N-ethyl-m-toluidine; purity not stated
Flag:             Critical study for SIDS endpoint
09-APR-2001                                                              (3)
```

2.3.1 Granulometry

-

2.4 Vapour Pressure

```
Value:            .33 hPa at 25 degree C
Method:           other (calculated): MPBPWIN (v1.31)
Testsubstance:    other TS:  molecular structure
Result:           Vapor Pressure Estimations (25 deg C):
                    (Using BP: 208.09 deg C (estimated))
                    (MP not used for liquids)
                      VP:  0.26 mm Hg (Antoine Method)
                      VP:  0.221 mm Hg (Modified Grain Method)
                      VP:  0.364 mm Hg (Mackay Method)
                    Selected VP:  0.24 mm Hg (Mean of Antoine & Grain methods)
Reliability:      (2)  valid with restrictions
                  Accepted calculation method
Flag:             Critical study for SIDS endpoint
```

16-AUG-2001 (1)

Value: 1.33 hPa at 54 degree C
Testsubstance: other TS: N-ethyl-m-toluidine; purity not stated
Flag: Critical study for SIDS endpoint
16-AUG-2001 (3)

2.5 Partition Coefficient

log Pow: 2.662
Method: other (calculated): KOWWIN Program (v1.65)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
16-AUG-2001 (1)

log Pow: 2.7
Method: other (calculated): A. Leo, CLOPG-3.54 MedChem Software 1989. Daylight, Chemical Information Systems, Claremont, CA 91711, USA
Year:
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
16-AUG-2001 (4)

2.6.1 Water Solubility

Value: 1131 mg/l at 20 degree C
Method: OECD Guide-line 105 "Water Solubility"
GLP: yes
Testsubstance: other TS: N-ethyl-m-toluidine; purity = 99.223% by GC (1992-09-14)
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
16-AUG-2001 (5)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: ca. 93 degree C
Type:
Method: other: DIN 51758
Year:
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
16-AUG-2001 (3)

2.8 Auto Flammability
-

2.9 Flammability
-

2.10 Explosive Properties
-

2.11 Oxidizing Properties

Result: maximum burning rate equal or higher than reference mixture
16-AUG-2001

2.12 Additional Remarks
-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: ca. .0000000001203522 cm3/(molecule * sec)
Degradation: 50 % after 1.1 hour(s)
Method: other (calculated): AOP v1.89
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
16-AUG-2001 (1)

3.1.2 Stability in Water

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 121-69-7.

3.1.3 Stability in Soil

-

3.2 Monitoring Data (Environment)

-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air, water, soil, sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: (calculation) Level III Fugacity Model
Year: 1999
Result:

Media	Distribution (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.176	2.13	1000	5.67e-012
Water	32.5	900	1000	1.31e-010
Soil	67	900	1000	6.27e-010
Sediment	0.305	3.6e+003	0	1.12e-010

Persistence Time: 595 hr
Reaction Time: 747 hr
Advection Time: 2.92e+003 hr
Percent Reacted: 79.6
Percent Advected: 20.4
Reliability: (2) valid with restrictions
Accepted calculation method

Flag: Critical study for SIDS endpoint
16-AUG-2001 (1)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, adapted
Degradation: 0 % after 20 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: 1976 GLP: no
Test substance: other TS: other TS: N-ethyl-m-toluidine; purity =99.5 %
Reliability: (1) valid without restriction
Flag: Critical study for SIDS endpoint
09-APR-2001

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation

Species: other
Exposure period:
Concentration:
BCF: 22.36
Elimination:
Method: other: BCF Program (v2.13)
Year: GLP:
Test substance: other TS: molecular structure
Result: Log Kow (estimated) : 2.66
Log Kow (experimental): not available from database
Log Kow used by BCF estimates: 2.66

Equation Used to Make BCF estimate:
Log BCF = 0.77 log Kow - 0.70

Estimated Log BCF = 1.350 (BCF = 22.36)
Reliability: (2) valid with restrictions
Accepted calculation method
16-AUG-2001 (1)

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: 49.5
Method: EPA OPP 72-1
Year: 1981 GLP: no data
Test substance: other TS: N-ethyl-m-toluidine; purity not stated
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
16-AUG-2001 (6)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: 50
LC100: 100
Method: other: Bestimmung der akuten Wirkung von Stoffen auf Fische. Arbeitskreis "Fischtest" in Hauptausschuß "Detergentien" (15.10.73)
Year: 1976 GLP: no
Test substance: other TS: N-ethyl-m-toluidine; purity = 99.5 %
Remark: range finding test
Reliability: (2) valid with restrictions
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
25-SEP-2001 (7)

Type: other: calculation
Species: other: Fish
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 24.022
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Remark: ECOSAR Class: Neutral Organics
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
16-AUG-2001 (1)

Type: other: calculation
Species: other: Fish
Exposure period: 14 day
Unit: mg/l Analytical monitoring: no
LC50: 48.323
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Remark: ECOSAR Class: Neutral Organics
Reliability: (2) valid with restrictions
Accepted calculation method
16-AUG-2001 (1)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: other: calculation
Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 26.941
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
19-JUN-2001 (1)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: other algae: Green Algae
Endpoint: other: calculation
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 17.495
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
19-JUN-2001 (1)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Pseudomonas fluorescens (Bacteria)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 1000
Method: other: Bestimmung der biologischen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L 8 (1968) modified
Year: 1976 GLP: no
Test substance: other TS: N-ethyl-m-toluidine; purity = 99.5 %
09-APR-2001 (7)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish
-

4.5.2 Chronic Toxicity to Aquatic Invertebrates
-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
Number of Animals:
Vehicle: other: corn oil
Value: 787 mg/kg bw
Method: other: USEPA TSCA Health Effects Testing Guidelines, 40 CFR 798.1175, "Acute Oral Toxicity", 1992.
Year: 1992 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity = 98.67%
Method: Animals used: 5 per sex/dose group;
Doses were: 100, 500, 750, 1000 mg/kg bw
Remark: Test material analysis not done under GLP
Result: LD 50 (95% CI)= 585-1058 mg/kg bw
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (8)

Type: LD50
Species: rat
Strain: Wistar
Sex: male/female
Number of Animals:
Vehicle: other: none
Value: 650 mg/kg bw
Method: Directive 84/449/EEC, B.1 "Acute toxicity (oral)"
Year: 1980 GLP: no data
Test substance: other TS: N-ethyl-m-toluidine; purity not stated
Method: 5 rats/sex/dose, single application by gavage;
6 doses: 0.5, 0.6,0.7, 0.8, 1.0, 1.2 ml/kg bw;
observation time 14 d, statistical evaluation
Remark: 0.5 ml was accepted without impairment, no mortality;
0.6,0.7, 0.8, 1.0, 1.2 ml/kg bw: all rats displayed slight symptoms of intoxication from 15 min. post appliation until death including cyanotic appearance and reduced general condition, females suffered additionally from decrease in body weight. Death occurred from 4 hours until the 4th day post treatment: 3/10, 7/10, 7/10, 9/10, 10/10
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (9)

5.1.2 Acute Inhalation Toxicity

Type:	LC50
Species:	rat
Strain:	no data
Sex:	no data
Number of Animals:	
Vehicle:	no data
Exposure time:	4 hour(s)
Value:	2.4 mg/l
Method:	other: no data
Year:	GLP: no data
Test substance:	other TS: N-ethyl-m-toluidine; purity not stated
Remark:	Toxic effects observed include labored breathing, decreased muscle tone, cyanosis, and loss of reflexes.

25-SEP-2001 (10)

5.1.3 Acute Dermal Toxicity

Type:	LD50
Species:	rabbit
Strain:	New Zealand white
Sex:	male/female
Number of Animals:	10
Vehicle:	
Value:	> 2000 mg/kg bw
Method:	other: USEPA TSCA Health Effects Testing Guidelines, 40CFR 798.1100, "Acute Dermal Toxicity", 1992
Year:	1992 GLP: yes
Test substance:	other TS: N-ethyl-m-toluidine; purity > 97%
Remark:	Animals used: 5/sex/dose group
Reliability:	(1) valid without restriction GLP guideline study
Flag:	Critical study for SIDS endpoint

25-SEP-2001 (11)

5.1.4 Acute Toxicity, other Routes
-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: undiluted

Exposure: Occlusive
Exposure Time: 4 hour(s)
Number of Animals: 6
PDII: .7
Result: slightly irritating
EC classificat.: not irritating
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1992 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity > 97%
Remark: 3 male and 3 female New Zealand white rabbits were exposed; all animals were scored after unwrapping and at day 7.
PDII = 0.7/8
Test matereial analysis was not done under GLP.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (12)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: slightly irritating
EC classificat.:
Method:
Year: GLP:
Test substance: other TS: N-ethyl-m-toluidine; purity not stated
Remark: exposure period: 24 hours
Flag: Critical study for SIDS endpoint
17-AUG-2001 (7)

5.2.2 Eye Irritation

Species: rabbit
Concentration: undiluted
Dose: .1 ml
Exposure Time:
Comment: not rinsed
Number of Animals: 6
Result: not irritating
EC classificat.: not irritating
Method: EPA OTS 798.4500
Year: 1992 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity = 98.67%
Remark: 6 female New Zealand white rabbits were exposed.
Test material analysis was not done under GLP.
Result: Maximum score of 9.8/110 at the 24 hour scoring iterval; all signs of irritation had cleared by 72 hours after dosing.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (13)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method:
Year: GLP:
Test substance: other TS: N-ethyl-m-toluidine; purity not stated
Flag: Critical study for SIDS endpoint
17-AUG-2001 (7)

5.3 Sensitization

Type: Buehler Test
Species: rabbit
Concentration: Induction undiluted
Challenge 50 %
Number of Animals:
Vehicle: other: acetone
Result: not sensitizing
Classification: not sensitizing
Method: other: according to Ritz, H.L., and Buehler, E.V., Current Concepts in Cutaneous toxicity, eds. Drill, V.A., and Lazar T. (Academic Press, 1980), pp. 25-40
Year: 1980 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity = 98.115

Remark: 20 test animals (10 male, 10 female) and 10 naive controls (5 male, 5 female);
Induction and challenge applications were dermal using 0.3 ml test substance in each Hilltop chamber;
Naive control was treated with 50% test material in acetone; controls were common to this study and one other. Test material analysis was not done under GLP.

Result:

Response:	Test animals	Naive controls
Grade 1	0/20	2/10
Grade +/-	16/20	8/10
Grade 0	4/20	0/10

At the time of the 24 hr reading, residual Neet (dipilatory) was noted on several of the dosing sites in the naive control group (including 2 animals with a grade 1 result). The Neet may have created artificial irritaion at the sites. The irritation in these animals was reduced to a grade of +/- by the 48 hr reading. The interpretation of the primary challenge data was not compromised by this occurrence. The responses produced in the test group were essentially comparable to the naive group, indicating that sensitization had not been induced.

Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
25-SEP-2001 (14)

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: inhalation
Exposure period: 2 weeks
Frequency of treatment: 6 hr/day, 5 days/week
Post. obs. period: 2 weeks, control and high exposure groups
Doses: 5.6, 32.8, 67.6 ppm
Control Group: yes, concurrent no treatment
NOAEL: = 5.6 ppm
Method: OECD Guide-line 412 "Repeated Dose Inhalation Toxicity: 28-day or 14-day Study"
Year: 1981 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity = 98.68%
Remark: Test material analysis not done under GLP. TSCA Substantial Risk notice.
Result: There were no deaths, and no changes in body weights, food consumption, clinical observations, or clinical chemistry. Methemoglobinemia was significantly increased across all exposure groups at both terminal and recovery necropsies in both sexes. Enlarged spleens, increased production of red cells in the spleen, bone marrow, and liver, and other hematology changes were consistent with induction of hemolytic anemia. Kidney effects were considered secondary to hemolytic anemia. This condition was not completely

reversed at the end of the 14 day recovery period. A "no effect level" was not established under the conditions of this study. However, the lowest exposure level of 5.6 ppm was considered a "no adverse effect level" because the increase in methemoglobin was not accompanied by adverse histopathology or clinical signs.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (15)

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 108-44-1; 121-69-7; 91-66-7.

5.5 Genetic Toxicity 'in Vitro'

Type: Bacterial reverse mutation assay
System of testing: Salmonella strains TA98, TA100, TA1535, TA1537,
Concentration: 100, 250, 500, 1000, 2500, 5000 ug/plate
Cytotoxic Conc.: 3330 ug/plate - S9 in TA100;
2500ug/plate - S9 in other strains
Metabolic activation: without
Result: negative
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: 1983 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity = 98.115%
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (16)

Type: Bacterial reverse mutation assay
System of testing: Salmonella strains TA98, TA100, TA1535, TA1537,
Concentration: 100, 250, 500, 1000, 2500, 5000 ug/plate
Cytotoxic Conc.: 3330 ug/plate + S9 in TA100;
5000ug/plate + S9 in other strains
Metabolic activation: with
Result: positive
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: 1983 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity = 98.115%
Remark: Test material analysis not done under GLP. The only deviation from guidelines was lack of a confirmatory assay. However, a separate study was done to confirm positive results in TA98 with activation (ChemFirst Study No. 18688-0-401SC)
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (16)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: up to 200 µg/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: Directive 84/449/EEC, B.14 "Other effects - Mutagenicity (Salmonella typhimurium - reverse mutation assay)"
Year: 1994 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity = 99.223 %
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (17)

Type: Escherichia coli reverse mutation assay
System of testing: E. coli strain WP2uvrA
Concentration: 100, 250, 500, 1000, 2500, 5000 ug/plate
Cytotoxic Conc.: 5000ug/plate +/- S9
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 472 "Genetic Toxicology: Escherichia coli Reverse Mutation Assay"
Year: 1983 GLP: yes
Test substance: other TS: N-ethyl-m-toluidine; purity = 98.115%
Remark: Test material analysis not done under GLP.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (16)

5.6 Genetic Toxicity 'in Vivo'

-

5.7 Carcinogenicity

-

5.8 Toxicity to Reproduction

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 108-44-1; 121-69-7.

5.9 Developmental Toxicity/Teratogenicity

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 121-69-7; 91-66-7.

5.10 Other Relevant Information
-

5.11 Experience with Human Exposure
-

(1) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(2) CRC Handbook of Chemistry and Physics. 80th edition (1999-2000) David R. Lide, ed. CRC Press, New York. p3-23 No. 747.

(3) Safety Data Sheet Bayer AG, 28.03.1989

(4) Calculation Bayer AG, UWS-Produktsicherheit

(5) Bayer AG study (1992-10-08)

(6) L.T. Brooke et al, Acute Toxicities of Organic Chemicals to Fathead Minnows(Pimephales Promelas) vol.1, Center for Lake Superior Environment Studies, Univ. of Wisconsin, Superior, WI (1984).

(7) Bayer AG data

(8) ChemFirst Study No. L08604-37

(9) E. Löser, Bayer AG data, N-Äthyl-m-toluidin rein: untersuchungen zur akuten Toxizität an männlichen und weiblichen Wistar Ratten, 25. Nov.1980

(10) Safety Data Sheet, DuPont de Nemours and Company, N-ethyl-m-toluidine, MSDS Number DU003000_00, revised 9/7/93.

(11) ChemFirst Study No. L08583-7

(12) ChemFirst Study No. L08583-8

(13) ChemFirst Study No. L08604-36

(14) ChemFirst Study No. 95-8607-21

(15) ChemFirst Study No.L08689-2

(16) ChemFirst Study No. 16861-0-409 (1995)

(17) Bayer AG, Report No. 23463, 08.11.1994

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 99-97-8
CAS No.	99-97-8
EINECS Name	N,N-dimethyl-p-toluidine
EINECS No.	202-805-4
Molecular Formula	C9H13N

Producer Related Part
  Company:
  Creation date: 21-OCT-1999

Substance Related Part
  Company:
  Creation date: 21-OCT-1999

Memo: Bayer Corporation

Printing date: 29-OCT-2001
Revision date:
Date of last Update: 29-OCT-2001

Number of Pages: 21

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association), Monocyclic Aromatic Amines and Nitro Aromatics (MAANA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States

21-AUG-2001

Type: cooperating company
Name: Albemarle Corpoiration
Country: United States

24-SEP-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

21-AUG-2001

Type: cooperating company
Name: Buffalo Color Corporation
Country: United States

21-AUG-2001

Type: cooperating company
Name: ChemFirst, Inc.
Country: United States

21-AUG-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information
-

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms
-

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: -6.6 degree C
Decomposition: no
Sublimation: no
Method: other: (calculated) MPBPWIN v 1.30
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Result: Melting Point: -10.56 deg C (Adapted Joback Method)
Melting Point: -2.61 deg C (Gold and Ogle Method)
Mean Melt Pt : -6.59 deg C (Joback; Gold,Ogle Methods)
Selected MP: -6.59 deg C (Mean Value)
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

2.2 Boiling Point

Value: 211 degree C at 1013 hPa
Decomposition: no
Method: other:
GLP: no data
Testsubstance: other TS: N,N,4-trimethyl-benzenamine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
21-AUG-2001 (2)

Value: 190.2 degree C
Method: other: MPBPWIN (v1.31)
GLP: no
Testsubstance: other TS: molecular structure
Remark: Adapted Stein and Brown Method
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

2.3 Density

Type: density
Value: .9366 g/cm3 at 20 degree C
Method: other
GLP: no data
Testsubstance: other TS: N,N,4-trimethyl-benzenamine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
21-AUG-2001 (2)

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: .78 hPa at 25 degree C
Method: other (calculated): MPBPWIN (v1.31)
GLP: no
Testsubstance: other TS: molecular structure
Result: Vapor Pressure Estimations (25 deg C):
(Using BP: 190.18 deg C (estimated))
(MP not used for liquids)
VP: 0.639 mm Hg (Antoine Method)
VP: 0.535 mm Hg (Modified Grain Method)
VP: 0.85 mm Hg (Mackay Method)

Selected VP: 0.587 mm Hg (Mean of Antoine & Grain methods)
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

Value: 1.33 hPa at 50 degree C
Method: other (measured)
GLP: no data
Testsubstance: other TS: N,N,4-trimethyl-benzenamine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
21-AUG-2001 (3)

2.5 Partition Coefficient

log Pow: 2.81 at 25 degree C
Method: other (measured)
Year:
GLP: no data
Testsubstance: other TS: N,N-dimethyl-p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
21-AUG-2001 (4) (5)

log Pow: 2.718
Method: other (calculated): KOWWIN Program (v1.65)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

log Pow: 2.61
Method:
Year:
Testsubstance: other TS: N,N-dimethyl-p-toluidine; purity not noted
Remark: Temperature: ambient
Method of equlibration: Shake-flask
Analytical method: absorption spectrophotometry
Aqueous phase: buffered solution of pH >7.0
Phase analyzed: aqueous
19-JUN-2001 (6) (7)

2.6.1 Water Solubility

Value: 455 mg/l
Qualitative: moderately soluble (100-1000 mg/L)
Method: other
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
24-SEP-2001 (8)

Value: 349.1 mg/l at 25 degree C
Qualitative: moderately soluble (100-1000 mg/L)
Method: other: (calculated) WSKOW (v1.36)
Year: 1999
GLP: no
Testsubstance: other TS: molecular structure
Remark: Log Kow (estimated) : 2.72
Log Kow (experimental): 2.81
Cas No: 000099-97-8
Name : Benzenamine, N,N,4-trimethyl-
Refer : Sangster 1993
Log Kow used by Water solubility estimates: 2.81

Equation Used to Make Water Sol estimate:
Log S (mol/L) = 0.796 - 0.854 log Kow - 0.00728 MW

Log Water Solubility (in moles/L) : -2.588
Water Solubility at 25 deg C (mg/L): 349.1
Reliability: (2) valid with restrictions
Accepted calculation method
21-AUG-2001 (1)

2.6.2 Surface Tension
-

2.7 Flash Point
-

2.8 Auto Flammability
-

2.9 Flammability
-

2.10 Explosive Properties
-

2.11 Oxidizing Properties
-

2.12 Additional Remarks
-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .0000000002026656 cm3/(molecule * sec)
Degradation: 50 % after .6 hour(s)
Method: other (calculated): AOP Program v1.89
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

3.1.2 Stability in Water

Type: abiotic
Method:
Year: GLP:
Test substance:
Remark: Hydrowin v1.67 cannot estimate a hydrolysis rate constant for this structure.
Flag: Critical study for SIDS endpoint
24-SEP-2001 (1)

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 121-69-7.

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air - biota - sediment(s) - soil - water
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: EPIWIN Level III Fugacity Model
Year: 1999
Result:

Media	Distribution (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.156	1.27	1000	4.44e-012
Water	26.8	900	1000	1.48e-009
Soil	72.7	900	1000	6.68e-009
Sediment	0.329	3.6e+003	0	1.23e-009

Persistence Time: 525 hr
Reaction Time: 617 hr
Advection Time: 3.52e+003 hr
Percent Reacted: 85.1
Percent Advected: 14.9
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum:
Method: other: BIOWIN (v3.67) Program
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Result: Linear Model Prediction : Biodegrades Fast
Non-Linear Model Prediction: Does Not Biodegrade Fast
Ultimate Biodegradation Timeframe: Weeks-Months
Primary Biodegradation Timeframe: Days-Weeks
Flag: Critical study for SIDS endpoint
17-APR-2001 (1)

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 108-44-1; 121-69-7; 103-69-5; 102-27-2; 91-66-7.

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation

Species: other
Exposure period:
Concentration:
BCF: 29.09
Elimination:
Method: other: BCF Program (v2.13)
Year: GLP: no
Test substance: other TS: molecular structure
Remark: Log Kow (estimated) : 2.72
Log Kow (experimental): 2.81
Log Kow used by BCF estimates: 2.81
Equation Used to Make BCF estimate:
Log BCF = 0.77 log Kow - 0.70

Estimated Log BCF = 1.464 (BCF = 29.09)
Reliability: (2) valid with restrictions
Accepted calculation method
21-AUG-2001 (1)

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type:	flow through
Species:	Pimephales promelas (Fish, fresh water)
Exposure period:	96 hour(s)
Unit:	mg/l Analytical monitoring: yes
LC50:	52
EC50 :	52
Method:	EPA OPP 72-1
Year:	1980 GLP: no data
Test substance:	other TS: N,N-dimethyl-p-toluidine purchased from Aldrich Chemical Co., Milwaukee, WI; purity = 99%
Method:	pH was adjusted to approximate that of Lake Superior water (pH 7.8) with NaOH or HCL. Compound analyses were done by GLC: all exposure chambers at 0,24,48,72, and 96 hr. Fathead minnows used in this experiment were 35 days old and were cultured at US EPA Environmental Research Laboratory, Duluth, MN and University of Wisconsin - Superior campus. 20 fish/concentration and control. Behavior and toxic signs were noted at 4,24,48,72 and 96 hours.
Remark:	Affected fish lost schooling behavior and swam near the tank surface. They were hypoactive and under-reactive to external stimuli, and had increased respiration. Equilibrium loss was not observed prior to death. Alkalinity values increased with the exposure concentrations, due to a reaction between the titrant and the toxicant.

Test condition:	temperature = 25.7 degree C (+/-0.38);
	dissolved oxygen = 6.8 mg/l; pH =7.57;
	hardness = 38.9 mg/l CaCO3; tank volume = 1 liter;
	actual concentrations 11.1, 17.9, 26.2, 41.6, 65.1 mg/l.

Reliability:	(1) valid without restriction Guideline study
Flag:	Critical study for SIDS endpoint

24-SEP-2001 (9)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: 46
EC50 : 41.5
Method: EPA OPP 72-1
Year: 1980 GLP: no data
Test substance: other TS: N,N-dimethyl-p-toluidine purchased from Aldrich Chemical Co., Milwaukee, WI; purity = 99%
Method: pH was adjusted to approximate that of Lake Superior water (pH 7.8) with NaOH or HCL. Compound analyses were done by GLC: all exposure chambers at 0,24,48,72, and 96 hr.

Fathead minnows used in this experiment were 32 days old and were cultured at US EPA Environmental Research Laboratory, Duluth, MN and University of Wisconsin - Superior campus.

20 fish/concentration and control. Behavior and toxic signs were noted at 4,24,48,72 and 96 hours.
Remark: Affected fish lost schooling behavior and swam near the tank surface. They were hypoactive and under-reactive to external stimuli, and had increased respiration. Initial dissolved oxygen values were less than 60% of saturation. Equilibrium loss was not observed prior to death. The measured tank values were less than the nominal values. Alkalinity values increased with the exposure concentrations due to a reaction between the titrant and the toxicant.
Test condition: temperature = 24.9 degree C (+/-0.32);
dissolved oxygen = 5.0 mg/l; pH = 7.39;
hardness = 40.3 mg/l $CaCO_3$; tank volume = 1 liter;
actual concentrations 11.8, 19.4, 30.9, 49.1, 71.3 mg/l.
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
24-SEP-2001 (10)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: 52.8
Method: other: American Society for Testing and Materials, 1980. Standard practice for conducting acute toxicity tests with fishes, macroinvertebrates, and amphibians. Annual Book of ASTM Standards. Philadelphia, PA, E729-80.
Year: 1980 GLP: no
Test substance: other TS: N,N-Dimethyl-p-toluidine (99-97-8) , purchased from Aldrich Chemical Company; chemical was of high purity
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
21-AUG-2001 (11)

Type: static
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 20
Method: other: Japanese Industrial Standards Committee: "Testing Methods for Industrial Wastewater", JIS K0102, Japanese Industrial Standards Committee, p. 154 (1971)
Year: 1971 GLP: no data
Test substance: other TS: N,N-Dimethyl-p-toluidine (99-97-8) , purity: . not given
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
14-AUG-2000 (12)

Type: other: calculation
Species: other
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 21.097
Method: other: (calculated) ECOSAR v0.99d
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
17-APR-2001 (1)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 23.758
Method: other: (calculated) ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: other algae: green algae
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 15.481
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

4.4 Toxicity to Microorganisms e.g. Bacteria
-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish
-

4.5.2 Chronic Toxicity to Aquatic Invertebrates
-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
Number of Animals: 10
Vehicle: other: neat
Value: 1650 mg/kg bw
Method: OECD Guide-line 401 "Acute Oral Toxicity"
Year: 1987 GLP: yes
Test substance: other TS: N,N-dimethyl-p-toluidine; purity = 99%
Remark: No analysis of test material available; only method deviation - a constant dose volume was not used.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (13)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
Number of Animals: 10
Vehicle: other: neat
Exposure time: 4 hour(s)
Value: 1.4 mg/l
Method: other: TSCA 40CFR 798.1150, July 1, 1991
Year: 1991 GLP: yes
Test substance: other TS: N,N-dimethyl-p-toluidine; purity = 99%
Remark: Submitted as TSCA substantial risk notice. No analysis of test material available; specification given
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (14)

5.1.3 Acute Dermal Toxicity

Type:	LD50
Species:	rabbit
Strain:	New Zealand white
Sex:	male/female
Number of Animals:	10
Vehicle:	other: neat
Value:	> 2000 mg/kg bw
Method:	OECD Guide-line 402 "Acute dermal Toxicity"
Year:	1987 GLP: yes
Test substance:	other TS: N,N-dimethyl-p-toluidine; purity = 99%
Remark:	No analysis of test material available; product specification given.
Reliability:	(1) valid without restriction GLP guideline study
Flag:	Critical study for SIDS endpoint

21-AUG-2001 (15)

5.1.4 Acute Toxicity, other Routes
-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation
-

5.2.2 Eye Irritation
-

5.3 Sensitization
-

5.4 Repeated Dose Toxicity

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 108-44-1; 121-69-7; 91-66-7.

5.5 Genetic Toxicity 'in Vitro'

Type: Bacterial reverse mutation assay
System of testing: Salmonella strains TA98, TA100, TA1537, TA1538
Concentration: 100, 333, 667, 1000, 3300, 5000 ug/plate
Cytotoxic Conc.: with metabolic activation: none
without metabolic activation: 1000 ug/plate
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: 1983 GLP: yes
Test substance: other TS: N,N-dimethyl-p-toluidine; purity = 99%
Remark: No analysis of test material; specification given . Only deviation from the testing guideline was the lack of a confirmatory assay.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (16)

Type: Cytogenetic assay
System of testing: Chinese hamster V79 cells
Concentration: 0, 0.3, 0.9, 1.2 mM
Cytotoxic Conc.: > 10% survival at 1.2mM as estimated by colony formation
Metabolic activation: without
Result: positive
Method: other: S. Bonatti et al, Mutat. Res. 116, 149-154 (1983)
Year: GLP: no data
Test substance: other TS: N,N-dimethyl-p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
21-AUG-2001 (17)

Type: Bacterial reverse mutation assay
System of testing: Salmonella strains TA97, TA98, TA100
Concentration: 0, 1, 2.5, 5, 10, 40, 70, 100 ug/plate
Cytotoxic Conc.: 100 ug/plate
Metabolic activation: with and without
Result: negative
Method: other: Maron, D.M., and Ames, B.N., Mutat. Res. 113, 173-215
Year: 1983 GLP: no data
Test substance: other TS: N,N-dimethyl-p-toluidine; purity = 99%
Reliability: (2) valid with restrictions
24-SEP-2001 (17)

5.6 Genetic Toxicity 'in Vivo'

Type: other: Alkaline elution assay
Species: mouse Sex:
Strain: Balb/c
Route of admin.: i.p.
Exposure period: single dose
Doses: 0, 1, or 2 mmol/kg (0, 135, 270 mg/kg)
Result: negative
Method: other: Parodi, S. et al, Mutat. Res. 54, 39-46 (1978)
Year: 1978 GLP: no data
Test substance: other TS: N,N-dimethyl-p-touludine; purity = 99%
Remark: The author mentions that an increase of 3X controls is usually considered positive.
Result:

dose mmol/kg	2 hr	24 hr
0	2.15	2.06
1	2.05	3.43
2	2.39	----

28-SEP-2001 (17)

Type: other: Alkaline elution assay
Species: rat Sex:
Strain: Sprague-Dawley
Route of admin.: oral unspecified
Exposure period: single dose
Doses: 0 and 8 mmol/kg (0 and 1080 mg/kg)
Result: ambiguous
Method: other: Parodi, S. et al, Mutat. Res. 54, 39-46 (1978)
Year: 1978 GLP: no data
Test substance: other TS: N,N-dimethyl-p-touludine; purity = 99%
Remark: DNA fragmentation increased in liver cells to about 2.4 X control at one dose only. The author mentions that an increase of 3X controls is usually considered positive. That is why he considers this a weak positive.
Result: weak positive

dose mmol/kg	6 hr	24 hr
0	1.36	1.48
8	3.22**	1.85

DNA fragmentation increased in liver cells to about 2.4 X control at one dose only.

28-SEP-2001 (17)

Type: other: Alkaline elution assay
Species: rat Sex:
Strain: Sprague-Dawley
Route of admin.: i.p.
Exposure period: single dose
Doses: 0, 4, and 8 mmol/kg (0, 540, and 1080 mg/kg)
Result: ambiguous
Method: other: Parodi, S. et al, Mutat. Res. 54, 39-46 (1978)
Year: 1978 GLP: no data
Test substance: other TS: N,N-dimethyl-p-touludine; purity = 99%
Remark: DNA fragmentation increased in liver cells to about 2X control at one dose only. The author mentions that an increase of 3X controls is usually considered positive. That is why he considers this a weak positive.
Result: weak positive

dose mmol/kg	2 hr	24 hr
0	1.63	1.99
4	3.14	2.06
8	3.23*	----

DNA fragmentation increased in liver cells to about 2X control at one dose only.

28-SEP-2001 (17)

5.7 Carcinogenicity

-

5.8 Toxicity to Reproduction

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 108-44-1; 121-69-7.

5.9 Developmental Toxicity/Teratogenicity

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 121-69-7; 91-66-7.

5.10 Other Relevant Information

-

5.11 Experience with Human Exposure

-

(1) Meylan W. and Howard P. (1999) EPIWin Modeling Program. Syracuse Research Corporation. Environmental Science Center, 6225 Running Ridge Road, North Syracuse, NY 13212-2510.

(2) CRC Handbook of Chemistry and Physics. 80th ed. (1999) David
R. Lide, ed. CRC Press, New York. p. 3-26, No. 862.

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(8) Verschueren, K. (2001) Handbook of Environmemtal Data on Organic Chemicals. 4th edition. Vol. 1 p. 944

(9) Geiger, D.L. et al. (1986) "Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas), Vol. 3, Center for Lake Superior Environmental Studies, University of Wisconsin, Superior, WI, p.221-2 (test 1).

(10) Geiger, D.L. et al. (1986) "Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas), Vol. 3, Center for Lake Superior Environmental Studies, University of Wisconsin, Superior, WI, p.223-224 (test 2).

(11) Broderius, S. and Kahl, M. (1985) Aquat. Toxicol. 6: 307-322.

(12) Tonogai, Y. et al. (1982) J. Toxicol. Sci. 7, 193-203.

(13) ChemFirst Study No. 3888-91-0105-TX-001

(14) ChemFirst Study No. L08413

(15) ChemFirst Study No. 3888-91-0106-TX-001

(16) ChemFirst Study No. 14506-0-401

(17) Taningher, M. et al, (1993) Environ. Mol. Mutagen. 21: 349-356.

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 103-69-5
CAS No.	103-69-5
EINECS Name	N-ethylaniline
EINECS No.	203-135-5
TSCA Name	Benzenamine, N-ethyl-
Molecular Formula	C8H11N

Producer Related Part
  Company:
  Creation date: 15-JUL-1999

Substance Related Part
  Company:
  Creation date: 15-JUL-1999

Memo: Bayer Corporation

Printing date: 29-OCT-2001
Revision date:
Date of last Update: 29-OCT-2001

Number of Pages: 27

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: lead organisation
Name: American Chemistry Council (formerly Chemical Manufacturers Association), Monocyclic Aromatic Amines and Nitro Aromatics (MAANA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States

17-AUG-2001

Type: cooperating company
Name: Albemarle Corpoiration
Country: United States

24-SEP-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

24-SEP-2001

Type: cooperating company
Name: Buffalo Color Corporation
Country: United States

24-SEP-2001

Type: cooperating company
Name: ChemFirst Inc
Country: United States

24-SEP-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information

Substance type: organic
Physical status: liquid
21-OCT-1999

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms

Benzenamine, N-ethyl-
21-OCT-1999

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern

Type: type
Category: Use in closed system
21-OCT-1999

Type: industrial
Category: Chemical industry: used in synthesis
21-OCT-1999

Type: use
Category: Intermediates
21-OCT-1999

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: -64 degree C
Method: other
GLP: no data
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

Value: -63.5 degree C
Method: other:
GLP: no data
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (2)

2.2 Boiling Point

Value: 203 degree C at 1013 hPa
Decomposition: no
Method: other:
GLP: no data
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (2)

Value: 204.5 degree C at 1013 hPa
Decomposition: no
Method: other
GLP: no data
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (3)

Value: 207 degree C
Method: other
GLP: no data
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

2.3 Density

Type:
Value: .9625 at 20 degree C
Method: other:
GLP: no data
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (2) (1)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: = .4 hPa at 20 degree C
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

Value: 1 hPa at 38 degree C
Method: other (measured):
GLP: no data
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (4)

Value: 1.9 at 50 degree C
Method: other (measured)
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Handbook value
Flag: Critical study for SIDS endpoint
21-AUG-2001 (1)

2.5 Partition Coefficient

log Pow: 1.92 at 25 degree C
Method: other (measured): OECD Chemicals Testing Programme
Ecotoxicology Group
Year: 1979
GLP: yes
Testsubstance: other TS: N-ethylaniline; purity not stated
Remark: Octanol/Water partition coeffiecient P= 82.30
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (5)

log Pow: 2.26 at 25 degree C
Method: other (measured): shake-flask method according to Fujita t, Iwasa J, Hansch C. 1964. J. Am. Chem. Soc. 86:5175.
Year:
GLP: no data
Testsubstance: other TS: N-ethylaniline; purity not noted
Remark: Method of equlibration: Shake-flask
Analytical method: absorption spectrophotometry
Aqueous phase: octanol-saturated water
Phase analyzed: aqueous
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
21-AUG-2001 (6) (7)

log Pow: 2.16
Method: other (measured)
Year:
GLP: no
Testsubstance: other TS: N-ethylaniline; purity not stated
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
21-AUG-2001 (7) (8)

log Pow: 2.114
Method: other (calculated): KOWWIN Program (v1.65)
Year:
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (9)

2.6.1 Water Solubility

Value:	ca. 2700 mg/l at 20 degree C
Qualitative:	soluble (1000-10000 mg/L)
pH:	1
Method:	other
Testsubstance:	other TS: N-ethylaniline; purity not stated
Reliability:	(2) valid with restrictions Handbook value
Flag:	Critical study for SIDS endpoint

21-AUG-2001 (1)

2.6.2 Surface Tension
-

2.7 Flash Point
-

2.8 Auto Flammability
-

2.9 Flammability
-

2.10 Explosive Properties
-

2.11 Oxidizing Properties
-

2.12 Additional Remarks
-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: = .0000000000515114 cm3/(molecule * sec)
Degradation: 50 % after 2.5 hour(s)
Method: other (calculated): AOP v1.89
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (9)

3.1.2 Stability in Water

Type: abiotic
t1/2 pH : 1.1 day
Method: other: careful sampling of Rhine river water at Lobith and 24.5 hours later at Gorinchem as carried out by GC-MS analysis of concentrates prepared by closed-loop gas-stripping and XAD adsorption techniques.
Year: GLP: no
Test substance: other TS: N-ethylaniline; 97.5% purity
Remark: The half life is much longer in stagnant waters or groundwaters due to limited volatilization, aerobic biodegradation and photochemical decomposition.
Test condition: Under field conditions, in running water, the half life of N-ethylaniline is estimated to be 1.1. days.
21-AUG-2001 (10)

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 121-69-7.

3.1.3 Stability in Soil

-

3.2 Monitoring Data (Environment)

Type of measurement: other: field study
Medium: surface water
Method: On July 16, 1979 a careful sampling of Rhine river water at Lobith and 24.5 hours later at Gorinchem as carried out by GC-MS analysis of concentrates prepared by closed-loop gas-stripping and XAD adsorption techniques.
Concentration .3 - µg/l
Result: Relevant concentration at Lobith was 0.3 ug/l and estmated half-life was 1.1 days.
19-JUN-2001 (10)

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: Air Water Soil Sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: (calculation) EPIWIN Level III Fugacity Model
Year: 1999
Result:

Media	Distribution (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.88	4.98	1000	1.46e-011
Water	42.2	360	1000	2.34e-010
Soil	56.8	360	1000	2.03e-009
Sediment	0.149	1.44e+003	0	1.7 e-010

Persistence Time: 275 hr
Reaction Time: 320 hr
Advection Time: 1.96e+003 hr
Percent Reacted: 86
Percent Advected: 14
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (9)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum:
Degradation: 0 % after 28 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: 1977 GLP: no data
Test substance: other TS: N-ethylaniline; purity not noted
Reliability: (1) valid without restriction
Guideline Study
Flag: Critical study for SIDS endpoint
24-SEP-2001 (11)

Type: aerobic
Inoculum:
Concentration: 19.1 mg/l related to DOC (Dissolved Organic Carbon)
23.7 mg/l related to Test substance
Degradation: 97 % after 14 day
Method: ISO 7827 "Evaluation in an aqueous medium of the 'ultimate' aerobic biodegradability of organic compounds - method by anlaysis of dissolved organic carbon (DOC)"
Year: GLP: no data
Test substance: other TS: N-ethylaniline; purity not noted
Remark: BOD = 0.048 g/g
BOD5/COD = 64.3%
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
24-SEP-2001 (12)

3.6 BOD5, COD or BOD5/COD Ratio

Method: other: Modified OECD Screening Test, ISO 7827

Result: 19.1 mg DOC of N-ethylaniline (23.7 mg) eliminated in 14 days to an extent of 97% (BOD5/COD = 64.3%)
BOD = 0.048 g/g
Reliability: (2) valid with restrictions
Guideline study with acceptable restrictions
21-AUG-2001 (13)

3.7 Bioaccumulation

Species:
Exposure period:
Concentration:
BCF: 9.19
Elimination:
Method: other: BCF Program (v2.13) no
Year: GLP:
Test substance: other TS: molecular structure
Remark: Log Kow (estimated) : 2.11
Log Kow (experimental): 2.16
Log Kow used by BCF estimates: 2.16

Equation Used to Make BCF estimate:
Log BCF = 0.77 log Kow - 0.70

Estimated Log BCF = 0.963 (BCF = 9.188)
Reliability: (2) valid with restrictions
Accepted calculation method
21-AUG-2001 (9)

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type:
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: = 33
Method: other: other: according to Japan Industrial Standards
Year: 1971 GLP: no data
Test substance: other TS: N-ethylaniline; purity not noted
Remark: Substances which were difficult to dissolve in water were dissolved in 1 ml. of ethanol then diluted with water.
Result: LC50 (24 hr) = 71 mg/l
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
21-AUG-2001 (14)

Type: other: calculation
Species: other: Fish
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: 70.802
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (9)

Type:
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no data
LC0: = 50
Method: other: No data
Year: GLP: no data
Test substance: no data
19-JUN-2001 (15)

Type: other: calculation
Species: other: Fish
Exposure period: 14 day
Unit: mg/l Analytical monitoring: no
LC50: 130.507
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
24-APR-2001 (9)

Type:
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 10
Method: other: No data
Year: GLP: yes
Test substance:
24-APR-2001 (16)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: other: calculation
Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 76.444
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (9)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
EC0: 6.3
EC50: 18
EC100: 50
Method: other: no data
Year: GLP: yes
Test substance: no data
Flag: Critical study for SIDS endpoint
21-AUG-2001 (16)

Type:
Species: other: Tetrahymena pyriformis
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: yes
EC50: 160
Method:
Year: GLP: yes
Test substance: no data
Method: T. pyriformis was pre-cultured at 30 degree C for 24 hr. Concentration for stock solution was 1.8 in 10 ml 2% protease peptone. Slightly soluble chemicals were dissolved in dimethylsulfoxide (DMSO). Stock solutions were inoculated with 0.2 ml of T. pyriformis and cultivated at 30 degree C for 24 hr without agitation. Cells were then counted by Coulter Counter and microscope (correlation coefficient was 0.998, n=32)

Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
28-SEP-2001 (18)

Type:
Species: other: Chaetogammarus marinus
Exposure period: 90 hour(s)
Unit: mg/l Analytical monitoring: no data
EC50: 44
Method: other: no data
Year: GLP: no data
Test substance: no data
24-APR-2001 (17)

Type: other: calculation
Species: Mysidopsis bahia (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 18.877
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
24-APR-2001 (9)

Type: other: calculation
Species: Daphnia sp. (Crustacea)
Exposure period: 16 day
Unit: mg/l Analytical monitoring: no
EC50: 4.114
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
24-APR-2001 (9)

Type:
Species: other: Tubitex species
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50 : 160
Method: other: no data
Year: GLP: no data
Test substance: no data
Result: LC50 (24 hr) = 470 mg/l
09-AUG-2000 (19)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: other algae: green algae
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 48.094
ChV : 5.125
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
21-AUG-2001 (9)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no data
EC10: 17
EC50: 98
Method: other: no data
Year: GLP: no data
Test substance: no data
Flag: Critical study for SIDS endpoint
21-AUG-2001 (20) (16)

Species: Agmenellum quadruplicatum (Algae)
Endpoint: other: algal lawn assay (growth inhibition
Exposure period: 7 day
Unit: Analytical monitoring: no
Method:
Year: GLP:
Test substance: other TS: N-ethylaniline; purity not noted
Method: Algal lawns were initially seeded with 1.0 x 10e+5 cells/ml in 1% agarized (Difco 0140) medium. The test chemical was absorbed onto antibiotic sensitivity disks (12.7 mm; Schleicher and Schuell, No. 740-E) which were placed directly onto the agar surface. The petri dish cultures were sealed with Scotch Tape and incubated in light from a tungsten lamp for 3-7 days at 28-30 degree C. Zone of inhibition was measured from the edge of the disk in mm. The radius of growth inhibition around the disk was judged visually and microscopically.
Result:

Concentration (ug/disk)	zone of inhibition (mm)
0	0
1	0
10	0
100	0
500	2
1000	10

0 indicates no inhibition,36 indicates complete inhibition.
No inhibittion was noted with ethanol controls.

LC50 >1000 ug/disk
Reliability: (3) invalid
Not a Guideline method
21-AUG-2001 (21)

4.4 Toxicity to Microorganisms e.g. Bacteria
-

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

Species: other
Endpoint: other
Exposure period: 30 day
Unit: mg/l Analytical monitoring: no
ChV : 9.284
Method: other: ECOSAR v0.99e
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
21-AUG-2001 (9)

4.5.2 Chronic Toxicity to Aquatic Invertebrates
-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type:	other: calculation
Species:	Eisenia fetida (Worm (Annelida), soil dwelling)
Endpoint:	other
Exposure period:	14 day
Unit:	other: ppm
LC50:	689.546
Method:	other: ECOSAR v0.99e
Year:	1999 GLP: no
Test substance:	other TS: molecular structure
Remark:	Chemical may not be soluble enough to measure this predicted effect.
Reliability:	(2) valid with restrictions Accepted calculation method

21-AUG-2001 (9)

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks
-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
Number of Animals: 10
Vehicle: other: corn oil
Value: = 478 mg/kg bw
Method: other: USEPA TSCA Health Effects Testing Guidelines, 40 CFR 798.1175, "Acute Oral Toxicity"
Year: 1992 GLP: yes
Test substance: other TS: N-Ethylaniline, purity 99.19%
Remark: Test material analysis not done under GLP
Result: 95% CI = 308-741 mg/kg bw
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (22)

Type: LD50
Species: rat
Strain: Sprague-Dawley
Sex: male/female
Number of Animals: 10
Vehicle: other: undiluted
Value: 332.2 - 401.6 mg/kg bw
Method: other: OECD Acute Oral Toxicity Protocol - modified
Year: GLP: yes
Test substance: other TS:Commercial purity: 97.5%
Remark: Undiluted N-ethylaniline was administered in a single dose at 275.0 mg/kg, 307.0 mg/kg, 342.0 mg/kg, 381.0 mg/kg, and 425.0 mg/kg to groups of five female and five male Sprague-Dawley rats. Animals were fasted overnight. Where possible, the volume of dosing solution did not exceed 5 ml. per animal. Pale skin was noted at the 275.0 and 342.0 mg/kg doses. Ataxia, pale skin, and deaths were noted at the 307.0 and 381.0 doses. Ataxia and death were noted at 425.0 mg/kg. Lungs which were dark in color were observed at necropsy.
LD50 calculated according to Finney DJ. "Statistical Methods in Biological Assay. 2nd ed. London:Griffin Press. 1971.
Result:

	Male	Female	Combined
LD50(mg/kg)	323.2	402.1	362.7
95% CI	(268.8-360.3)	(362.3-636.4)	(332.2-401.6)

Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (23)

Type: LD50
Species: rat
Strain: no data
Sex: no data
Number of Animals:
Vehicle: no data
Value: 290 mg/kg bw
Method:
Year: GLP: no data
Test substance: other TS: monoethylaniline; purity not noted
Remark: When given at one-half its LD50, monoethylaniline caused normochromic anemia and increased by 50-60% the blood methemoglobin content in rats. After chronic administration at 5% the LD50, a decrease in hemoglobin and erythrocytes, and an increase in methemoglobin and leukocytes was observed.
24-APR-2001 (24)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 300 mg/kg bw
Method: other: no data
Year: GLP: no data
Test substance: no data
10-AUG-2000 (25)

Type: LD50
Species: mouse
Strain: no data
Sex: no data
Number of Animals:
Vehicle: no data
Value: 500 mg/kg bw
Method: other: no data
Year: GLP: no data
Test substance: other TS: monoethylaniline; purity not noted
24-APR-2001 (24)

Type: LD50
Species: cat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 25 - 200 mg/kg bw
Method: other: no data
Year: GLP: no data
Test substance: no data
Remark: Report outlines environmental health data from published literature and industry.
Result: No deaths ocurred at 25 mg/kg bw. All animals dies at 200 mg/kg bw.
10-AUG-2000 (16)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain:
Sex: male/female
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: 1.13 - 1.48 mg/l
Method: other: OECD Acute Inhalation Toxicity Protocol - Modified
Year: GLP: yes
Test substance:
Remark: Groups of 5 male and 5 female Sprague Dawley rats (70 total animals) were exposed to chamber concentrations of N-ethylaniline at 0.01, 0.026, 0.30, 1.13, 1.48, 1.38, and 1.42 mg/L. The average particle size (mass median diameter) ranged form 3.8 to 5.8 um (standard deviation of 2.5 to 6.0). Daily observations indicated that body weight loss, nasal discharge, decreased activity, and possible slight respiratory difficulty occurred subsequent to exposure. No lesions definitely attributable to N-ethylaniline exposure were noted during post mortem examination. The LC50 (based on actual chamber concentration) was found to be greater than 1.13 and less than 1.48 mg/L.
Test substance: Commercial purity: 97.5%
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (26)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Strain: New Zealand white
Sex: male/female
Number of Animals: 5
Vehicle: other: undiluted
Value: > 2000 mg/kg bw
Method: other: USEPA TSCA Health Effects Testing Guidelines, 40CFR 798.1100, "Acute Dermal Toxicity"
Year: 1992 GLP: yes
Test substance: other TS: N-ethylaniline, purity 99.19%
Remark: 5 animals/sex/dose group;
Test material analysis not done under GLP
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (27)

Type: LD50
Species: rat
Strain:
Sex: male
Number of Animals:
Vehicle:
Value: = 1915.1 mg/kg bw
Method: other: OECD Protocol - Modified
Year: GLP: yes
Test substance:
Remark: Six male and 6 female rats were assigned to each of the five dosage groups (1200, 1483, 1833, 2265, and 2800 mg/kg). The clipped test area constituted no less than 10% of the entire body surface and was abraded in 3 males and 3 females per group prior to application. Clinical observations included black urine, loss of appetite, decreased activity and death.
Test substance: Commercial purity: 97.5%
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (28)

Type: LD50
Species: rat
Strain:
Sex: female
Number of Animals:
Vehicle:
Value: = 1347 mg/kg bw
Method: other: OECD Protocol - Modified
Year: GLP: yes
Test substance:
Remark: Six male and 6 female rats were assigned to each of the five dosage groups (1200, 1483, 1833, 2265, and 2800 mg/kg). The clipped test area constituted no less than 10% of the entire body surface and was abraded in 3 males and 3 females per group prior to application. Clinical observations included black urine, loss of appetite, decreased activity and death.
Test substance: Commercial purity: 97.5%
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (28)

5.1.4 Acute Toxicity, other Routes
-

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation
-

5.2.2 Eye Irritation
-

5.3 Sensitization
-

5.4 Repeated Dose Toxicity

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 108-44-1; 121-69-7; 91-66-7.

5.5 Genetic Toxicity 'in Vitro'

Type: Bacterial reverse mutation assay
System of testing: S. typhimurium strains TA97, TA98, TA100, and TA1535
Concentration: 0, 10.0, 33.0, 100.0, 333.0, 1000.0, and 1666.0 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: 1983 GLP: yes
Test substance: other TS: N-Ethylaniline (103-69-5), purity: 97% by label
Remark: Procedure: Preincubation protocol used.
Max. 0.05 ml DMSO solvent used/plate.
Plates/test: 1.
Activation system: 10 and 30% S-9 fraction of Arochlor 1254-induced male Sprague-Dawley rat and Syrian hamster livers.
Media: Histidine dependent (Vogel-Bonner).
Assay was done at SRI International.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (29)

Type: Bacterial reverse mutation assay
System of testing: Species/Strain: S. typhimurium TA98, TA100, TA1535, TA1537
Concentration: No Data
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: similar to OECD Guide-line 471
Year: GLP: yes
Test substance: no data
Remark: Procedure: Pre-incubation.
Plates/test: No data.
Activation system: S-9 liver fraction from Arochlor 1254 or methylcholanthrene induced rats.
Media: histidine dependent.
No. of replicates: No data.
Reliability: (1) valid without restriction
Comparable to Guideline study
Flag: Critical study for SIDS endpoint
21-AUG-2001 (30)

5.6 Genetic Toxicity 'in Vivo'
-

5.7 Carcinogenicity

-

5.8 Toxicity to Reproduction

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 106-49-0; 108-44-1; 121-69-7.

5.9 Developmental Toxicity/Teratogenicity

See IUCLID data sets on CAS# 62-53-3; 95-53-4; 121-69-7; 91-66-7.

5.10 Other Relevant Information

-

5.11 Experience with Human Exposure

-

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7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 62-53-3
CAS No.	62-53-3
EINECS Name	aniline
EINECS No.	200-539-3
TSCA Name	Benzenamine
Molecular Formula	C6H7N

Producer Related Part
  Company: EUROPEAN COMMISSION - European Chemicals Bureau
  Creation date: 11-FEB-2000

Substance Related Part
  Company: EUROPEAN COMMISSION - European Chemicals Bureau
  Creation date: 11-FEB-2000

Printing date:	21-JUN-2001
Revision date:	11-FEB-2000
Date of last Update:	11-FEB-2000

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Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

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Country: France
Phone: 33147420633
Telefax: 33147421204

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Country: Netherlands
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Telefax: 020-6254449
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Name: BASF AG
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Town: 67056 Ludwigshafen
Country: Germany

Name: BASF Antwerpen N. V.
Town: 2040 Antwerpen 4
Country: Belgium

Name: BASF Schwarzheide GmbH
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Country: Germany

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Country: United Kingdom

Name: Imperial Chemical Industries PLC
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Country: United Kingdom
Phone: 0044/71/834-4444
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Country: Netherlands
Phone: 31-172-431601
Telefax: 31-172-432494

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information

Substance type: element
Physical status: liquid

Substance type: element
Physical status: solid

Substance type: organic
Physical status: liquid

1.1.0 Details on Template

-

1.1.1 Spectra

-

1.2 Synonyms

1-Aminobenzol
Source: BASF Antwerpen N. V. Antwerpen 4
OXON Italia SpA Pero (MI)

1-AMINOBENZOL
Source: Bayer AG Leverkusen

Aminobenzeen
Source: B.V. CONSOLCO Amsterdam
Bayer Shell Isocyanates N.V. Antwerpen
OXON Italia SpA Pero (MI)

AMINOBENZENE
Source: VIOCHROM SA AGHIA VARVARA ATHENS

Aminobenzene
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Goodyear Chemicals Europe LES ULIS Cedex
OXON Italia SpA Pero (MI)
Imperial Chemical Industries PLC London
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

aminobenzene
Source: Monsanto Europe N.V. Bruxelles

Aminobenzene, Phenylamine.
Source: Hickson & Welch Ltd. Castleford

AMINOBENZENE; AMINOPHEN; ANILIN OIL; PHENYLAMINE
Source: Enichem Synthesis Milan

Aminobenzene; aniline oil; phenylamine;
Source: Mallinckrodt Specialty Chemicals Ltd Stavely, Chesterfield

Aminobenzol
Source: OXON Italia SpA Pero (MI)
Sigeco GmbH Duisburg

AMINOBENZOL
Source: Bayer AG Leverkusen

Aminobenzol; Phenylamin;
Source: Raschig GmbH Ludwigshafen

Aminophen
Source: BASF Antwerpen N. V. Antwerpen 4
Goodyear Chemicals Europe LES ULIS Cedex
OXON Italia SpA Pero (MI)
Imperial Chemical Industries PLC London
BASF AG Ludwigshafen
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide
Sigeco GmbH Duisburg

AMINOPHEN
Source: Bayer AG Leverkusen

Aminophenol
Source: OXON Italia SpA Pero (MI)

AMMINOBENZENE
Source: Enichem S.p.A. Milan

Amminobenzene
Source: OXON Italia SpA Pero (MI)

Anilin
Source: OXON Italia SpA Pero (MI)
Sigeco GmbH Duisburg

anilin
Source: Imperial Chemical Industries PLC London

ANILIN
Source: Bayer AG Leverkusen

anilin oil
Source: OXON Italia SpA Pero (MI)

Aniline
Source: VOS B.V. Alphen aan den Rijn
OXON Italia SpA Pero (MI)

Aniline (8CI)
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

Aniline oil
Source: Goodyear Chemicals Europe LES ULIS Cedex

Aniline Olie
Source: B.V. CONSOLCO Amsterdam

Aniline olie
Source: OXON Italia SpA Pero (MI)

Anilinöl, Amidobenzol
Source: NEUBER GES.M.B.H. WIEN

Anyvim
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
OXON Italia SpA Pero (MI)
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

Benzeenamine
Source: Bayer Shell Isocyanates N.V. Antwerpen
OXON Italia SpA Pero (MI)

benzenamine
Source: Monsanto Europe N.V. Bruxelles

Benzenamine
Source: Goodyear Chemicals Europe LES ULIS Cedex
OXON Italia SpA Pero (MI)
Sigeco GmbH Duisburg

Benzenamine (9CI)
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

Benzenamine, Aminophenol
Source: UniroyalChemical Company Latina Scalo

BENZENAMMINA
Source: Enichem S.p.A. Milan

Benzenammina
Source: OXON Italia SpA Pero (MI)

Benzene, amino-
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Goodyear Chemicals Europe LES ULIS Cedex
OXON Italia SpA Pero (MI)
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

Benzeneamine
Source: OXON Italia SpA Pero (MI)
Imperial Chemical Industries PLC London

BENZENEAMINE
Source: Bayer AG Leverkusen

Benzolamin
Source: BASF Antwerpen N. V. Antwerpen 4
OXON Italia SpA Pero (MI)
Sigeco GmbH Duisburg

BENZOLAMIN
Source: Bayer AG Leverkusen

Blue Oil
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
OXON Italia SpA Pero (MI)
Imperial Chemical Industries PLC London
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

C.I. 76000
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

FENILAMMINA
Source: Enichem S.p.A. Milan

Fenilammina
Source: OXON Italia SpA Pero (MI)

Fenylamine
Source: Bayer Shell Isocyanates N.V. Antwerpen
OXON Italia SpA Pero (MI)

noir solvant 7
Source: ALMIMET PARIS

Phenylamin
Source: BASF Antwerpen N. V. Antwerpen 4
OXON Italia SpA Pero (MI)
Imperial Chemical Industries PLC London
Sigeco GmbH Duisburg

PHENYLAMIN
Source: Bayer AG Leverkusen

PHENYLAMINE
Source: VIOCHROM SA AGHIA VARVARA ATHENS

Phenylamine
Source: Bayer Shell Isocyanates N.V. Antwerpen
BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Goodyear Chemicals Europe LES ULIS Cedex
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

phenylamine
Source: Monsanto Europe N.V. Bruxelles
OXON Italia SpA Pero (MI)

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity

Quantity more than 1 000 000 tonnes

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: T
N
other RM: H
Specific limits: yes
R-Phrases: (20/21/22) Harmful by inhalation, in contact with skin and if swallowed
(40) Possible risks of irreversible effects
(48/23/24/25) Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed
(50) Very toxic to aquatic organisms
S-Phrases: (1/2) Keep locked up and out of reach of children
(28) After contact with skin, wash immediately with plenty of ...

(36/37) Wear suitable protective clothing and gloves
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)
(61) Avoid release to the environment. Refer to special instructions/Safety data sets

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: carcinogenic, category 3
R-Phrases: (40) Possible risks of irreversible effects

Classification: as in Directive 67/548/EEC
Class of danger: corrosive
R-Phrases: (20/21/22) Harmful by inhalation, in contact with skin and if swallowed

Classification: as in Directive 67/548/EEC
Class of danger: dangerous for the environment
R-Phrases: (50) Very toxic to aquatic organisms

Classification: as in Directive 67/548/EEC
Class of danger: toxic
R-Phrases: (48/23/24/25) Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use in closed system

Type: type
Category: Use resulting in inclusion into or onto matrix

Type: industrial
Category: Agricultural industry

Type: industrial
Category: Basic industry: basic chemicals

Type: industrial
Category: Chemical industry: used in synthesis

Type: industrial
Category: Paints, lacquers and varnishes industry

Type: industrial
Category: Photographic industry

Type: industrial
Category: Polymers industry

Type: industrial
Category: Textile processing industry

Type: industrial
Category: other: industra farmaceutica

Type: industrial
Category:

Type: industrial
Category: other

Type: use
Category: Colouring agents

Type: use
Category: Intermediates

Type: use
Category: Oxidizing agents

Type: use
Category: Pharmaceuticals

Type: use
Category: Photochemicals

Type: use
Category: other: agricultural intermediates,mdi,dye stuffs,rubber chemicals and intermediate for pharmaceuticals.

Type: use
Category:

Type: use
Category: other

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values

Type of limit: MAC (NL)
Limit value: 2 other
Limit value: other
Remark: Andere meeteenheid : PPM
Grenswaarde voor blootstelling van korte duur:
a) Numerieke waarde : onbekend
b) Meeteenheid : onbekend
c) Numerieke waarde : onbekend
d) Tijdschema : onbekend
e) Frequentie : onbekend

Referentie : Onbekend
Source: B.V. CONSOLCO Amsterdam

Type of limit: MAK (DE)
Limit value: 2 ml/m3
Short term expos.
Limit value: 10 ml/m3
Schedule: 30 minute(s)
Frequency: 2 times
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide
(1)

Type of limit: MAK (DE)
Limit value: 8 mg/m3
Remark: hautresorptiv
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide
(1)

Type of limit: MAK (DE)
Limit value:
Remark: krebserzeugend EG-Kategorie 3
fortpflanzungsgefaehrdend Gruppe D
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide
(2)

Type of limit: MAK (DE)
Limit value: 8 mg/m3
Short term expos.
Limit value: 40 mg/m3
Schedule: 30 minute(s)
Frequency: 8 times
Remark: limit value: 2 ppm
Source: Monsanto Europe N.V. Bruxelles

Type of limit: MAK (DE)
Limit value: 8 mg/m3
Source: Enichem Synthesis Milan

Type of limit: MAK (DE)
Limit value: 2 ml/m3
Short term expos.
Limit value: 10 ml/m3
Schedule: 30 minute(s)
Frequency: 2 times
Source: BASF AG Ludwigshafen
OXON Italia SpA Pero (MI)

Type of limit: MAK (DE)
Limit value: 8 mg/m3
Short term expos.
Limit value: 40 mg/m3
Schedule: 30 minute(s)
Frequency: 8 times
Remark: valore limite: 2 ppm
Source: Monsanto Europe N.V. Bruxelles
OXON Italia SpA Pero (MI)

Type of limit: MAK (DE)
Limit value: 8 mg/m3
Source: Enichem Synthesis Milan
OXON Italia SpA Pero (MI)

Type of limit: MAK (DE)
Limit value: 2 ml/m3
Short term expos.
Limit value: 10 ml/m3
Schedule: 30 minute(s)
Frequency: 2 times
Source: BASF AG Ludwigshafen
OXON Italia SpA Pero (MI)

Type of limit: MAK (DE)
Limit value: 2 ml/m3
Short term expos.
Limit value: 10 ml/m3
Schedule: 30 minute(s)
Frequency: 2 times
Source: BASF AG Ludwigshafen
OXON Italia SpA Pero (MI)

Type of limit: MAK (DE)
Limit value: 8 mg/m3
Short term expos.
Limit value: 40 mg/m3
Schedule: 30 minute(s)
Frequency: 2 times
Source: Sideco GmbH Duisburg
OXON Italia SpA Pero (MI)
Bayer AG Leverkusen
OXON Italia SpA Pero (MI)
Sigeco GmbH Duisburg

Type of limit: MAK (DE)
Limit value: 8 mg/m3
Short term expos.
Limit value: 40 mg/m3
Schedule: 30 minute(s)
Frequency: 2 times
Remark: Grenzwert: 2 ppm
Source: Bayer AG Leverkusen

Type of limit: MAK (DE)
Limit value: 8 mg/m3
Short term expos.
Limit value: 32 mg/m3
Schedule: 15 minute(s)
Frequency: 4 times
Source: Raschig GmbH Ludwigshafen

Type of limit: OES (UK)
Limit value: 10 mg/m3
Short term expos.
Limit value: 20 mg/m3
Schedule: 10 minute(s)
Source: Enichem Synthesis Milan
Enichem Synthesis Milan
OXON Italia SpA Pero (MI)

Type of limit: OES (UK)
Limit value: 10 mg/m3
Short term expos.
Limit value: 20 mg/m3
Schedule: 15 minute(s)
Source: Imperial Chemical Industries PLC London
OXON Italia SpA Pero (MI)

Type of limit: OES (UK)
Limit value: 10 mg/m3
Short term expos.
Limit value: 20 mg/m3
Schedule: 15 minute(s)
Remark: Skin Notation
Source: Imperial Chemical Industries PLC London

Type of limit: TLV (US)
Limit value: 10 mg/m3
Source: VIOCHROM SA AGHIA VARVARA ATHENS

Type of limit: TLV (US)
Limit value: 2 ml/m3
Source: Bayer Shell Isocyanates N.V. Antwerpen
Bayer Shell Isocyanates N.V. Antwerpen
OXON Italia SpA Pero (MI)

Type of limit: TLV (US)
Limit value: 7.6 mg/m3
Remark: Gilt fuer Anilin und Homologe.
Wert bezieht sich auf Haut.
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide
(3)

Type of limit: TLV (US)
Limit value:
Remark: Limit value: 2 ppm
Gilt fuer Anilin und Homologe. Wert bezieht sich auf Haut.
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide
(3)

Type of limit: TLV (US)
Limit value: 7.6 mg/m3
Source: Goodyear Chemicals Europe LES ULIS Cedex

Type of limit: TLV (US)
Limit value: 7.6 mg/m3
Remark: TLV-TWA=2 ppm = 7.6 mg/m3
Source: Enichem Synthesis Milan

Type of limit: TLV (US)
Limit value: 7.6 mg/m3
Source: Enichem S.p.A. Milan
(4)

Type of limit: TLV (US)
Limit value: 7.6 mg/g
Remark: There is no STEL published for this chemical.
Source: UniroyalChemical Company Latina Scalo

Type of limit: TLV (US)
Limit value: 7.6 mg/m3
Remark: TLV-TWA = 2 ppm = 7.6 mg/m3
Source: Enichem Synthesis Milan
OXON Italia SpA Pero (MI)

Type of limit: TLV (US)
Limit value: 7.6 mg/m3
Source: Enichem S.p.A. Milan
OXON Italia SpA Pero (MI)

Type of limit: other
Limit value: .1 mg/m3
Remark: MAC (ex URSS), 1980-1987
Source: Enichem Synthesis Milan

Type of limit: other
Limit value: 2 mg/m3
Short term expos.
Limit value: 6 mg/m3
Schedule: 8 hour(s)
Source: Hickson & Welch Ltd. Castleford

1.9 Source of Exposure

Method: Aniline is shipped in 200 lts steel drums. Upon receipt, the drums are stored in the wharehouse on ground level. racked whare
Source: VIOCHROM SA AGHIA VARVARA ATHENS

Remark: - Produktieproces: Door catalytische reductie van nitrobenzeen met stikstof of catalytische reactie van chloorbenzeen met ammoniak in waterige oplossing.

- Plaatsen van productie zover ons bekend:
  - Duitsland
  - Engeland
  - Tsjechië
  - Rusland
  - Japan
  - USA

Source: B.V. CONSOLCO Amsterdam

Remark: Artificial sources: Wastewater and emissions from its manufacture, transport, storage and use in the manufacture of polyurethanes (MDI), rubber processing chemicals, pesticides, fibers, dyes and pigments.. (re.1)

Aniline.. has.. een found in industrial effluents from oil shale recovery e oil refineries and from chemical e coal conversion plants (re.2)
Many industrial precesses:
-Catalytic liquid-phase hydrogenation of nitrobenzene
-Catalytic vapor-phase hydrogenation of nitrobenzene
-Reduction of nitrobenzene with iron and iron salts
-Amination of phenol
Source: Enichem Synthesis Milan

(5) (6)

Remark: LA SOSTANZA VIENE IMPORTATA E UTILIZZATA NEL SITO INDUSTRIALE DI BRINDISI PER LA SINTESI DI DIAMMINODIFENILMETANO IN UN SISTEMA CHIUSO. LE EMISSIONI SONO TRASCURABILI E VENGONO ADEGUATAMENTE ABBATTUTE IN MODO DA PREVENIRE QUALSIASI FORMA DI ESPOSIZIONE SIA ALL'INTERNO CHE ALL'ESTERNO DEL SITO.
Source: Enichem S.p.A. Milan

Remark: Aniline is used in the production of fluorescent whitening agents.
Source: Hickson & Welch Ltd. Castleford

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution

Classified by: KBwS (DE)
Labelled by: KBwS (DE)
Class of danger: 2 (water polluting)
Source: Bayer Shell Isocyanates N.V. Antwerpen
BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Bayer AG Leverkusen
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

1.14.2 Major Accident Hazards

Legislation: Directive 82/502/EEC
Substance listed: yes
No. in Directive: Annex II Part II No. 2
Source: Bayer Shell Isocyanates N.V. Antwerpen

Legislation: Stoerfallverordnung (DE)
Substance listed: no
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

(7)

Legislation: Stoerfallverordnung (DE)
Substance listed:
Remark: Anlage 2 Nr. 4 c
Source: Bayer AG Leverkusen

1.14.3 Air Pollution

Classified by: TA-Luft (DE)
Labelled by:
Number: 3.1.7 (organic substances)
Class of danger: I
Source: Bayer Shell Isocyanates N.V. Antwerpen

Classified by: TA-Luft (DE)
Labelled by: TA-Luft (DE)
Number: 3.1.7 (organic substances)
Class of danger: I
Source: BASF AG Ludwigshafen
BASF Antwerpen N. V. Antwerpen 4
Bayer AG Leverkusen
BASF AG Ludwigshafen
BASF Schwarzheide GmbH Schwarzheide

1.15 Additional Remarks

Method: dfdfdf
Source: VIOCHROM SA AGHIA VARVARA ATHENS

Remark: Transportinformatie: Volgens ADR/VLG 6.1 cijfer 11b - UN no. 1547
Source: B.V. CONSOLCO Amsterdam

Remark: COMBUSTIONE DI QUESTA SOSTANZA IN INCENERITORE IDONEO ALLO SMALTIMENTO DI RESIDUI CHIMICI PERICOLOSI.
Source: Enichem S.p.A. Milan

Remark: Avoid all personal contact with this chemical.
Disposal Information: In accordance with local or national environmental control regulations. Do Not Reuse Containers!
Product reacts vigorously with acids, oxidising agents and hexachloromelamine.
SPILL, LEAK and DISPOSAL INFORMATION: Cleanup perosnnel should wear suitable protective equipment (SCBA).
Transportation Information: ADR/RID, IMO, ICAO/IATA classification = 6.1, poison.

ID Number = UN1547
Source: UniroyalChemical Company Latina Scalo

Remark: Aniline is transported in road tankers and handled in bulk storages and enclosed pipework.
Source: Hickson & Welch Ltd. Castleford

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: = -6.2 degree C
Source: BASF AG Ludwigshafen
(8)

2.2 Boiling Point

Value: = 183.5 - 184 degree C
Source: BASF AG Ludwigshafen
(8)

2.3 Density

Type: density
Value: = 1.0213 g/cm3
Source: BASF AG Ludwigshafen
(8)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: = .5 hPa at 20 degree C
Source: BASF AG Ludwigshafen
(8)

2.5 Partition Coefficient

log Pow: = .91
Method:
Year:
Source: BASF AG Ludwigshafen
(8)

2.6.1 Water Solubility

Value: 36 g/l at 20 degree C
pH: 8.8 at 36 g/l and 20 degree C
Source: BASF AG Ludwigshafen
(8)

2.6.2 Surface Tension

-

2.7 Flash Point

Value: = 76 degree C
Type:
Method: other: DIN 51 758
Year:
Source: BASF AG Ludwigshafen

(8)

2.8 Auto Flammability

Value: = 540 degree C
Method: other: DIN 51 794
Source: BASF AG Ludwigshafen

(8)

2.9 Flammability

-

2.10 Explosive Properties

Result: other: Explosionsgrenzen in Luft: 1.2-11.0 Vol.%
Source: BASF AG Ludwigshafen

(8)

2.11 Oxidizing Properties

-

2.12 Additional Remarks

Remark: Gefaehrliche Reaktionen: Exotherme Reaktion mit Saeuren.
Viskositaet: 4.4 mPa.s bei 20 Grad C
Source: BASF AG Ludwigshafen

(8)

3.1.1 Photodegradation
-

3.1.2 Stability in Water
-

3.1.3 Stability in Soil

Type: Radiolabel:
Concentration:
Cation exch.
capac.
Microbial
biomass:
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: adsorption
Media: water - soil
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: berechnet
Year: 1994
Remark: log Koc = 1.65
Computer Programm: PCKOC, PC Software to Estimate Soil Sorption Coefficients, Version 1.22, PH.Howard, W.Meylan (Mai 1993), Syracuse Research Corporation, New York.
Source: BASF AG Ludwigshafen

(9)

Type: adsorption
Media: water - soil
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: gemessen
Year:
Remark: log Koc = 2.07
Source: BASF AG Ludwigshafen

(9) (10)

Type: adsorption
Media: water - soil
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: gemessen
Year:
Remark: log Koc = 2.14
Source: BASF AG Ludwigshafen

(9) (11)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: other: BASF-Belebtschlamm
Concentration: 596 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 97 % after 5 day
Method: other: Modified OECD Screening Test
Year: 1981 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen

(12)

Type: aerobic
Inoculum: other: BASF-Belebtschlamm
Concentration: 100 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: = 92 % after 6 day
Testsubstance: 3 hour(s) = 15 %
1 day = 39 %
3 day = 91 %
Method: other: Standversuch
Year: 1980 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen

(13)

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation

-

3.8 Additional Remarks

-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish
-

4.2 Acute Toxicity to Aquatic Invertebrates
-

4.3 Toxicity to Aquatic Plants e.g. Algae
-

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: other bacteria: BASF-Belebtschlamm
Exposure period: 30 minute(s)
Unit: mg/l Analytical monitoring: no
EC20 : = 2800
Method: other: Kurzzeitatmungstest
Year: 1979 GLP: no
Test substance: other TS: Substanz aus EG-Test
Remark: Keine Atmungshemmung bis 1400 mg/l
Source: BASF AG Ludwigshafen

(14)

Type: aquatic
Species: other bacteria: BASF-Belebtschlamm
Exposure period: 30 minute(s)
Unit: mg/l Analytical monitoring: no
EC20 : = 550
Method: other: Kurzzeitatmungstest
Year: 1980 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen

(15)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

-

4.6.2 Toxicity to Terrestrial Plants

-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

-

4.7 Biological Effects Monitoring

-

4.8 Biotransformation and Kinetics

-

4.9 Additional Remarks

-

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 200 - 2000 mg/kg bw
Method: other
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Bericht und Ergebnis sind nachvollziehbar und akzeptabel
(16)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: ca. 572 mg/kg bw
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Bericht und Ergebnis sind nachvollziehbar und akzeptabel
(17)

Type: other
Species: cat
Strain:
Sex:
Number of Animals:
Vehicle:
Value:
Method: other
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Anilin fuehrte nach oraler Applikation zu starker Methaemoglobinbildung.
Eines der beiden Tiere die 100 mg/kg erhielten starben, in den niederen Dosierungen (1 - 50 mg/kg) trat keine Mortaliaet auf, jedoch wurden in allen Dosierungen erhoehte Methaemoglobinwerte gemessen.
Source: BASF AG Ludwigshafen
Test substance: Untersucht wurden das BASF-Produkt XIX/405 Anilin und

Anilin p.a.
Reliability: (2) valid with restrictions
Bericht und Ergebnis sind nachvollziehbar und akzeptabel
(18) (19) (20)

Type: other
Species: cat
Strain:
Sex:
Number of Animals:
Vehicle:
Value:
Method: other
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Die einmalige orale Gabe von 50 mg/kg fuehrte bei den beiden in den Versuch eingesetzten Katzen zu starker Methaemoglobinbildung und Cyanose. Ein Tier starb.
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Bericht und Ergebnis sind nachvollziehbar und akzeptabel
(21)

5.1.2 Acute Inhalation Toxicity

Type: other: IRT
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value:
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Die 3-stuendige Exposition von 12 Ratten in einer bei 20 Grad Celsius mit der Substanz gesaettigten Atmosphaere wirkte bei keinem der Tiere letal. Die 8-stuendige Exposition von 6 Ratten fuehrte zum Tod der Tiere.
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Bericht und Ergebnis sind nachvollziehbar und akzeptabel
(17)

5.1.3 Acute Dermal Toxicity
-

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: ca. 368 mg/kg bw
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Bericht und Ergebnis sind nachvollziehbar und akzeptabel
(17)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Bericht und Ergebnis sind nachvollziehbar und akzeptabel
(17)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.:
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
Reliability: (2) valid with restrictions
Bericht und Ergebnis sind nachvollziehbar und akzeptabel
(17)

5.3 Sensitization
-

5.4 Repeated Dose Toxicity
-

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA102
Concentration: bis 5000 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: nach Maron und Ames: Mutat. Res.,113, 173-215, (1983)
Year: GLP: no data
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
Reliability: (1) valid without restriction
Guidelinekonforme Studie, valide Studie
(22)

5.6 Genetic Toxicity 'in Vivo'
-

5.7 Carcinogenicity
-

5.8 Toxicity to Reproduction

-

5.9 Developmental Toxicity/Teratogenicity

-

5.10 Other Relevant Information

-

5.11 Experience with Human Exposure

Remark: Von 1967-1992 wurden 13 Faelle von Zyanose und Atembeschwerden nach Einwirkung von Anilin beobachtet, die zur weiteren Behandlung in die Klinik eingewiesen wurden.
Source: BASF AG Ludwigshafen

(23)

Remark: A cluster of ten cases of Hodgkin`s disease was identified within the active workforce of a large chemical manufacturing firm over a 23-year period. In the total workforce of 62000 person-years, an expected number of 2.01 cases was calculated, giving a standardized incidence ratio of 497 (95 % CI 238-915). A nested case-control study was undertaken with 200 controls. For 11 selected chemicals (incl. aniline) exposure odds ratios were calculated. No substance emerged as a likely candidate for explaining the observed Hodgkin`s disease cluster.
Source: BASF AG Ludwigshafen

(24)

(1) TRGS 900 (1993)

(2) TRGS 500 (1993)

(3) ACGIH (1991-1992)

(4) ACGIH (1993 - 1994) - DOCUMENTAZIONE DI VALORI LIMITE DI SOGLIA E DEGLI INDICI DI ESPOSIZIONE BIOLOGICA.

(5) (re.1) Chemical marketing Reporter, Chemical profile, 7 sept. (1985)

(re.2) IARC, Monographs on the evaluation of the carcinogenic risk of chemical to man. Geneva, World Health Organization, Int. Ag. for research on cancer, 1972-present. (Multivolume work), p. V27 45 (1982).

(6) Re: Ullmann, Encyclopedia of Industrial Chemistry, 1985 Vol. A2, pag. 303-312, VCH

(7) Stoerfall-Verordnung vom 20.09.1991

(8) BASF AG, Sicherheitsdatenblatt Anilin (04.01.1994)

(9) BASF AG, Umweltanalytik, Notiz vom 27.09.94

(10) Van Oepen,B. et al., Chemosphere 22, 285, (1991)

(11) Gerstel,Z., Personal communication, The Volcani Center, Institute of Soils, Israel, zitiert nach: Koerdel,W.: Report: Validation of the HPLC-Screening Method for the determination of the adsorption coefficient Koc in soil, (August 1993), Fraunhofer Institut fuer Umweltchemie und Oekotoxikologie, Schmallenberg

(12) BASF AG, Labor Oekologie, unveroeffentlichte Untersuchung: Biotic Degradation: Modified OECD Screening Test vom 05.06.1981

(13) BASF AG, Labor Oekologie, unveroeffentlichte Untersuchung: Standversuch vom 06.05.1980

(14) BASF AG, Labor Oekologie, unveroeffentlichte Untersuchung: Kurzzeitatmungstest vom 10.01.1979

(15) BASF AG, Labor Oekologie, unveroeffentlichte Untersuchung: Kurzzeitatmungstest vom 24.01.1980

(16) BASF AG: Abt. Toxikologie, unveroeffentlichte Untersuchung, Project No. 10A257/891044, 06.07.1989

(17) BASF AG: Abt. Toxikologie, unveroeffentlichte Untersuchung, (XXI/214), 14.03.1972

(18) BASF AG: Abt. Toxikologie, unveroeffentlichte Untersuchung, (XIX/405), 17.04.1970

(19) BASF AG: Abt. Toxikologie, unveroeffentlichte Untersuchung, (XIX/405), 23.04.1970

(20) BASF AG: Abt. Toxikologie, unveroeffentlichte Untersuchung, 16.04.1970

(21) BASF AG: Abt. Toxikologie, unveroeffentlichte Untersuchung, (XXI/46), 11.03.1971

(22) Jung R. et al.: Mutat. Res., 278, 265-270, (1992)

(23) unveroeffentlichte Mitteilung, BASF Werksaerztlicher Dienst (1992)

(24) Swaen, G., M., H., Slangen, J., M., M., Ott, M., G., Kusters, E., Van Den Langenbergh, G., Arends, J., W., Zober, A.; Int. Arch Occup. Environ. Health 68, 224-228, (1996)

7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 121-69-7
CAS No.	121-69-7
EINECS Name	N,N-dimethylaniline
EINECS No.	204-493-5
TSCA Name	Benzenamine, N,N-dimethyl-
Molecular Formula	C8H11N

Producer Related Part
  Company: EUROPEAN COMMISSION - European Chemicals Bureau
  Creation date: 11-FEB-2000

Substance Related Part
  Company: EUROPEAN COMMISSION - European Chemicals Bureau
  Creation date: 11-FEB-2000

Printing date:	25-SEP-2001
Revision date:	11-FEB-2000
Date of last Update:	11-FEB-2000

Number of Pages: 126

Chapter (profile):	Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile):	Reliability: without reliability, 1, 2, 3, 4
Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

-

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: liquid

1.1.0 Details on Template

-

1.1.1 Spectra

-

1.2 Synonyms

(Dimethylamino)benzene
Source: BASF AG Ludwigshafen

Aniline, N,N-dimethyl- (8CI)
Source: BASF AG Ludwigshafen

BENZENAMINE, N,N-DIMETHYL-
Source: VIOCHROM SA AGHIA VARVARA ATHENS

Benzenamine, N,N-dimethyl- (9CI)
Source: BASF AG Ludwigshafen

Dimethylanilin
Source: BASF AG Ludwigshafen

Dimethylaniline
Source: ZENECA Specialties Manchester
BASF AG Ludwigshafen

Dimethylphenylamine
Source: BASF AG Ludwigshafen

DMA
Source: ZENECA Specialties Manchester

N,N-Dimethylaminobenzene
Source: BASF AG Ludwigshafen

N,N-dimethylaniline
Source: ZENECA Specialties Manchester

N,N-Dimethylaniline
Source: BASF AG Ludwigshafen

N,N-Dimethylbenzenamine
Source: BASF AG Ludwigshafen

N,N-Dimethylphenylamine
Source: BASF AG Ludwigshafen

Versneller NL 63/10
Source: BASF AG Ludwigshafen

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: T
N
other RM: H
Specific limits: no data
R-Phrases: (23/24/25) Toxic by inhalation, in contact with skin and if swallowed
(40) Possible risks of irreversible effects
(51/53) Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment
S-Phrases: (1/2) Keep locked up and out of reach of children
(28) After contact with skin, wash immediately with plenty of ...
(36/37) Wear suitable protective clothing and gloves
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)
(61) Avoid release to the environment. Refer to special instructions/Safety data sets

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: carcinogenic, category 3
R-Phrases: (40) Possible risks of irreversible effects

Classification: as in Directive 67/548/EEC
Class of danger: dangerous for the environment
R-Phrases: (51) Toxic to aquatic organisms
(53) May cause long-term adverse effects in the aquatic environment

Classification: as in Directive 67/548/EEC
Class of danger: toxic
R-Phrases: (23/24/25) Toxic by inhalation, in contact with skin and if swallowed

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values

Type of limit: MAK (DE)
Limit value: 5 ml/m3
Short term expos.
Limit value: 10 ml/m3
Schedule: 30 minute(s)
Frequency: 4 times
Source: BASF AG Ludwigshafen
(1)

Type of limit: MAK (DE)
Limit value: 25 mg/m3
Remark: hautresorptiv
Source: BASF AG Ludwigshafen
(1)

Type of limit: MAK (DE)
Limit value:
Remark: krebserzeugend Gruppe III B.
Source: BASF AG Ludwigshafen
(2)

Type of limit: OES (UK)
Limit value: 25 mg/m3
Short term expos.
Limit value: 50 mg/m3
Schedule: 10 minute(s)
Remark: OES carries skin notation.
Source: ZENECA Specialties Manchester
(3)

Type of limit: TLV (US)
Limit value: 25 mg/m3
Source: VIOCHROM SA AGHIA VARVARA ATHENS

Type of limit: TLV (US)
Limit value: 25 mg/m3
Remark: Wert bezieht sich auf Haut.
Source: BASF AG Ludwigshafen
(4)

Type of limit: TLV (US)
Limit value:
Remark: Wert bezieht sich auf Haut.
Source: BASF AG Ludwigshafen
(4)

Type of limit: TLV (US)
Limit value: 25 mg/m3
Remark: Wert bezieht sich auf Haut.
Source: BASF AG Ludwigshafen
(4)

1.9 Source of Exposure

Remark: N,N-dimethylaniline is manufactured in an enclosed system at one manufacturing site.Exposures are low and well-controlled.The substance is solely used as a fine chemical intermediate and hence subsequent exposures are limited.The material is rapidly consumed within contained systems and the potential for exposure is low.
Source: ZENECA Specialties Manchester

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution

Classified by: KBwS (DE)
Labelled by:
Class of danger: 2 (water polluting)
Source: BASF AG Ludwigshafen

Classified by: other: BASF
Labelled by: other: BASF
Class of danger: 2 (water polluting)
Source: BASF AG Ludwigshafen

1.14.2 Major Accident Hazards

Legislation: Stoerfallverordnung (DE)
Substance listed: no
Source: BASF AG Ludwigshafen

(5)

1.14.3 Air Pollution

Classified by:
Labelled by:
Number: 3.1.7 (organic substances)
Class of danger: I
Remark: Vorlaeufige Zuordnung (durch andere Firmen)
Source: BASF AG Ludwigshafen

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: ca. 2 degree C
Source: BASF AG Ludwigshafen
(6)

2.2 Boiling Point

Value: = 194 - 195 degree C
Source: BASF AG Ludwigshafen
(6)

2.3 Density

Type: density
Value: = .96 g/cm3 at 20 degree C
Source: BASF AG Ludwigshafen
(6)

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: = .53 hPa at 20 degree C
Source: BASF AG Ludwigshafen
(6)

2.5 Partition Coefficient

log Pow: = 2.278
Method: other (calculated): Inkrementenmethode von Rekker mit Computerprogramm der Firma CompuDrug Ltd.
Year:
Source: BASF AG Ludwigshafen
(7)

log Pow: = 2.31
Method: other (calculated): gemaess Rekker, R.F., The hydrophobic fragmental constant, Elsevier, Amsterdam 1988
Year:
Source: BASF AG Ludwigshafen
(8)

log Pow: = 2.62
Method:
Year:
Source: BASF AG Ludwigshafen
(9)

2.6.1 Water Solubility

Value: = 1.2 g/l at 20 degree C
pH: 7.4 at 1.2 g/l and 20 degree C
Source: BASF AG Ludwigshafen
(10)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: = 75 degree C
Type: closed cup
Method: other: DIN 51 758
Year:
Source: BASF AG Ludwigshafen
(10)

Value: = 83 degree C
Type: open cup
Method: other: DIN ISO 2592
Year:
Remark: Nach dem Entflammen brannte die Probe weiter. Flammpunkt und Brennpunkt liegen bei der gleichen Temperatur.
Source: BASF AG Ludwigshafen
(11)

2.8 Auto Flammability

Value: 370 degree C
Method: other: DIN 51 794
Source: BASF AG Ludwigshafen
(10)

2.9 Flammability
-

2.10 Explosive Properties

Result:
Source: BASF AG Ludwigshafen
(10)

2.11 Oxidizing Properties
-

2.12 Additional Remarks

Remark: Gefaehrliche Reaktionen: exotherme Reaktion mit Saeuren
Source: BASF AG Ludwigshafen

(10)

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: O3
Degradation: = 50 % after 1.2 day
Method: other (calculated)
Year: GLP:
Test substance: other TS: Reinheitsgrad 99%
Remark: Concentration of Sensitizer: 7.2*10^-11 molecules/cm^3
Rate Constant: 9.1*10^-18 cm^3/molecule*sec
Source: BASF AG Ludwigshafen
Test condition: Reaktionskammer; Temperatur 296 K; Reaktionsprodukte: Wasserstoffperoxid, Ameisensaeure, Formaldehyd, N-Methylformanilid
(12)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Degradation: = 50 % after 2.6 hour(s)
Method:
Year: GLP:
Test substance: other TS: Reinheitsgrad 99%
Remark: Rate Constant: 1.48*10^-10 cm^3/molecule*sec
Source: BASF AG Ludwigshafen
Test condition: Blitzlichtphotolyse; Resonanzfluoreszenz; Temperaturbereich 278-464 K
(12)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 3000000 molecule/cm3
Method:
Year: GLP:
Test substance:
Remark: Atmospheric transformation: lifetime less than 1 day
Source: BASF AG Ludwigshafen
(13)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: other: HNO3 (Gasphase)
Degradation: = 50 % after 1.6 day
Method:
Year: GLP:
Test substance: other TS: Reinheitsgrad 99%
Remark: Concentration of Sensitizer: 2.6 ug/m^3
Rate Constant: >/= 2*10^-16 cm^3/molecule*sec
Source: BASF AG Ludwigshafen
Test condition: Reaktionskammer
(14)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: other: HNO3 (Gasphase)
Degradation: = 50 % after 1.6 day
Method:
Year: GLP:
Test substance: other TS: Reinheitsgrad 99%
Remark: Concentration of Sensitizer: 2.6 ug/m^3
Rate Constant: >/= 2*10^-16 cm^3/molecule*sec
Source: BASF AG Ludwigshafen
Test condition: Reaktionskammer

(12)

Type: water
INDIRECT PHOTOLYSIS
Sensitizer: OH
Degradation: = 50 % after 15 day
Method:
Year: GLP:
Test substance:
Remark: Concentration of Sensitizer: 10^-16 mol/l
Rate Constant: 5.3*10^9 cm^3/molecule*sec
Source: BASF AG Ludwigshafen
Test condition: 25 Grad C; pH 9

(15)

Type: water
INDIRECT PHOTOLYSIS
Sensitizer: other: Carbonatradikale
Degradation: = 50 % after 3 hour(s)
Method:
Year: GLP:
Test substance:
Remark: Concentration of Sensitizer: 3*10^-14 mol/l; Rate Constant: 1.8*10^9 l/mol*sec.
In einem Vergleich des Abbaus von N,N-Dimethylanilin in Wasser zwischen den konkurrierenden Abbauwegen durch die Reaktion mit Carbonatradikalen, Hydrogencarbonatradikalen und der direkten Photolyse bei 313 nm war der Weg ueber den Abbau durch Carbonatradikale am schnellsten. Die nachgewiesenen Geschwindigkeitskonstanten unter den gewaehlten Laborbedingungen (20 Grad C) betrugen fuer den Abbau durch Carbonatradikale 0.072 min^-1, fuer Hydrogencarbonat 0.1 min^-1 und fuer die direkte Photolyse 0.0011 min^-1 aus denen sich Halbwertszeiten von 10, 7, 63 Minuten ableiten lassen.
Source: BASF AG Ludwigshafen

(16)

Type: water
INDIRECT PHOTOLYSIS
Sensitizer: other: Singulett Sauerstoff
Degradation: = 50 % after 9.6 hour(s)
Method:
Year: GLP:
Test substance:
Remark: Concentration of Sensitizer: 2*10^-13 mol/l
Rate Constant: 1*10^8 l/mol*sec
Source: BASF AG Ludwigshafen
(17)

3.1.2 Stability in Water

Type:
Method: other
Year: GLP:
Test substance:
Remark: Unter Umweltbedingungen kann N,N-Dimethylanilin als hydrolysebestaendig angesehen werden.
Source: BASF AG Ludwigshafen
(18)

Type:
Method: other
Year: GLP:
Test substance:
Remark: Bei Lobith in den Niederlanden betrug die Konzentration von N,N-Dimethylanilin im Rhein waehrend einer einmaligen Messkampagne 1979 0.3 ug/l. Nach einer Fliesszeit von 24.5 h wurde die Konzentration von DMA bei Gorinchem erneut bestimmt (keine Konzentrationsangabe in der Originalliteratur). Bei Annahme einer Reduktion der Konzentration nach dem Geschwindigkeitsgesetz 1.Ordnung berechneten die Autoren fuer DMA eine Halbwertszeit fuer die Abnahme der DMA-Konzentration von 2.3 Tagen. Ueber den Verbleib des Stoffes (z.B. Bindung an Schwebstoffe, Volatilisierung, abiotische und biotische Transformation) macht die Untersuchung keine Aussage.
Source: BASF AG Ludwigshafen
(19)

Type:
Method: other
Year: GLP:
Test substance:
Remark: Bei Lobith in den Niederlanden betrug die Konzentration von N,N-Dimethylanilin im Rhein waehrend einer einmaligen Messkampagne 1979 0.3 ug/l. Nach einer Fliesszeit von 24.5 h wurde die Konzentration von DMA bei Gorinchem erneut bestimmt (keine Konzentrationsangabe in der Original-literatur). Bei Annahme einer Reduktion der Konzentration nach dem Geschwindigkeitsgesetz 1.Ordnung berechneten die Autoren fuer DMA eine Halbwertszeit fuer die Abnahme der DMA-Konzentration von 2.3 Tagen. Ueber den Verbleib des Stoffes (z.B. Bindung an Schwebstoffe, Volatilisierung, abiotische und biotische Transformation) macht die Unter-suchung keine Aussage.
Source: BASF AG Ludwigshafen

(19)

3.1.3 Stability in Soil

Type: laboratory Radiolabel:
Concentration:
Content of clay: = 15.9 %
silt: = 14.4 %
sand: = 69.7 %
Organ. carbon: = 1.3 %
pH: = 6.7
Cation exch.
capac. = 12.3 other: mval/100 g
Microbial
biomass:
Method: other: Adsorptions-/Desorptionstest gemaess OECD Richtlinie 106
Year: GLP:
Test substance:
Remark: Koc=97; aufgrund der Koc-Werte ist mit einer insgesamt mittleren aber pH-Wert-gesteuerten Bodensorption zu rechnen. Parabraunerde
Source: BASF AG Ludwigshafen

(20)

Type: laboratory Radiolabel:
Concentration:
Content of clay: = 2.6 %
silt: = 8.2 %
sand: = 89.2 %
Organ. carbon: = 4.9 %
pH: = 2.8
Cation exch.
capac. = 15.1 other: mval/100 g
Microbial
biomass:
Method: other: Adsorptions-/Desorptionstest gemaess OECD Richtlinie 106
Year: GLP:
Test substance:
Remark: Koc=337; aufgrund der Koc-Werte ist mit einer insgesamt mittleren aber pH-Wert-gesteuerten Bodensorption zu rechnen. Waldpodsol
Source: BASF AG Ludwigshafen
(21)

Type: laboratory Radiolabel:
Concentration:
Content of clay: = 35.7 %
silt: = 58.8 %
sand: = 5.5 %
Organ. carbon: = 1.6 %
pH: = 7.1
Cation exch.
capac. = 13.4 other: mval/100 g
Microbial
biomass:
Method: other: Adsorptions-/Desorptionstest gemaess OECD Richtlinie 106
Year: GLP:
Test substance:
Remark: Koc=116; aufgrund der Koc-Werte ist mit einer insgesamt mittleren aber pH-Wert-gesteuerten Bodensorption zu rechnen. Sediment
Source: BASF AG Ludwigshafen
(21)

Type: laboratory Radiolabel:
Concentration:
Content of clay: = 2.6 %
silt: = 8.2 %
sand: = 89.2 %
Organ. carbon: = 4.9 %
pH: = 2.8
Cation exch.
capac. = 15.1 other: mval/100 g
Microbial
biomass:
Method: other: Adsorptions-/Desorptionstest gemaess OECD Richtlinie 106
Year: GLP:
Test substance:
Remark: Koc=337; aufgrund der Koc-Werte ist mit einer insgesamt mittleren aber pH-Wert-gesteuerten Bodensorption zu rechnen. Waldpodsol
Source: BASF AG Ludwigshafen
(20)

Type: laboratory Radiolabel:
Concentration:
Content of clay: = 35.7 %
silt: = 58.8 %
sand: = 5.5 %
Organ. carbon: = 1.6 %
pH: = 7.1
Cation exch.
capac. = 13.4 other: mval/100 g
Microbial
biomass:
Method: other: Adsorptions-/Desorptionstest gemaess OECD Richtlinie 106
Year: GLP:
Test substance:
Remark: Koc=116; aufgrund der Koc-Werte ist mit einer insgesamt mittleren aber pH-Wert-gesteuerten Bodensorption zu rechnen. Sediment
Source: BASF AG Ludwigshafen
(20)

Type: Radiolabel:
Concentration:
Cation exch. capac.
Microbial biomass:
Method: other
Year: GLP:
Test substance:
Remark: Die Autoren beschreiben die Aufbringung von kommunalem Belebtschlamm, der Restgehalte verschiedener organischer Verbindungen enthielt, auf Sandboden (Rubicon Sand) in Muskegon (Michigan,USA) und die Elimination dieser Verbindungen im Boden. Die Konzentration an N,N-Dimethylanilin im Schlamm betrug 223 ug/kg. Nach der Aufbringung des Schlammes auf den Boden in ueberhoehten Mengen von 448 bzw. 224 t/ha (entsprechend 44.8 bzw. 22.4 kg/m^2) wurden nach 5 Tagen in der oberen Bodenschicht (0-15.2 cm Tiefe) 24 bzw. 25 ug/kg N,N-Dimethylanilin, nach 122 Tagen 19 bzw. 4 ug/kg und nach 241 Tagen 30 ug/kg bzw. unterhalb der Nachweisgrenze (keine Angabe der Nachweisgrenze) gefunden. Diese widerspruechlichen Ergebnisse fuehren die Autoren auf die schon im Klaerschlamm relativ geringe N,N-Dimethylanilin-Konzentration zurueck. Eine Verlagerung in tiefere Bodenschichten (22.9-38.1 cm Tiefe) konnte fuer N,N-Dimethylanilin nicht gefunden werden.
Source: BASF AG Ludwigshafen

(22)

3.2 Monitoring Data (Environment)

Type of measurement: background concentration
Medium: soil
Method:
Concentration
Remark: In einem sandigen Boden aus Muskegon (Michigan,USA) wurde kein DMA nachgewiesen. Die Bodenproben wurden aus einer Tiefe von 0-15.2 cm und 22.9-38.1 cm entnommen. Eine Nachweisgrenze wurde nicht angegeben.
Source: BASF AG Ludwigshafen

(22)

Type of measurement: concentration at contaminated site
Medium: other: Klaerschlamm
Method:
Concentration
Remark: Im Klaerschlamm einer staedtischen Klaeranlage mit hohem Anteil an industriellen Abwaessern in Muskegon (Michigan, USA) wurden 223 ug/kg (vermutlich Trockengewicht) N,N-Dimethylanilin gefunden.
Source: BASF AG Ludwigshafen

(22)

Type of measurement: concentration at contaminated site
Medium: soil
Method:
Concentration
Remark: 1978 entnommene Bodenproben im Uferbereich des Flusses Buffalo (New York,USA) ergaben N,N-Dimethylanilin-Konzentrationen von 10 und 40 ppm (entsprechend 10 und 40 mg/kg, vermutlich Trockengewicht). Eine Nachweisgrenze ist nicht angegeben. Der Uferbereich wurde auch als Deponie der farbstoffproduzierenden Industrie genutzt.
Source: BASF AG Ludwigshafen

(23)

Type of measurement: concentration at contaminated site
Medium: sediment
Method:
Concentration
Remark: Die Autoren nahmen im Juni 1979 Sedimentproben aus dem Fluss Buffalo (New York,USA), der stark mit Industrieabwaessern aus der Farbstoffproduktion belastet ist. DMA konnte in den an 3 Stellen genommenen Proben nicht nachgewiesen werden (Nachweisgrenze nicht angegeben). Der Fluss wird jedoch jaehrlich ausgebaggert, wodurch sich N,N-Dimethylanilin nur ueber den Zeitraum von 7-8 Monaten anreichern konnte.
Source: BASF AG Ludwigshafen

(23)

Type of measurement: other: Konzentration im Flusswasser
Medium: surface water
Method:
Concentration
Remark: Konzentrationen im Untersuchungszeitraum 1989:
arithmetischer Mittelwert/Maximalwert (mg/m^3) ->
RHEIN: Oehningen -0.05/<0.05; Village-Neuf 0.06/0.27;
Seltz <0.05/0.10; Karlsruhe <0.05/0.11; Worms 0.14/0.53;
Mainz 0.09/0.32; Koblenz <0.05/0.26; Duesseldorf <0.05/0.11;
Lobith <0.05/0.22; Bimmen <0.05/0.25.
MAIN: Bischofsheim <0.05/0.27.
Bei den meisten Stationen handelt es sich um 24-h-Mischproben, die zur Analyse zu 14-Tagessammelproben vereinigt wurden.
Source: BASF AG Ludwigshafen

(24)

Type of measurement: other: Konzentration im Flusswasser
Medium: surface water
Method:
Concentration
Remark: Hoechste im Rahmen der Gewaesserueberwachungsstufe 1 (1988) und der Trendueberwachung (1989) gemessene Konzentrationen an N,N-Dimethylanilin in ug/l (n=13, 24-h-Mischproben):
1988 -> Bad Honnef,Rhein Sued; Duesseldorf,Rhein Mitte; Kleve-Bimmen,Rhein Nord; Muendung Wupper, Sieg, Erft, Ruhr, Lippe: <=0.1 ug/l; Muendung Emscher: 0.7 ug/l.
1989 -> saemtliche obengenannte Messstellen: <=0.1 ug/l.
Source: BASF AG Ludwigshafen
(25) (26)

Type of measurement: other: Konzentration im Flusswasser
Medium: surface water
Method:
Concentration
Remark: Hoechste im Rahmen der Gewaesserueberwachungsstufe 1 (1988) und der Trendueberwachung (1989) gemessene Konzentrationen an N,N-Dimethylanilin in ug/l (n=13, 24-h-Mischproben):
1988 -> Bad Honnef,Rhein Sued; Duesseldorf,Rhein Mitte; Kleve-Bimmen,Rhein Nord; Muendung Wupper, Sieg, Erft, Ruhr, Lippe: <=0.1 ug/l; Muendung Emscher: 0.7 ug/l.
1989 -> saemtliche obengenannte Messstellen: <=0.1 ug/l.
Source: BASF AG Ludwigshafen
(25) (26)

Type of measurement: other: Konzentration im Trinkwasser
Medium: drinking water
Method:
Concentration
Remark: Bei Untersuchungen des Pruefungs- und Forschungsinstituts der Niederlaendischen Wasserwerke (KIWA) im Zeitraum 1979-1982 wurde im Trinkwasser (Rheinuferfiltrat) eine maximale Rheinwasserkonzentration von >1 ug/l bestimmt (Nachweisgrenze nicht angegeben).
Source: BASF AG Ludwigshafen
(27)

3.3.1 Transport between Environmental Compartments

Type: volatility
Media: water - air
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method:
Year:
Remark: Aufgrund der chemisch/physikalischen Eigenschaften ist sowohl ein Uebertritt aus der Hydrosphaere in die Atmosphaere als auch eine Deposition aus der Atmosphaere moeglich. Nach den Kriterien von Thomas (1982) ist N,N-Dimethylanilin als ein aus waessriger Loesung maessig fluechtiger Stoff anzusehen.
Henry-Konstante (berechnet): 5.4 Pa*m^3/mol (20 Grad C).
Source: BASF AG Ludwigshafen
(28)

Type: volatility
Media: water - air
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method:
Year:
Remark: Aufgrund der chemisch/physikalischen Eigenschaften ist sowohl ein Uebertritt aus der Hydrosphaere in die Atmosphaere als auch eine Deposition aus der Atmosphaere moeglich. Nach den Kriterien von Thomas (1982) ist N,N-Dimethylanilin als ein aus waessriger Loesung maessig fluechtiger Stoff anzusehen.
Henry-Konstante (berechnet): 5.4 Pa*m^3/mol (20 Grad C).
Source: BASF AG Ludwigshafen
(18)

3.3.2 Distribution

Media: water - air
Method: Calculation according Mackay, Level I
Year:
Remark: Luft: 64.6%; Wasser: 34.3%
Source: BASF AG Ludwigshafen
(18)

3.4 Mode of Degradation in Actual Use

Remark: N,N-Dimethylanilin kann unter Umweltbedingungen als hydrolysebestaendig angesehen werden. In der Atmosphaere kann der Stoff durch Reaktion mit Hydroxylradikalen bei Halbwertszeiten von wenigen Stunden und bei Reaktion mit Ozon oder Salpetersaeure innerhalb von wenigen Tagen rasch transformiert werden.
Source: BASF AG Ludwigshafen
(28)

Remark: N,N-Dimethylanilin kann unter Umweltbedingungen als hydrolysebestaendig angesehen werden. In der Atmosphaere kann der Stoff durch Reaktion mit Hydroxylradikalen bei Halbwertszeiten von wenigen Stunden und bei Reaktion mit Ozon oder Salpetersaeure innerhalb von wenigen Tagen rasch transformiert werden.
Source: BASF AG Ludwigshafen
(18)

3.5 Biodegradation

Type: aerobic
Inoculum: other bacteria: BASF-Belebtschlamm, adaptiert
Concentration: 95.5 mg/l related to Test substance
Degradation: = 75 % after 28 day
Method: Directive 84/449/EEC, C.7 "Biotic degradation - modified MITI test"
Year: GLP:
Test substance:
Remark: Abbaugrad bezogen auf BSB/THSB-Verhaeltnis.
Biologische Abbauvorgaenge sind moeglich.
Potentiell biologisch abbaubar.
Source: BASF AG Ludwigshafen
(29)

Type: aerobic
Inoculum: other bacteria: Belebtschlamm, nicht adaptiert/kommunal
Degradation: < 10 % after 28 day
Method: Directive 84/449/EEC, C.7 "Biotic degradation - modified MITI test"
Year: GLP:
Test substance:
Remark: Anfangskonzentration: 50/100/200 mg/l (Testsubstanz)
BSB des CSB
Source: BASF AG Ludwigshafen
(30)

Type: aerobic
Inoculum: activated sludge
Degradation: ca. 65 % after 28 day
Result: readily biodegradable
Method: OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year: 1983 GLP: yes
Test substance:
Source: BASF AG Ludwigshafen
(31)

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Degradation: = 95 % after 28 day
Method: OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year: 1983 GLP: yes
Test substance:
Remark: 95% bioelimination (DOC removal)
Source: BASF AG Ludwigshafen
(31)

Type: aerobic
Inoculum: other bacteria: BASF-Belebtschlamm, adaptiert
Concentration: 95.5 mg/l related to Test substance
Degradation: = 75 % after 28 day
Method: OECD Guide-line 301 F "Ready Biodegradability: Manometric Respirometry Test"
Year: GLP:
Test substance:
Remark: Abbaugrad bezogen auf BSB/THSB-Verhaeltnis.
Biologisch abbaubar.
Source: BASF AG Ludwigshafen
(29)

Type: aerobic
Inoculum: other bacteria: Belebtschlamm, nicht adaptiert/kommunal
Degradation: < 10 % after 28 day
Method: OECD Guide-line 301 F "Ready Biodegradability: Manometric Respirometry Test"
Year: GLP:
Test substance:
Remark: Anfangskonzentration: 50/100/200 mg/l (Testsubstanz)
BSB des CSB
Source: BASF AG Ludwigshafen
(30)

Type: aerobic
Inoculum: other bacteria: Belebtschlamm, adaptiert/industriell
Concentration: 400 mg/l
Degradation: = 100 % after 6 day
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: GLP:
Test substance:
Remark: Einsatzkonzentration bezogen auf TOC
Ergebnis verweist auf Strippen und Adsorption als Eliminationsmechanismus.
Hinweise auf biologische Abbauprozesse sind nicht gegeben.
Konzentration liegt im Bereich der Hemmung der Atmungsaktivitaet des Belebtschlamms.
Source: BASF AG Ludwigshafen
(32)

Type: aerobic
Inoculum: other bacteria: Belebtschlamm, adaptiert/industriell
Concentration: 400 mg/l
Degradation: = 100 % after 6 day
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: GLP:
Test substance:
Remark: Einsatzkonzentration bezogen auf TOC
Ergebnis verweist auf Strippen und Adsorption als Eliminationsmechanismus.
Konzentration liegt im Bereich der Hemmung der Atmungsaktivitaet des Belebtschlamms.
Source: BASF AG Ludwigshafen
(32)

Type: aerobic
Inoculum: other bacteria: adaptiertes Inokulum
Degradation: = 22 % after 5 day
Method: other: BSB-Test (BSB des THSB)
Year: GLP:
Test substance:
Remark: Ausserdem: BSB5 des THSB = 0%; keine Angaben zum Inokulum.
Source: BASF AG Ludwigshafen
(33)

Type: aerobic
Inoculum: other bacteria: adaptiertes Inokulum
Degradation: = 43 % after 5 day
Method: other: BSBx-Bestimmung, DEV H5 DIN 38409, Teil 51, Deutsche Einheitsverfahren zur Wasser-, Abwasser- und Schlammuntersuchung, Bestimmung des biochemischen Sauerstoffbedarfs
Year: GLP:
Test substance:
Remark: BSB des THSB; berechnet aus THSB- und BSB5-Angaben
Source: BASF AG Ludwigshafen

(34)

Type: aerobic
Inoculum: other bacteria: nicht adaptiertes Inokulum
Degradation: < 5 % after 5 day
Method: other: BSBx-Bestimmung, DEV H5 DIN 38409, Teil 51, Deutsche Einheitsverfahren zur Wasser-, Abwasser- und Schlammuntersuchung, Bestimmung des biochemischen Sauerstoffbedarfs
Year: GLP:
Test substance:
Remark: BSB des CSB
Source: BASF AG Ludwigshafen

(30)

Type: aerobic
Inoculum: domestic sewage
Method: other: ETAD 103 (effect on treatment)
Year: 1983 GLP: yes
Test substance:
Remark: Result: IC50 >100 mg/l
Source: BASF AG Ludwigshafen

(31)

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Degradation: = 1.9 % after 14 day
Method: other: MITI-Test (BOD of THOD)
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Concentration of sludge: 30 mg/l

(35)

Type: aerobic
Inoculum: other: microorganisms from the secondary aeration basins of an industrial wastewater treatment plant
Method: other: two different acclimation procedures (enrichment procedure and single-flask procedure) followed by assessing biodegradation by measuring CO2 evolution
Year: GLP:
Test substance:
Remark: Percentage loss of DOC during the single-flask acclimation procedure: not detected/nd/nd/42/60/80/- after 1/2/3/4/5/6/7 days.
Primary and ultimate biodegradation:
Enrichment procedure: 28 (+-16) max.% CO2 evolved after 7 days; 72 (+-49)% chemical remaining.
Single-flask procedure: 78 (+-0.5) max.% CO2 evolved after 7 days; 0.15 (+-0.05)% chemical remaining.
Source: BASF AG Ludwigshafen
Test condition: Single-flask procedure: microorganisms were acclimated for 2 to 7 d in a single acclimation flask at constant or increasing concentrations of the test chemical without transfer of microorganisms.
Enrichment procedure: microorganisms were acclimated in a series of flasks over a 21-d period by making adaptive transfers to increasing concentrations of the test chemical.
(36)

Type: aerobic
Inoculum: other bacteria: Belebtschlamm kommunaler u. industrieller Abwaesser
Concentration: 20 mg/l related to Test substance
Degradation: <= 3 %
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Testergebnis bezogen auf Testzeit von 6 h
(37)

Type: anaerobic
Inoculum: domestic sewage
Method: other: ETAD 103 (effect on treatment NOEL)
Year: 1983 GLP: yes
Test substance:
Remark: Result: 1.0% w/w vss
Source: BASF AG Ludwigshafen
(31)

3.6 BOD5, COD or BOD5/COD Ratio

Method: Directive 84/449/EEC, C.8 "Biodegradation: Biochemical Oxygen Demand"
Year: 1983 GLP: yes
Concentration: 4 mg/l related to Test substance

C O D

Method: Directive 84/449/EEC, C.9 "Biodegradation: Chemical Oxygen Demand"
Year: 1983 GLP:
COD: = 2040 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: < .05

Remark: BOD5 <100 mg/g
Source: BASF AG Ludwigshafen
(31)

Method: other: BSB-Test nach DIN 38409/51

C O D

Method: other: CSB-Test nach DIN 38409/41
COD: = 1880 mg/g substance

R A T I O B O D 5 / C O D

BOD5/COD: ca. .001

Result: BSB5 kleiner 2 mg/g
Source: BASF AG Ludwigshafen
(30)

3.7 Bioaccumulation

Species: Carassius auratus (Fish, fresh water)
Exposure period: 48 hour(s)
Concentration: 808 mg/l
BCF: = 6.8
Elimination:
Method:
Year: GLP:
Test substance:
Remark: Die getesteten Konzentrationen von 80/90/100/200/300 mg/l lagen ueber dem LC50-Wert der Fischart.
Die DMA-Gehalte im Fisch stiegen nicht proportional mit der Konzentration im Wasser an, sondern blieben, sobald die Tiere betaeubt waren, konstant. Erst nach dem Tod stieg die Konzentration in den Fischkoerpern wieder an.
Source: BASF AG Ludwigshafen

(38)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .05 mg/l
BCF: ca. 4.7 - 10.1
Elimination:
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(35)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .5 mg/l
BCF: ca. 5.4 - 13.6
Elimination:
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(35)

Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 48 hour(s)
Concentration: 80 mg/l
BCF: = 8.7
Elimination:
Method:
Year: GLP:
Test substance:
Remark: Die getesteten Konzentrationen von 80/90/100/200/300 mg/l lagen ueber dem LC50-Wert der Fischart.
Die DMA-Gehalte im Fisch stiegen nicht proportional mit der Konzentration im Wasser an, sondern blieben, sobald die Tiere betaeubt waren, konstant. Erst nach dem Tod stieg die Konzentration in den Fischkoerpern wieder an.
Source: BASF AG Ludwigshafen

(38)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .05 mg/l
BCF: ca. 4.7 - 10.1
Elimination:
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(35)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 42 day at 25 degree C
Concentration: .5 mg/l
BCF: ca. 5.4 - 13.6
Elimination:
Method: OECD Guide-line 305 C "Bioaccumulation: Test for the Degree of Bioconcentration in Fish"
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(35)

Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Concentration: 80 mg/l
BCF: = 7.3
Elimination:
Method:
Year: GLP:
Test substance:
Remark: Die getesteten Konzentrationen von 80/90/100/200/300 mg/l lagen zum Teil ueber den LC50-Werten der Fischart.
Die DMA-Gehalte im Fisch stiegen nicht proportional mit der Konzentration im Wasser an, sondern blieben, sobald die Tiere betaeubt waren, konstant. Erst nach dem Tod stieg die Konzentration in den Fischkoerpern wieder an.
Source: BASF AG Ludwigshafen

(38)

Species: other: 3 verschiedene Fischarten
Exposure period:
Concentration:
BCF:
Elimination:
Method:
Year: GLP:
Test substance:
Remark: Fische 3 verschiedener Arten wurden Stoffkonzentrationen ausgesetzt, die einen narkotischen Effekt bewirkten. Anschliessend reduzierte sich die Konzentration an N,N-Dimethylanilin beim Reiskaerpfling nach ca.30 Minuten, beim Goldfisch nach ca.60 Minuten und beim Karpfen nach ca.90 Minuten um 50% (Zahlenwerte aus Graphik abgelesen).
Source: BASF AG Ludwigshafen

(39)

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: flow through
Species: Carassius auratus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 69
Method: other: 25 Grad Celsius
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(40)

Type: flow through
Species: Carassius auratus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 69
SC50 : = 56
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: SC50 is a concentration causing 50% of the test fish to turn sideways in 48 hours.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data
(41)

Type: flow through
Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 69
Method: other: 25 Grad Celsius
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(40)

Type: flow through
Species: Cyprinus sp. (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 69
SC50 : = 56.6
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: SC50 is a concentration causing 50% of the test fish to turn sideways in 48 hours.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data
(41)

Type: flow through
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 78
Method: other: 25 Grad Celsius
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(42)

Type: flow through
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: = 102
Method: other: Japanese Industrial Standard (JIS K 0102-1986-71)
Year: 1986 GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data
(43)

Type: flow through
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 78
SC50 : = 64
Method: other: no data
Year: 1983 GLP: no
Test substance: other TS
Remark: The concentration of the test solution causing 50% of the test fish to turn sideways (still alive) in 48 hours (SC50) was established.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data
(41)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 78.2
Method: other: 23.4 Grad Celsius
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(44)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 52.6
Method: other: 25.3 Grad Celsius
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(44)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: = 65.6
Method: other: Benoit D.A et al. Water Res. 16:457-464
Year: 1982 GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of high purity.
(45)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 78
Method: other: data collected from the multi-volume series "Acute toxicities of organic chemicals to fathead minnow." Centre for Lake Superior Env. Studies, U. of Wisconsin-Superior, Vol. 1-5, 1984 - 1986, 1988, 1990
Year: GLP: no data
Test substance: other TS
Remark: LC50 value was calculated from the original value (0.65 mmol/l) given as a log of inverse the 96 h 50% mortality concentration in mol/l (log LC50 -1).
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >95%
(46)

Type: other: bioaccumulation
Species: Cyprinus carpio (Fish, fresh water)
Exposure period:
Unit: Analytical monitoring: no data
Method: other: Bioaccumulation test of chemical substance in fish and shellfish
Year: 1974 GLP: no
Test substance: other TS
Method: Test method is stipulated in the Japanise Order Prescribing the Items of the Test Relating to the New Chemical Substances (1974). This guideline corresponds to OECD Guideline for Testing Chemicals No 305C (May 12, 1981). Two nominal concentrations of the compound were used for 6 weeks: 0.5 and 0.05 mg/l. Bioconcentration factors established were 5.4 - 13.6 and 4.7 - 10.1, respectively.
Remark: NN-dimethylaniline; no further data
Source: BASF AG Ludwigshafen

Type: semistatic
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 51.1
Method: other: EEC Methods for determination of ecotoxicity C1 Acute toxicity for fish.
Year: 1989 GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline from Fluka; > 99.5% purity

(47)

Type: static
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 33
Method: other: 25 Grad Celsisus
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(48)

Type: static
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 98
Method: other: 25 Grad Celsisus
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(42)

Type: static
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
TLm : = 33
Method: other: Japanese Industrial Standards Committee (JIS K0102) p. 154
Year: 1971 GLP: no
Test substance: other TS
Remark: TLm value of 56 mg/l was established for 24 hours.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data

(49)

Type: static
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC50: = 98
Method: other: no data
Year: GLP: no
Test substance: no data
Method: no data
Source: BASF AG Ludwigshafen

(41)

Type:
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50: 76
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(50)

Type:
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
LC50: = 65.6
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(51)

Type: other
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
NOEC: = .039
LC50: = .183 - .186
LC100: = .242
Method: other: Baumann M. and Sander K. J. Exp. Zool.230:363-374
Year: 1984 GLP: no
Test substance: other TS
Remark: Fertilized zebrafish eggs were treated continuously with up to seven concentrations of NN-dimethylaniline from the 8-cell stage until hatching. The original data were expressed in umol/l and were: 0.33, 1.51 and 2 for NOEC, LC50 and LC100, respectively.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline from Merck; no futher data

(52)

Type: other
Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 72 hour(s)
Unit: Analytical monitoring: no
Method: other: Loeb H.A. and Kelly W.H. New York Fish and Game J. 7:(2) 160
Year: 1960 GLP: no
Test substance: other TS
Remark: NN-dimethylaniline in 3 different doses was placed in one ortwo No 5 gelatin capsules and force-fed to at least 3 fish. No effects were observed at doses of 80, 97 and 136 mg/kg within the 72 hour observation period.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data

(53)

Type: other
Species: Cyprinus sp. (Fish, fresh water)
Exposure period: 24 hour(s)
Unit: µg/l Analytical monitoring: no data
LC50: ca. 10
Method: other: EPA, 1989 and RIZA/BKH AQUATOX
Year: 1989 GLP: no data
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data

(54)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = 8
EC50: = 13
EC100: = 40
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Geprueft mit 100 mg/l Tween 80 als Loesungsvermittler.
(55)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = .8
EC50: = 5
EC100: = 20
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Geprueft mit 100 mg/l Tween 80 als Loesungsvermittler.
(55)

Type:
Species: other aquatic arthropod: Chaetogammarus marinus
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
LC50 : = 85
Method:
Year: GLP:
Test substance:
Remark: LC50(24h)= 85(73-99) mg/l; LC50(48h)= 61(53-71) mg/l;
LC50(96h)= 38(33-44) mg/l; NOEC(96h)= 10 mg/l.
Source: BASF AG Ludwigshafen
(56)

Type:
Species: other aquatic arthropod: Daphnia magna Straus
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = 8
EC50: = 13
EC100: = 40
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Geprueft mit 100 mg/l Tween 80 als Loesungsvermittler.
(55)

Type:
Species: other aquatic arthropod: Daphnia magna Straus
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
EC0: = .8
EC50: = 5
EC100: = 20
Method: Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Geprueft mit 100 mg/l Tween 80 als Loesungsvermittler.
(55)

Type:
Species: other aquatic worm: Tubifex sp.
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
LC50 : = 640 - 1100
Method:
Year: GLP:
Test substance:
Remark: Entweder Mortalitaet der Kontrolltiere >10% oder Anzahl der toten Tiere stieg nicht kontinuierlich mit der Konzentration, sondern zeigte Unregelmaessigkeiten.
LC50(48h)=200-360 mg/l.
Source: BASF AG Ludwigshafen
Test condition: Temperatur 20 Grad C; Laenge der Versuchstiere 3-5 cm
(57)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Agmenellum quadruplicatum (Algae)
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method: other: Wachstumshemmtest
Year: GLP:
Test substance:
Remark: Keine toxische Wirkung bei 1000 ug/disk.
Source: BASF AG Ludwigshafen
(58)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring:
EC10: = 210
EC50: = 340
Method: other: Scenedesmus-Zellvermehrungs-Hemmtest, DIN 38412 Teil 9, Bestimmung der Hemmwirkung von Wasserinhaltsstoffen auf Gruenalgen
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Geprueft mit 100 mg/l Tween 80 als Loesungsvermittler.
(55)

Species: other algae: Cyclotella meneghiniana (marine Algen)
Endpoint:
Exposure period:
Unit: mg/l Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: Bei Zugabe von 5 mg N,N-Dimethylanilin/l erhoehte sich die Initialgeschwindigkeit der Phosphodiesterase im Rohextrakt um 7.8-12.1%. Ein Einfluss auf die alkalische Phosphatase-Aktivitaet war bei stark streuenden Messwerten nicht zu erkennen.
Source: BASF AG Ludwigshafen
(59)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type:
Species: activated sludge, domestic
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring:
EC50: = 100
Method: other: OECD-Richtlinie (01.08.83, Nr.210)
Year: GLP:
Test substance:
Remark: Belebtschlamm einer kommunalen Klaeranlage (Japan)
Source: BASF AG Ludwigshafen
(60)

Type:
Species: Pseudomonas putida (Bacteria)
Exposure period: 16 hour(s)
Unit: mg/l Analytical monitoring:
TGK : > 1050
Method: other: Pseudomonas-Zellvermehrungs-Hemmtest, DIN 38412 Teil 8, zum Gelbdruck verabschiedet, Bestimmung der Hemmwirkung von Wasserinhaltsstoffen auf Bakterien
Year: GLP:
Test substance:
Remark: Keine Hemmwirkung bei einer Konzentration von 1050 mg/l. (1050 mg/l entspricht einer gesaettigten Loesung, hergestellt aus 25 g/l mit anschliessender Filtration.)
Source: BASF AG Ludwigshafen
(61)

Type:
Species: Tetrahymena pyriformis (Protozoa)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC50: = 110
Method: other: Wachstumshemmtest
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: 30 Grad C
(62)

Type:
Species: Tetrahymena pyriformis (Protozoa)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC50: = 110
Method: other: Zellvermehrungshemmtest
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
Test condition: Temperatur 30 Grad C; Anzucht der Organismen bei 30 Grad C unter sterilen Bedingungen in 2%iger Peptonloesung
(62)

Type:
Species: Vibrio fisheri (Bacteria)
Exposure period:
Unit: mg/l Analytical monitoring:
EC50: ca. 61
Method:
Year: GLP:
Test substance:
Remark: Hemmung der Biolumineszenz; Zahlenwert aus Graphik berechnet
Source: BASF AG Ludwigshafen
(63)

Type:
Species: other bacteria: Agmenellum quadruplicatum (Stamm PR 6)
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: Nach einer Expositionsdauer von 3-7 Tagen konnten bei einer maximalen Konzentration von 1000 ug je Petrischale keine Hemmhoefe im Bakterienrasen beobachtet werden.
Source: BASF AG Ludwigshafen
(58)

Type:
Species: other bacteria: BASF-Belebtschlamm
Exposure period: 30 minute(s)
Unit: mg/l Analytical monitoring:
EC50: ca. 650
EC20 : ca. 140
Method: other: Kurzzeitatmungstest
Year: GLP:
Test substance:
Remark: Atmungshemmung
EC80(30 min.) ca.2000 mg/l.
Source: BASF AG Ludwigshafen
(64)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: other
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: no data are available
Source: BASF AG Ludwigshafen

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

Type: other
Species:
Endpoint:
Exposure period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: no data are available
Source: BASF AG Ludwigshafen

4.6.2 Toxicity to Terrestrial Plants

Species:
Endpoint:
Expos. period:
Unit:
Method: other
Year: GLP:
Test substance:
Remark: no data are available
Source: BASF AG Ludwigshafen

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

Species: other
Endpoint:
Expos. period:
Unit:
Method:
Year: GLP:
Test substance:
Remark: no data are available
Source: BASF AG Ludwigshafen

4.7 Biological Effects Monitoring

Remark: no data are available
Source: BASF AG Ludwigshafen

4.8 Biotransformation and Kinetics

Type: animal
Remark: Eine im Cytosol lokalisierte NADPH-abhaengige Monooxygenase aus Trypanosoma cruzi oxidiert N,N-Dimethylanilin zum entsprechenden N-Oxid.
Source: BASF AG Ludwigshafen
(65)

Type: plant
Remark: Aus Polyporus versicolor isolierte Laccase konnte N,N-Dimethylanilin oxidieren.
Source: BASF AG Ludwigshafen
(66)

Type: plant
Remark: Chloroperoxidase des Pilzes Caldariomyces fumago demethyliert N,N-Dimethylanilin zum N-Methylanilin.
Source: BASF AG Ludwigshafen
(67)

Type: plant
Remark: Chloroperoxidase des Pilzes Caldariomyces fumago demethyliert N,N-Dimethylanilin zum N-Methylanilin.
Source: BASF AG Ludwigshafen
(67)

4.9 Additional Remarks

Remark: Weitere Informationen sind dem BUA-Bericht N,N-DIMETHYLANILIN zu entnehmen.
Source: BASF AG Ludwigshafen

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1120 mg/kg bw
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
(68)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1300 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(69)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1410 mg/kg bw
Method: other: Thompson W.R. Use of moving averages and interpolation to estimate median effective dose. Bacteriol. Rev. 11:115 using the tables of Weil (Weil C.S. Biometrics 8:249, 1952)
Year: 1947 GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data
(70) (71) (72) (73)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 700 - 1400 mg/kg bw
Method: other: no data
Year: GLP: yes
Test substance: other TS
Remark: 1300 mg/kg was calculated for male rats, for females LD50 could not be calculated because 100% mortality occured over a very narrow dose range.
NTP study
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, purity >98%.
(74) (75)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1348 mg/kg bw
Method: other: no data
Year: GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.
(75) (73)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: ca. 1170 mg/kg bw
Method: other: BASF test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
(76)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1440 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(69)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1500 mg/kg bw
Method: other: no data
Year: GLP: yes
Test substance: other TS
Remark: LD50s of 1500 mg/kg and 1375 mg/kg were established for males and females, respectively.
NTP study
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, purity >98%.
(77) (75)

Type: LDLo
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 350 mg/kg bw
Method: other: no data
Year: GLP: yes
Test substance: other TS
Remark: NTP study
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, purity >98%.
(77) (71)

Type: other: MetHb formation
Species: cat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 50 mg/kg bw
Method: other: BASF test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Result: Meth-Hb-level was 77.3% after 4 hours and 72.2% after 6 hours. Reversible after 24-30 hours.
Source: BASF AG Ludwigshafen

(78)

Type:
Species: cat
Strain:
Sex:
Number of Animals:
Vehicle:
Value:
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: 50 mm3/kg (50 mg/kg) p.o.: Met-Hb-Spiegel = 77%
Source: BASF AG Ludwigshafen

(79)

Type: other: MetHb formation
Species: dog
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 50 mg/kg bw
Method: other
Year: 1942 GLP: no
Test substance: no data
Remark: Dogs (no other details given) were given 50 mg/kg NN-dimethylaniline by gavage. After 4 hours 20% of the totalblood hemoglobin was metHb. The highest metHb level of 40% was attained after 8 hours; in the 10th hour, it had decreased to 30%.
Source: BASF AG Ludwigshafen

(80)

Type:
Species: dog
Strain:
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: GLP:
Test substance:
Remark: 50 mg/kg per Schlundsonde: erhoehter Methaemoglobinaemie-Spiegel (maximal 40%, gemessen 8 h nach Applikation)
Source: BASF AG Ludwigshafen

(81)

Type: other: mortality
Species: guinea pig
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 2000 mg/kg bw
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: Tremors, tonic and clonic convulsions, deaths due to the respiratory paralysis were observed.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(82)

Type:
Species: guinea pig
Strain:
Sex:
Number of Animals:
Vehicle:
Value:
Method:
Year: GLP:
Test substance:
Remark: Zufuhrweg: p.o. und s.c.: 2000 mg/kg letal
Source: BASF AG Ludwigshafen

(83)

Type: LDLo
Species: human
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 50 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(84)

Type: LDLo
Species: human
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 50 mg/kg bw
Method: other
Year: GLP: no
Test substance: other TS
Remark: No data on symptoms observed
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data
(85) (71) (72)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: > 5.1 mg/l
Method: other: OECD Acute Inhalation Toxicity Protocol
Year: 1981 GLP: yes
Test substance: other TS
Method: Liquid - Aerosol
Remark: At a NN-dimethylaniline concentration of 4900 mg/m3 no mortality was observed; however, 2/5 males died 3 days after exposure and 1/5 females died 3 days and 1/5 females died 4 days after exposure, when rats were exposed to the compound concentration of 4600 mg/m3. Two/five male rats exposed to a concentration of 5100 mg/m3 died on day 3; no mortality was observed among females.

Result:	Geometric Mean Particl.	Nominal Concentr.	Time-weighted Measured	Mortality in 14 days

	+ SD in um	mg/l	mg/l	Males	Females
	4.8+5.1	5.1	1.9	2/5	0/5
	5.2+3.4	4.6	2.0	2/5	2/5
	5.8+3.3	4.9	1.0	0/5	0/5

Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline: no further data.
(75) (86) (87) (88)

Type: LCLo
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: = .25 mg/l
Method: other: no data
Year: 1972 GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline: no further data.
(71) (72) (89)

Type: LCLo
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 30 minute(s)
Value: = .98 - 4.8 mg/l
Method: other
Year: 1978 GLP: no
Test substance: other TS
Remark: Test was performed with the method of the Utah Biomedical Test Laboratory to establish "Immediately dangerous to life or health" values. The aim was to determine test compound concentrations which will produce "no effect", a "minimal effect" and a "frank effect" in exposed animals.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of "commercial technical grade".
(75) (90)

Type: other: IRT
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value:
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Keine Letalitaet nach 8 h Exposition in einer bei 20 Grad C angereicherten Atmosphaere (Dampf).
Source: BASF AG Ludwigshafen
(68)

Type: other: IRT
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value:
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: Keine Letalitaet nach 3 h Exposition in einer bei 100 Grad C angereicherten Atmosphaere (Dampf); Letalitaet nach laengerer Exposition
Source: BASF AG Ludwigshafen
(68)

Type: other: IRT
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value:
Method: other
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Remark: No mortality was observed when 12 rats were exposed for 8 hours to an atmosphere that has been saturated at 20 degrees centigrade with the volatile part of the compound.
Source: BASF AG Ludwigshafen
(76)

Type: other: LDLo
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value: = .25 mg/l
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(91) (92)

Type:
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 4 hour(s)
Value:
Method:
Year: GLP:
Test substance:
Remark:

Partikel-groesse (um)	Kammer (Nominal-) Konz. (mg/l)	gemess.Konz. (mg/l)	Letalitaet
4,8	5,1	1,9	2/10
5,2	4,6	2,0	4/10
5,8	4,9	1,0	0/10

Source: BASF AG Ludwigshafen
(93) (94) (95)

Type:
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 30 minute(s)
Value:
Method:
Year: GLP:
Test substance:
Remark: 0,98; 4,8 mg/l: keine irreversiblen Schaeden.
Source: BASF AG Ludwigshafen
(96)

Type:
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 4 hour(s)
Value:
Method:
Year: GLP:
Test substance:
Remark: Schwellenwert fuer Met-Hb-Bildung bei 0,25 mg/l
Source: BASF AG Ludwigshafen
(97)

Type: LCLo
Species: guinea pig
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 30 minute(s)
Value: = .98 - 4.8 mg/l
Method: other: no data
Year: 1978 GLP: no
Test substance: other TS
Remark: Test was performed with the method of the Utah Biomedical Test Laboratory to establish "Immediately dangerous to life or health" values. The aim was to determine test compound concentrations which will produce "no effect", a "minimal effect" and a "frank effect" in exposed animals.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of "commercial technical grade".
(75) (90)

Type:
Species: guinea pig
Strain:
Sex:
Number of
Animals:
Vehicle:
Exposure time: 30 minute(s)
Value:
Method:
Year: GLP:
Test substance:
Remark: 0,98; 4,8 mg/l: keine irreversiblen Schaeden
Source: BASF AG Ludwigshafen
(96)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1770 mg/kg bw
Method: other: Draize J.H. et al. J. Pharmacol. Exp. Therap. 82: 377
Year: 1944 GLP: no
Test substance: no data
Source: BASF AG Ludwigshafen
(98) (71) (72) (73)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 960 mg/kg bw
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
(68)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: ca. 1000 mg/kg bw
Method: other: BASF test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen

Type: other: MetHb formation
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 60 mg/kg bw
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: The highest metHb level in blood (22.9%) was measured 30 minutes post-exposure; after 90 minutes it had dropped to 10.1 % and after 150 minutes to 2.7%. Sulfhemoglobin could not be detected.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, no further data.
(99)

Type: other: MetHb formation
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value:
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: When mice were injected (i.p.) with 65 mg/kg NN-dimethylaniline for 3 days, 1.8 % metHb and 2.0 % sulfhemoblobin were found 48 hours after the last dose.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, no further data.
(99)

Type: other: metHb formation
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value:
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: When a single dose (39 mg/kg) of NN-dimetylaniline was administered to Sprague-Dawley rats the maximum level of metHb induced was 2.9%
Source: BASF AG Ludwigshafen

Test substance: NN-dimethylaniline, no further data.

(100)

Type:
Species: mouse
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: i.p.
Value:
Method:
Year: GLP:
Test substance:
Remark: 60 mg/kg: erhoehter Methaemoglobinaemie-Spiegel (maximal 23%, gemessen 30 min nach Applikation)
Source: BASF AG Ludwigshafen

(101)

Type: LD100
Species: guinea pig
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: s.c.
Value: = 2000 mg/kg bw
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: Tremors, tonic and clonic convulsions, deaths due to the respiratory paralysis were observed.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, no further data.

(82)

Type: LDLo
Species: rat
Strain:
Sex:
Number of
Animals:
Vehicle:
Route of admin.: s.c.
Value: = 100 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(102)

Type: LDLo
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: = 100 mg/kg bw
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: Russian study, no further informations given.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, no further data.

(103) (70)

Type: other: MetHb formation
Species: dog
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value:
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: A dog weighing 15 kg was injected s.c. on days 1 and 3 with 1.5 g NN-dimethylaniline in 15 ml of water. After the first dose, anorexia and lethargy developed; after the second dose, extensive vomiting, salivation and severe general weakness were observed. The cyanosis and marked metHb formation observed 3 hours after each injection had regressed 24 hours later. In addition, the number of erythrocytes increased during the study from 5.1 million to 9.6 million.
Source: BASF AG Ludwigshafen
Test substance: Hydrochloride salt of NN-dimethylaniline.

(104)

Type: other: skin irritation
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value:
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: A depot of 0.2, 0.4 or 1.0 ml of a 3% NN-dimethylaniline in olive oil was injected under the ear skin of 8 rabbits. After a few days the only finding was slight redness without marked inflammation. Microscopic examination revealed only insignificant thickening of the epithelium.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(105)

Type:
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value:
Method:
Year: GLP:
Test substance:
Remark: (Ohr), 0,2-1,0 ml einer 3%igen Loesung in Olivenoel: nach wenigen Tagen leichte Roetung.
Source: BASF AG Ludwigshafen

(106)

Type:
Species: cat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.v.
Value:
Method:
Year: GLP:
Test substance:
Remark: 24 mg/kg: Ueber einen Zeitraum von 2 Stunden erhoehter Methaemoglobinaemie-Spiegel von 30%; Maximalwert nach 3 Stunden
Source: BASF AG Ludwigshafen

(107)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: irritating
EC classificat.:
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
(68)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: irritating
EC classificat.:
Method: other: Smyth Carpenter
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(91) (108)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: irritating
EC classificat.:
Method: other: Methode: 500 mg/ 24 h
Year: GLP:
Test substance:
Remark: Sekundaerzitat ohne weitere Angaben; der Effekt wird als "mild" bezeichnet
Source: BASF AG Ludwigshafen
(109)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: irritating
EC classificat.:
Method: other
Year: GLP: no
Test substance: other TS
Remark: Primary skin irritation on rabbits was recorded on a 10-grade ordinal series and was based upon the severest reaction that developed on the clipped skin of belly of each of five albino rabbits within 24 hours of the uncovered application of 0.01 ml undiluted sample. Grade 1 indicates no irritation, grade 6 indicates necrosis when undiluted. Skin irritation properties of NN-dimethylaniline was estimated as grade 3.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(71) (73)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: slightly irritating
EC classificat.:
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: RTECS data
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further information given.

(110)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: irritating
EC classificat.: irritating
Method: other: BASF test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
(76)

Species: guinea pig
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: irritating
EC classificat.:
Method: Draize Test
Year: GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.
(111)

Species: human
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: not irritating
EC classificat.:
Method: other: no data
Year: GLP: no
Test substance: other TS
Method: Approximately 0.1 g of petrolatum containing 0.6% NN-dimethylaniline was applied to a 1.5 square inch "Band-Aid" Sheer patch and applied to the backs of 5 male human subjects for 24 hours. At 24 hours the patches were removed, the area wiped with a paper towel and reactions observed. Observations were also made at 48 and 72 hours.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.
(112)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.:
Method: other: Smyth Carpenter
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(108)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.:
Method: other: Methode: 20 mg/ 24 h
Year: GLP:
Test substance:
Remark: Sekundaerzitat ohne weitere Angaben; der Effekt wird als "moderate" bezeichnet
Source: BASF AG Ludwigshafen
(109)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: not irritating
EC classificat.:
Method: other: BASF-Test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG Ludwigshafen
(68)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.:
Method: other: Carpenter C.P. and Smyth Jr H.F. Am. J. Ophtal. 29:1363
Year: 1946 GLP: no
Test substance: other TS
Method: Eye irritation in rabbits was recorded in a 10-grade ordinal series and was based upon the degree of corneal necrosis that results from instillation of various volumes and concentrations of chemical. Grade 1 indicated at most a very small area of necrosis resulting from 0.5 ml of undiluted chemical in the eye. Grade 5 indicated a severe burn from 0.005 ml.
Corneal injury caused by NN-dimethylaniline in rabbits was estimated as grade 5.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(73)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: moderately irritating
EC classificat.:
Method: other: no data
Year: GLP: no
Test substance: other TS
Remark: RTECS data.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(110)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.: irritating
Method: other: BASF test
Year: GLP: no
Test substance: as prescribed by 1.1 - 1.4

Source: BASF AG Ludwigshafen

(76)

5.3 Sensitization

-

5.4 Repeated Dose Toxicity

Species: rat Sex: male
Strain: no data
Route of admin.: inhalation
Exposure period: 4 Monate
Frequency of treatment: 5 Std./Tag; 6 Tage/Woche
Post. obs. period: keine Angaben
Doses: 0,011; 0,001 mg/l
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Result: Im Vordergrund standen haematotoxische Effekte: Anaemie sowie Methaemoglobinanstieg gegen Versuchsende auf 12% in der oberen, bzw. auf 5,5% in der unteren Dosisgruppe. Die beobachtete Beeinflussung der Katalase und Peroxidase der roten Blutzellen in der 0,011 mg/l-Gruppe wird methodisch nicht praezise beschrieben und erscheint in ihrem Aussagegehalt nicht eindeutig. Auch die Interpretation der Ergebnisse der zu Ende der Studie durchgefuehrten Untersuchungen (u.a. Thymoltruebungstest bzw. Hyper-gamma-globulinaemie) als Nachweis einer Leberfunktionsstoerung erscheint fraglich. Klinische Parameter, wie Symptomatik, Koerpergewicht, Futterverzehr sind ebensowenig beschrieben, wie eine pathologische Begutachtung.
Source: BASF AG Ludwigshafen

(92)

Species: rat Sex: male
Strain: no data
Route of admin.: inhalation
Exposure period: 100 Tage
Frequency of treatment: kontinuierlich
Post. obs. period: keine Angaben zur Zeitdauer
Doses: 0,0000055; 0,0004; 0,0003 mg/l
Control Group: other: Luft
NOAEL: .000006 mg/l
Method:
Year: GLP:
Test substance:
Result: Bei einer Dosierung von 0,0003 mg/l wurde ein erhoehter Methaemoglobin-Spiegel beobachtet (max. 22%). In der zweiten Versuchshaelfte wurden vereinzelt Heinzkoerperchen gefunden, daneben Retikulozytose und Leukopenie. Aus einem pathologischen Bromsulphthalein-Test, einer Abnahme des Gesamteiweisses mit Veraenderungen im Verhaeltnis der einzelnen Eiweissfraktionen sowie der Senkung des SH-Gruppen-Spiegels im Serum schliessen die Autoren auf eine Leberfunktionsstoerung. Bei der histochem. Untersuchung der Milz fand sich eine Zunahme des Haemosiderins. Histologische Veraenderungen fanden sich in Gehirn, Leber und Lunge. Zur klin. Symptomatik finden sich keine Angaben. Die in einer Nachbeobachtungsphase (Zeitdauer nicht angegeben) durchgefuehrten Untersuchungen ergaben eine "Normalisierung bei der Mehrzahl der Werte" (keine naehren Angaben). Die Interpretation der geschilderten Befunde ist aufgrund fehlender Informationen zur Untersuchungsmethodik sowie aufgrund rein qualitativer Angaben nicht moeglich.
Source: BASF AG Ludwigshafen

(113)

Species: rat Sex: male
Strain: no data
Route of admin.: inhalation
Exposure period: 100 days
Frequency of treatment: daily, for 24 hours
Post. obs. period: not stated
Doses: 0.000005 or 0.0003 mg/l
Control Group: no data specified
NOAEL: = .000005 mg/l
LOAEL: = .0003 mg/l
Method: other
Year: GLP: no
Test substance: other TS
Method: Male white rats (strain not specified) were exposed to NN-dimethylaniline for 24 hours for 100 days (12 weeks?), then observed for the recovery for unspecified period (2 weeks?).
Remark: No adverse effects were found in rats exposed to

NN-dimethylaniline at a concentration of 0.005 mg/m3. At a higher concentration of 0.3 mg/m3 the following symptoms were observed: increased metHb concentration (maximum of 22%), reduced erythrocyte number and Hb concentration, reticulocytosis, leukopenia, hypoproteinaemia, reduced concentration of SH groups in blood serum, accumulation of pyruvic acid in the liver, chromatolysis in brain cells, increased excretion of coproporphyrin in urine and reduced level of ascorbic acid in the adrenals. There were changes in the chronaxial ratios of the antagonistic muscle observed.
Russian publication. Protocol differs from the international standards; methods are not sufficiently described, no information on clinical observations. In the author's opinion, most of the adverse effects observed were reversible during recovery period.

Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(114)

Species: rat Sex: male
Strain: no data
Route of admin.: inhalation
Exposure period: 4 months
Frequency of treatment: 5 hours daily, 6 days per week
Post. obs. period: not stated
Doses: 1.1 or 10.7 mg/m3 (0.0011 or 0.0107 mg/l)
Control Group: yes
Method: other
Year: GLP: no
Test substance: other TS
Method: Fifteen white male rats (strain not specified) in each group, including controls, were used. There is no data on clinical observation and description of methods used. No information is given, if animals were observed for the reversibility of changes.
Remark: Russian publication. Quality of data is poor, because many important informations are lacking.
Towards the end of the exposure period, the metHb level in animals of the high dose group increased to 11.6%, the total Hb level decreased by 8.8% and the number of erythrocytes decreased to 5 415 000/mm3 (in controls = 6000000/mm3). The blood catalase activity was reduced by almost one half while peroxidase activity increased by about 25%. At the end of the exposure period, liver function disorders (higher thymol score, dysproteinaemia and lower level of vit. C). In the first month of exposure only, the coproporphyrin level in urine was increased slightly. In addition, hyperplasia of lymphatic tissue in the spleen were found.
In animals exposed to NN-dimethylaniline in concentration of1.1 mg/m3, similar changes were observed but of much lower intensity. The metHb level in the blood increased to 5.6% by the end of the exposure period; however, the total Hb

level decreased by 13.1%.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(89)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 2 Wochen
Frequency of treatment: 5 Tage/Woche
Post. obs. period: keine Angaben
Doses: 94; 188; 375; 750; 1500 mg/kg in Maisoel
Control Group: yes, concurrent vehicle
Method:
Year: GLP:
Test substance:
Result: Es handelt sich um Range-finding-Versuche fuer eine anschliessende Kanzerisierungsstudie. Pro Dosisgruppe wurden 10 Tiere eingesetzt.
In der obersten Dosisgruppe starben alle Tiere innerhalb von 3 Tagen; die zweithoechste Dosierung ueberlebte nur ein maennliches Tier. In den 3 unteren Dosisgruppen kam es zu keinen Todesfaellen. Dosisabhaengig zeigten diese Tiere Splenomegalien; ab einer Dosis von 375 mg/kg wurde eine verminderte Koerpergewichtsentwicklung beobachtet. Bei 6 von 10 Tieren, die einer Dosis von 375 mg/kg ausgesetzt waren, fand sich eine extramedullaere Blutbildung und Haemosiderose der Milz. Klinisch waren Zyanose, Lethargie und Tremor auffaellig.
Source: BASF AG Ludwigshafen

(69)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 13 Wochen
Frequency of treatment: 5 Tage/Woche
Post. obs. period: keine Angaben
Doses: 32; 63; 125; 250; 500 mg/kg jw. geloest in 10 ml/kg Maiskeimoel
Control Group: yes, concurrent vehicle
NOAEL: < 32 mg/kg
Method:
Year: GLP:
Test substance:
Result: Es handelt sich um Range-finding-Versuche fuer eine anschliessende Kanzerisierungsstudie. Pro Dosisgruppe wurden 10 Tiere eingesetzt. Keine substanzbedingte Mortalitaet. Das Koerpergewicht der maennl. Tiere der beiden obersten Dosisgruppen war gegenueber den Kontrollen um 15 bzw. 27% erniedrigt. Bei allen Tieren war ab einer

Dosis von 125 mg/kg eine Abnahme der motorisschen Aktivitaet zu beobachten. Tiere der beiden hoechsten Dosisgruppen zeigten Zyanose; Splenomegalien fanden sich dosisabhaengig bei Tieren aller Gruppen. Histologisch zeigten beinahe alle Tiere Haemosiderose und Haematopoese in der Milz sowie - dosisabhaengig - Haemosiderinablagerungen in Leber (ab 63 mg/kg), Niere und Hoden. Weiterhin fand sich - ab einer Dosierung von 63 mg/kg - eine Knochenmarkshyperplasie. Nach Ansicht der Autoren sind Splenomegalie und die genannten histopathologischen Befunde eine Sekundaerfolge der toxischen Wirkung von N,N-Dimethyl-anilin auf Erythrozyten mit intravaskulaerer Haemolyse und gesteigertem Erythrozytenabbau.

Source: BASF AG Ludwigshafen

(115) (116) (69)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 14 days
Frequency of treatment: daily
Post. obs. period: no data
Doses: 93.75, 187.5, 375, 750 or 1500 mg/kg/day in corn oil.
Control Group: yes, concurrent vehicle
NOAEL: < 93.75 mg/kg
Method: other
Year: GLP: yes
Test substance: other TS
Method: NTP study comparable to guideline study.
Remark: Five males and 5 females were used in each group. All animals survived doses of 93.75 to 375 mg/kg; all animals, apart from one male, died 6 days after a dose of 750 mg/kg and all animals died at the highest dose after 3 days. Symptoms observed were: cyanosis, lethargy, slight tremor, diarrhea, discharge from nose and eyes. Splenomegaly was observed in 2 males and 1 female dosed with 93.75 mg/kg, in all animals apart from 1 female in the 187.5 mg/kg dose group, and in all animals in group given 375 mg/kg. One surviving male rat in the group given 750 mg/kg also showed splenomegaly. Extramedullary haematopoiesis and hemosiderosis were observed in the spleen of 3 males and 3 females given the dose of 375 mg/kg.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.

(117)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 13 weeks
Frequency of treatment: 5 days/week
Post. obs. period: no data
Doses: 31.25, 62.5, 125, 250 or 500 mg/kg dissolved in 5 ml corn oil/kg
Control Group: yes, concurrent vehicle
NOAEL: < 31.25 mg/kg
Method: other
Year: GLP: yes
Test substance: other TS
Method: NTP study, comparable to guideline study.
Remark: Ten males and 10 females were used in each group. No compound-related mortality was noted. A significant decrease in body weight gain was observed in male rats at 250 and 500 mg/kg. Cyanosis was seen in rats of these two groups. Animals with splenomegaly were found in all dose groups. Bone marrow hyperplasia and increased hematopoiesis in the spleen occured. The severity of these lesions was dose-related.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.

(118) (117)

Species: rat Sex: no data
Strain: no data
Route of admin.: dermal
Exposure period: 10 Tage
Frequency of treatment: keine Angabe
Post. obs. period: nicht angegeben
Doses: nicht angegeben
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Result: Im Resorptionsversuch an der Schwanzhaut der Ratte wurde eine ausgepraegte Resorption von Dimethylanilin durch die Haut hindurch beobachtet. Es traten Todesfaelle auf. Die toedliche Dosis laesst sich jedoch in diesem Versuchsmodell nicht quantifizieren; Methodik bzw. Details der Versuchsdurchfuehrung - z.B. Pinselung oder Tauchversuch - werden nicht beschrieben. Anaemie mit Methaemoglobinaemie-Bildung (bis 30%) waren die herausragenden Effekte.
Source: BASF AG Ludwigshafen

(92)

Species: rat Sex: no data
Strain: no data
Route of admin.: dermal
Exposure period: 10 days
Frequency of treatment: daily
Post. obs. period: no data
Doses: undiluted compound, amount not given
Control Group: no data specified
Method: other
Year: GLP: no
Test substance: other TS
Remark: It was found that during application of undiluted NN-dimethylaniline to the rat tail for 10 days, 62.5 % (5/8) of exposed rats died between day 2 and 10. In surviving animals, body weight was significantly lower than that of controls; methemoglobinemia (29.6 %), reduced Hb (47.8 %), erythropenia and reticulosis were also observed. Russian publication; data of poor quality.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, no further data.

(89)

Species: rat Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 10 Tage
Frequency of treatment: taeglich
Post. obs. period: nicht angegeben
Doses: 100 mg/kg/d
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Result: Methaemoglobinaemie-Bildung, Erniedrigung des Haemoglobin-Gehaltes sowie der Erythrozyten-Zahl, Heinzkoerper-Bildung sowie andere Effekte auf Serum- und Harnparameter (z.B. Urobilinurie). Aus Dysproteinaemie und positivem Thymoltruebungstest schliessen die Autoren auf eine Leberschaedigung. Nebennieren und Milz waren hypertrophisch, die Milzgewichte erhoeht.
Source: BASF AG Ludwigshafen

(92)

Species: rat Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 10 days
Frequency of treatment: daily
Post. obs. period: no data
Doses: 0.1 g/kg/day
Control Group: no data specified
Method: other
Year: GLP: no
Test substance: other TS
Remark: Methemoglobinaemia, a decrease in total Hb, a decrease in the number of erythrocytes, and reticulocytosis were found. Blood catalase activity was reduced while peroxidase activity increased. Liver function disorders expressed by increased thymol score, dysproteinemia and a lower vit. C level.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(89)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: gavage
Exposure period: 2 Wochen
Frequency of treatment: 5 Tage/Woche
Post. obs. period: keine Angaben
Doses: 94; 188; 375; 750; 1500 mg/kg in Maisoel
Control Group: yes, concurrent vehicle
NOAEL: 94 mg/kg
Method:
Year: GLP:
Test substance:
Result: Es handelt sich um Range-finding-Versuche fuer eine anschliessende Kanzerisierungsstudie. Pro Dosisgruppe wurden 10 Tiere eingesetzt.
In den beiden obersten Dosisgruppen starben alle Tiere innerhalb von 3 bzw. 12 Tagen, in den anderen Dosisgruppen kam es zu keinen Todesfaellen. 1 Tier in der 188 mg/kg-Gruppe sowie 5 Tiere unter einer Dosierung von 375 mg/kg zeigten Splenomegalie. Ferner fand sich bei 3 weiblichen Tieren der letztgenannten Gruppe extra-medullaere Blutbildung und Haemosiderose in der Milz. Klinisch waren Lethargie und Tremor auffaellig.
Source: BASF AG Ludwigshafen

(69)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: gavage
Exposure period: 13 Wochen
Frequency of treatment: 5 Tage/Woche
Post. obs. period: keine Angaben
Doses: 32; 63; 125; 250; 500 mg/kg jw.geloest in 10 ml/kg Maiskeimoel
Control Group: yes, concurrent vehicle
NOAEL: 32 mg/kg
Method:
Year: GLP:
Test substance:
Result: Es handelt sich um Range-finding-Versuche fuer eine anschliessende Kanzerisierungsstudie. Pro Dosisgruppe wurden 10 maennliche und weibliche Tiere eingesetzt. Keine substanzbedingte Mortalitaet. Das Koerpergewicht aller behandelten maennlichen Tiere war gegenueber den Kontrollen vermindert. Bei allen Tieren - mit Ausnahme der weiblichen Tiere in den beiden niedrigen Dosierungen - war eine Abnahme der motorischen Aktivitaet zu beobachten. Splenomegalien fanden sich - dosisabhaengig - bei Tieren aller Dosisgruppen. Histologisch zeigte sich - ebenfalls dosisabhaengig ab 63 mg/kg - Haemosider- ose und Haematopoese in Milz und Leber sowie - ab einer Dosis von 250 mg/kg - Haemosiderinablagerungen in der Niere. Nach Ansicht der Autoren sind Splenomegalie und die genannten histopatholog- ischen Befunde eine Sekundaerfolge der tox. Wirkung von N,N-Dimethylanilin auf Erythrozyten mit intravaskulaerer Haemolyse und gesteigertem Erythrozytenabbau.
Source: BASF AG Ludwigshafen
(119) (120) (121)

Species: mouse Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: 8 Tage
Frequency of treatment: taeglich
Post. obs. period: 8 Tage
Doses: 365; 725; 1455; 2910; 5815 mg/kg; jw. in 5 ml/kg Maisoel
Control Group: yes, concurrent vehicle
NOAEL: < 365 mg/kg
Method:
Year: GLP:
Test substance:
Result: Es handelt sich um eine Range-finding Studie fuer einen anschliessenden Screening-Versuch zur Reproduktionstoxizitaet. Die Versuchsgruppen umfassten jeweils 10 Tiere.
Die 3 hoechsten Dosierungen waren fuer alle Tiere nach 1 (5815 mg/kg), 2 (2910 mg/kg) bzw. 4 Tagen (1455 mg/kg) letal. In der 725 mg/kg-Gruppe ueberlebten 3/10 Tiere, in

der untersten Dosisgruppe 6/10 Tiere. In allen Dosisgruppen zeigte ein Grossteil der Tiere ab dem 2.Behandlungstag Erschoepfung, Lethargie und Tremor. In der Nachbeobachtungsphase waren die Tiere klinisch unauffaellig. Die Koerpergewichtsentwicklung war mit derjenigen der Kontrolltiere vergleichbar. Eine Sektion der Tiere wurde nicht durchgefuehrt.

Source: BASF AG Ludwigshafen

(122) (123) (124) (125)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: gavage
Exposure period: 15 days
Frequency of treatment: daily
Post. obs. period: no data
Doses: 93.75, 187.5, 375, 750 and 1500 mg/kg/day in corn oil.
Control Group: yes, concurrent vehicle
NOAEL: = 93.75 mg/kg bw
LOAEL: = 187.5 mg/kg bw
Method: other
Year: GLP: yes
Test substance: other TS
Method: NTP study, comparable to OECD guideline 407.
Remark: Five males and 5 females were used in each group, except that the dose of 187.5 mg/kg/day was given to 4 males. The doses of 93.75, 187.5 and 375 mg/kg were survived by all animals. In groups given higher doses (750 and 1500 mg/kg), all animals died after 12 days and 3 days, respectively. Symptoms observed were: lethargy, marked salivation and tremor. Splenomegaly was observed in 1 male dosed with 187.5 mg/kg and in 2 males and 3 females given the dose of 375 mg/kg. Haematoma and extramedullary haematopoiesis or haemosiderosis were observed in 3 males and 3 females in the group given 375 mg/kg.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.

(117)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: gavage
Exposure period: 13 weeks
Frequency of treatment: 5 days/week
Post. obs. period: no data
Doses: 31.25, 62.5, 125, 250 or 500 mg/kg in 10 ml corn oil/kg;
Control Group: yes, concurrent vehicle
NOAEL: = 31.25 mg/kg
LOAEL: = 62.5 mg/kg
Method: other
Year: GLP: yes
Test substance: other TS
Method: NTP study, comparable to guideline study.
Remark: Ten males and 10 females were used in each group. No substance-related mortality was demonstrated. The final mean body weight of male and female mice were within 12% of those of vehicle controls. Compound-related clinical signs included lethargy and salivation. Splenomegaly was observed in all dose groups; the severity was dose related, although reported to be minimal in 4/10 mice at the 31.25 mg/kg/day dose level. Extramedullary hematopoiesis and hemosiderosis occured in the spleen of dosed mice. The severity of these lesions was dose-related, although reported to be mild in 1/10 mice at the 31.25 mg/kg/day dose level.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.

(118) (126) (117)

Species: mouse Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: 8 days
Frequency of treatment: daily
Post. obs. period: 8 days
Doses: 365, 725, 1455, 2910 or 5815 mg/kg in corn oil
Control Group: yes, concurrent vehicle
Method: other: no data
Year: GLP: no data
Test substance: other TS
Remark: Ten animals were used in each group. The 365 mg/kg dose was survived by 7/9 animals (1 animal died due to dosing error), 725 mg/kg by 3/10. In groups given higher doses, all animals died on exposure days 4, 2 or 1, respectively. The symptoms of intoxication which appeared with increasing dose in all animals during the exposure period included lethargy, exhaustion, tremor and ataxia. The body weights of survivors were only minimally reduced at the end of the observation period.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, no further data.

The undiluted NN-dimethylaniline was used for the group given 5815 mg/kg.

(75) (127)

Species: mouse Sex: no data
Strain: no data
Route of admin.: i.p.
Exposure period: 3 Tage
Frequency of treatment: taeglich
Post. obs. period: 48 Stunden
Doses: 60 mg/kg
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Result: 48 Stunden nach der letzten Applikation wurde ein Methaemoglobinaemie-Spiegel von 1,8% sowie 2,0% Sulfhaemoglobin im Blut gemessen (Kontrollen: 0,9% Met-Hb; 0,1% S-Hb)
Source: BASF AG Ludwigshafen

(101)

Species: dog Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 3 Tage
Frequency of treatment: am 1. und am 3. Tag
Post. obs. period: keine Angaben
Doses: 1500 mg (100 mg/kg) als salzsaures Salz in 15 ml Wasser
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Result: Nach der ersten Gabe zeigte das Tier Fressunlust und Lethargie, nach der zweiten Applikation starkes Erbrechen, Speichelfluss und Erschoepfung. Jeweils 3 Stunden post injectionem war eine Zyanose der Schleimhaeute und eine starke Methaemoglobinaemie-Bildung auffaellig, die nach 24 Stunden abgeklungen war.
Source: BASF AG Ludwigshafen

(128)

Species: guinea pig Sex: male
Strain: no data
Route of admin.: s.c.
Exposure period: 12 Monate
Frequency of treatment: 6 Tage/Woche
Post. obs. period: keine Angaben
Doses: 0,2 ml einer 2%igen Loesg. von DMA in Olivenoel(ca.10mg/kg/Appl.)
Control Group: yes, concurrent vehicle
Method:
Year: GLP:
Test substance:
Result: Der Versuch wurde mit 6 Tieren durchgefuehrt. 4 Tiere verendeten nach 36, 63, 84 bzw. 389 Tagen. Die Koerpergewichtszunahme war verzoegert. Ab dem 50. Tag zeigte sich eine Abnahme der Erythrozytenzahl; die Retikulozytenzahl stieg bis zum 140. Tag an, um danach wieder abzufallen. Ferner fand sich eine Hyperaemie und truebe Schwellung parenchymatoeser Organe, sowie eine hyperaemische und verdickte Harnblasenwand. Ein Tier zeigte bronchiale Metaplasie.
Source: BASF AG Ludwigshafen

(129)

Species: guinea pig Sex: male
Strain: no data
Route of admin.: s.c.
Exposure period: over a year (> 389 days, exact duration not given)
Frequency of treatment: once a day, 6 days a week
Post. obs. period: no data
Doses: 1.3 to 5.3 mg/kg
Control Group: yes, concurrent vehicle
Method: other
Year: GLP: no
Test substance: other TS
Remark: To six animals 0.1 to 0.2 ml of NN-dimethylaniline were given s.c. as a 1 to 2 % olive-oil solutions.
Four out of 6 animals died after 36 to 389 days. At the early stage of the experiment, a weight gain was hampered and followed by a gradual increase. The number of erythrocytes showed a trend of gradual decrease after the 50th day. The number of reticulocytes showed an increasing trend which peaked between the 110th and the 140th day and gradually decreased to the level observed at the beginning of the experiment. Hyperemia and cloudy swelling of parenchmatous organs, as well as hyperemia and slight thickening of the wall of the urinary bladder were observed. Metaplasia in the epithelium of bronchi was found in one animal administered NN-dimethylaniline for 389 days.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(130)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration: up to 333 ug/plate (in DMS0)
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: yes
Test substance: other TS
Remark: NTP study.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.
(131) (132) (133) (117) (134)

Type: Ames test
System of testing: Salmonella typhimurium TA 98
Concentration: up to 0.05 mg/plate
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other: Ames B.N. et al. Mutat. Res. 31:347-364
Year: 1975 GLP: no data
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.
(135)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1538
Concentration: up to 5000 ug/plate
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: Ames B.N. et al. Mutat. Res. 31:347-364
Year: 1975 GLP: no
Test substance: other TS
Remark: Positive in TA 98 with norharman.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.
(136)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration: 0.121 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Ames B.N. et al. Mutat.Res. 31:347-364
Year: 1975 GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline od reagent grade.

(137)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100
Concentration: up to 70 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Maron D.M. and Ames B.N. Mutat. Res. 113:173-215
Year: 1983 GLP: no data
Test substance: other TS
Remark: Preincubation test, S9 of male rats and male hamsters.
Source: BASF AG Ludwigshafen
Test substance: Purity of 99%.

(138)

Type: Ames test
System of testing: Salmonella typhimurium
Concentration: no data
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: no data
Year: GLP: no data
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.

(139)

Type: Ames test
System of testing: Salmonella thyphimurium; TA98
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP:
Test substance:
Remark: Sekundaerzitat; in der zitierten Originalliteratur finden sich keine Angaben zum N,N-Dimethylanilin
Source: BASF AG Ludwigshafen

(140)

Type: Ames test
System of testing: Salmonella typhimurium
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(141)

Type: Ames test
System of testing: Salmonella typhimurium; TA98 TA100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen

(142)

Type: Ames test
System of testing: Salmonella typhimurium; TA98 TA100 TA1535 TA1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(143) (144)

Type: Ames test
System of testing: Salmonella typhimurium; TA98 TA100 TA1535 TA1537 TA1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(145)

Type: Ames test
System of testing: Salmonella typhimurium TA98 TA100 TA1535 TA1537 TA1538, TA97, TA2637
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method:
Year: GLP:
Test substance:
Remark: Testverfahren: modifizierter Ames-Test
Ergebnis: positiv (nur nach Zusatz von Norhaman bei TA98, sonst negativ)
Source: BASF AG Ludwigshafen
(146) (147)

Type: Bacterial reverse mutation assay
System of testing: E. coli; WP2uvrA and WP2uvrA/pKM
Concentration: up to 5000 ug/plate
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: no data
Year: GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: N,N-dimethyl aniline
(136)

Type: Mouse lymphoma assay
System of testing: L5178Y mouse lymphoma cells
Concentration: 192-576 ug/ml (without S9-Mix), 9.6-57.6 ug/ml (with S9-Mix)
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: according to Clive et al., 1979 and Myhr, 1985
Year: GLP: yes
Test substance: other TS
Remark: NTP study. Original values 200-600 nl/ml and 10-60 nl/ml, repectively. Positiv at concentrations higher 384 ug/ml without S9 and 19.2 ug/ml with S9.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline, purity >98%.
(148) (117) (75)

Type: Mouse lymphoma assay
System of testing: L5178Y
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(149)

Type: Sister chromatid exchange assay
System of testing: Chinese hamster ovary cells
Concentration: up to 1010 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: no data
Year: GLP: yes
Test substance: other TS
Remark: NTP study.
Result: Negative without S9; positive with S9.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.
(150) (151) (117) (152)

Type: Sister chromatid exchange assay
System of testing: CHO-Zellen
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP:
Test substance:
Remark: Ergebnis: positiv (ohne metabolische Aktivierung: negativ)
Source: BASF AG Ludwigshafen
(153) (154)

Type: Unscheduled DNA synthesis
System of testing: primary cultured rat hepatocytes
Concentration: up to 0.12 mg/ml
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other: Williams G.M. Cancer Res. 37:1845-1851
Year: 1977 GLP: no
Test substance: other TS
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.
(155)

Type: Unscheduled DNA synthesis
System of testing: Ratten-Hepatozyten
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(156)

Type: other: Chromosomenanalyse
System of testing: CHO-Zellen
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP:
Test substance:
Source: BASF AG Ludwigshafen
(153) (154)

Type: other: Chromosomal abberations
System of testing: Chinese hamster ovary cells
Concentration: up to 1010 ug/ml
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: no data
Year: GLP: yes
Test substance: other TS
Remark: NTP study.
Result: Without S9 mix: positive in the highest dose only.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.
(150) (151) (117) (75) (152)

Type: other: micronuclei induction
System of testing: Chinese hamster V79 cells
Concentration: up to 0.14 mg/ml
Cytotoxic Conc.:
Metabolic activation: without
Result: positive
Method: other: Bonatti S. et al. Mutagen. 7:111-114
Year: 1992 GLP: no data
Test substance: other TS
Method: Micronuclei formation was matched with an immunofluorescent staining for kinetochore protein (CREST-antibodies).
Result: Aneugenic effect: slight positive (2.5 times higher than in the negative control).
Source: BASF AG Ludwigshafen
Test substance: Purity of 99%.

(138)

5.6 Genetic Toxicity 'in Vivo'

Type: other: alkaline DNA elution test
Species: rat Sex: male
Strain: Sprague-Dawley
Route of admin.: i.p.
Exposure period: 2 hours
Doses: 484 or 969 mg/kg
Result:
Method: other: Parodi S. et al. Mutat. Res. 54: 39-46
Year: 1978 GLP: no data
Test substance: other TS
Result: The compound produced a weakly positive result in rat liver.
Source: BASF AG Ludwigshafen
Test substance: N,N-dimethyl aniline; purity of 99%.

(138)

Type: other: alkaline DNA elution test
Species: rat Sex: male
Strain: Sprague-Dawley
Route of admin.: i.p.
Exposure period: 24 hours
Doses: 484 mg/kg
Result:
Method: other: Parodi S. et al. Mutat. Res. 54: 39-46
Year: 1978 GLP: no data
Test substance: other TS
Result: The compound produced a negative result in rat liver.
Source: BASF AG Ludwigshafen
Test substance: N,N-dimethyl aniline; purity of 99%.

(138)

Type: other: alkaline DNA elution test
Species: mouse Sex: male
Strain: Balb/c
Route of admin.: i.p.
Exposure period: 2 hours
Doses: 242 or 484 mg/kg
Result:
Method: other: Parodi S. et al. Mutat. Res. 54:39-46
Year: 1978 GLP: no
Test substance: other TS
Result: The compound produced a weakly positive result in mouse liver
Source: BASF AG Ludwigshafen
Test substance: N,N-dimethyl aniline; purity of 99%.
(138)

Type: other: alkaline DNA elution test
Species: mouse Sex: male
Strain: Balb/c
Route of admin.: i.p.
Exposure period: 24 hours
Doses: 242 mg/kg
Result:
Method: other: Parodi S. et al. Mutat. Res. 54:39-46
Year: 1978 GLP: no data
Test substance: other TS
Result: The compound produced a weakly positive result in mouse liver.
Source: BASF AG Ludwigshafen
Test substance: N,N-dimethyl aniline; purity of 99%.
(138)

Type: other: alkaline DNA elution test
Species: rat Sex: male
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: 6 and 24 hours
Doses: 969 mg/kg
Result:
Method: other: Parodi S. et al. Mutat. Res. 54:39-46
Year: 1978 GLP: no data
Test substance: other TS
Result: The compound was negative in rat liver when tested at 6 hours and 24 hours after administration.
Source: BASF AG Ludwigshafen
Test substance: N,N-dimethyl aniline; purity of 99%.
(138)

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: other: F-344/N
Route of admin.: gavage
Exposure period: 103 Wochen
Frequency of treatment: 5 Tage/Woche
Post. obs. period: keine Angabe
Doses: 3; 30 mg/kg in Maisoel
Result:
Control Group: yes, concurrent vehicle
Method:
Year: GLP:
Test substance:
Result: (Die Versuchsgruppen umfassten jeweils 50 maennliche und 50 weibliche Tiere)
Koerpergewichtsentwicklung und Ueberlebensrate blieben durch die Substanzzufuhr unbeeinflusst. Zielorgan der Substanzwirkung war die Milz; bei den maennlichten Tieren der oberen Dosisgruppe war die Inzidenz fettiger Umwandlung (10/50) und Fibrose (22/50) signifikant erhoeht. Weibliche Tiere der hohen Dosisgruppe wiesen vermehrt chronisch fokale Entzuendungen der Leber auf. In allen Gruppen - auch den Kontrollen - fanden sich Haemosiderose und Erythropoese in dern Milz; jedoch waren die Befunde bei den mit Dimethylanilin behandelten Tiere ausgepraegter. In der oeberen Dosisgruppe wurde bei den maennlichen Tieren eine erhoehte Anzahl von Sarkomen (n=3) und Osteosarkomen (n=1) der Milz beobachtet (4/50=8%; hist. Kontrollen: 3/2081=0,1%), die der Substanzzufuhr zugeschrieben wird. Ein maennliches Tier der oberen Dosisgruppe zeigte ein Thymus-Sarkom. Bei beiden Geschlechtern fand sich eine gegenueber den Kontrollen erniedrigte Anzahl von monozytaeren Leukaemien, moeglicherweise als Ausdruck direkter Substanzwirkung auf die Milz, dem Ursprungsort dieser Leukaemien bei F344-Ratten.
Source: BASF AG Ludwigshafen

(157) (158) (69)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: gavage
Exposure period: 2 years
Frequency of treatment: 5 days/week for 103 weeks
Post. obs. period: no data
Doses: 3 or 30 mg/kg/day in corn oil
Result:
Control Group: yes, concurrent vehicle
Method: other
Year: GLP: no data
Test substance: other TS
Remark: Groups of 50 rats of each sex were used. Mean body weights of vehicle control and dosed rats were comparable throughout the studies. The survival of rats among all respective groups was similar, except for the lower survival of vehicle control female rats (vehicle control, 21/50; low dose, 32/50; high dose, 36/50). Final survival for male rats were: 29/50; 32/50; 28/50, respectively.
Fatty metamorphosis and fibrosis in the spleen of high dose male rats were increased: 0/49; 1/49; 10/50, and 5/49; 2/49 and 22/50, respectively. SPLENIC HEMOSIDEROSIS and HEMATOPOIESIS were present at an incidence greater than 85% in all groups; however, the severity of lesions was greater in dosed groups than in controls. SACROMAS OF THE SPLEEN were seen in 3/50 high dose male rats, and an OSTEOSARCOMA was seen in another high dose male rat. One additional high dose male rat had a sarcoma of the thymus. Splenic sarcomas are uncommon in corn oil vehicle control male Fisher 344/N rats (0.1%); thus, these neoplasms were considered to be chemically related.
LOWER INCIDENCES OF MONONUCLEAR CELL LEUKEMIA (which apparently originates in the spleen) were seen in experimental male and female rats than in vehicle controls (male: 13/50; 4/50; 3/50, respectively; female: 11/50; 7/50; 0/50, respectively).
NTP study.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.

(159) (117)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: gavage
Exposure period: 103 Wochen
Frequency of treatment: 5 Tage/Woche
Post. obs. period:
Doses: 15; 30 mg/kg in Maisoel
Result:
Control Group: yes, concurrent vehicle
Method:
Year: GLP:
Test substance:
Result: (Die Versuchsgruppen umfassten jeweils 50 maennliche und 50 weibliche Tiere).
Waehrend der Expositionszeit wurden keine Zeichen der Intoxikation beobachtet. Bei 2 weiblichen Tieren der niedrigen und bei 8 weiblichen Tieren der oberen Dosisgruppe fanden sich Vormagen-Papillome (Kontrollgruppe: 2 Tiere)
Source: BASF AG Ludwigshafen
(158) (69)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: gavage
Exposure period: 2 years
Frequency of treatment: 5 days/week for 103 weeks
Post. obs. period: no data
Doses: 15 and 30 mg/kg/day in corn oil
Result:
Control Group: yes, concurrent vehicle
Method: other
Year: GLP: no data
Test substance: other TS
Remark: Groups of 50 mice of each sex were used. Mean body weights of vehicle control and experimental mice were similar throughout the study. Final survival was as follows: male mice - vehicle control: 34/50; low dose: 30/50; high dose: 34/50; female mice - 35/50; 39/50; 33/50.
The incidence of squamous cell papillomas of the forestomach in high dose female mice was marginally greater than in vehicle controls (2/50; 2/50; 8/50).
NO other EFFECTS were seen.
NTP study.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of purity >98%.
(117)

Species: rat Sex: male/female
Strain: Wistar
Route of admin.: s.c.
Exposure period: 249 Tage (im NTP TR 360(1990) mit 21 Wochen angegeben)
Frequency of treatment: in den ersten 13 Wochen: 2 Tage/Woche; anschliessend taeglich
Post. obs. period: 19 Wochen
Doses: 100 mg/kg in Arachis-Oel(im NTP TR 360(1990) mit 500 mg/kg ang.)
Result:
Control Group: no data specified
Method:
Year: GLP:
Test substance:
Remark: In der Originalarbeit finden sich keinerlei Hinweise zur Versuchsdurchfuehrung; eine Bewertung der Substanz kann aus den Ergebnissen dieser Studie nicht erfolgen.
Result: Die Substanz zeigte unter den gewaehlten Versuchsbedingungen keine kanzerogene Wirkung.
Source: BASF AG Ludwigshafen
(160) (69) (161)

Species: rat Sex: male
Strain: Wistar
Route of admin.: s.c.
Exposure period: 21 weeks
Frequency of treatment: twice /week for the first 13 weeks and once a day thereafter for 21 weeks
Post. obs. period: 19 weeks
Doses: 500 mg/kg
Result:
Control Group: no data specified
Method: other: Walpole A.L. Acta Un. Int. Canc. 1:483
Year: 1963 GLP: no
Test substance: other TS
Remark: NO EFFECT. No further information given.
These studies are considered to be inadequate for evaluationof a potential carcinogenic effect because of the short period of exposure and the incomplete reporting.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline; no further data.
(162) (163)

5.8 Toxicity to Reproduction
-

5.9 Developmental Toxicity/Teratogenicity

Species: mouse Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: 7.-14. Traechtigkeitstag
Frequency of treatment: taeglich
Duration of test:
Doses: 365 mg/kg in Maiskeimoel
Control Group:
Method:
Year: GLP:
Test substance:
Result: Maternale Toxizitaet: Erschoepfung, Lethargie, Letalitaet. Es wurden keine Effekte auf die Koerpergewichtsentwicklung der Muttertiere sowie auf Geburtsgewicht und Ueberlebensrate der Jungtiere waehrend der ersten 3 Tage p.p. beobachtet. Die Wurfgroesse war mit derjenigen der Kontrolltiere (Vehikelkontrollen) vergleichbar.
Von 50 traechtigen Tieren starben 2 Tiere nach der Applikationsphase, eines musste moribund getoetet werden.
Source: BASF AG Ludwigshafen
(164) (165) (166) (124) (125)

Species: mouse Sex: female
Strain: CD-1
Route of admin.: gavage
Exposure period: 8 days
Frequency of treatment: 8 consecutive days, Day 7 through Day 14 of gestation (vaginal plug = day 0)
Duration of test: up to postnatal day 3
Doses: 365 mg/kg/day
Control Group: yes, concurrent vehicle
Method: other: Chernoff N. and Kavlock R.J. In: Short-term bioassays in the analysis of complex environmental mixtures, Ed. Waters et al. New York, Plenum Publishing Co. Vol. III: 417-427
Year: 1983 GLP: yes
Test substance: other TS
Remark: Fifty female mice were used. Three females died during the first 4 days after exposure; this effect was considered compound-related. No significant effect on maternal body weight or litter weight 3 days postpartum was observed. Three dams died; there were no deaths in the control group. Seven dams in the NN-dimethylaniline group and nine in the control group were not pregnant. Three dams in the treated group, but none in the control group, had been fertilized without subsequent implantation. One dam in the treated group had a dead litter which was not delivered by day 23 of gestation. Treatment with NN-dimethylaniline had no apparent effect on time to delivery and on reproduction outcome which was 97%. The average number of live pups per litter at birth was 9 ± 3 for the control group and 9 ± 3 for the treated group. The average number of live pups per litter 3 days

postpartum was 8 ± 3 for the treated group and 9 ± 3 for the control group. Although the Offspring Viability Ratio was reported to be significantly (Student's t-test) reduced in the treated group compared with the control group, the reported mean ratios for treated (0.98 ± 0.04) and control (1.00 ± 0.02) group do not appear to be different.

Source: BASF AG Ludwigshafen

Test substance: NN-dimethylaniline; no further data.

(167) (168) (169) (127) (170) (171) (172)

5.10 Other Relevant Information

Type: Biochemical or cellular interactions

Remark: When 60 mg/kg NN-dimethylaniline was administered by intraperitoneal injection on each of 3 consecutive days, 1.8% metHb and 2.0% sulfhaemoglobin were found in the blood 48 hours after the last application.

Source: BASF AG Ludwigshafen

(99)

Type: Biochemical or cellular interactions

Remark: Male Wistar rats were fed diets of varying selenium content in order to obtain selenium-deficient and selenium-supplemented rats. After 5-6 weeks rats were used to investigate how selenium influences the effect of dimethylnitrosamine (DMN) on the microsomal N-, and C-oxygenation of NN-dimethylaniline (DMA). For this purpose the liver of rats were perfused with 5 mM of DMN prior to the preparation of microsomes and postmitochondrial supernatant S9.
It was found that DMN-perfused livers from rats fed a Se-defficient diet exhibited a lower N-oxygenation activity towards DMA than did those from Se-supplemented rats. The same relative difference was observed in another set of experiments performed with non-perfused livers. Diet did notaffect C-oxygenation activity.
Chinese hamster V79 cells were exposed directly to the circulating perfusate of the liver of male Wistar rats fed for 5-6 weeks diets of varying selenium content in order to obtain Se-deficient and Se-supplemented rats. Perfusate contained 5 mM dimethylnitrosamine (DMN) and V79 cells were exposed for 2 hours. A negative correlation between NN-dimethylaniline-N-oxygenation in microsomes isolated from these livers and mutagenicity of DMA to V79 cells was observed, whereas no correlation was demonstrated between the mutagenicity of DMA to V79 cells and NN-dimethylaniline-C-oxygenation.

Source: BASF AG Ludwigshafen

(173)

Type: Biochemical or cellular interactions
Remark: Weanling rats were fed a Se-deficient diet with or without sodium selenite (0.2 ppm selenium) in the drinking water. Cadmium-induced effects on N-, and C-oxygenation of NN-dimethylaniline in the liver microsomes were measured. Cd in vitro caused a decrease in C-oxygenation. This effect tended to be more prominent in the Se-defficient groups. On the other hand, N-oxygenation was increased when Cd was added, and no differences were found between Se-deficient and Se-supplemented groups. However, there was a tendency for lower N-oxygenation in the Se-deficient rat.
Source: BASF AG Ludwigshafen

(174)

Type: Biochemical or cellular interactions
Remark: Groups of male Sprague-Dawley rats were pretreated (p. o.) with 7.5 mM/kg acetone, methyl isobutyl ketone (MBK), methyl n-butyl ketone (MnBK) or octanone (OCT), given either as a single dose or as three consecutive doses. This was followed, 18 hours later, by the i.p. administration of 0.8 or 2.4 mM/kg of NN-dimethylaniline (DMA). It was found that pretreatments with MBK, MnBK and OCT enhanced significantly the metHb production by DMA. In other experiments (3-days of pretreatments p.o. followed by 0.8 mM/kg DMA i.p.) metHb formation was related to the pretreatments as follows: OCT (7.5 mM/kg) > phenobarbital (50 mg/kg) > 3-methylcholantrene (25 mg/kg) > pregnenolone-1,6a-carbonitrile (20 mg/kg) > corn oil = saline.
Source: BASF AG Ludwigshafen

(175)

Type: Biochemical or cellular interactions
Remark: It was shown that liver microsomes metabolize NN-dimethylaniline to: NN-dimethylaniline-N- oxide, 4-NN-dimethylaminophenol, 2-NN-dimethylaminophenol, 4-N-methylaminophenol, 2-aminophenol, 4-aminophenol and phenylhydroxylamine. All the metabolites were able to oxidize hemoglobin in erythrocytes.
Source: BASF AG Ludwigshafen

(176)

Type: Biochemical or cellular interactions
Remark: NN-dimethylaniline was oxidized with hydrogen peroxide according to Belov and Savich (J. Gen. Chem. USSR, 17, 257, 1947) to NN-dimethylaniline-N-oxide. It was shown that the formation of metHb by NN-dimethylaniline-N-oxide in beef hemoglobin was not due to a direct oxidation of the ferrohemoglobin by the N-oxide. Oxygen was needed for the reaction. Pretreatment of the hemoglobin with -SH reagents accelerated its reaction with NN-dimethylaniline-n-oxide.
Source: BASF AG Ludwigshafen

(177)

Type: Biochemical or cellular interactions
Remark: Covalent binding of NN-dimethylaniline to hemoglobin was studied in female Wistar rats. The compound (0.6mM/kg) was dissolved in 1,2-propanediol and administered by gavage. The hemoglobin binding index (fraction of the dose that binds to hemoglobin expressed as mM/molHb/dose) for NN-dimethylaniline was 11.4.
Source: BASF AG Ludwigshafen
(178)

Type: Biochemical or cellular interactions
Remark: NN-dimethylaniline has been shown to oxidize thiols in the reaction in which oxygen is taken up and superoxide radical is formed. Horseradish peroxidase catalyzes this reaction and GSH is the thiol employed.
Source: BASF AG Ludwigshafen
(179)

Type: Biochemical or cellular interactions
Remark: Male Wistar rats were fed a Se-deficient diet with or without sodium selenite (0.2 ppm) in the drinking water. The liver of rats were perfused with 5mM 1,1-dimethylhydrazine (UDMH) for 2 hours.
It was found that the microsomal metabolism of NN-dimethylaniline was not significantly affected by the UDMH treatment although there was a tendency towards reduced C-oxygenation when selenium-deficient livers were used.
Source: BASF AG Ludwigshafen
(180)

Type: Metabolism
Remark: Dimethylanilin wirkt als indirekter Methaemoglobinaemiebildner, d.h. Dimethylanilin reagiert nicht direkt mit Haemoglobin, sondern erst nach metabolischer Umwandlung in aktive Formen, vermutlich durch mischfunktionelle Oxidasen.
Source: BASF AG Ludwigshafen
(181)

Type: Metabolism
Remark: Die intravenoese Verabreichung von Dimethylanilin und N,N-Dimethylanilin-N-oxid an Hunde sowie in vitro-Experimente mit N,N-Dimethylanilin-N-oxid und Haemoglobin zeigten, dass das N-oxid keine wesentliche Rolle bei der Methaemoglobinaemie-Bildung spielen kann.
Source: BASF AG Ludwigshafen
(182) (183)

Type: Metabolism
Remark: Als Metabolit des Dimethylanilins wurde im Urin von Kaninchen N,N-Dimethyl-4-aminophenol nachgewiesen.
Source: BASF AG Ludwigshafen
(184)

Type: Metabolism
Remark: Ratten, die an 6 aufeinanderfolgenden Tagen intraperitoneale Injektionen von Dimethylanilin (jw. 24 mg/kg) erhielten, schieden durchschnittlich 6% der applizierten Dosis als N-Oxid im Harn aus.
Source: BASF AG Ludwigshafen
(185)

Type: Metabolism
Remark: Bei in vitro-Studien konnten die folgenden Hauptmetaboliten identifiziert werden: N-Methylanilin, N,N-Dimethylanilin-N-oxid, N,N-Dimethyl-4-aminophenol, N,N-Dimethylanilin-2-aminophenol; in geringerer Menge auch Anilin, N-Methyl-4-aminophenol, 4-Aminophenol.
Source: BASF AG Ludwigshafen
(181)

Type: Metabolism
Remark: In Untersuchungen mit Kaninchenleber-Mikrosomen wurde kein Dimethyl-N-oxid als Zwischenprodukt der Demethylierung durch verschiedene Cytochrom P450-Isoenzyme nachgewiesen.
Source: BASF AG Ludwigshafen
(186)

Type: Metabolism
Remark: Eine N-Demethylierung kann auch durch die Prostaglandin-Synthetase erfolgen.
Source: BASF AG Ludwigshafen
(187)

Type: Metabolism
Remark: Bei Inkubation von Rattenhepatozyten mit N,N-Dimethylanilin wurde als Metabolisierungsprodukt neben dem N-oxid, dem N-Methylanilin und dem Anilin ein N-Methylanilin-Konjugat indentifiziert, bei dem es sich wahrscheinlich um das N-Glukuronid handelt.
Source: BASF AG Ludwigshafen
(188)

Type: Metabolism
Remark: In Rattenlebermikrosomen wurde die Demethylierung von Dimethylanilin durch eine Vorbehandlung mit 3-Methylcholanthren ebenso wenig beeinflusst wie durch den Zusatz von Dimethylnitrosamin.
Source: BASF AG Ludwigshafen
(189)

Type: Metabolism
Remark: Eine Behandlung mit dem Cytochrom P450-induzierenden Phenobarbital erhoehte die Reaktionsgeschwindigkeit der N-Dimethylierung in Rattenlebermikrosomen; beta-Naphtylamin, welches Cytochrom P448 induziert, hatte keinen Einfluss.
Source: BASF AG Ludwigshafen
(190)

Type: Metabolism
Remark: Dimethylanilin soll in etwa gleichem Masse wie Monomethylanilin demethyliert werden (in vitro-Versuche mit Kaninchenlebermikrosomen)
Source: BASF AG Ludwigshafen
(191)

Type: Metabolism
Remark: In Lebermikrosomen von Vitamin E-defizienten sowie von Corticoid- bzw. 2-Aminofluoren-behandelten Ratten wurde eine gegenueber der N-Demethylierung verstaerkte N-Oxidation von Dimethylanilin beobachtet.
Source: BASF AG Ludwigshafen
(192)

Type: Metabolism
Remark: Bei Katzen wird das Auftreten von Dimethylanilin-N-oxid im Blut nach intravenoeser Dimethylanilin-Injektion beschrieben.
Source: BASF AG Ludwigshafen
(193)

Type: Metabolism
Remark: Im Gegensatz zu tierischen Mikrosomen, bei denen die N-Demethylierung im Vordergrund steht, soll nach Untersuchungen mit menschlichen Lebermikrosomen primaer die N-Oxidation des Dimethylanilins stattfinden.
Source: BASF AG Ludwigshafen
(194) (195)

Type: Metabolism
Remark: Eine N-Oxidation des Dimethylanilins konnte auch mit humanen fetalen Lebermikrosomen gezeigt werden.
Source: BASF AG Ludwigshafen
(196)

Type: Metabolism
Remark: Dimethylanilin fuehrt in Leberzellen zur GSH-Oxidation und zur Freisetzung von GSSG.
Source: BASF AG Ludwigshafen
(197)

Type: Metabolism
Remark: In Untersuchungen zur Bindung von verschiedenen monozyklischen aromatischen Aminen an Haemoglobin nach Sondierung bei Ratten wurde fuer N,N-Dimethylanilin ein dem des Anilins vergleichbarer "Haemoglobin-Bindungs-Index" gemessen (Dimethylanilin: 11; Anilin: 22; z.Vgl. p-Chloranilin: 569)
Source: BASF AG Ludwigshafen
(198)

Type: Metabolism
Remark: Eine ein- bis 3malige perorale Vorbehandlung mit verschiedenen Ketonen fuehrte bei Ratten zu signifikant erhoehter Methaemoglobin-Bildung nach i.p.-Gabe von Dimethylanilin (0,8 bzw. 2,4 nmol/kg). Die Autoren vermuten eine Mikrosomen-induzierende Wirkung der Ketone.
Source: BASF AG Ludwigshafen
(199)

Type: Metabolism
Remark: In einer Untersuchung an Katzen wurden 10 min nach intravenoeser Injektion nur noch 50% der nach 2 min gemessenen Dimethylanilin-Konzentration im Blut nachgewiesen. Im Laufe weiterer 90 min sank die Konzentration nochmals auf etwa die Haelfte. Bereits 2 min post injectionem wurde im Blut Nitrosobenzol identifiziert.
Source: BASF AG Ludwigshafen
(200)

Type: Metabolism
Remark: Rattenleber
In der Rattenleber wird die Bildung des Dimethylanilin-N-oxids durch eine Flavin-Monooxygenase katalysiert.
Source: BASF AG Ludwigshafen
(201)

Type: Metabolism
Remark: Als Metabolit des Dimethylanilins wurde im Urin von Hunden 2-Aminophenol nachgewiesen.
Source: BASF AG Ludwigshafen
(202)

Type: Metabolism
Remark: Im Urin von Hunden, denen 40mg/kg Dimethylanilin i.v. injiziert worden war, fanden sich nach 48 Std. geringe Mengen von 4-Aminophenol, N-Methyl-4-Aminophenol, N,N-Dimethyl-4-Aminophenol, 2-Aminophenol und N-Methylanilin; N,N-Dimethyl-2-Aminophenol und N-Methyl-2-Aminophenol konnten lediglich in untergeordnetem Masse nachgewiesen werden. Im Urin wurde kein Anilin gefunden, jedoch in geringer Konzentration im Blut(2x10e-5 mol). Nach Meinung der Autoren sind die zahlreich nachgewiesenen Aminophenole - die auch aus dem durch Demethylierung entstandenen N-Methyl- anilin und Anilin gebildet werden - massgeblich fuer die Methaemoglobinaemie-Bildung verantwortlich.
Source: BASF AG Ludwigshafen
(203)

Type: Metabolism
Remark: Dimethylanilin wird durch Mikrosomen von Meerschweinchen, Kaninchen und Ratten N-demethyliert, N-oxidiert sowie in geringem Umfang am Ring hydroxyliert; neben Lungen- und Darmgewebe zeigten v.a. Lebermikrosomen hohe Aktivitaet.
Source: BASF AG Ludwigshafen

(204)

Type: Metabolism
Remark: In einer Studie mit Ratten- und Schweinelebermikrosomen-Praeparationen wurde der Mechanismus der direkten N-Demethylierung belegt.
Source: BASF AG Ludwigshafen

(205)

Type: Metabolism
Remark: Metabolism of NN-dimethylaniline was investigated in rabbit liver microsomes in vitro. It was found that N-demethylation and N-oxidation are the major routes of metabolism with Km values 0.25 mM and 0.072 mM, respectively. It indicates the presence of two distinct enzyme systems.
A good correlation was found between the hydrofobic bonding constant (pi) =2.29 and the extent of demethylation (pKa = 4.98) of NN-dimethylaniline.
Source: BASF AG Ludwigshafen

(206)

Type: Metabolism
Remark: Metabolism of NN-dimethylaniline in vitro using microsomal preparations from different species has confirmed N-demethylation and N-oxidation and established ring hydroxylation as metabolic routes. However, different metabolites were found in the rat, ferret, hamster, rabbit and guinea pig. N-methylaniline, aniline and NN-dimethyl-4-aminophenol were present in all preparations, N-methyl-4-aminophenol was not present in ferret microsomes,4-aminophenol was present in rabbit and guinea pig preparations only, and NN-dimethylaniline-N-oxide was found in the rabbit and guinea pig only. Ring hydroxylase, N-demethylase and N-oxidase enzyme activities were measured in washed microsomal preparations of various male New Zealand White rabbit organs. The total metabolism was greatest in the liver (24% of initial substrate) and smaller in the lung (6.3%), the intestine (4.4%) kidney (2.9%) and heart (1.0%). Apparent Km values of N-demethylation, N-oxidation and 4-hydroxylation of NN-dimetylaniline established in rabbbit microsomes were 0.549 mM/l, 0.153 mM/l, 0.157 mM/l, respectively. Corresponding Vmax values were: 9.12, 3.99 and 0.68, respectively.
Apparent Km values for N-demethylation, N-oxidation and 4-hydroxylation of NN-dimethylaniline established in guinea pig microsomes were: 0.427 mM/l, 0.041 mM/l and 0.53 mM/l, respectively. Corresponding Vmax values were: 4.29, 1.94 and 0.83, respectively.
Source: BASF AG Ludwigshafen

(207)

Type: Metabolism
Remark: Triethyllead chloride was added directly to male rat liver microsomes (0, 0.25, 0.5, 1.0 and 3.0 mM), or rats were pretreated with ip injections, once a day for 2 days (0, 1.5 and 3.0 mg triethyllead chloride/kg), and microsomes prepared without any further treatment on Day 3. The effects of these treatments on microsomal N-oxygenation and C-oxygenation of NN-dimethylaniline were studied in vitro. Increased microsomal N-oxygenation was obtained by in vivo treatment and decreased C-oxygenation by in vitro treatment. It was also found that triethyllead chloride added in vitro to a concentration of 0.25 mM and above produced a statistically significant reduction in the content of cytochrome P-450.
Source: BASF AG Ludwigshafen

(208)

Type: Metabolism
Remark: Hepatic microsomal metabolism of NN-dimethylaniline was studied in vitro using control ad phenobarbital-induced microsomes. When the compound was incubated with phenobarbital-induced hepatic microsomes, a significant decrease of its metabolism from 4.92 ± 0.28 to 3.65 ± 0.13 (expressed as nM formaldehyde formed/min/mg of protein) was observed. Phenobarbital pretreatment also resulted in a significant decrease in the specific activity of hepatic microsomal FAD-containing monooxygenase.
The metabolism of NN-dimethylaniline in the microsomes prepared from rat respiratory and olfactory nasal mucosa was also studied. It was found that compound metabolism is higher in olfactory microsomes (6.04 nM of formaldehyde/min/mg of protein) than in respiratory microsomes; 2.52 nM.
Source: BASF AG Ludwigshafen

(209)

Type: Metabolism
Remark: It was found that N-oxidation of NN-dimethylaniline is not enhanced in microsomes from rats pretreated with phenobarbitone and beta-naphtoflavone. Cytochrome P-450 inhibitors had no effect on N-oxidation, but inhibit N-demethylation of the compound. N-oxidation was stimulated by n-octylamine, and strongly inhibited by naphtylthiourea. From this study it is concluded that in rats, N-oxidation of NN-dimethylaniline is mediated exclusively via the flavin-containing monooxygenase, whereas N-demethylation is mediated via a cytochrome P-450 system.
Source: BASF AG Ludwigshafen

(210)

Type: Metabolism
Remark: It was found that N-oxidation of 14C-NN-dimethylaniline occured in an isolated, ventilated and perfused lung preparation as well as in an in vitro rabbit lung preparation. The Km value of rabbit lung microsomal N-oxidase was 0.71 mM, and the Vmax value was 12.59 (mM/min/mg protein).
It was also found that N-oxidation of NN-dimethylaniline occured in an isolated, ventilated and perfused rat lung preparation as well as in an in vitro rat lung preparation. Using 14C-labeled compound, the Km value of N-oxidase activity in the rat microsomal preparation was 0.09 mM; the Vmax was 2.93 mM/min/mg/protein.
Source: BASF AG Ludwigshafen

(211)

Type: Metabolism
Remark: It was found that in vitro, N,N',N,N'-(CH3)-benzidine (TMB) can be an intermediate in the N-demethylation of NN-dimethylaniline by a peroxidase-H2O2 system, but not with a cytochrome P-450-cumene hydroperoxide system. The N-demethylation of TMB and NN-dimethylaniline by peroxidase-H2O2 is readily inhibited by a wide range of hydrogen donors in contrast to that of the cytochrome P-450-cumene hydroperoxide system.
Source: BASF AG Ludwigshafen

(212)

Type: Metabolism
Remark: N-oxidation of NN-dimethylaniline has been measured with whole homogenates of human hepatic tissue obtained by needle or surgical biopsy on over 100 patients. The rate of N-oxidation was compared with the demethylation rate of aminopyrine. It is concluded that N-oxidation appears to be more a significant route in humans than it is in laboratory animals.
Source: BASF AG Ludwigshafen

(213)

Type: Metabolism
Remark: In an in vitro assay with post-mortem liver tissue from 4 men, 2 to 5 times more NN-dimethylaniline was metabolized by N-oxidation than by N-demethylation.
Source: BASF AG Ludwigshafen

(214)

Type: Metabolism
Remark: N-oxidation of NN-dimethylaniline was demonstrated with liver microsomes from human fetuses. The rate of formation of NN-dimethylaniline-N-oxide was 0.3 to 2.4 nmole/min/mg protein and varied greatly among individuals. The authors ascribes this variations predominantly to differences between stages of development (week 13 - week 21). Their studies indicated that N-oxygenation of the compound is independent of the cytochrome P-450 system.

Source: BASF AG Ludwigshafen
(215) (216)

Type: Metabolism
Remark: The microsomal fraction of the rat seminal vesicle, when fortified with the arachidonic acid, catalyzed N-demethylation of NN-dimethylaniline. It shows that N-demethylation of NN-dimethylaniline can be catalyzed not only by cytochrome P-450 but also by prostaglandin synthase.
Source: BASF AG Ludwigshafen
(217)

Type: Metabolism
Remark: After i.v. injection of 40 mg of NN-dimethylaniline/kg into mongrel dogs, N-methylaniline and the ring-hydroxylated metabolites (NN-dimethyl-2-aminophenol, NN-dimethyl-4-aminophenol, N-methyl-2-aminophenol, N-methyl-4-aminophenol, 2-aminophenol and 4-aminophenol) were detected in the urinewithin 48 hours, mostly in the form of the glucuronic or sulfuric acid conjugates. The major metabolites were 4-aminophenol and 2-aminophenol. In the blood of beagle dogs injected (i.v.) with 40 mg NN-dimethylaniline/kg, the highest concentration of aniline, 2.4 ug/ml, was detected after 2 hours.
Source: BASF AG Ludwigshafen
(218)

Type: Metabolism
Remark: In the blood of cats which had received 0.209 mM NN-dimethylaniline/kg i.v., 0.15 ug/ml nitrobenzene was detected after only 2 minutes. The highest level, 0.25 ug/ml, was observed after 20 - 40 minutes. The blood aniline concentration reached the peak value of 1.7 ug/ml after 2 hours.
Source: BASF AG Ludwigshafen
(219)

Type: Metabolism
Remark: Cats were given 24.2 mg NN-dimethylaniline/kg i.v. NN-dimethylaniline-N-oxide was detected in the blood after only 10 minutes. The highest concentration, 4 - 6 ug/ml, was attained after 40 - 60 minutes.
Source: BASF AG Ludwigshafen
(220)

Type: Metabolism
Remark: Four dogs were injected intravenously with 92 mg NN-dimethylaniline/kg. The highest concentration of NN-dimethylaniline-N-oxide in the blood (8.5 ug/ml) after 30 minutes was measured.
Source: BASF AG Ludwigshafen
(221)

Type: Metabolism
Remark: It is demonstrated that N-oxide is formed at a sufficiently rapid rate for it to be an intermediate in the oxidative demethylation of NN-dimethylaniline catalyzed by microsomes isolated from rat or pig liver.
Source: BASF AG Ludwigshafen

(222)

Type: Metabolism
Remark: The effect of the oxidative N-dealkylation inhibitor, SKF 525-A, on the excretion of NN-dimethylaniline (DMA) by the rat was investigated. For this purpose male albino rats were injected i.p. as follows: six injections of DMA at one-day intervals, four injections of DMA + SKF 525-A at seven-day intervals and one injection of DMA alone on the day 18. About 6% of the injected DMA was recovered as the N-oxide during 6-days the amine was injected alone. However, the simultaneous injection of SKF 525-A with DMA nearly doubled the amount of N-oxide excreted (11.6 %). The effect of SKF 525-A was reversible. The excretion of N-oxide returned to the original level when DMA alone was administered again on day 18.
Source: BASF AG Ludwigshafen

(223)

Type: Metabolism
Remark: It was found that rat liver microsomal preparations enzymatically catalyze the N-demethylation and N-oxidation of NN-dimethylaniline. Apparent Km values for N-demethylation and for N-oxidation were: 0.128 mM/l, and 0.093 mM/l, respectively. Apparent Vmax values for N-demethylation and N-oxidation were: 1.93 and 0.75 nM/min/mg protein, respectively.
It was shown that pig liver microsomal prepartions enzymatically catalyze the N-demethylation and N-oxidation of NN-dimethylaniline. Apparent Km values for N-demethylation and N-oxydation were: 0.67 and 0.16 mM/l, respectively. Apparent Vmax values for N-demethylation and N-oxydation were: 0.71 and 0.35 nM/min/mg protein, respectively.
It was also demonstrated that in rat liver microsomal preparations, SKF 525-A inhibitis and phenobarbital pretreatment stimulates N-oxide demethylation; EDTA inhibits both the latter reaction and N-oxidation; EGTA and nicotinamide stimulate C-oxidation and inhibit N-oxide demethylation; SH-blocking agents inhibit C-oxidation and stimulate both N-oxidation and N-oxide demethylation.
Source: BASF AG Ludwigshafen

(224)

Type: Metabolism
Remark: Preincubation of phenobarbital-induced rat liver microsomal fractions with 1 mM revenast, an antiallergic drug, decreased NN-dimethylaniline N-demethylation by 49%.
Source: BASF AG Ludwigshafen

(225)

Type: Metabolism
Remark: Evidence is presented for the existence of alternate metabolic routes for N-oxidation of NN-dimethylaniline.One pathway involves the cytochrome P-450-linked mixed function oxidase system. The other pathway is represented by a mixed function amine oxidase, which lacks NADPH diaphorase activity and is insensitive to treatment with 2-bromo-4'-nitroacetophenone and lipase.
Source: BASF AG Ludwigshafen

(226)

Type: Metabolism
Remark: The abilities of several cytochrome P-450 isoenzymes from rabbit liver (P-450 form 2 and P-450 form 4) and rat liver (P-450b and P-450c) to catalyze N-oxide formation and their abilities to catalyze the demethylation of N-oxide were determined and compared with their abilities to catalyze the demethylation of NN-dimethylaniline. The results obtained suggest that the N-oxide of NN-dimethylaniline is not an intermediate in the demethylation of NN-dimethylaniline by these forms of cytochrome P-450 and that N-oxidase activity is not associated with these isozymes.
Source: BASF AG Ludwigshafen

(227)

Type: Metabolism
Remark: Male rats were pretreated with daily i.p. injections of either phenobarbital, 3-methylcholantrene, or the corresponding vehicles for up to 9 days, administered carbon tetrachloride (CCl4) by gavage (2.5 ml/kg) and sacrificed 3hours later. Hepatic microsomes were isolated and assayed for cytochrome P-450 content and mixed-function oxidase activity. In the saline pretreated controls, CCl4 treatment produced only a minor decrease in the demethylation of NN-dimethylaniline. In the animals pretreated with phenobarbital, CCl4 decreased demethylation activity to 47 % of the induced level. In contrast, a small and statistically insignificant decrease was noted in the demethylation of NN-dimethylaniline in animals pretreated with 3-methylcholantrene. The data suggest that the specificcytochrome P-450(s) in the saline-treated as well as the cytochrome P-450(s) induced by phenobarbital, but not the 3-methylcholantrene-induced cytochrome P-450, are susceptible to CCl4-induced destruction.
Source: BASF AG Ludwigshafen

(228)

Type: Metabolism
Remark: It was shown that in a reconstituted system consisting of purified rat liver microsomal P-450, the ratio of the rates of N-dealkylation and N-oxidation varied from 100 to 1000.
Source: BASF AG Ludwigshafen

(229)

Type: Metabolism
Remark: Carbon monoxide (CO) was found to diminish the maximum velocity of N-oxide formation from NN-dimethylaniline in rabbit liver microsomes. The oxygen affinity of the system is increased in the presence of CO. Furthermore, CO modified both the dissociation constant, pK, of one oxygen-linked group and the pH optimum of the N-oxidation reaction.
Source: BASF AG Ludwigshafen

(230)

Type: Metabolism
Remark: Effect of dimethylnitrosamine (DMN) on microsomal metabolism of NN-dimethylaniline in perfused rat liver was studied. Livers were perfused for 4.5 hours and DMN was added to the initial perfusate at concentrations of 1, 5 or 25 mM.
It was found that 1 mM had no effect on the microsomal N- and C-oxygenation of NN-dimethylaniline. Perfusion with 5 mM DMN caused a decrease in C-oxygenation (20%), and slight increase of N-oxygenation, which resulted in a statistically significant increase in the N/C ratio (40%). Following perfusion with 25 mM DMN, a 50 % increase in N-oxygenation was observed, whereas C-oxygenation remained at approximately the same level as that observed after perfusion with 5 mM DMN. Thus, a further increase in the N/C ratio was obtained.
Effect of dimethylnitrosoamine (DMN) on in vivo metabolism of NN-dimethylaniline by rat liver microsomes was studied. DMN was dissolved in 0.9 % saline and administered i.p. as a single dose of 20 mg DMN/kg. The i.p. administration was done 15 hours before exsanguination. It was shown that in vivo treatment with DMN had a pronounced effect on hepatic microsomal NN-dimethylaniline metabolism: N-oxygenation was increased by 40% and C-oxygenation decreased by about 30%. Thus, increasing the N/C ratio by 105%.
It was found that less than 7% of the NN-dimethylaniline wasmetabolized by C- and N-oxygenation in the rat liver microsomal prepartions.
When rat liver microsomes were incubated with both dimethylnitrosamine (5 mM) and NN-dimethylaniline (5 mM), a small but significant decrease (10 %) in both N- and C-oxygenation was observed.
Source: BASF AG Ludwigshafen

(231)

Type: Metabolism
Remark: It was demonstrated that NN-dimethylaniline, when incubated with mouse liver microsomes, underwent oxidative N-demethylation to free formaldehyde.
Source: BASF AG Ludwigshafen

(232)

Type: Metabolism
Remark: It was demonstrated that chick liver microsomal enyzmes catalyze the demethylation of NN-dimethylaniline-N-oxide at a rate greater than the oxidative demethylation of NN-dimethylaniline. Corresponding Km values were: 155 and 16mM; corresponding Vmax values were: 200 and 66.6 uM of CH20/min/mg protein.
The demethylation of NN-dimethylaniline (DMA) activity of chick liver microsomes was almost completly inhibited by SKF525-A at a concentration of 0.1 mM. The inhibitory effect appeared to be competitive with the substrate (Ki value of 4uM). Demethylation of NN-dimethylaniline-N-oxide was also found to be competitively inhibited by SKF 525-A (Ki value =15 uM). The effects of additional compounds on demethylase activity were also studied. Incubation of the microsomal fraction with NADPH gave 2.29 uM-CH20/min/mg protein. By omitting NADPH and incubating the microsomal enzymes with different ferric ions, i.e. FeCl3, Fe2(S04)2 and Fe(ClO4)3, DMA was oxidized, but to a lesser extent when NADPH was present. In the presence of ferrous ions, i.e. FeSO4, Fe(ClO4)2 and Fe(NH4)SO4, microsomal oxidation of DMA was higher than in the presence of NADPH. Copper sulfate and actetate had almost the same effect as ferric ions. HgCl2, MnSO4, MgCl2, ZnSO4, ZnCl2, KCN, GSH and EDTA gave no demethylation when incubated separately with the microsomal fraction with no NADPH. Ascorbic acid and catechol, when incubated separately with the microsomal fraction, gave activity slightly more than when NADPH was incubated with the microsomes. Ascorbic acid, catechol and EDTA activated the oxidation reaction in the microsomal fraction containing NADPH, while GSH inactivated it and KCN inhibited it completely.
Ascorbic acid, catechol and EDTA activated the demethylationreaction when each compound was incubated separately with the microsomal fraction and a H202-generating system. GSH greatly inactivated this reaction and KCN inhibited it completely.
The demethylation of NN-dimethylaniline (DMA) of livers taken from normal chicken and livers taken from chicks hatched from eggs injected with DDT (1,1,1-trichloro-2,2-bis(p-chlorophenyl) ethane, DDD (1,1-dichloro-2,2-bis (p-chlorophenyl) ethane and DDE (1,1-dichloro-2,2-bis (p-chlorophenyl) ethylene was determined. It has been found that DDT injection caused the greatest DMA demethylation activity and DDE the least, while DDD was intermediate; the demethylation activities were: 3.45, 2.63 and 3.07 uM CH20/min/mg protein, respectively. Michaelis constans (Km) calculated for the effects of DDT,

DDD and DDE on the demethylase activity were similar; 0.16mM. DDT, DDD and DDE stimulated microsomal oxidative acitivity; the maximum velocities (Vmax) of chick microsomal DMA demethylase activity were: 156, 90 and 75 uM CH20/min/mg protein, respectively.

Source: BASF AG Ludwigshafen

(233)

Type: Metabolism

Remark: N-oxidation and demethylation of NN-dimethylaniline by adult rabbit liver and lung microsomes were investigated. It was demonstrated that lung N-oxidase enzyme activity was about three times higher than liver N-oxidase at the pH optimum, about 8.9, whereas the activities were nearly the same at a more physiological pH ranges.
The effects of various divalent cations on N-oxidation and demethylation of NN-dimethylaniline by adult liver and lung microsomes were investigated. The lung N-oxidase was stimulated about 2-fold by 100 mM Mg and 0.1 mM Hg, whereas liver N-oxidase activity was inhibited by these concentrations of ions. In contrast to the effects of Hg and Mg, 1 mM Ni enhanced liver N-oxidase activity about 30 % and 5 mM Ni stimulated lung enzyme activity about 30%, whereas concentrations above 10 mM were inhibitory to both N-oxidases. Both liver and lung demethylase activities were inhibited by these concentrations of Mg, Hg and Ni.
Effects of various sulhydryl reagents were tested for their effects on N-oxidation and demethylation of NN-dimethylaniline by adult rabbit liver and lung microsomes. At a concentration of 0.1 mM, HgCl2 and the mercurials, p-chloromercurybenzoate and phenylmercury acetate inhibited both demethylases and liver N-oxidase, but stimulated lung N-oxidase activity. However, 0.1 mM to 1 mM N-ethylmaleimide and iodoacetimide had little effect on either liver or lung N-oxidase.
It was also demonstrated that microsomal N-oxidation in lungs from 2 year-old rabbits was stimulated by 0.1 mM mercury just as in the adult.
Changes in NN-dimethylaniline metabolism with age were followed in rabbits from 4 days old to adulthood. There was a steady increase in lung demethylase activity and N-oxidase acitivity in the liver and lung to adult levels. However, liver demethylase activity increased sharply between 2 weeks and 1 month. Activities of N-demethylase in liver and lung,and of N-oxidase in liver from newborn rabbits were 10-20% of adult levels. However, lung N-oxidase activities in the newborn were about 50% of adult levels.

Source: BASF AG Ludwigshafen

(234)

Type: Metabolism
Remark: The effects of carbon disulphide (CS2) on N-oxidation and N-demethylation of NN-dimethylaniline by the mice liver microsomes were studied 1 hour after the oral administration of 30 or 300 mg CS2/kg. A statisically significant decreasein N-demethylation was observed. N-oxidase activity was increased, but not significantly.
Source: BASF AG Ludwigshafen
(235)

Type: Metabolism
Remark: The oxidative dealkylation of NN-dimethylaniline in rabbit microsomes was not inhibited by SKF 525-A.
Source: BASF AG Ludwigshafen
(236)

Type: Metabolism
Remark: The liver microsomes from guinea pigs had a capacity to N-demethylate (2.9 muM CH2O formed/mg protein/min.), and to N-oxygenate (1.2 muM CH2O formed/mg protein/min.) NN-dimethylaniline.
Increased rat hepatic microsomal N-oxygenation of NN-dimethylaniline, and to a considerably smaller extent N-demethylation, was obtained by in vivo treatment with either 2-acetylaminofluorene (rats were fed a standard diet containing 0.06 % for 20 - 25 days) or 2-aminofluorene (i.p.). Vitamin E depletion, protein deficiency and stress caused an increase in N-oxygenation accompanied by a decrease in N-demethylation.
Source: BASF AG Ludwigshafen
(237)

Type: Metabolism
Remark: Weanling male Sprague-Dawley rats were pretreated with i.p. administration of methylcholantrene (single 40 mg/kg dose in corn oil, 23 -24 hours prior to sacrifice). It was demonstrated that N-demethylation of NN-dimethylaniline by hepatic microsomes was not affected by methylcholantrene pretreatment. The demethylation of NN-dimethylaniline was not affected by the co-presence of dimethylnitrosoamine.
Source: BASF AG Ludwigshafen
(238)

Type: Metabolism
Remark: Male CD-COBS rats were preatreated either with phenobarbital in saline (80 mg/kg i.p. daily for 3 days) or with beta-naphthoflavone dissolved in corn oil (60 mg/kg i.p. daily for two days). The Michaelis constants (Km) for the N-demethylation of NN-dimethylaniline with untreated, beta-naphthoflavone and phenobarbital treated rat liver microsomes were: 52, 49 and 16 uM, respectively. Corresponding Vmax values were: 10, 10 and 45 uM/min/mg protein, respectively.
Source: BASF AG Ludwigshafen
(239)

Type: Metabolism
Remark: The metabolism of NN-dimethylaniline in vitro was 2 times greater in freshly isolated rabbit Clara cells than in freshly isolated rabbit pneumocyte II cells.
Source: BASF AG Ludwigshafen
(240)

Type: Metabolism
Remark: Rat hepatocytes were isolated by collagenase perfusion and used for NN-dimethylaniline metabolism studies in vitro. Incubation of the compound with rat hepatocytes results in N-demethylation, NN-didemethylation and N-oxidation. A metabolite, tentatively identified as the N-glucuronide of N-methylaniline, was also observed. No attempts were made to isolate or quantify any ring hydroxylated products.
Source: BASF AG Ludwigshafen
(241) (242)

Type: Metabolism
Remark: Hepatic microsomes were prepared from few species of mammals and birds and incubated with NN-dimethylaniline. Formaldehyde and NN-dimethylaniline-N-oxide produced from the compound were measured. Red-winged blackbirds (Agelaius phoeniceus) were found to have significantly lower N-demethylation activities than rats, and had only marginal or no N-oxidation activities. The N-oxidation and N-demethylation activities of hepatic microsomes from brown-headed cowbirds (Molothrus ater), common grackles (Quiscalus quiscula) and starlings (Sturnus vulgaris) were similar to those of redwings.
Result:

	N-oxidation	N-demethylation
Red-winged blackbirds	0.05 ± 0.04 0.036 ± 0.078	12.76 ± 1.84 20.38 ± 12.96
CD rat	5.87 ± 1.57	63.67 ± 3.54
Rabbit	56	128
Brown-headed cowbird	0.1 ± 0.097	11.55 ± 5.9
Common grackle	0.05 ± 0.054	12.55 ± 5.78
Starling	0.118 ± 0.108	26.52 ± 21.58

N-oxidation is expressed in nmol NN-dimethylaniline-N-oxide formation/mg microsomal protein/10 min. N-demethylation is expressed in nmol formaldehyde formation/mg microsomal protein/10 min.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline purchased from Fluka and further purified as described by Devereux and Fouts in Chem-Biol. Interactions. 8:91-105, 1974.
(243)

Type: Metabolism
Remark: Induction of rabbit hepatic microsomal cytochrome P-450 by Imidazole: Enhanced metabolic activity and altered substrate specifity
Source: BASF AG Ludwigshafen
(244)

Type: other
Remark: Induction of flavine-containing monooxygenase in rabbit lung and kidney by sex steroids and glucocorticoids
Source: BASF AG Ludwigshafen
(245)

Type: other: Pharmakodynamik
Remark: in vitro; Rattenleber-Mikrosomen
Applikationsweg: Inkubation
Vorbehandlung von Leber-Mikrosomen (Ratte) mit "Revenast" fuehrte zu einer -reversiblen- Hemmung der N-Demethylierung von N,N-Dimethylanilin.
Source: BASF AG Ludwigshafen
(246)

Type: other: Review
Remark: Zusammenfassende Darstellungen
Source: BASF AG Ludwigshafen
(247) (181) (248) (249) (250)

Type: other: MetHb formation in humans
Remark: Increased level of metHb to 1.84 % was found in the blood of workers exposed to NN-dimethylaniline for the long period (not given). In few cases metHb level reached 5.2 %. Erythropenia and reticulocytosis were also found in the exposed workers. There were no changes in the blood catalase and peroxidase activities demonstrated.
Source: BASF AG Ludwigshafen
(89)

Type: other: Structural relationship between mutagenicity, maximum tolerated dose and carcinogenicity in rodents
Remark: The CASE was applied to a study of the structural bases of toxicity as expressed in the MTD, carcinogenicity and mutagenicity. NN-dimethylaniline was one out of the compounds analyzed. A high overlap between the structural determinants of the MTD of mice and rats and mutagenicity in Salmonella was observed.
Source: BASF AG Ludwigshafen
(251)

Type: other: accumulation in fish
Remark: The accumulation of 5 aniline derivatives, NN-dimethylaniline among them, in killfish, gold fish and carp were determined. It was found that the concentration rate of NN-dimethylaniline expressed as a concentration in fish/concentration in the test solution after 48 hours exposure ratio in killfish, gold fish and carp were: 7.3,

6.8 and 8.7, respectively. Partition coefficient (n-octanol/water) of 415.7 for the compound was established. It was concluded that the partition coefficient corresponds to the amount of the compound accumulated in the fish body. It was found that the amounts of NN-dimethylaniline in killfish did not increase proportionally to the concentration of the compound in test solution. The concentration in killfish stayed at constant level and syncopic state was observed; they were able to survive in syncopic state in the solution containing up to 200 mg/l NN-dimethylaniline for 3 hours and in the test solution containing 80 mg/l of the compound for 24 hours. It was sugessted that the threshold level (of ca 500 ug/g fish) exists and may be a kind of selfguard action to prevent the accumulation of NN-dimethylaniline.

Source: BASF AG Ludwigshafen

(252)

Type: other: carcinogenicity classification

Remark: A new stratification scheme for rodent carcinogens, in relation to human carcinogen hazard, is proposed. The lowest ranking was accorded to chemicals that induced a highly restricted pattern of tumor induction (i.e. in a specific site in a single sex of a single species). NN-dimethylaniline was classified to this category.

Source: BASF AG Ludwigshafen

(253)

Type: other: carcinogenicity classification

Remark: The relationship between the use of the maximum tolerated dose and study sensitivity for detecting rodent carcinogenicity in studies conducted on 216 chemicals by theNTP was studied. NN-dimethylaniline was one of only 13 rodent carcinogens which had increased tumor rates limited to the top dose (estimated MTD). Seventy five per cent of carcinogens showed numerically elevated site-specific tumor rates at lower doses (1/2 MTD, 1/4 MTD).

Source: BASF AG Ludwigshafen

(254) (117)

Type: other: carcinogenicity classification

Remark: NN-dimethylaniline was put on the list of NTP chemicals for which evidence of carcinogenicity should be confirmed before use in mechanistic or validation studies, based on no structural alert, a negative Salmonella response and a unique tumor site (spleen) in a single sex of a single species (male rat).

Source: BASF AG Ludwigshafen

(255)

Type: other: relationship between general toxicity and carcinogenicity
Remark: Concordance was found between the sites of toxicity and mutagenicity and carcinogenicity of NN-dimethylaniline. Conclusions were drawn based on the results of subchronic (13-week) and chronic (2-years) studies by the NTP Programme (NTP Report No. 360, 1989) In rats, the spleen was the target organ; lesions found were: fibrosis/metaplasia/sarcomas. In mice, the forestomach was the target organ; lesions found were: hyperplasia/squamous cell tumors.
Source: BASF AG Ludwigshafen

(256)

Type: other: review
Remark: Critical data evaluation for NN-dimethylaniline for MAK value and classification of carcinogens has been done by a Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area. It was concluded that a well-founded MAK value for NN-dimethylaniline cannot be derived because there are so few human data. Since in the animal studies with N,N-dimethylaniline, both the acute toxicity and the methaemoglobin formation is less marked than with aniline, the MAK value of 5 ml/m3 and the classification in category II, 1 for the limitation of exposure peaks can be retained provisionally. Biological monitoring of exposure is possibile by measurement of haemoglobin binding. The BAT value for aniline could be applied for this purpose. Because of the suspicion that N,N-dimethylaniline could have carcinogenic activity, it was classified in Section III B in the List of MAK Values. The substance is designated with an "H" because it has been shown to be absorbed through the skin in toxic amounts. The available reproductive toxicity data are insufficient for a classification in one of the pregnancy groups.
Source: BASF AG Ludwigshafen

(75)

Type: other: review
Remark: Critical data evaluation for carcinogenicity classification of NN-dimethylaniline has been done by IARC.
It was concluded that there is inadequate evidence in humans and limited evidence in experimental animals for the carcinogenicity of NN-dimethylaniline.
Overall evaluation was that NN-dimethylaniline is not classifiable as to its carcinogenicity to humans (Group 3).
Source: BASF AG Ludwigshafen

(257)

Type: other: review
Remark: The Health and Environmental Effects Profile for NN-dimethylaniline was prepared by the Office of Health and Environmental Assessment of EPA USA. Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.
NN-dimethylaniline has been determined to be a systemic toxicant. A Reference Dose (RfD) for NN-dimethylaniline is 0.002 mg/kg/day for oral exposure. The Reportable Quantity (RQ) value for NN-dimethylaniline is 100 pounds.
Source: BASF AG Ludwigshafen
(258)

Type: other: structure-activity relationship
Remark: A weak correlation between acute dermal toxicity to rabbits (log LD50), dermal solubility thermodynamic parameter (sigma c) and log P for 20 aromatics was found.
NN-dimethylaniline was one of the aromatics tested.
Source: BASF AG Ludwigshafen
(98)

Type: other: structure-activity relationship
Remark: The nonmutagenic activity of NN-dimethylaniline was predicted correctly by the computerized SAR system (ADAPT) using the 19 molecular descriptors.
Source: BASF AG Ludwigshafen
(134)

Type: other: structure-activity relationship
Remark: No correlation was found between the mutagenic structural alert (electropholic potential of N(CH3)2) of NN-dimethylaniline and the induction of mutations in Salmonella mutagenesis assay.
Source: BASF AG Ludwigshafen
(259) (256)

Type: other: structure-activity relationship
Remark: It was found that using CASE (Computer Automated Structure Evaluation) the positive result of cytogenetic effects observed in CHO cells (i.e, SCE and chromosomal abberations) could be predicted with 65% and 47.9% probability, respectively.
Source: BASF AG Ludwigshafen
(152)

Type: other: structure-activity relationship
Remark: Nonmutagenic activity of chemicals in the Ames test was accurately predicted with CASE (Computer Automated Structure Evaluator).
It should be noted that the authors used data from Connor etal. (Mutat. Res. 118:49-59, 1983) where, according to them, it was found that NN-dimethylaniline is not mutagenic to S. typhimurium (TA 98 with S9). In fact, this compound

was not among 19 chemicals tested by Connor et al. However, it should be stated that good prediction on nonmutagenic activity was obtained with CASE four years later, when authors used data from Mori Y et al. (Carcinogenesis 1:121-127, 1980).
Source: BASF AG Ludwigshafen
(258) (260) (261) (262)

Type: other: structure-activity relationship
Remark: After analysis of activity data for several N-heterocyclic, nitro- amino- (primary, secondary and tertiary), and amino-N-heterocyclic aromatic compounds, it is suggested that since it is not possible to form the N-hydroxyamino metabolite, no mutagenic activity in Ames test could be found for NN-dimethylaniline.
Source: BASF AG Ludwigshafen
(135)

Type: other: structure-activity relationship
Remark: Multinominal model was applied on the mortality data of the acute toxicity of NN-dimethylaniline to zebrafish (Brachydanio rerio). By fitting the model on the experimental mortality data the parameters a (decrease of the LC50 with time), b (log LC50) and beta (decrease of the probability of survival with increasing compound concentration) were estimated. There were: a=0.777 ± 0.159 mg/hr/l; b=1.7 ± 0.065 mg/l and beta= 0.094 ± 0.023. Discriminant analysis was used then to test whether it is possible to discriminate between narcotic chemical such as NN-dimethylaniline and non-narcotic compounds with statistical modelling. It was concluded that parameter a succesfully categorized the compound, but parameter beta misclassified it.
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline from Fluka; > 99.5% purity
(47)

Type: other: structure-activity relationship
Remark: A good correlation was found between NN-dimethylaniline Log 96-h LC50 to fathead minnows (-3.36) and log n-octanol/water partition coeficient P (2.38).
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline of high purity.
(45)

Type: other: structure-activity relationship
Remark: The log EC50 value of NN-dimethylaniline showed a good correlation with 48 h log LC50 value for Himadaka (Orizias latipes) and log P (partition coefficient n-octanol/water).
Source: BASF AG Ludwigshafen
Test substance: NN-dimethylaniline: no further data
(263)

5.11 Experience with Human Exposure

Remark: N,N-Dimethylanilin kann als Dampf inhaliert bzw. ueber den Magen-Darm-Trakt un die Haut resorbiert werden.
Source: BASF AG Ludwigshafen
(264) (265)

Remark: Bei oraler Aufnahme betraegt die niedrigste toedliche Dosis 50 mg/kg.
Source: BASF AG Ludwigshafen
(266)

Remark: Eine akute gesundheitliche Gefaehrdung durch inhalation ist bei Dimethylanilinkonzentrationen in der Luft ab 500 mg/m3 zu erwarten.
Source: BASF AG Ludwigshafen
(267)

Remark: Als Symptome einer akuten Intoxikation werden Kopfschmerzen, Muskelschwaeche, Tremor, Beschleunigung von Puls- und Atemfrequenz, Methaemoglobinaemie, Cyanose, Atemnot, Verwirrtheit, tonisch-klonische Kraempfe , Kreislaufkollaps, Bewusstlosigkeit und schliesslich Atemstillstand beschrieben.
Source: BASF AG Ludwigshafen
(268) (265)

Remark: Zwei Arbeiter, die offensichtlich erheblich exponiert waren, kollabierten augenblicklich unf klagten nach achtstuendiger Bewusstlosigkeit lediglich ueber Sehstoerungen und starke Bauchschmerzen.
Source: BASF AG Ludwigshafen
(269)

Remark: Positive Reaktion im Epikutantest bei einem Polyesterverarbeiter.
Source: BASF AG Ludwigshafen
(270)

Remark: Nach Langzeiteinwirkung von N,N-Dimethylanilin wird bei Arbeitern eine signifikante Erhoehung des Methaemoglobins (1,84 % gegenueber 0,38 % in der Kontrollgruppe), eine signifikante Erythropenie ud Retikulozytose und eine Tendenz zur Verringerung des Haemoglobingehalts beschrieben.
Source: BASF AG Ludwigshafen
(271)

Remark: Eine Ueberwachungs- bzw. Querschnittsuntersuchung bei 139 bzw. 174 Beschaeftigten in einem chemischen Produktionsbetrieb mit Exposition gegenueber N,N-Dimethylanilin und anderen Stoffen zeigte keine auf N,N-Dimethylanilin zurueckzufuehrende Gesundheitsstoerungen, z. B. keine MetHb-Bildung.
Source: BASF AG Ludwigshafen
(272)

Remark: Bei oraler Aufnahme betraegt die niedrigste toedliche Dosis 50 mg/kg.
Source: BASF AG Ludwigshafen
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Source: BASF AG Ludwigshafen
(272)

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7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 95-53-4
CAS No.	95-53-4
EINECS Name	o-toluidine
EINECS No.	202-429-0
TSCA Name	Benzenamine, 2-methyl-
Molecular Formula	C7H9N

Producer Related Part	
Company:	Bayer Corporation
Creation date:	23-SEP-1999
Substance Related Part	
Company:	Bayer Corporation
Creation date:	23-SEP-1999

Memo:	Bayer Corporation

Printing date:	08-OCT-2001
Revision date:	
Date of last Update:	08-OCT-2001

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Flags (profile):	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type:	other: co-sponsoring organization
Name:	American Chemistry Council (formerly Chemical Manufacturers Association), Monocyclic Aromatic Amines and Nitro Aromatics (MAANA) HPV Panel
Street:	1300 Wilson Boulevard
Town:	22209 Arlington, VA
Country:	United States

04-OCT-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information
-

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms
-

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: -16.3 degree C
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: o-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
04-OCT-2001 (1)

Value: >= -23.5 degree C
Source: Bayer AG Leverkusen
16-FEB-1994 (2)

Value: -22.6 - -23.1 degree C
Source: Bayer AG Leverkusen
04-MAR-1994 (3)

Value: -16.3 degree C
Source: Du Pont de Nemours DeutschlandBayer AG Leverkusen
08-APR-1994 (4)

Value: < -15 degree C
Source: Bayer AG Leverkusen
08-APR-1994 (5)

2.2 Boiling Point

Value: 200.3 degree C
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: o-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
04-OCT-2001 (1)

Value: 199.8 degree C at 760 hPa
Source: Du Pont de Nemours DeutschlandBayer AG Leverkusen
08-APR-1994 (4)

Value: 200 degree C at 1013 hPa
Source: Bayer AG Leverkusen
08-APR-1994 (3)

Value: > 200 degree C
Decomposition: yes
Method: other: DTA
Source: Bayer AG Leverkusen
Test condition: 10 K/min
16-FEB-1994 (2)

Value:
Remark: Decomposition: no exotherm reaction up to 400 degree C (DTA)
Source: Bayer AG Leverkusen
08-APR-1994 (6)

2.3 Density

Type: relative density
Value: .9984 at 20 degree C
Method: other: Handbook value
GLP: no data
Testsubstance: other TS: o-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
04-OCT-2001 (1)

Type: density
Value: 1 - 1.004 g/cm3 at 20 degree C
Method: other: DIN 51757
Source: BASF AGBayer AG Leverkusen
16-FEB-1994 (7)

Type: density
Value: 1 g/cm3 at 20 degree C
Source: Bayer AG Leverkusen
31-JUL-1997 (2) (3)

Type: density
Value: 1.004
Source: Du Pont de Nemours DeutschlandBayer AG Leverkusen
08-APR-1994 (4)

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: 1 hPa at 42.6 degree C
Method: other (measured): Handbook value
GLP: no data
Testsubstance: other TS: o-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
04-OCT-2001 (8)

Value: .53 hPa at 20 degree C
Source: Bayer AG Leverkusen
10-AUG-2000 (3)

Value: 3.7 hPa at 50 degree C
Source: Bayer AG Leverkusen
10-AUG-2000 (3)

Value: .24 hPa at 20 degree C
Source: Bayer AG Leverkusen
31-JUL-1997 (2)

Value: .3 hPa at 20 degree C
Source: BASF AGBayer AG Leverkusen
31-JUL-1997 (7)

Value: 1 hPa at 44 degree C
Source: Du Pont de Nemours DeutschlandBayer AG Leverkusen
08-APR-1994 (4)

Value: 1.33 hPa at 44 degree C
Source: Bayer AG Leverkusen
31-JUL-1997 (2)

2.5 Partition Coefficient

log Pow: 1.4 at 24.5 degree C
Method: Directive 84/449/EEC, A.8 "Partition coefficient"
Year:
GLP: yes
Testsubstance: other TS: o-toluidine; purity not noted
Source: BASF AGBayer AG Leverkusen
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
04-OCT-2001 (9)

log Pow: 1.3
Method: other (calculated): ClogP, Leo, Hansch: Leo et al. (1971): Chem. Rev. 71, 525
Year:
GLP: no
Testsubstance: other TS: molecular structure
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Data from Handbook or collection of data;
Accepted calculation method
Flag: Critical study for SIDS endpoint
04-OCT-2001 (10) (11) (12)

log Pow: 1.54
Method: other (calculated)
Year:
Source: Bayer AG Leverkusen
01-AUG-1997 (13)

2.6.1 Water Solubility

Value: 8.292 g/l at 25 degree C
Method: other: WSKOW (v1.36)
GLP: no
Testsubstance: other TS: molecular structure
Result: Log Kow (estimated) : 1.62
Log Kow (experimental): 1.32
Cas No: 000095-53-4
Name : o-Toluidine
Refer : Hansch et al; 1995
Log Kow used by Water solubility estimates: 1.32

Equation Used to Make Water Sol estimate:
Log S (mol/L) = 0.796 - 0.854 log Kow - 0.00728 MW

Log Water Solubility (in moles/L) : -1.111
Water Solubility at 25 deg C (mg/L): 8292
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
05-OCT-2001 (14)

Value: 8 g/l at 20 degree C
pH: 7.5 at 8 g/l and 20 degree C
Source: BASF AGBayer AG Leverkusen
31-JUL-1997 (7)

Value: 17 g/l at 20 degree C
pH: 8.5 at 17 g/l and 20 degree C
Source: Bayer AG Leverkusen
31-JUL-1997 (3)

Value: 15 g/l at 40 degree C
Source: Bayer AG Leverkusen
31-JUL-1997 (2)

Value: 19 g/l at 60 degree C
Source: BASF AGBayer AG Leverkusen
31-JUL-1997 (7)

Value: 25 g/l at 60 degree C
Source: Bayer AG Leverkusen
31-JUL-1997 (3)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: 85 degree C
Type: closed cup
Method: other: DIN 51758
Year:
Source: BASF AGBayer AG Leverkusen
31-JUL-1997 (7) (3)

Value: 86 degree C
Type:
Method:
Year:
Source: Bayer AG Leverkusen
31-JUL-1997 (2)

2.8 Auto Flammability

Value: > 450 degree C
Remark: Ingition temperature
Source: Bayer AG Leverkusen
23-JUL-1997 (2)

Value: 480 degree C
Method: other: DIN 51794
Remark: Ignition temperature
Source: BASF AGBayer AG Leverkusen
31-JUL-1997 (7) (3) (12)

Value:
Remark: Ignition temperature: not below 500 degree C
Source: Bayer AG Leverkusen
08-APR-1994 (5)

2.9 Flammability

-

2.10 Explosive Properties

-

2.11 Oxidizing Properties

-

2.12 Additional Remarks

Remark: Untere Exposionsgrenze: 1 Vol-%
Obere Explosionsgrenze: 7 Vol-%
Gefaehrliche Zersetzungsprodukte: Nitrose Gase
Unvertraegliche Substanz: Mineralsaeuren (Reaktion zu Salzen)
Source: Bayer AG Leverkusen
24-JUL-1997 (3) (12)

Remark: Explosionsgrenzen: 1.5 - 7.5 Vol. %
Source: BASF AGBayer AG Leverkusen
16-FEB-1994 (7)

Remark: Henry-Konstante: H = 0.334 Pa x m3/mol
Source: Bayer AG Leverkusen
16-FEB-1994 (15)

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Rate constant: .0000000000000000000143 cm3/(molecule * sec)
Degradation: 50 % after .1 day
Method: other (calculated): Medchem Software CLOGP3, Release 3.42
Year: 1986 GLP:
Test substance:
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
11-AUG-2000 (16)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .00000000000132 cm3/(molecule * sec)
Degradation: 50 % after 9.7 hour(s)
Method: other (calculated): AOPWIN vers. 1.89
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
05-OCT-2001 (14)

3.1.2 Stability in Water

Type:
Method: other: Schultz et al. (1989) Bull. Environ. Toxicol. Chem. 42:192-198
Year: GLP:
Test substance: other TS: o-toluidine; purity not noted
Result: A solution of 1.62 mg/l in distilled water lost 4.0-5.6% in 48 hours
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
05-OCT-2001 (17)

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: air, water, soil, sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: (calculation) Level III Fugacity Model
Year:
Result:

Media	Distribution (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.355	1.94	1000	6.53e-012
Water	50.4	360	1000	4.19e-011
Soil	49.1	360	1000	8.97e-010
Sediment	0.099	1.44e+003	0	3.41e-011

Persistence Time: 269 hr
Reaction Time: 314 hr
Advection Time: 1.85e+003 hr
Percent Reacted: 85.5
Percent Advected: 14.5
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
05-OCT-2001 (14)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: other: sludge samplings from different sewage plants, rivers, bays and a lake, 30 mg/l
Concentration: 100 mg/l related to Test substance
Degradation: 65.4 % after 28 day
Method: OECD Guide-line 301 C "Ready Biodegradability: Modified MITI Test (I)"
Year: GLP: no
Test substance: other TS: o-toluidine; purity not noted
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
05-OCT-2001 (18)

Type: aerobic
Inoculum: activated sludge, industrial, non-adapted
Degradation: 96 % after 15 day
Result: inherently biodegradable
Testsubstance: 3 hour(s) 20 - 30 %
5 day 20 %
10 day 77 %
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 1986 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
05-OCT-2001 (19)

Type: aerobic
Inoculum: activated sludge
Degradation: > 90 % after 28 day
Method: OECD Guide-line 301 A (old version) "Ready Biodegradabiltiy: Modified AFNOR Test"
Year: GLP: no
Test substance: no data
Remark: Specific (gas chromatography) analysis:
7 day (>90 %)
14 day (>90 %)
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
11-AUG-2000 (20)

Type: aerobic
Inoculum: activated sludge
Degradation: > 90 % after 28 day
Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: GLP: no
Test substance: no data
Remark: DOC Analysis:
7 day (57 - >90 %)
14 day (>90 %)
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
11-AUG-2000 (20)

Type: aerobic
Inoculum: activated sludge
Degradation: > 90 % after 28 day
Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: GLP: no
Test substance: no data
Remark: Specific (gas chromatography) analysis:
7 day (57 - >90 %)
14 day (>90 %)
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
11-AUG-2000 (20)

Type: aerobic
Inoculum: other bacteria: soil bacteria, enrichment culture
Degradation: 100 %
Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: GLP: no
Test substance: no data
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
11-AUG-2000 (21) (22)

Type: aerobic
Inoculum: activated sludge, industrial
Degradation: 96 % after 11 day
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: GLP: no
Test substance: no data
Remark: approx. 14 % of the elimination caused by physical mechanisms
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
11-AUG-2000 (22)

Type: aerobic
Inoculum: activated sludge
Degradation: 88 - 90 % after 28 day
Method: OECD Guide-line 301 A (old version) "Ready Biodegradabiltiy: Modified AFNOR Test"
Year: GLP: no
Test substance: no data
Remark: DOC Analysis:
7 day (74 - 89 %)
14 day (73 - >90 %)
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
11-AUG-2000 (20)

Type: aerobic
Inoculum: other: effluent of BASF waste water treatment plant
Concentration: 20 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: 97 % after 21 day
Testsubstance: 7 day 86 %
14 day 95 %
Method: OECD Guide-line 301 E "Ready biodegradability: Modified OECD Screening Test"
Year: 1981 GLP: no
Test substance:
Source: BASF AGBayer AG Leverkusen
Reliability: (1) valid without restriction
11-AUG-2000 (23)

Type: aerobic
Inoculum: other bacteria: soil microflora from Niagara silt loam
Concentration: 25 mg/l related to Test substance
Degradation: 100 % after 64 day
Method: other: Closed bottle test
Year: GLP: no
Test substance: no data
Remark: soil microorganisms in aqueous mineral medium; determination of primary degradation
Source: Bayer AG Leverkusen
Test condition: Spectrophotometrical measurement at 265 nm
Reliability: (2) valid with restrictions
11-AUG-2000 (24)

Type: aerobic
Inoculum: other: activated sludge, acclimated
Degradation: 97.7 % after 5 day
Method: other: batch test, similar to Zahn-Wellens Test
Year: GLP: no
Test substance:
Remark: Test compound as sole C source, mineral salts, dark, stirred.
Source: Bayer AG Leverkusen
11-AUG-2000 (25)

Type: aerobic
Inoculum: other bacteria: adapted to the test substance
Degradation: ca. 60 %
Method: other: Respirometer test
Year: GLP: no
Test substance: no data
Source: Bayer AG Leverkusen
11-AUG-2000 (26) (22)

Type: aerobic
Inoculum: activated sludge
Concentration: 100 mg/l related to Test substance
Degradation: 92 % after 1 day
Method: other: Activated sludge degradability test
Year: GLP: no
Test substance: no data
Remark: Degradation 92 % related to COD, 83 % related to TOC
Source: Bayer AG Leverkusen
11-AUG-2000 (27) (28)

Type:
Inoculum: other: activated sludge, adapted
Method: other: Warburg respirometer
Year: GLP: no
Test substance: no data
Remark: degradation by a mutant Aerobacter sp.:
500 mg/ at 30 degree C
parent: 100 % ring disruption in 64 h
mutant: 100 % ring disruption in 6 h
Source: Bayer AG Leverkusen
11-AUG-2000 (29)

3.6 BOD5, COD or BOD5/COD Ratio

Remark: ThoD: 3136 mg/g (NO2)
2538 mg/l (NH3)
Source: Bayer AG Leverkusen
31-JUL-1997

3.7 Bioaccumulation

Species: other
Exposure period:
Concentration:
BCF: 2.07
Elimination:
Method: other: BCF Program (v2.13)
Year: GLP: no
Test substance: other TS: molecular structure
Result: Log Kow (estimated) : 1.62
Log Kow (experimental): 1.32
Log Kow used by BCF estimates: 1.32

Equation Used to Make BCF estimate:
Log BCF = 0.77 log Kow - 0.70

Estimated Log BCF = 0.316 (BCF = 2.072)
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
05-OCT-2001 (14)

Species: other: Crassostrea gigas, Pacific oyster; static
Exposure period: 24 hour(s)
Concentration: 5 mg/l
BCF: 4.6
Elimination:
Method:
Year: GLP: no data
Test substance:
Source: Bayer AG Leverkusen
31-JUL-1997 (30)

Species: other: Mytilus edulis, Common bay mussel; static
Exposure period: 24 hour(s)
Concentration: 5 mg/l
BCF: 4.2
Elimination:
Method:
Year: GLP: no data
Test substance:
Source: Bayer AG Leverkusen
31-JUL-1997 (30)

3.8 Additional Remarks

Remark: Degradation in soil:
- 500 mg/kg Chernozem soil
- degr. in 3 days leaving very stable prod. that persists > 3 months
Source: Bayer AG Leverkusen
31-JUL-1997 (31)

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no data
NOEC: 31.6
LC50: 68 - 100
Method: other: Bestimmung der Wirkung von Wasserinhaltsstoffen auf Fische, DIN 38412 Teil 15
Year: 1979 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AGBayer AG Leverkusen
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
05-OCT-2001 (32)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: 30
LC50: 117
LC100: 178
Method: other: DIN 38412 L15
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
05-OCT-2001 (33)

Type: flow through
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 100
Method: other: no data
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
31-JUL-1997 (34)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 14 day
Unit: µmol/l Analytical monitoring: no data
LC50: 2.88
Method: other: see Koenemann, H., Toxicology 19, 209-221 (1981)
Year: GLP: no
Test substance: no data
Source: Bayer AG Leverkusen
31-JUL-1997 (35) (36)

Type: static
Species: Carassius auratus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 124
Method: other: no data
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
31-JUL-1997 (34)

Type: static
Species: Cyprinus carpio (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 78.5
Method: other: no data
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
31-JUL-1997 (34)

Type: static
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 103
Method: other: Static, no further information
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
31-JUL-1997 (34)

Type: static
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 14 day
Unit: mg/l Analytical monitoring: no
LC50: 81.3
Method: other: Koenemann, 1981
Year: GLP: no
Test substance: other TS: purity: > 99.5 %
Source: Bayer AG Leverkusen
23-JUL-1997 (13)

Type:
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 42
Method: other: no data
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
31-JUL-1997 (37)

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
EC50: .52
Method: other: NEN 6501
Year: 1980 GLP: no data
Test substance: other TS: o-toluidine; purity > 99.5 %
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
05-OCT-2001 (13)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 1.6 - 5
EC50: 9 - 50
EC100: 100
Method: other: Daphnia Immobilization test; s. Authors of this publication
Year: GLP: no
Test substance: other TS: o-toluidine; purity not noted
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
05-OCT-2001 (38)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
LC0 : 2.5
Method: other: Daphnia Immobilization test; s. Authors of this publication
Year: GLP: no
Test substance: no data
Source: Bayer AG Leverkusen
01-AUG-1997 (39)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
LC50 : 26
Method: other: Daphnia Immobilization test; s. Authors of this publication
Year: GLP: no
Test substance: no data
Source: Bayer AG Leverkusen
01-AUG-1997 (39)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
LC100 : 60
Method: other: Daphnia Immobilization test; s. Authors of this publication
Year: GLP: no
Test substance: no data
Source: Bayer AG Leverkusen
01-AUG-1997 (39)

Type:
Species: Daphnia magna (Crustacea)
Exposure period:
Unit: mg/l Analytical monitoring: no data
LC50 : 26
Method: other: no data
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
Test condition: no information about exposure period (24 h oder 48 h)
04-MAR-1994 (40)

Type:
Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: <= 8
Method: other: no data
Year: GLP: no
Test substance: no data
Remark: EC50 here pronounced effect to over 50 % of test animals
Source: Bayer AG Leverkusen
Test condition: System: static; beta-mesosaprobic to mesotrophic river water used for dilution
31-JUL-1997 (41)

Type:
Species: Elasmopus pectenicrus (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50 : > 40
Method: other: see this publication
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
31-JUL-1997 (42)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Chlorella pyrenoidosa (Algae)
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 55
Method: OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year: 1984 GLP: no data
Test substance: other TS: o-toluidine; purity: > 99.5%
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
05-OCT-2001 (13)

Species: Scenedesmus subspicatus (Algae)
Endpoint: biomass
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 3.9
Method: other: DIN 38412 part 9
Year: GLP: no
Test substance:
Source: Bayer AG Leverkusen
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
05-OCT-2001 (43)

Species: Microcystis aeruginosa (Algae, blue, cyanobacteria)
Endpoint: biomass
Exposure period: 8 day
Unit: mg/l Analytical monitoring: no
TT : .31
Method: other: cell multiplication inhibition test
Year: GLP: no
Test substance: no data
Remark: TT = Toxicity Threshold
Source: Bayer AG Leverkusen
Test condition: pH: 7
31-JUL-1997 (44) (45) (46)

Species: Scenedesmus quadricauda (Algae)
Endpoint: biomass
Exposure period: 7 day
Unit: mg/l Analytical monitoring: no
TT : 6.3
Method: other: cell multiplication inhibition test
Year: GLP: no
Test substance: no data
Remark: TT = Toxicity Threshold
Source: Bayer AG Leverkusen
Test condition: pH: 7
31-JUL-1997 (45) (46) (47) (48)

Species: Scenedesmus sp. (Algae)
Endpoint: growth rate
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
TT : 10
Method: other: cell multiplication inhibition test
Year: GLP: no
Test substance: no data
Remark: TT = Toxicity Threshold
Source: Bayer AG Leverkusen
Test condition: System: static; beta-mesosaprobic to mesotrophic river water used for dilution
31-JUL-1997 (41)

Species: Scenedesmus subspicatus (Algae)
Endpoint: biomass
Exposure period: 7 day
Unit: mg/l Analytical monitoring: no
EC10: 9.4
Method: other: cell multiplication inhibition test
Year: GLP: no
Test substance: no data
Source: Bayer AG Leverkusen
31-JUL-1997 (49)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Chilomonas paramaecium (Protozoa)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
TT : 237
Method: other: cell multiplcation inhibition
Year: GLP: no
Test substance: no data
Remark: TT = Toxicity Threshold
Source: Bayer AG Leverkusen
31-JUL-1997 (50) (51)

Type: aquatic
Species: Entosiphon sulcatum (Protozoa)
Exposure period: 72 hour(s)
Unit: mg/l Analytical monitoring: no
TT : 76
Method: other: cell multiplcation inhibition
Year: GLP: no
Test substance: no data
Remark: TT = Toxicity Threshold
Source: Bayer AG Leverkusen
31-JUL-1997 (47) (52) (50) (53) (49)

Type: aquatic
Species: Photobacterium phosphoreum (Bacteria)
Exposure period: 15 minute(s)
Unit: mg/l Analytical monitoring: no
EC50: 33
Method: other: Beckmann Instruments Manual
Year: 1982 GLP: no
Test substance: other TS: purity: > 99.5 %
Source: Bayer AG Leverkusen
23-JUL-1997 (13)

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 16 hour(s)
Unit: mg/l Analytical monitoring: no
TT : 16
Method: other: cell multiplication inhibition test
Year: GLP: no
Test substance: no data
Remark: TT = Toxicity Threshold
Source: Bayer AG Leverkusen
31-JUL-1997 (44) (47) (48) (49)

Type: aquatic
Species: Tetrahymena pyriformis (Protozoa)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
TT : 520
Method: other: cell multiplication inhibition
Year: GLP: no data
Test substance:
Remark: TT = Toxicity Threshold
Source: Bayer AG Leverkusen
31-JUL-1997 (54)

Type: aquatic
Species: Uronema parduzci (Protozoa)
Exposure period: 20 hour(s)
Unit: mg/l Analytical monitoring: no
TT : 21
Method: other: cell multiplcation inhibition
Year: GLP: no
Test substance: no data
Remark: TT = Toxicity Threshold
Source: Bayer AG Leverkusen
31-JUL-1997 (50) (55)

Type: aquatic
Species: anaerobic bact. from a domestic water treatment plant
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 1250
Method: ETAD Fermentation tube method "Determination of damage to effluent bacteria by the Fermentation Tube Method"
Year: 1986 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: Bayer AG Leverkusen
04-MAR-1994 (56)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish

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4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species:	Daphnia magna (Crustacea)
Endpoint:	mortality
Exposure period:	21 day
Unit:	mg/l Analytical monitoring: no
NOEC:	1
EC50:	2.2
Method:	other: NEN 6502
Year:	1980 GLP: no data
Test substance:	other TS: purity: > 99.5 %
Source:	Bayer AG Leverkusen

23-JUL-1997 (13)

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms

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4.6.2 Toxicity to Terrestrial Plants

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4.6.3 Toxicity to other Non-Mamm. Terrestrial Species

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4.7 Biological Effects Monitoring

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4.8 Biotransformation and Kinetics

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4.9 Additional Remarks

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5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex: male
Number of Animals:
Vehicle:
Value: = 900 mg/kg bw
Method: other: BASF-Test
Year: GLP: no
Test substance: other TS: o-toluidine; purity >= 99.5 % w/w
Source: BASF AGBayer AG Leverkusen
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
08-OCT-2001 (57) (58)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 635 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: male
Source: Bayer AG Leverkusen
16-FEB-1994 (59)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 670 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (60)

Type: LD50
Species: rat
Strain:
Sex: male
Number of
Animals:
Vehicle:
Value: = 940 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
11-AUG-2000 (61)

Type: LD50
Species: rat
Strain:
Sex: male
Number of
Animals:
Vehicle:
Value:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: value: 0.75 ml/kg Kgw.
Source: Bayer AG Leverkusen
11-AUG-2000 (62)

Type: LD50
Species: rat
Strain:
Sex: male
Number of
Animals:
Vehicle:
Value: = 2951 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS: Hydrochloride salt
Source: Bayer AG Leverkusen
11-AUG-2000 (63)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1710 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (64)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 520 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (60)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 760 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (64)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 840 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (60)

Type: LD50
Species: cat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: >= 50 mg/kg bw
Method: other: BASF-Test
Year: GLP: no
Test substance: other TS
Remark: Zufuhrweg: Schlundsonde
Es wurde eine starke Methaemoglobinbildung beobachtet.
Source: BASF AGBayer AG Leverkusen
Test substance: 0.5 %ige waessrige Loesung
16-FEB-1994 (57)

5.1.2 Acute Inhalation Toxicity

Type: other: IRT
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 7 hour(s)
Value:
Method: other: According to: Smyth et al. (1962): Am. Ind. Hyg. Ass. J. 23, 95-107
Year: GLP: no
Test substance: other TS: o-toluidine; purity >= 99.5 % w/w
Remark: No deaths in a saturated atmosphere (vapor) at 20 deg C. [Keine Letalitaet in einer bei 20 Grad C angereicherten Atmosphaere (Dampf)].
Source: BASF AG; Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint

08-OCT-2001 (57)

Type: other: Zeitsaettigungstest
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 8 hour(s)
Value:
Method: other: Smyth et al. (1962): Am. Ind. Hyg. Ass. J. 23, 95-107
Year: GLP: no data
Test substance: other TS: o-toluidine; purity not noted
Remark: Not lethal [Nicht letal]
Source: Bayer AG Leverkusen
08-OCT-2001 (61)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Strain:
Sex: male
Number of Animals:
Vehicle:
Value: 3250 mg/kg bw
Method: other: according to Smyth et al. (1962): Am. Ind. Hyg. Ass. J. 23, 95-107
Year: GLP: no data
Test substance: other TS: o-toluidine; purity not noted
Source: Bayer AG Leverkusen
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
05-OCT-2001 (61)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 164 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: male
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
16-FEB-1994 (65)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 246 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: female
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
16-FEB-1994 (65)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 150 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (63)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 179 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: male
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
16-FEB-1994 (65)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 113 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: female
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
16-FEB-1994 (65)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: = 1115 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (66)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time: 24 hour(s)
Number of Animals:
PDII:
Result: not irritating
EC classificat.: not irritating
Method: other: no data
Year: GLP: yes
Test substance: no data
Remark: on rabbit ear: Exposure Time: 24 hr
[Am Kaninchenohr; Einwirkzeit: 24 h
Source: Bayer AG Leverkusen
08-OCT-2001 (67)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: moderately irritating
EC classificat.:
Method: other: Patch-Test
Year: GLP: no data
Test substance: no data
Remark: Exposure Time: 24 hr [Einwirkzeit: 24 h]
Source: Bayer AG Leverkusen
08-OCT-2001 (63)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: moderately irritating
EC classificat.: irritating
Method: Draize Test
Year: 1959 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AG; Bayer AG Leverkusen
08-OCT-2001 (57)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time: 24 hour(s)
Comment:
Number of Animals:
Result: highly irritating
EC classificat.:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Exposure Time: 24 hr [Einwirkzeit: 24 h]
Source: Bayer AG Leverkusen
08-OCT-2001 (63)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Ohne Auswaschen, Cornea oberflaechlich veraetzend
Source: Bayer AG Leverkusen
16-FEB-1994 (67)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: moderately irritating
EC classificat.: not irritating
Method: Draize Test
Year: 1959 GLP: no
Test substance: as prescribed by 1.1 - 1.4
Source: BASF AGBayer AG Leverkusen
16-FEB-1994 (57)

5.3 Sensitization
-

5.4 Repeated Dose Toxicity

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 7 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 1000 - 50000 ppm
Control Group: no data specified
Method: other: according to Griesemer, Cueto (1980): IARC Sci. Publ. 27,259-281
Year: GLP: no data
Test substance: other TS: o-toluidine, hydrocloride; purity not noted
Remark: 5 animals/sex/group [5 Tiere/Geschlecht/Gruppe]
Result: In the highest dose group 4 males and 3 females died as a consequence of retarded body weight gain (up to 58%). From 12500 ppm, pigmentation in the kidneys, liver, and spleen. [In der hoechsten Dosisgruppe starben 4 m und 3 w, dosisabhaengige Verzoegerung der Koerpergewichtsentwicklung (bis zu 58 %), ab 12500 ppm Pigmentierungen in Niere, Leber und Milz.]
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
Flag: Critical study for SIDS endpoint
08-OCT-2001 (68) (69)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: oral feed
Exposure period: 7 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 1000 - 50000 ppm
Control Group: no data specified
Method: other: according to Griesemer, Cueto (1980): IARC Sci. Publ. 27,259-281
Year: GLP: no data
Test substance: other TS: o-toluidine, hydrocloride; purity not noted
Remark: 5 animals/sex/group [5 Tiere/Geschlecht/Gruppe]
Result: Dose-dependent d3lay in body weight gain (up to 37%), pigment deposition in the spleen in the highest dose group.

[Dosisabhaengige Verzoegerung der Koerpergewichtsentwickung (bis zu 37 %), in der hoechsten Dosisgruppe Pigmentablagerungen in der Milz.]
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
Flag: Critical study for SIDS endpoint
08-OCT-2001 (68) (69) (70)

Species: rat Sex: male/female
Strain: no data
Route of admin.: dermal
Exposure period: 4 Months
Frequency of treatment: 4 h/day
Post. obs. period:
Doses: 8, 80 mg/kg Kgw.
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Applied to 2/3 of the area of the tail skin.
[Auf 2/3 der Flaeche der Schwanzhaut appliziert; 15 Tiere/Geschlecht/Gruppe]
Result: In the males of the highest dose group a reduction in the RNA content of the testes homogenate and an increase in that of the sertoli cells. In the females, a prolonged estrus and an increased number of corpora lutea.

[Bei den m der hohen Dosierung Verminderung des RNA-Gehaltes des Hodenhomogenates und Vergroesserung der Sertoli-Zellen, bei den w verlaengerte Oestrusphase und erhoehte Anzahl an Gelbkoerpern.]
Source: Bayer AG Leverkusen
Flag: Critical study for SIDS endpoint
08-OCT-2001 (71)

Species: rat Sex: no data
Strain: no data
Route of admin.: dermal
Exposure period: keine Angabe
Frequency of treatment: jeden 2. Tag
Post. obs. period:
Doses: 0.5 % Loesung in Chloroform
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Haemorrhagien in der Blase, Vakuolisierung der Epithelzellen, papilloese Proliferation der Epithelzellen der Blase.
Source: Bayer AG Leverkusen
16-FEB-1994 (72)

Species: rat Sex: male
Strain: Fischer 344
Route of admin.: oral unspecified
Exposure period: 5, 10, 20 days
Frequency of treatment: daily
Post. obs. period:
Doses: 225 mg/kg bw/day
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Verzoegerte Koerpergewichtszunahme und erhoehte Mortalitaet, fuer Erythrozytenschaedigung typische Organbefunde (erhoehtes Milzgewicht sowie Kongestion und extramedullaere Haematopoese, renale Haemosiderose, erhoehte Knochenmarksdichte).
Source: Bayer AG Leverkusen
11-AUG-2000 (58) (73)

Species: rat Sex: no data
Strain: no data
Route of admin.: oral unspecified
Exposure period: 91 Tage
Frequency of treatment: taeglich
Post. obs. period:
Doses: 15 - 24 mg/Tier (gesenkt wegen Toxizitaet auf 7.5 - 12 mg/Tier)
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Bei 3/10 Tieren Veraenderungen in der Mucosa der Blase mit Metaplasien und beginnender Epithelproliferation.
Source: Bayer AG Leverkusen
16-FEB-1994 (74)

Species: rat Sex: no data
Strain: no data
Route of admin.: oral unspecified
Exposure period: 2.5 Monate
Frequency of treatment: taeglich
Post. obs. period:
Doses: 35 mg/kg Kgw./Tag
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Erhoehte Methaemoglobin-Bildung, Erythropenie, Retikulozytose.
Source: Bayer AG Leverkusen
16-FEB-1994 (60)

Species: rat Sex: male
Strain: Wistar
Route of admin.: i.p.
Exposure period: 3 consecutive days
Frequency of treatment: once a day for 3 consecutive days
Post. obs. period: no
Doses: 75 mg/kg bw
Control Group: no data specified
Method: other: Determination of long metabolzing enzymes
Year: GLP: no data
Test substance: no data
Remark: increased activity of AHH in liver, kidney and lung; increased activity of NADPH-cytochrome c reductase in liver.
Source: Bayer AG Leverkusen
18-APR-1994 (75)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1537, TA 1538, G 46
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
11-AUG-2000 (76)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 1535, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
11-AUG-2000 (77) (78)

Type: other: 8-Azaguanin-Resistenz-Test (HGPRT-Lokus)
System of testing: Salmonella typhimurium
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
11-AUG-2000 (79)

Type: Ames test
System of testing: Escherichia coli WP2, WP2uvrA, C 3076, D 3052
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
05-OCT-2001 (76)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
05-OCT-2001 (80) (81)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
05-OCT-2001 (82) (83)

Type: DNA damage and repair assay
System of testing: primaere Ratten- und Hamsterhepatocyten
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
05-OCT-2001 (84)

Type: DNA damage and repair assay
System of testing: E. coli K-12 343/113 uvrB-/recA-, E. coli K-12 343/113 uvrb+/recA+
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
05-OCT-2001 (85)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
15-APR-1994 (86)

Type: Ames test
System of testing: Salmonella typhimurium
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (87) (88)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
15-APR-1994 (89)

Type: Ames test
System of testing: Salmonella typhimurium TA 100, TA 1535, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (90)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (91)

Type: Ames test
System of testing: Salmonella typhimurium TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (92) (93)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (94)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Remark: positive only in presence of norharman
Source: Bayer AG Leverkusen
18-APR-1994 (95)

Type: Ames test
System of testing: Salmonella typhimurium
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (96)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (97)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 102
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (98)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (99) (100)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 104
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: ambiguous
Method: other
Year: GLP: no data
Test substance: no data
Remark: positive in TA 100
Source: Bayer AG Leverkusen
03-MAY-1994 (101)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Remark: positive only with norharman
Source: Bayer AG Leverkusen
03-MAY-1994 (102)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (103)

Type: Ames test
System of testing: Salmonella Typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: hydrochloride
Source: Bayer AG Leverkusen
03-MAY-1994 (104)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Ames, B.N. et al. (1975): Mutat. Res. 31, 347-364
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
18-APR-1994 (105)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Metabolische Aktivierung: S9-Mix und Norharman
Source: Bayer AG Leverkusen
16-FEB-1994 (106)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 102
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (107)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (108)

Type: Ames test
System of testing: Salmonella typhimurium TA 102
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (109)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: urine method
Year: GLP: no data
Test substance: no data
Remark: posive result only with urine extract collected from rats given 80 mg/kg bw.
Source: Bayer AG Leverkusen
03-MAY-1994 (110)

Type: Ames test
System of testing: Salmonella typhimurium (no further information)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: urine methode
Year: GLP: no data
Test substance: no data
Remark: Substance administered to rats, urine tested, abstract only
Source: Bayer AG Leverkusen
03-MAY-1994 (111) (112)

Type: Ames test
System of testing: Salmonella typhimurium TA 92, TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
15-APR-1994 (113)

Type: Ames test
System of testing: Salmonella typhimurium TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (114)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (115)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1353, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (116)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (117)

Type: Ames test
System of testing: salmonella typhimurium TA 97, TA 98, TA 100, TA 1535
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (118)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (119)

Type: Bacillus subtilis recombination assay
System of testing: B. subtilis M45 Rec-
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
15-APR-1994 (120) (121)

Type: Bacillus subtilis recombination assay
System of testing: Bacillus subtilis H 17 rec+, M 45 rec-
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid

16-FEB-1994 (122)

Type: Bacterial forward mutation assay
System of testing: Salmonella typhimurium BA 13, BA 9
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

18-APR-1994 (123)

Type: Bacterial gene mutation assay
System of testing: E.coli rec-
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen

15-APR-1994 (120) (124)

Type: Bacterial gene mutation assay
System of testing: E. coli RecA-/PolA-
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen

15-APR-1994 (120) (125)

Type: Bacterial gene mutation assay
System of testing: salmonella typhimurium TA 98, TA 100; Escherichia Coli WP2, WP2uvrA(P)
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (126)

Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1538, Escherichia coli WP2uvrA
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other: Mutascreen
Year: GLP: no data
Test substance:
Source: Bayer AG Leverkusen
18-APR-1994 (127)

Type: Bacterial reverse mutation assay
System of testing: Salmonella typhimurium TA 98, TA 100; Escherichia coli WP2uvrA
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other: Mutascreen
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (128)

Type: Cytogenetic assay
System of testing: Chinese hamster lung (CHL) fibroblast cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (80) (129)

Type: Cytogenetic assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (80) (130)

Type: Cytogenetic assay
System of testing: Chinese hamster primary liver (CH1-L) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Remark: mitosis and mitotic spindle
Source: Bayer AG Leverkusen

03-MAY-1994 (131) (132)

Type: Cytogenetic assay
System of testing: RL 4 (Rattenleber)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (133)

Type: Cytogenetic assay
System of testing: CH1-L (Fibroblasten)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (134) (135)

Type: Cytogenetic assay
System of testing: CHO-Zellen
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (136)

Type: Cytogenetic assay
System of testing: CHO-Zellen
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (136)

Type: DNA damage and repair assay
System of testing: primaere Hepatocyten (Mensch, Ratte)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Remark: Abstract of Congress Report
Source: Bayer AG Leverkusen
15-APR-1994 (137)

Type: DNA damage and repair assay
System of testing: Escherichia coli W 3110, P 3478
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (138)

Type: DNA damage and repair assay
System of testing: Escherichia coli po1A
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
16-FEB-1994 (139)

Type: Escherichia coli reverse mutation assay
System of testing: Escherichia coli WP
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (140)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: Saccharomyces cervisiae D4
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
18-MAY-1994 (141) (142)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: Strain XV185-14C
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (143) (144) (145)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: Strains D/-144, XV185-14C, RM52
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (146) (145)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: Strain C658-K42
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (147)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: strain D7
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Remark: point mutation, mitotic gene conversion, mitotic segregation
Source: Bayer AG Leverkusen
03-MAY-1994 (148)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: strain D61-M, D6
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Remark: mitotic aneuploidy
Source: Bayer AG Leverkusen
03-MAY-1994 (149)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: strain D6
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: hydrochloride
Remark: mitotic aneuploidy
Source: Bayer AG Leverkusen
03-MAY-1994 (150) (151) (152) (153)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: strain JD1
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP: no data
Test substance: other TS: hydrochloride
Remark: Mitotic gene conversion
Source: Bayer AG Leverkusen
03-MAY-1994 (154)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: strain D61.M
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (155)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: strain D3
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (156) (157)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: strain D7
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (150) (158)

Type: HGPRT assay
System of testing: Chinese hamster V79
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (159) (160)

Type: HGPRT assay
System of testing: V 79
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (161)

Type: HGPRT assay
System of testing: CHO-Zellen
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (162)

Type: HGPRT assay
System of testing: AHH-1-Zellen (Human-Zellen)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (163)

Type: Mammalian cell gene mutation assay
System of testing: Chinese hamster V79 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: Fox, M. (1975): Mutat. Res. 29, 449-466
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (159) (164) (165)

Type: Mammalian cell gene mutation assay
System of testing: Chinese hamster V79 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Kuroki, T. et al. (1977): Cancer Res. 37, 1044-1050
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (159) (166)

Type: Mitotic recombination in Saccharomyces cerevisiae
System of testing: strain D61-M, D6
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Remark: mitotic crossing over, point mutation
Source: Bayer AG Leverkusen
03-MAY-1994 (149)

Type: Mouse lymphoma assay
System of testing: L5178Y TK-/TK+
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (159) (167)

Type: Mouse lymphoma assay
System of testing: L5178Y TK+/TK+
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (159) (168)

Type: Mouse lymphoma assay
System of testing: L5178Y TK-/TK+
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (169) (159)

Type: Mouse lymphoma assay
System of testing: L5178Y TK-/TK+
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (170) (171)

Type: Mouse lymphoma assay
System of testing: L15178Y TK-/TK+
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (159) (172) (173) (174)

Type: Mouse lymphoma assay
System of testing: L5178Y TK+/TK-
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Clive, D., Spector, J.F.S. (1975): Mutat. Res. 31, 17-29
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

18-MAY-1994 (159) (160)

Type: Mouse lymphoma assay
System of testing: L5178Y TK-/TK+
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

03-MAY-1994 (175)

Type: Mouse lymphoma assay
System of testing: L5178Y TK-/TK+
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

16-FEB-1994 (176)

Type: Salmonella typhimurium reverse mutation assay
System of testing: Samonella typhimurium TA 98
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other: Reddy, B.S. et al. (1974): J. Natl. Cancer Inst. 52, 507-511
Year: GLP: no data
Test substance: no data
Remark: Addition of lithocholic acid inhibits the mutagenic acitivity of o-toluidine
Source: Bayer AG Leverkusen

18-APR-1994 (177)

Type: Salmonella typhimurium reverse mutation assay
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP: no data
Test substance: no data
Remark: positive only with Norharman
Source: Bayer AG Leverkusen
03-MAY-1994 (178) (179)

Type: Salmonella typhimurium reverse mutation assay
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP: no data
Test substance: no data
Remark: posive only with Norharman
Source: Bayer AG Leverkusen
03-MAY-1994 (180)

Type: Sister chromatid exchange assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochloride
Source: Bayer AG Leverkusen
18-MAY-1994 (181) (182) (183)

Type: Sister chromatid exchange assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (184)

Type: Sister chromatid exchange assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (80) (83)

Type: Sister chromatid exchange assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (80) (185)

Type: Sister chromatid exchange assay
System of testing: Lymphocytes (human)
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (186)

Type: Sister chromatid exchange assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: Induction of SCE in CHO cells treated with plasma of rats pretreated with o-Toluidine
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (187)

Type: Sister chromatid exchange assay
System of testing: human lymphocytes co-cultured with rat hepatocytes
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: Krishna, G.J.N. and Oug, T. (1986): Teratogen. Carcinogen. Mutagen. 6, 321-330
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (188)

Type: Sister chromatid exchange assay
System of testing: CHO
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
16-FEB-1994 (189)

Type: Sister chromatid exchange assay
System of testing: RL 4 (Rattenleber)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (133)

Type: Sister chromatid exchange assay
System of testing: V 79
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (190)

Type: Unscheduled DNA synthesis
System of testing: HeLa cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochloride
Source: Bayer AG Leverkusen
15-APR-1994 (181) (191)

Type: Unscheduled DNA synthesis
System of testing: HeLa S3 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (192)

Type: Unscheduled DNA synthesis
System of testing: primaere Rattenhepatocyten
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (193)

Type: Unscheduled DNA synthesis
System of testing: HeLa S3 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (194)

Type: Unscheduled DNA synthesis
System of testing: rat hepatocytes
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (195)

Type: Unscheduled DNA synthesis
System of testing: HeLa S3
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Metabolische Aktivierung: nicht dosisabhaengig
Source: Bayer AG Leverkusen

16-FEB-1994 (196)

Type: Unscheduled DNA synthesis
System of testing: primaere Ratten- und Hamsterhepatozyten
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

16-FEB-1994 (197)

Type: Unscheduled DNA synthesis
System of testing: primaere Rattenhepatozyten
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

16-FEB-1994 (76)

Type: Unscheduled DNA synthesis
System of testing: rat hepatocytes
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: urine methode
Year: GLP: no data
Test substance: no data
Remark: Substance administered to rats, urine tested, abstract only
Source: Bayer AG Leverkusen

03-MAY-1994 (111) (112)

Type: Yeast Cytogenetic assay
System of testing: Saccharomyces cerevisiae PG-148, PG-154, PG-155, PG-166
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
18-MAY-1994 (150) (198)

Type: Yeast Cytogenetic assay
System of testing: strain 197/2d; strain rad3, rad18, rad52, trp2
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (199) (200)

Type: Yeast gene mutation assay
System of testing: Schizosaccharomyces pombe P1
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Loprieno, N. (1981): Prog. Mutt. Res. 1, 424,433
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (150) (201) (202)

Type: other: 6-Thioguanin-Resistenz-Test (HGPRT-Lokus)
System of testing: V 79
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (203)

Type: other: 8-Azaguanin-Resistenz-test
System of testing: Salmonella typhimurium TM 677
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (204)

Type: other: DNA binding
System of testing: leucocytes (guinea pig)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (205)

Type: other: DNA damage
System of testing: Escherichia coli PolA-/PolA+
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: Slater, E.E. et al. (1971): Cancer Res. 31, 970-973
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (206)

Type: other: DNA damage
System of testing: chinese hamster fibroblas (V79) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other: alkaline elution method
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (119)

Type: other: DNA damage
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: alkaline sucrose gradient
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (185)

Type: other: DNA fragmentation
System of testing: primaere Hepatocyten (human, rat)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: alkaline elution technique
Year: GLP: no data
Test substance: no data
Remark: abstract only
Source: Bayer AG Leverkusen
18-APR-1994 (207)

Type: other: DNA single strand breaks
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: alkaline sucrose sedimention
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (208)

Type: other: DNA-single-strand break
System of testing: Rattenhepatocyten
Concentration: 319, 1063, 3190 ug/ml in Ethanol
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: alkalische Elution
Year: GLP: no data
Test substance: other TS: solved in Ethanol
Source: Bayer AG Leverkusen
15-APR-1994 (209)

Type: other: Degranulations test
System of testing: postmitochondrial supernatent (PMS) from rat liver
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (210)

Type: other: Differential killing assay
System of testing: Escherichia coli WP2, WP67, CM871
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (211)

Type: other: Enhancement of anchorage-independent survival
System of testing: Rauscher leukemia virus (RLV) infected Fischer rat-embryo (RIFRE) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

03-MAY-1994 (212)

Type: other: Fluctuation test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: ambiguous
Method: other: Green, M.H.L. et al. (1977): Mutat. Res. 48, 287-294
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen

18-APR-1994 (213)

Type: other: Human lymphoblast gene-locus mutation assay
System of testing: human lymphoblasts TK6, AHH-1
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

18-MAY-1994 (214) (215)

Type: other: Induction f gene mutation in A. nidulans
System of testing: Aspergillus nidulans
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

15-APR-1994 (216) (217)

Type: other: Inhibition of oxidative metabolism
System of testing: brown fat cells, hamster
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (218) (219)

Type: other: MVL assay (integration enhancement test)
System of testing: Mouse kidney C3H2K cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
03-MAY-1994 (220)

Type: other: Membrane damage
System of testing: Human diploid embryonic lung fibroblasts (line MRC 5)
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (221) (222)

Type: other: Micronucleaus Test in vitro
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (185)

Type: other: Micronucleus assay in vitro
System of testing: lymphocytes (human)
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (223)

Type: other: Microtiter fluctuation test
System of testing: Escherichia coli WP2uvrA, Salmonella typhimurium TA 98, TA 1535, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: ambiguous
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (224)

Type: other: Mitotische Rekombination + Genkonversion
System of testing: Saccharomyces cerevisiae D 3
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (225)

Type: other: Mitotische Rekombination + Genkonversion
System of testing: Saccharomyces cerevisiae D 7
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (226)

Type: other: Mitotische Rekombination + Genkonversion
System of testing: Saccharomyces cerevisiae XV 185-14
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (227)

Type: other: Mitotische Rekombination + Genkonversion
System of testing: Saccharomyces cerevisiae JD 1
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (228)

Type: other: Mitotische Rekombination und Genkonversion
System of testing: Saccharomyces cerevisiae D61.M
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (229)

Type: other: Recombination-Assay
System of testing: Escherichia coli
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (230)

Type: other: Zelltransformation
System of testing: Baby hamster kidney cells (BHK 21 C13/HRC 1)
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochloride
Source: Bayer AG Leverkusen
15-APR-1994 (231) (232)

Type: other: Zelltransformation
System of testing: BHK 21/clone
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
15-APR-1994 (181) (233)

Type: other: Zelltransformation
System of testing: Syrian hamster embryo cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (234)

Type: other: Zelltransformation
System of testing: BHK 21C13-Zellen
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
16-FEB-1994 (235) (236)

Type: other: Zelltransformation
System of testing: SHE-Zellen
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
16-FEB-1994 (237)

Type: other: Zorotest
System of testing: E. coli
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other: bacterial assay, based on expression of gal genes under control of lambda prophage repressors
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
15-APR-1994 (120) (238)

Type: other: cell transformation assay
System of testing: Syrian hamster embryo (SHE) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
18-APR-1994 (239)

Type: other: cell transformation assay
System of testing: Balb/c-3T3
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (240) (241)

Type: other: cell transformation assay
System of testing: AKR leukemia virus infected NIH Swiss mouse embryo (AKH-NIH-ME) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (242) (243)

Type: other: cell transformation assay
System of testing: Syrian hamster embryo (SHE) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: positive
Method: other: Adenovirus (SA7) transformation assay as prescribed by Casto, B.C. (1973): Progr. Esp. Tumor Res. 18, 166-198
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (244)

Type: other: cell transformation assay
System of testing: embryonic mouse fibroblasts (C3H/10T1/2 Clone 8)
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method: other: Reznikoff, C.A. et al. (9173): Cancer Res. 33, 3231-3238
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-MAY-1994 (245) (246) (247)

Type: other: cell transformation assay
System of testing: Chinese hamster ovary (CHO) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (159) (248)

Type: other: inhibition of cell growth
System of testing: Ascites sarcoma B P8 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (221) (249)

Type: other: inhibition of metabolic activation
System of testing: Chinese hamster V79 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (250) (251)

Type: other: inhibition of metabolic cooperation
System of testing: Chinese hamster V79 cells
Concentration: see remarks
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Remark: inhibition of metabolic cooperation at concentration higher than 0.5 mM
Source: Bayer AG Leverkusen
15-APR-1994 (252)

Type: other: inhibition of metabolic cooperation
System of testing: Chinese hamster V79 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: positive
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (250) (253)

Type: other: inhibition of metabolic cooperation assay
System of testing: Chinese hamster V79 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
18-APR-1994 (254) (255) (250)

Type: other: lambda-induction assay (lysis)
System of testing: E. coli
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Source: Bayer AG Leverkusen
15-APR-1994 (120) (256)

Type: other: see remark
System of testing: Arabidopsis (Columbia wild type)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other
Year: GLP: no data
Test substance: no data
Remark: type: Arabidopsis assay (Pflanze)
Source: Bayer AG Leverkusen

15-APR-1994 (257) (258)

Type: other: t-RNA acceptance assay
System of testing: different t-RNA preperations
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method: other: Hradec, J. (1988): Carcinogenesis 9, 837-842
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (259)

Type: other: umu gene expression
System of testing: Salmonella typhimurium TA 1535/psk1002
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
03-MAY-1994 (260)

5.6 Genetic Toxicity 'in Vivo'

Type: Cytogenetic assay
Species: mouse Sex: male
Strain: B6C3F1
Route of admin.: i.p.
Exposure period: single administration
Doses: 150, 300, 600 mg/kg bw
Result: negative
Method: other
Year: GLP: no data
Test substance: other TS: hydrochloride
Source: Bayer AG Leverkusen
05-OCT-2001 (261)

Type: Sister chromatid exchange assay
Species: Chinese hamster Sex: female
Strain: no data
Route of admin.: oral unspecified
Exposure period:
Doses: 100, 200, 300 mg/kg Kgw.
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
05-OCT-2001 (262)

Type: Sister chromatid exchange assay
Species: mouse Sex: male
Strain: B6C3F1
Route of admin.: i.p.
Exposure period: single administration
Doses: 150, 300, 600 mg/kg bw
Result: positive
Method: other
Year: GLP: no data
Test substance: other TS: hydrochloride
Source: Bayer AG Leverkusen
05-OCT-2001 (261)

Type: other: Drosophila reversion assay
Species: Drosophila melanogaster Sex: male/female
Strain: other: stock: unstable zeste-white somatic eye color
Route of admin.: other: oral feed of larvae
Exposure period: 48 h
Doses: 10, 25, 50, 100 mM (ca. 1.1, 2.7, 5.4, 10.7 g)
Result: negative
Method: other: Rasmuson et al. (1978): Mut. Res. 54, 33-38
Year: GLP: no data
Test substance: no data
Remark: control: yes, concurrent vehicle
Result: negative
Source: Bayer AG Leverkusen
05-OCT-2001 (263) (264)

Type: Cytogenetic assay
Species: hamster Sex: no data
Strain: no data
Route of admin.: oral unspecified
Exposure period:
Doses: 100 - 300 mg/kg Kgw.
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
05-OCT-2001 (72)

Type: Cytogenetic assay
Species: mouse Sex: no data
Strain: no data
Route of admin.: i.p.
Exposure period:
Doses: 45 mg/kg Kgw.
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Positiv
Source: Bayer AG Leverkusen
16-FEB-1994 (72)

Type: Cytogenetic assay
Species: mouse Sex: no data
Strain: other: Lacca
Route of admin.: other: injection (no further information)
Exposure period: 24 hours
Doses:
Result:
Method:
Year: GLP: no data
Test substance: no data
Result: positive
Source: Bayer AG Leverkusen
03-MAY-1994 (265)

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex: no data
Strain: no data
Route of admin.: other: feeding (adults and larves)
Exposure period: no data
Doses: no data
Result:
Method: other
Year: GLP: no data
Test substance: no data
Remark: abstract only: several compounds tested
Result: positive in larves; no further information
Source: Bayer AG Leverkusen
15-APR-1994 (266)

Type: Drosophila SLRL test
Species: Drosophila melanogaster Sex: male/female
Strain: other: stock canton S
Route of admin.: other: larval feeding
Exposure period: no data
Doses: no data
Result:
Method: other: Valencia, R. (1988): environ. Mol. Mutagen. 14, 245-251
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Remark: control: yes, concurrent vehicle
Result: negative
Source: Bayer AG Leverkusen
03-MAY-1994 (267)

Type: Inhibition of DNA-Synthesis
Species: mouse Sex: no data
Strain: CBA
Route of admin.: i.p.
Exposure period:
Doses: 15-30 % der LD50
Result:
Method: other
Year: GLP: no data
Test substance: no data
Result: positiv
Source: Bayer AG Leverkusen
15-APR-1994 (268) (269) (270)

Type: Inhibition of DNA-Synthesis
Species: mouse Sex: no data
Strain: no data
Route of admin.: i.p.
Exposure period:
Doses: 15-30 % der LD50
Result:
Method: other
Year: GLP: no data
Test substance: no data
Result: negativ
Source: Bayer AG Leverkusen
15-APR-1994 (88)

Type: Micronucleus assay
Species: mouse Sex: male
Strain: B6C3F1
Route of admin.: i.p.
Exposure period: single administration
Doses: 75, 150, 300 mg/kg bw
Result:
Method: other
Year: GLP: no data
Test substance: other TS: hydrochloride
Result: negative
Source: Bayer AG Leverkusen
03-MAY-1994 (261)

Type: Micronucleus assay
Species: mouse Sex: no data
Strain: no data
Route of admin.: i.p.
Exposure period:
Doses: 40, 80, 160, 169, 270, 338 ul/kg Kgw.
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS
Result: Negativ
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
03-MAY-1994 (271) (272) (273)

Type: Micronucleus assay
Species: other: Wassermolchlarve (Erythrozyten) Sex: no data
Strain: no data
Route of admin.: other: keine Daten
Exposure period:
Doses:
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Positiv
Source: Bayer AG Leverkusen
16-FEB-1994 (274)

Type: Sister chromatid exchange assay
Species: mouse Sex: no data
Strain: Balb/c
Route of admin.: i.p.
Exposure period:
Doses: 45 mg/kg Kgw.
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Positiv
Source: Bayer AG Leverkusen
16-FEB-1994 (275)

Type: other: DNA Single-strand break
Species: mouse Sex: male
Strain: other: Swiss CD-1
Route of admin.: i.p.
Exposure period:
Doses: 100 mg/kg Kgw.
Result:
Method: other: alkaliche Elution
Year: GLP: no data
Test substance: no data
Remark: Leber- und Nieren-DNA
Result: Positiv
Source: Bayer AG Leverkusen
15-APR-1994 (276)

Type: other: DNA binding
Species: rat Sex: male
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: single administration
Doses: 500 mg/kg bw given in corn oil
Result:
Method: other
Year: GLP: no data
Test substance:
Result: positiv
Source: Bayer AG Leverkusen
15-APR-1994 (277)

Type: other: DNA binding
Species: rat Sex: male
Strain: Sprague-Dawley
Route of admin.: i.p.
Exposure period: single administration
Doses: 10, 20, 50, 100 mg/kg bw
Result:
Method: other: 32P post-labelling
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
15-APR-1994 (278)

Type: other: Hemmung testikulaerer DNA-Synthese
Species: mouse Sex: no data
Strain: no data
Route of admin.: oral unspecified
Exposure period:
Doses: 200 mg/kg Kgw.
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Positiv
Source: Bayer AG Leverkusen
16-FEB-1994 (279)

Type: other: Mouse-sperm-abnormality-Test
Species: mouse Sex: male
Strain: no data
Route of admin.: i.p.
Exposure period: 5 Tage
Doses: 0.05 - 0.5 mg/kg/Kgw./Tag
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Result: Negativ
Source: Bayer AG Leverkusen
03-MAY-1994 (271) (280) (281)

Type: other: SMART-Test
Species: other: Drosophila Sex: no data
Strain: no data
Route of admin.: oral feed
Exposure period:
Doses:
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Positiv (Fluegel)
Source: Bayer AG Leverkusen
03-MAY-1994 (264) (282)

Type: other: SMART-Test
Species: other: Drosophila Sex: no data
Strain: no data
Route of admin.: other: keine Daten
Exposure period:
Doses:
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Positiv (Augenfaerbung)
Source: Bayer AG Leverkusen
16-FEB-1994 (283)

Type: other: Somatic recombination and mutation (SRM) assay
Species: Drosophila melanogaster Sex: male/female
Strain: other: stock: white coral somatic eye color
Route of admin.: oral feed
Exposure period: 4 days
Doses: 2.0 - 8.0 mM (ca. 215 - 864 mg
Result:
Method: other: Becker, H.J. (1966): Curr. Topics Develop. Biol. 1,155-171
Year: GLP: no data
Test substance: no data
Remark: control: yes, concurrent vehicle
Result: positive
Source: Bayer AG Leverkusen
03-MAY-1994 (284) (285)

Type: other: Sperm abnormalities
Species: mouse Sex: no data
Strain: other: Lacca
Route of admin.: other: injection (no further information)
Exposure period: 24 hours
Doses: 0.01 mmol/kg, 0.1 mmol/kg, 1 mmol/kg (ca. 1.08 mg/kg, 10.8 mg/kg, 108 mg/kg bw)
Result:
Method:
Year: GLP: no data
Test substance: no data
Result: positive
Source: Bayer AG Leverkusen
03-MAY-1994 (265)

Type: other: zeste-white (UZ) somatic mutation assay
Species: Drosophila melanogaster Sex: male/female
Strain: other: Drosophila melanogaster UZ stock
Route of admin.: other: oral feed of larvae
Exposure period: single administration
Doses: 0.5, 1.0, 2.0 mM in Ethanol/Tween 80
Result:
Method: other: Rasmuson et al. (1984): Eye pigmentation changes in Drosophila melanogaster in "Handbook of Mutagenicity" (Kilbey et al eds), 603-613
Year: GLP: no data
Test substance: other TS: solved in 5 % ethanol/1 % Tween 80
Result: positiv
Source: Bayer AG Leverkusen
15-APR-1994 (286)

5.7 Carcinogenicity

Species: rat Sex: male
Strain: other: Charles River
Route of admin.: oral feed
Exposure period: 18 Months
Frequency of treatment: daily
Post. obs. period: 6 Months
Doses: 0, 8000, 16000 ppm
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS: o-toluidine; purity not noted
Remark: 25 animals/sex/group
Dosage resulted in a retarded body weight gain of >10% after 3 months; at that time [the dosage] was lowered by half.

[25 Tiere/Gruppe; Dosierung aufgrund einer verzoegerten Koerpergewichtsentwicklung von >10 % nach 3 Monaten auf jeweils die Haelfte gesenkt]
Result: The lower dose increased the incidence of subcutaneous fibromas and fibrosarcomas, transitional cell carcinomas of the bladder and multiple tumors (bladder cancers, pituitary and adrenal adenomas)

[Dosisabhaengig erhoehte Inzidenzen an subkutanen Fibromen und Fibrosarkomen, Uebergangszellkarzinomen der Blase und multiplen Tumoren (Blasenkarzinome, Hypophysen- und Nebennierenadeome).]
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
08-OCT-2001 (287) (288) (289) (290) (65)

Species: rat Sex: male/female
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 104 Weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 3000, 6000 ppm
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS: o-toluidine; purity not noted
Remark: 50 Tiere/Geschlecht/Gruppe; Kontrollgruppe: 20 Tiere/ Geschlecht
Result: The lower dose retarded body weight gain and increased mortalities in both sexes (all males of the high dose group were dead after 101 weeks); the lower dose increased the incidence of fibrosarcomas, angiosarcomas, and osteosarcomas in the spleen and other organs (spleen sarcomas are rare tumors in F344 rats), transitional cell carcinomas and papillomas of the urinary bladder, fibromas of the subcutaneous tissues of the skin, fibroadenomas of the mammary glands and mesotheliomas in various organs.

[Dosisabhaengig verzoegerte Koerpergewichtszunahme und erhoehte Mortalitaet bei beiden Geschlechtern (alle m der hohen Dosierung waren nach 101 Wochen tot), dosisabhaengig erhoehte Inzidenzen an Fibrosarkomen, Angiosarkomen und Osteosarkomen in der Milz und anderen Organen (Milzsarkome sind v. a. bei der F 344-Ratte seltene Tumoren), Uebergangszellkarzinomen und Papillomen der Harnblase, Fibromen des Subkutangewebes der Haut, Fibroadenomen der Brustdruese und Mesotheliomen in verschiedenen Organen.]
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
08-OCT-2001 (291) (292) (69) (288)

Species: rat Sex: male
Strain: Fischer 344
Route of admin.: oral feed
Exposure period: 73 Wochen
Frequency of treatment: taeglich
Post. obs. period:
Doses: 0, 4000 ppm
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS
Remark: 30 Tiere/Gruppe
Result: Verzoegerte Koerpergewichtszunahme und erhoehte Mortalitaet im 2. Jahr, gering erhoehte Inzidenz an Blasen- und Lebertumoren (Blase 4/30, Leber 3/30), hohe Inzidenz an Mammatumoren (13/30, vor allem Fibroadenome), hohe Inzidenz an Mesotheliomen, Sarkomen und Milzfibromen, 25/30 Tieren wiesen Hautfibrome auf.
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
03-MAY-1994 (293) (294)

Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure period: 18 Monate
Frequency of treatment: taeglich
Post. obs. period: 3 Monate
Doses: 0, 16000, 32000 ppm
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS
Remark: 25 Tiere/Geschlecht/Gruppe; aufgrund einer verzoegerten Koerpergewichtsentwicklung von >10 % nach 3 Monaten auf jeweils die Haelfte gesenkt
Result: Signifikanter dosisabhaengiger Anstieg von Gefaesstumoren bei m/w Tieren (Haemangiome, Haemangiosarkome).
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
03-MAY-1994 (288) (289) (294) (290) (65)

Species: mouse Sex: male/female
Strain: B6C3F1
Route of admin.: oral feed
Exposure period: 102 - 103 Wochen
Frequency of treatment: taeglich
Post. obs. period:
Doses: 0, 1000, 3000 ppm
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS
Remark: 50 Tiere/Geschlecht/Gruppe; Kontrollgruppe: 20 Tiere/ Geschlecht
Result: Dosisabhaengig verzoegerte Koerpergewichtszunahme, keine signifikant erhoehte Mortalitaet bei beiden Geschlechtern, dosisabhaengig erhoehte Inzidenzen an hepatozellulaeren Karzinomen und Adenomen (w) und Haemangiosarkomen aller Lokalisationen (m).
Source: Bayer AG Leverkusen
Test substance: Hydrochlorid
03-MAY-1994 (69) (288)

Species: rat Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 85 Wochen
Frequency of treatment: 1mal/Woche
Post. obs. period:
Doses: 0, 30 mg/Tier
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: 0 mg: 75 Tiere; 30 mg: 50 Tiere
Result: 12/30 behandelten Tieren und 10/48 Kontrolltieren entwickelten Tumoren.
Source: Bayer AG Leverkusen
16-FEB-1994 (295)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: s.c.
Exposure period: 24 Monate
Frequency of treatment: 1mal/Woche
Post. obs. period:
Doses: 0, 25, 75 mg/kg Kgw.
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: 30 Tiere/Geschlecht/Gruppe
Result: Kein Einfluss auf Koerpergewicht oder Mortalitaet, bei den m dosisabhaengig erhoehte Inzidenzen an malignen Tumoren an der Einstichstelle.
Source: Bayer AG Leverkusen
16-FEB-1994 (66)

Species: mouse Sex: no data
Strain: other: CC 57
Route of admin.: s.c.
Exposure period: 23 Wochen
Frequency of treatment: 1mal/Woche
Post. obs. period:
Doses: 0, 5 mg/Tier
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Bei 0 mg: 195 Tiere; bei 5 mg: 75 Tiere
Result: 7/36 behandelte Tiere und 19/140 Kontrolltiere entwickelten Tumoren.
Source: Bayer AG Leverkusen
16-FEB-1994 (295)

Species: rabbit Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 16 Monate
Frequency of treatment: 6mal/Woche
Post. obs. period:
Doses: 1, 0.5 ml
Result:
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: 15 Tiere
Result: Erhoehte Mortalitaet, Blasenpapillome bei Tieren, die laenger als 100 Tage lebten.
Source: Bayer AG Leverkusen
03-MAY-1994 (296) (294)

Species: Syrian hamster Sex: male/female
Strain: other: Goldhamster
Route of admin.: s.c.
Exposure period: 53 Wochen
Frequency of treatment: 1mal/Woche
Post. obs. period:
Doses: 0, 1.9 mmol/kg Kgw.
Result:
Control Group: yes
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: 15 Tiere/Geschlecht/Gruppe
Result: Kein Einfluss auf Koerpergewichtsentwicklung, keine erhoehte Tumorinzidenz.
Source: Bayer AG Leverkusen
03-MAY-1994 (297) (294)

Species: guinea pig Sex: no data
Strain: no data
Route of admin.: s.c.
Exposure period: 16 Monate
Frequency of treatment: 6mal/Woche
Post. obs. period:
Doses: 1, 0.5 ml
Result:
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: 10 Tiere
Result: Die Tiere lebten nicht lange genug, um Tumoren zu entwickeln.
Source: Bayer AG Leverkusen
16-FEB-1994 (296)

5.8 Toxicity to Reproduction

Type:
Species: rat Sex: male/female
Strain: no data
Route of admin.: dermal
Exposure Period: 4 Months
Frequency of treatment: 4 h/Day
Duration of test:
Doses: 8, 80 mg/kg Kgw.
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS: o-toluidine; purity not noted
Remark: Applied to 2.3 of the area of the tail skin; mated with untreated animals.

[Auf 2/3 der Flaeche der Schwanzhaut appliziert; verpaart mit unbehandelten Tieren]
Result: In the offspring of the high dose dams in 1, delayed body weight gain in first month and non-significant change in the relative weights of kidneys, ovaries, heart, and lungs.

[Bei den Nachkommen der hochdosierten Muttertiere im 1. Lebensmonat verzoegerte Koerpergewichtsentwicklung und geringfuegige Veraenderungen des relativen Gewichtes von Nieren, Ovarien, Herz und Lunge.]
Source: Bayer AG Leverkusen
08-OCT-2001 (71)

Type:
Species: mouse Sex: female
Strain: Balb/c
Route of admin.: s.c.
Exposure Period: waehrend der gesamten Schwangerschaft
Frequency of
treatment: alle 4 - 5 Tage
Duration of test:
Doses: 2 mg/Tier
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Kurz vor der Geburt wurde embryonales Nierengewebe entnommen und kultiviert.
Result: In den Versuchskulturen kam es im Gegensatz zu den Kontrollkulturen zu ungleichmaessigen Hyperplasien und Herdwucherungen.
Source: Bayer AG Leverkusen
15-APR-1994 (298) (299)

5.9 Developmental Toxicity/Teratogenicity

Species: mouse Sex: female
Strain: Balb/c
Route of admin.: s.c.
Exposure period: during the last week of gestation [waehrend der letzten Woche der Gestation]
Frequency of
treatment: 4 - 5mal
Duration of test:
Doses: 2 mg/Tier
Control Group: no data specified
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Result: Increased tumor frwequency in the offspring [Erhoehte Tumorfrequenz bei den Nachkommen]
Source: Bayer AG Leverkusen
08-OCT-2001 (300)

5.10 Other Relevant Information

Type: Metabolism
Remark: Verabreichung einer LD50-Dosis von Toluidin (Isomer nicht spezifiziert) an Versuchstiere (keine naeheren Angaben) erniedrigt die Aktivitaet der Succinat-Dehydrogenase um circa 5 %.
Source: Bayer AG Leverkusen
15-APR-1994 (301)

Type: Metabolism
Remark: Nach einmaliger oraler Verabreichung von 50 mg/kg KGW 14C-markiertem o-Toluidin an maennlichen Sprague-Dawley Ratten werden 94.7 der Dosis mit dem Urin ausgeschieden.
Source: Bayer AG Leverkusen
15-APR-1994 (302)

Type: Metabolism
Remark: Ratte (Fischer 344), maennlich, 0.82 mmol/kg KGW (ca. 88 mg(kg KGW), s.c.
Wirkung: Ausscheidung von 0.02 - 0.18 % der Dosis im 0-6 h Urin als N-Hydroxy-o-toluidin.
Source: Bayer AG Leverkusen
18-APR-1994 (303)

Type: Metabolism
Remark: Ratte (Sprague-Dawley), maennlich, 50 mg/kg bw s.c.
Wirkung:
Nach 72 h waren 91% der Dosis mit dem Urin, 1,7% mit den Faeces und 0,3% als CO2 ausgeschieden. Haupmetabolit im Urin: 4-Amino-m-kresol (40% bzw. 10% als Sulfat und 3% bzw. 1% als Glucoronid)
Source: Bayer AG Leverkusen
03-MAY-1994 (304)

Type: Metabolism
Remark: Ratte (Fischer), maennlich, 400 mg/kg bw s.c.
Wirkung:
Nach 48 h waren 83.9% der Dosis mit dem Urin, 3.3% mit den Faeces und 1.4% als CO2 ausgeschieden. Haupmetabolit im Urin: 4-Amino-m-kresol und N-Acetyl-4-amino-m-kresol(27.8% bzw. 8.5% als Sulfat und 32.6 bzw. 2.8% als Glucoronid)
Source: Bayer AG Leverkusen
03-MAY-1994 (305)

Type: other
Remark: Ratte (Sprague-Dawley), maennlich, 50 mg/kg Kgw., p.o. bzw. 10, 20, 40, 50, 100 mg/kg Kgw., i.p.
Wirkung:
Nachweis von Addukten mit Haemoglobin und Albumin (dosisabhaengige Zunahme).
Source: Bayer AG Leverkusen
15-APR-1994 (306) (307)

Type: other
Remark: Methylsubstitution am Ring verringert die neuromuskulaere Wirkung von Anilinderivaten
Source: Bayer AG Leverkusen
15-APR-1994 (308)

Type: other
Remark: Verabreichung von o-Toluidin mitt dem Futter an Albinoratten (keine naeheren Angaben) verursacht metaplastische Veraenderungen am Blasenepithel.
Source: Bayer AG Leverkusen
18-MAY-1994 (309) (294)

Type: other: Binding characteristics
Remark: Einmalige s.c. Injektion von 10, 20, 40, 50 oder 100 mg 14C-o-Toluidin/kg KGW in maennliche Sprague Dawley Ratten und Gewinnung des Serums nach 2, 4, 8, 18, 24, 168, 336 oder 672 h. Maximale Bindung von o-Toluidin an Albumin nach 4 h (2.5 ng o-Tol/mg Alb) und an Haemoglobin nach 24 h (3.7 ng o-Toluidin/mg/Hb).
Source: Bayer AG Leverkusen
18-APR-1994 (310) (311) (312)

Type: other: Biological N-oxidation
Remark: Hund (keine naeheren Angaben), 111.1 mg o-Tol-HCl/kg KGW, i.v., Einzeldosis, 4 Tiere
Wirkung:
Methaemoglobinbildung, kein Nachweis von Nitrosotoluol.
Source: Bayer AG Leverkusen
03-MAY-1994 (313)

Type: other: Biotransformation
Remark: Ratte (Sprague Dawley), maennlich, 10 bzw. 100 mg/kg KWG i.p. an 7 Tagen
Wirkung: erhoehte Aktivitaet von Cytochrom P-450, Ethoxyresorufin-O-deethylase, Ethoxycoumarin-O-deethylase und Aldrin Epoxidase.
Source: Bayer AG Leverkusen
18-APR-1994 (314)

Type: other: Haematotoxizitaet
Remark: Katze, 27 mg/kg Kgw., i.v.
Wirkung:
Erhoehte Methaemoglobin-Bildung (70.1 %)
Source: Bayer AG Leverkusen
16-FEB-1994 (315)

Type: other: Haematotoxizitaet
Remark: Katze, 1-80 mg/kg KGW, i.p.
Wirkung:
erhoehte Methaemoglobinbildung (max. 7.4. g5/Met-HB
Source: Bayer AG Leverkusen
03-MAY-1994 (316)

Type: other: Hemoglobin binding
Remark: After single oral dose of 0.6 mmol/kg (ca.=64.2 mg/kg) o-toluidine to female Wistar rats and 1 mmol/kg (ca.=107 mg/kg) to female B6C3F1 mice by gavage a hemoglobin binding index (HBI: mmol/mol Hb/dose (mmol/kg)) of 4.0 in rats and 2.1 in mice was found.
Source: Bayer AG Leverkusen

18-APR-1994 (317)

Type: other: Industion of Cytochrome P-448 activity using EROD as model substrate
Remark: i.p. Injektion von je 50 mg o-Toluidin-Hydrochlorid/kg KGW an drei Tagen in Wistar Ratten fuehrt zu Erhoehung der EROD-Aktivitaet in der Leber
Source: Bayer AG Leverkusen
18-MAY-1994 (318) (319) (320)

Type: other: Inhibition of viral interferon induction in mammalian cell cultures
Remark: o-Toluidine shows no effect on induction of interferon by influenza virus (Ao/PR/8/34) in Rhesus monkey kidney (LLC-MK2) cells. Test done with and without metabolic activation.
Source: Bayer AG Leverkusen
18-APR-1994 (321)

Type: other: hemoglobin binding
Remark: Ratte (Wistar), weiblich, 0.5 mmol/kg (ca. 54 mg/kg), Schlundsonde, Einzeldosis
Wirkung:
HBI: 4.0; HBI: (mmol compound/mole Hb)/(mmol compound/kg bw)
Source: Bayer AG Leverkusen
03-MAY-1994 (322)

Type: other: internal respiration of brain tissue
Remark: Single s.c.-administration of 8.95 mMol o-toluidine to male and female Wistar rats resulted in lower activity of cerebral succinatedehydrogenase; no changes in internal respiration of brain tissue or cerebral cyctochromeoxidase
Source: Bayer AG Leverkusen
18-APR-1994 (323)

5.11 Experience with Human Exposure

Remark: Positive Reaktion im Epikutantest bei 25 % der primaer durch PPD (p-Phenylendiamin) sensibilisierten Personen (Gruppensensibilisierung).
Source: Bayer AG Leverkusen
16-FEB-1994 (324)

Remark: Es wurde eine statistisch signifikante Zunahme der Inzidenz an Blasenkrebs festgestellt bei 1749 in einer chemischen Fabrik (USA) beschaeftigten Arbeitern, die gegen o-Toluidin und Anilin exponiert waren. In einer Untergruppe von 708 eindeutig exponierten Arbeitern gab es 7 Faelle von Blasenkrebs (erwartet wurde 1 Fall).
Source: Bayer AG Leverkusen
16-FEB-1994 (325)

Remark: Methaemoglobinbildung bei einem Schlosser nach akzidentieller lokaler Einwirkung von o-Toluidin bei Reparaturarbeiten. Unter Behandlung mit Toluoniumchlorid ging der initiale Methaemoglobinwert von 39.7 % auf 2.6 % zurueck.
Source: BASF AGBayer AG Leverkusen
16-FEB-1994 (326)

Remark: Untersuchung einer nach Rauchern und Nicht-Rauchern ausgewaehlten Turiner Bevoelkerungsgruppe zeigt eine erhoehte Bildung von Haemoglobin-Addukten bei Rauchern.
Source: Bayer AG Leverkusen
18-MAY-1994 (327)

Remark: Nachweis und quantitative Bestimmung von o-Toluidin im Urin von Rauchern (6.3 ug/24 h , n=16) und Nichtrauchern (4.1 ug/24 h, n=12).
Source: Bayer AG Leverkusen
18-MAY-1994 (328) (329)

Remark: Re-Analyse der Untersuchungsergebnisse von Bryant et al. fuehrt zu einer Korrelation der unterschiedlichen Haemolglobin-Bindung mit individuellen Stoffwechselunterschieden.
Source: Bayer AG Leverkusen
03-MAY-1994 (330)

Remark: Bei Rauchern wurde eine leichte Tendenz zu hoeheren Haemoglobin-Addukt-Werten beobachtet; keine strenge Assoziation zwischen Raucher-Status und Haemoglobin-Addukt-bildung.
Source: Bayer AG Leverkusen
03-MAY-1994 (331)

Remark: Bei einer Gruppe von 35 maennlichen Arbeitern, die zwischen 1924 und 1953 in der Produktion von 4-Chlor-o-toluidin aus o-Toluidin beschaeftigt waren, wurden keine Blasentumoren gefunden.
Source: Bayer AG Leverkusen
Test substance: no data
03-MAY-1994 (332)

Remark: Bei der zytoskopischen Untersuchung an 75 von 81 Beschaeftigten in der o/p-Toluidin-Produktion (Raumluft-Konzentration: 0.7-28.6 mg/mu) wurden 2 Faelle von Blasenpapillomen und mehrere Faelle von Veraenderungen der Blasenmuscua gefunden
Source: Bayer AG Leverkusen
Test substance: no data
03-MAY-1994 (333)

Remark: Bei einer Studie an Arbeitern in der farbstoffindustrie (Italien) wurden bei einer untergruppe von 53 Beschaeftigten, die gegenueber einem gemisch aus Toluol, o-Nitrotoluol, o-Toluidin und 4,4¦-Methylen-bis(2-methylanilin exponiert waren, 5 Todesfaelle in Folge von Blasenkrebs registriert.
Source: Bayer AG Leverkusen
Test substance: no data
03-MAY-1994 (334)

Remark: Exposition gegenueber o-Toluidin in einer Konzentration von 40 ppm (176 mg/mu) ueber 60 Minuten fuehrt zu schweren Vergiftungserscheinungen, 10 ppm (44 mg/mu) rufen Krankheitssymptome hervor und langfristige Exposition gegenueber 5 ppm (22mg/mu) verursacht Unwohlsein.
Source: Bayer AG Leverkusen
Test substance: no data
03-MAY-1994 (335)

Remark: Zwischen 1905-1935 wurde bei Arbeitern, die in einer chemischen Fabrik (Deutschland) gegenueber o-Toluidin und Anilin exponiert waren, 11 Faelle von Blasenkrebs beobachtet.
Source: Bayer AG Leverkusen
Test substance: no data
03-MAY-1994 (336)

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7.1 End Point Summary

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7.2 Hazard Summary

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7.3 Risk Assessment

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I U C L I D

D a t a S e t

Existing Chemical	ID: 108-44-1
CAS No.	108-44-1
EINECS Name	m-toluidine
EINECS No.	203-583-1
TSCA Name	Benzenamine, 3-methyl-
Molecular Formula	C7H9N

Producer Related Part
  Company: EUROPEAN COMMISSION - European Chemicals Bureau
  Creation date: 10-FEB-2000

Substance Related Part
  Company: EUROPEAN COMMISSION - European Chemicals Bureau
  Creation date: 10-FEB-2000

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1.0.1 OECD and Company Information

Name: Bayer AG
Town: 51368 Leverkusen
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Name: Hickson & Welch Ltd.
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Cedex: 09

Name: YORKSHIRE CHEMICALS plc
Street: 27 KIRKSTALL ROAD
Town: LS31LL LEEDS
Country: United Kingdom
Phone: 0113 244 3111
Telefax: 0113 242 1670
Telex: 55366

1.0.2 Location of Production Site

-

1.0.3 Identity of Recipients

-

1.1 General Substance Information

Substance type: organic
Physical status: liquid

1.1.0 Details on Template

-

1.1.1 Spectra

-

1.2 Synonyms

1-AMINO-3-METHYLBENZENE
Source: Bayer AG Leverkusen

3-AMINO-1-METHYLBENZENE
Source: Bayer AG Leverkusen

3-AMINO-1-METHYLBENZOL
Source: Bayer AG Leverkusen

3-AMINOPHENYLMETHAN
Source: Bayer AG Leverkusen

3-AMINOPHENYLMETHANE
Source: Bayer AG Leverkusen

3-AMINOTOLUEN
Source: Bayer AG Leverkusen

3-AMINOTOLUENE
Source: YORKSHIRE CHEMICALS plc LEEDS
Bayer AG Leverkusen

3-Aminotoluene, 3-Methylaniline.
Source: Hickson & Welch Ltd. Castleford

3-AMINOTOLUOL
Source: Bayer AG Leverkusen

3-METHYLANILIN
Source: Bayer AG Leverkusen

3-METHYLANILINE
Source: YORKSHIRE CHEMICALS plc LEEDS

3-METHYLBENZENAMINE
Source: YORKSHIRE CHEMICALS plc LEEDS

3-METHYLBENZOLAMIN
Source: Bayer AG Leverkusen

3-TOLUIDINE
Source: YORKSHIRE CHEMICALS plc LEEDS
Bayer AG Leverkusen

BENZENAMINE, 3-METHYL-
Source: Bayer AG Leverkusen

M-AMINOTOLUENE
Source: Bayer AG Leverkusen

M-AMINOTOLUOL
Source: Bayer AG Leverkusen

M-METHYLANILINE
Source: Bayer AG Leverkusen

M-TOLUIDIN
Source: Bayer AG Leverkusen

M-TOLUIDINE
Source: Bayer AG Leverkusen

m-Tolylamine
Source: RHONE-POULENC AGRO LYON

M-TOLYLAMINE
Source: Bayer AG Leverkusen

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity

Quantity 5 000 - 10 000 tonnes

1.6.1 Labelling

Labelling: as in Directive 67/548/EEC
Symbols: T
N
Nota: C
other RM: H
Specific limits: no data
R-Phrases: (23/24/25) Toxic by inhalation, in contact with skin and if swallowed
(33) Danger of cumulative effects
(50) Very toxic to aquatic organisms
S-Phrases: (1/2) Keep locked up and out of reach of children
(28) After contact with skin, wash immediately with plenty of ...
(36/37) Wear suitable protective clothing and gloves
(45) In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible)
(61) Avoid release to the environment. Refer to special instructions/Safety data sets

1.6.2 Classification

Classification: as in Directive 67/548/EEC
Class of danger: dangerous for the environment
R-Phrases: (50) Very toxic to aquatic organisms

Classification: as in Directive 67/548/EEC
Class of danger: toxic
R-Phrases: (23/24/25) Toxic by inhalation, in contact with skin and if swallowed

Classification: as in Directive 67/548/EEC
Class of danger:
R-Phrases: (33) Danger of cumulative effects

1.7 Use Pattern

Type: type
Category: Non dispersive use

Type: type
Category: Use in closed system

Type: industrial
Category: Chemical industry: used in synthesis

Type: use
Category: Intermediates

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values

Type of limit:
Limit value:
Remark: No Occupational Exposure Limit assigned.
Source: Hickson & Welch Ltd. Castleford

1.9 Source of Exposure

Remark: Substance is used as an intermediate in the production of agrochemicals and dyestuffs.
Source: Hickson & Welch Ltd. Castleford

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution

Classified by:	KBwS (DE)
Labelled by:	KBwS (DE)
Class of danger:	2 (water polluting)
Source:	Bayer AG Leverkusen

1.14.2 Major Accident Hazards

Legislation:	Stoerfallverordnung (DE)
Substance listed:	
Remark:	4C
Source:	Bayer AG Leverkusen

1.14.3 Air Pollution

Classified by:	other: Hoechst AG
Labelled by:	
Number:	3.1.7 (organic substances)
Class of danger:	II
Remark:	no classification
Source:	Bayer AG Leverkusen
	Bayer AG Leverkusen

1.15 Additional Remarks

Remark:	Substance is packed in road tankers and 200 litre steel drums.
Source:	Hickson & Welch Ltd. Castleford

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: = -50.5 degree C
Source: RHONE-POULENC AGRO LYON

Value: = -32 degree C
Source: Bayer AG Leverkusen
(1)

Value: = -31.5 degree C
Source: Bayer AG Leverkusen
(2)

Value: ca. -30 degree C
Source: Bayer AG Leverkusen
(3)

2.2 Boiling Point

Value: = 203 degree C
Source: Bayer AG Leverkusen
(1)

Value: = 203.3 degree C
Source: RHONE-POULENC AGRO LYON

Value: = 203.4 degree C at 1013 hPa
Source: Bayer AG Leverkusen
(4)

Value: ca. 204 degree C at 1013 hPa
Source: Bayer AG Leverkusen
(3)

2.3 Density

Type: density
Value: ca. .988 g/cm3 at 20 degree C
Source: Bayer AG Leverkusen
(3)

Type: relative density
Value: = .989 at 20 degree C
Source: RHONE-POULENC AGRO LYON

2.3.1 Granulometry

-

2.4 Vapour Pressure

Value: = .3 hPa at 20 degree C
Remark: calculation Bayer AG; based on data from Weast, Handbook of Chemistry and Physics
Source: Bayer AG Leverkusen
(3)

Value: = .37 hPa at 20 degree C
Source: RHONE-POULENC AGRO LYON

Value: = .36 hPa at 25 degree C
Source: Bayer AG Leverkusen
(4)

2.5 Partition Coefficient

log Pow: = 1.4
Method:
Year:
Source: RHONE-POULENC AGRO LYON

log Pow: = 1.4
Method: other (measured): Flask-Shaking-Method
Year:
Source: Bayer AG Leverkusen
(5)

log Pow: = 1.42
Method: other (measured): experimentally determined according to Fujita et al. (1964)
Year:
Source: Bayer AG Leverkusen
(6)

log Pow: = 1.54
Method: other (calculated): calculated according to Rekker (1977)
Year:
Source: Bayer AG Leverkusen
(7)

log Pow: = 1.56
Method: other (calculated): calculated using the Med-Chem-C log P program
Year:
Source: Bayer AG Leverkusen
(8)

log Pow: = 1.64
Method: other (calculated): calculated using the Genstat program
Year:
Source: Bayer AG Leverkusen
(8)

2.6.1 Water Solubility

Value: = 12 g/l at 20 degree C
Source: Bayer AG Leverkusen
(9)

Value: = 17 g/l at 25 degree C
Source: Bayer AG Leverkusen
(10)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: = 86 degree C
Type:
Method:
Year:
Source: RHONE-POULENC AGRO LYON

Value: ca. 90 degree C
Type: closed cup
Method: other: DIN 51758
Year:
Source: Bayer AG Leverkusen
(3)

2.8 Auto Flammability

Value: = 481 degree C
Source: RHONE-POULENC AGRO LYON

Value:
Method: other: DIN 51794
Remark: Ignition temperature: not below 500 degree C
Source: Bayer AG Leverkusen
(3)

2.9 Flammability

Result: flammable
Remark: Production risk of carbon oxide and nitrogen oxide in smokes
Source: RHONE-POULENC AGRO LYON

2.10 Explosive Properties
-

2.11 Oxidizing Properties

-

2.12 Additional Remarks

Remark: Corrosive to aluminium and alloys
Source: RHONE-POULENC AGRO LYON

Remark: Air saturation at 20 degree C = 1318 mg m-toluidine/m3.
Source: Bayer AG Leverkusen
(11)

Remark: Negative logarithm of ionization constant of protonated base (pkBH+): 4.73 at 25 degree C, in aqueous HCl
Source: Bayer AG Leverkusen
(4)

Remark: pKa = 4.70
Source: Bayer AG Leverkusen
(10)

Remark: Henry's law constant = 0.27 Pa x m3 x mol-1, calculated according to the following equation: vapour pressure at 20 degree C (30 Pa) x molecular weight (107.16 g/mol) divided by water solubility (12000 g/m3)
Source: Bayer AG Leverkusen

3.1.1 Photodegradation

Type:
Method:
Year: GLP:
Test substance:
Remark: Photochemical degradation:
calculated according to Atkinson (1985)
KOH = 2.2 x 10E-10 cm3/molecules x s
t1/2= 105.12 minutes, assuming a mean OH radical
concentration of 5 x 10E5 molecules/cm3
Source: Bayer AG Leverkusen
(12)

3.1.2 Stability in Water
-

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments
-

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge
Concentration: 8.4 mg/l related to COD (Chemical Oxygen Demand)
Degradation: 63 % after 28 day
Method: OECD Guide-line 301 D "Ready Biodegradability: Closed Bottle Test"
Year: GLP:
Test substance: other TS: m-Toluidine D, CAS-No. 25640-74-8
Remark: degradation was measured as COD (CSB);
degradation was 64 % after 21 days
Source: Bayer AG Leverkusen
(13)

Type: aerobic
Inoculum: other bacteria: mainly secondary effluent
Concentration: 20 mg/l related to DOC (Dissolved Organic Carbon)
Degradation: 64 - 84 % after 28 day
Method: other: Modified OECD Screening Test, OECD Guideline 301 E adopted 12 May 81, Directive 84/449/EEC, C.3; ISO 7824 (1984) (precursor)
Year: GLP:
Test substance:
Remark: degradation measured as DOC decrease,
2 parallels (64 and 84 % degradation, respectively);
recovery = 57 % DOC in a separate test
Source: Bayer AG Leverkusen

(14)

Type: aerobic
Inoculum: activated sludge, adapted
Concentration: 200 mg/l related to COD (Chemical Oxygen Demand)
Degradation: 97.7 % after 5 day
Method: other: The test was performed in a batch system, inoculum concentration: 100 mg dry weight/l, 20 days adaptation.
Year: GLP:
Test substance:
Remark: degradation was measured as COD decrease
Source: Bayer AG Leverkusen

(15)

Type: aerobic
Inoculum: other: sludge samples from different sewage plants, rivers, bays and a lake
Concentration: 100 mg/l related to Test substance
Degradation: 0 - 1 % after 28 day
Method: other: see remarks
Year: GLP: no data
Test substance:
Remark: Method:
"Biodegradation test of chemical substance by microorganisms etc." stipulated in the Order Prescribing the Items of the Test Relating to the New Chemical Substance (1974, Order of the Prime Minister, Minister of Health and Welfare, the MITI No. 1). This guideline corresponds to "301C, Ready Biodegradability: Modified MITI Test I" stipulated in the OECD Guidelines for Testing of Chemicals (May 12, 1981).
sludge conc.: 30 mg/l
degradation was measured as BOD
Source: Bayer AG Leverkusen

(16)

Type:
Inoculum: other bacteria: soil microorganisms, adapted
Concentration: 6.3 mg/l related to Test substance
Degradation: 68 % after 56 day
Method: other: A model wastewater was used as test substance, the biomass concentration in the sand reactor was 3.1 g/l, dilution rate during the 6-8 week experiment was 0.45 per hour. No further data available.
Year: GLP:
Test substance:
Remark: sand was used as a biofilm carrier; degradation was measured as disappearance of test substance (initial DOC concentration: 500 mg/l)
Source: Bayer AG Leverkusen

(17)

Type:
Inoculum: other bacteria: soil microorganisms
Concentration: 25 mg/l related to Test substance
Degradation: 100 % after 8 day
Method: other: Decrease of absorption was measured at 275 nm.
Year: GLP:
Test substance:
Remark: soil microorganisms in aqueous medium
Source: Bayer AG Leverkusen

(18)

3.6 BOD5, COD or BOD5/COD Ratio

Remark: ThOD: 2538 mg/g
COD : 2545 mg/g
Source: Bayer AG Leverkusen

(13)

3.7 Bioaccumulation
-

3.8 Additional Remarks
-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC100: 283
LC10 : 100
Method: other: Lethal effect on Brachydanio rerio LC0, LC50, LC100; 48-96h, UBA-procedural proposal May 1984, static system, aerated
Year: 1989 GLP: yes
Test substance: other TS: 99.62 %
Remark: geom. mean: 168
test substance precipitates in the test medium within the first minutes, effective concentrations were determined, but the LC values based on nominal concentrations
analytical monitoring: HPLC
Source: Bayer AG Leverkusen

(11)

Type:
Species: other: Poecilia reticulata (Guppy)
Exposure period: 14 day
Unit: mg/l Analytical monitoring:
LC50: 36.31
Method: other: Semi-static test
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(7)

Type:
Species:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance:
Remark: Highly toxic to aquatic organisms
Source: RHONE-POULENC AGRO LYON

4.2 Acute Toxicity to Aquatic Invertebrates

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC0: .244
EC100: 133
Method: other: Acute Immobilisation Test; initial pH = 8.0; 20 degree C
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen
(14)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 16 day
Unit: mg/l Analytical monitoring:
NOEC: .012
EC10 : .012
Method: other: Concept NEN report 6502 from the Dutch Standard Organization (1980), reduction of growth; medium was renewed 3 times a week
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen
(19) (7)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 16 day
Unit: mg/l Analytical monitoring:
EC50: .038
Method: other: Concept NEN reports 6501 and 6502 from the Dutch Standard Organisation (1980), Inhibition of reproduction; medium was renewed 3 times a week
Year: GLP:
Test substance:
Remark: EC50 after correction of nominal concentrations for the average measured recoveries: 0.043 mg/l (113 % recovery)
Source: Bayer AG Leverkusen
(19) (20)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC50 : .75
Method: other: Concept NEN reports 6501 and 6502 from the Dutch Standard Organization (1980), Mortality; static test
Year: GLP:
Test substance:
Remark: LC50 after correction of nominal concentrations for the average measured recoveries: 0.73 mg/l
Source: Bayer AG Leverkusen

(21)

Type:
Species: Daphnia sp. (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring:
LC 50 : = .73
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: RHONE-POULENC AGRO LYON

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Chlorella vulgaris (Algae)
Endpoint:
Exposure period:
Unit: mg/l Analytical monitoring:
EC50: 66.1 - 141.3
Method: other: Inhibition of growth, EC50 for 6-9 h, 36.5 degree C
Year: GLP:
Test substance:
Remark: the EC50 value depended on the method of the growth inhibition determination:
cell multiplication after sporulation: EC50 : 66.1 mg/l; photometric extinction of the Chlorella-suspension at 680 nm and determination of the total chlorophyll content: EC50 : 117.5 mg/l; photometric extinction of the suspension at 750 nm and dry weight determination: EC50 : 141.3 mg/l
Source: Bayer AG Leverkusen

(22)

Species: Scenedesmus quadricauda (Algae)
Endpoint:
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
EC3 : 10
Method: other: German standard methods for the examination of water, wastewater and sludge; bioassay (group L); determination of the inhibitory effects of water constituents on green algae (Scenedesmus cell multiplication inhibition test) (L9)
Year: GLP: no
Test substance:
Source: Bayer AG Leverkusen

(23)

Species: Scenedesmus subspicatus (Algae)
Endpoint:
Exposure period: 7 day
Unit: mg/l Analytical monitoring:
EC3 : 6.1
Method: other: German standard methods for the examination of water, wastewater and sludge; bioassay (group L); determination of the inhibitory effects of water constituents on green algae (Scenedesmus cell multiplication inhibition test) (L9)
Year: GLP:
Test substance:
Remark: 57 % recovery (DOC) in a separate test, initial pH = 7.5
Source: Bayer AG Leverkusen

(14)

Species: other algae: Agmenellum quadruplicatum (marine blue-green algae)
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method: other: Growth Inhibition Test, conventional lawn technique (agar plates), 3-7 days incubation
Year: GLP:
Test substance:
Remark: complete growth inhibition at 100 ug/plate
no further data available
Source: Bayer AG Leverkusen

(24)

Species: other algae: Agmenellum sp. (blue-green algae)
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method: other: Growth Inhibition Test, conventional lawn technique (agar plates), 3-7 days incubation
Year: GLP:
Test substance:
Remark: complete growth inhibition at 100 ug/plate
no further data available
Source: Bayer AG Leverkusen
(25)

Species: other algae: Chlorella autotrophica
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method: other: Growth Inhibition Test, conventional lawn technique (agar plates), 3-7 days incubation
Year: GLP:
Test substance:
Remark: complete growth inhibition at 10 mg/plate
no further data available
Source: Bayer AG Leverkusen
(24)

Species: other algae: Cylindrotheca sp. (marine diatom)
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method: other: Growth Inhibition Test, conventional lawn technique (agar plates), 3-7 days incubation
Year: GLP:
Test substance:
Remark: complete growth inhibition at 10 mg/plate
no further data available
Source: Bayer AG Leverkusen
(24)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: Pseudomonas putida (Bacteria)
Exposure period: 18 hour(s)
Unit: mg/l Analytical monitoring:
EC10: 151
Method: other: German standard methods for the examination of water, wastewater and sludge; bioassay (group L); determination of the biological effects of the toxic wastewater on bacteria L8 (1968) modified
Year: GLP: no
Test substance:
Remark: nominal concentration; 57 % recovery (DOC) in a separate test
Source: Bayer AG Leverkusen
(14)

Type: aquatic
Species: other bacteria: activated sludge (from laboratory)
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring: no
EC50: 1572
EC05 : 437
Method: other: Test for Inhibition of Oxygen Consumption by Activated Sludge, ISO 8192
Year: 1989 GLP: yes
Test substance: other TS: 99.62 %
Remark: direct weight
Source: Bayer AG Leverkusen
(11)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish
-

4.5.2 Chronic Toxicity to Aquatic Invertebrates

Species: Daphnia sp. (Crustacea)
Endpoint:
Exposure period: 16 day
Unit: mg/l Analytical monitoring:
EC50: = .043
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: RHONE-POULENC AGRO LYON

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
-

4.9 Additional Remarks

Remark: Tetrahymena pyriformis (Protozoa), Inhibition of growth:
EC50 : 285.0 mg/l; 48 h
EC50 : 154.5 mg/l; 48 h
EC50 : 277.5 mg/l; 60 h
EC50 : 370.0 mg/l; 24 h
Source: Bayer AG Leverkusen
(26) (27) (28) (29)

Remark: 1071.6 mg m-toluidine/l ethanol (99 %) led to a 67 % mortality of the pine wood nematode, Bursaphelenchus lignicolus.
Source: Bayer AG Leverkusen
(30)

Remark: Several bacteria (Rhodococcus rhodochrous DSM 3954, Pseudomonas putida mt-2) could adapt their growth on m-toluidine.
Source: Bayer AG Leverkusen
(31) (32) (33)

Remark: m-toluidine was readily metabolized by soil microorganisms during the 32-day examination period. The degradation was measured using 14-C-m-toluidine.
Source: Bayer AG Leverkusen
(34)

Remark: No anaerobic degradation of m-toluidine could be detected after eight months, within ten months 73% of m-toluidine was biodegraded in the sulfate reducing aquifer slurries, but no degradation could be detected in the methanogenic aquifer slurries.
Source: Bayer AG Leverkusen
(35)

Remark: 3.91 - 7.81 mg m-toluidine/ml led to a complete growth inhibition of Staphylococcus aureus, Enterococcus, Escherichia coli, Proteus mirabilis and Pseudomonas aeruginosa.
Source: Bayer AG Leverkusen
(36)

Remark: m-toluidine led to a complete growth inhibition of Microsporum (1.95 mg/ml) and Trichophyton (0.24 - 1.95 mg/ml) species.
61 - 970 ng m-toluidine/ml led to a decrease in growth of Candida species.
Source: Bayer AG Leverkusen
(37)

Remark: m-toluidine was detected in waste water (no further data available) and in ground water in Minnesota (297 ug/l in 1981; influenced by coal tar distillation wastes) and Wyoming (1.5 - 3.3 ug/l; influenced by underground coal gasification sites; no further data available).
Source: Bayer AG Leverkusen
(38) (39)

Remark: m-toluidine was detected in oil from Montana (0.53 mg/l) and Baytown (0.24 mg/l) and in coal oil in Minnesota (no further data available).
Source: Bayer AG Leverkusen
(40) (24)

Remark: The degradation of m-toluidine was measured with yellow-pigmented, gram-negative bacteria. Assuming 10E13 organisms per liter the half-life of m-toluidine was calculated as 4 hours.
Source: Bayer AG Leverkusen
(41)

Remark: Partially purified enzymes (peroxidase and aniline oxidase) of the soil fungus Geotrichum candidum L-3 transformed m-toluidine to the corresponding azobenzene. No further data available.
Source: Bayer AG Leverkusen
(42)

Remark: Redwinged blackbird (Agelaius phoeniceus), acute oral toxicity: LD50 = 242 mg/kg b.w.; administration of m-toluidine by gavage.
Source: Bayer AG Leverkusen
(43)

Remark: European starling (Sturnus vulgaris), acute oral toxicity: LD50 > 1000 mg/kg b.w.; administration of m-toluidine by gavage.
Source: Bayer AG Leverkusen
(43)

Remark: Quail (Coturnix coturnix), acute oral toxicity: LD50 : 562 mg/kg b.w.; administration of m-toluidine by gavage.
Source: Bayer AG Leverkusen
(43)

Remark: In a batch culture of phenol-degrading methanogenic bacteria 50, 100 and 300 mg m-toluidine/l were not degraded to methane within a 15-week period.
Source: Bayer AG Leverkusen
(44)

Remark: For further ecotoxicological data see BUA Report (in press)
Source: Bayer AG Leverkusen

5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 450 mg/kg bw
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: RHONE-POULENC AGRO LYON

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 974 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(45)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: ca. 450 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(46)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1160 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(14)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1430 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(47)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 740 mg/kg bw
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: RHONE-POULENC AGRO LYON

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 740 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(47)

5.1.2 Acute Inhalation Toxicity
-

5.1.3 Acute Dermal Toxicity
-

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value:
Method:
Year: GLP:
Test substance:
Remark: males 690 mg/kg; females 660 mg/kg
data for m-toluidine-HCl
Source: Bayer AG Leverkusen
(48)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value:
Method:
Year: GLP:
Test substance:
Remark: males 714 mg/kg; females 650 mg/kg
data for m-toluidine-HCl
Source: Bayer AG Leverkusen
(48)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 116 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(49)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 150 mg/kg bw
Method:
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(50)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: other: keine Angabe
Value: = 750 mg/kg bw
Method:
Year: GLP:
Test substance:
Remark: no further data available.
Source: Bayer AG Leverkusen

(51)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: moderately irritating
EC classificat.:
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: RHONE-POULENC AGRO LYON

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: moderately irritating
EC classificat.:
Method: other: no data
Year: GLP:
Test substance:
Remark: 24 h exposure
Source: Bayer AG Leverkusen

(52)

5.2.2 Eye Irritation

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of
Animals:
Result: moderately irritating
EC classificat.:
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: RHONE-POULENC AGRO LYON

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: moderately irritating
EC classificat.:
Method: other: no data
Year: GLP:
Test substance:
Source: Bayer AG Leverkusen

(52)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result:
EC classificat.:
Method: other: no data
Year: GLP:
Test substance:
Remark: observation 2 hours after application: photosensitivity, lacrimation; oedema and erythema of the conjunctivae and opacity of the cornea at test day 2
Source: Bayer AG Leverkusen

(51)

5.3 Sensitization
-

5.4 Repeated Dose Toxicity

Species: rat Sex: no data
Strain: no data
Route of admin.: gavage
Exposure period: 30 d
Frequency of treatment: daily
Post. obs. period: no data
Doses: 280 mg/kg b.w./day
Control Group: yes
Method:
Year: GLP:
Test substance:
Result: decreased body weight, increased relative spleen weight, anemia (reduced oxygenated hemoglobin content, erythrocytopenia) increased sulfonated hemoglobin content, appearance of Heinz-Ehrlich bodies, decreased SH-groups in the blood, disturbed vitamin C content (no further data available)
Source: Bayer AG Leverkusen
(51)

Species: rat Sex: no data
Strain: no data
Route of admin.: gavage
Exposure period: 90 d
Frequency of treatment: 3 d/w
Post. obs. period: no data
Doses: 280 mg/kg b.w./day
Control Group: yes
Method:
Year: GLP:
Test substance:
Result: decreased body weight, increased spleen weight, anemia (reduced oxygenated hemoglobin content, erythrocytopenia) increased sulfonated hemoglobin content, appearance of Heinz-Ehrlich bodies, decreased SH-groups in the blood, disturbed vitamin C content (no further data available)
Source: Bayer AG Leverkusen
(51)

Species: rat Sex: male
Strain: Wistar
Route of admin.: i.p.
Exposure period: 3 d
Frequency of treatment: daily
Post. obs. period: no
Doses: 75 mg/kg b.w./day
Control Group: yes
Method:
Year: GLP:
Test substance:
Remark: The effect of m-toluidine treatment on cytochrome contents of microsomes of liver and kidney as well as the enzyme activities of microsomes of liver, kidney and lung was determined.
Result: Significantly ($p < 0.05$) enhanced glutathion S-transferase activity was found in the liver; the NADPH-cytochrome c reductase activity was significantly ($p < 0,05$) decreased in the kidney; the enzyme activities in the lungs were within the normal range. The cytochrome P-450 and cytochrome b5 contents in liver and kidney were not influenced by m-toluidine.
Source: Bayer AG Leverkusen

(53)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing:
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method:
Year: GLP:
Test substance: as prescribed by 1.1 - 1.4
Source: RHONE-POULENC AGRO LYON

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Remark: negative in the presence of the co-mutagen Norharman
no concentration data available
Source: Bayer AG Leverkusen
(54)

Type: Ames test
System of testing: Salmonella typhimurium TA 98
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP:
Test substance:
Remark: concentrations up to 200 ug/plate
Norharman absent/present in the test system
Source: Bayer AG Leverkusen
(55)

Type: Ames test
System of testing: Salmonella typhimurium TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Remark: concentrations up to 100 ug/plate
Source: Bayer AG Leverkusen
(56)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Remark: concentration = 535.8 or 1071.6 ug/ml (5; 10 mM)
no further data available
Source: Bayer AG Leverkusen
(57)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP:
Test substance:
Remark: no concentration data available
Source: Bayer AG Leverkusen
(58)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Remark: concentration = 321.5 ug/plate
Source: Bayer AG Leverkusen
(59)

Type: Ames test
System of testing: Salmonella typhimurium TA 102
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Remark: concentrations up to 5000 ug/plate
Source: Bayer AG Leverkusen

(60)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Remark: concentrations up to 107 ug/plate
Source: Bayer AG Leverkusen

(61)

Type: Unscheduled DNA synthesis
System of testing: rat liver hepatocyte
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Remark: concentrations up to 107.16 mg/ml
Source: Bayer AG Leverkusen

(62)

Type: other: other (see remarks)
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538, G46, C3076, D3052, Escherichia coli WP2, WP2 uvr A-
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP:
Test substance:
Remark: Gradient plate test for bacterial mutation (modified Ames Test) concentrations up to 1000 ug/ml of agar
Source: Bayer AG Leverkusen

(62)

Type: other: other (see remarks)
System of testing: Bacillus subtilis
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP:
Test substance:
Remark: Assay for loss of transforming DNA activity
1070 mg m-toluidine/l was mixed with transforming DNA and incubated 60 minutes, mixed with competent cells and incubated 30 minutes, mixed with soft agar and poured onto the minimal agar plate, the number of transforments was counted after incubation for 2 days at 37 degree C.
Source: Bayer AG Leverkusen

(57)

5.6 Genetic Toxicity 'in Vivo'

Type: Sister chromatid exchange assay
Species: mouse Sex: no data
Strain:
Route of admin.: i.p.
Exposure period: once
Doses: 10, 50, 100 and 200 mg/kg b.w.
Result:
Method:
Year: GLP:
Test substance:
Remark: result: negative
no further data available
Source: Bayer AG Leverkusen

(63)

Type: Sister chromatid exchange assay
Species: mouse Sex: no data
Strain:
Route of admin.: i.p.
Exposure period: single application
Doses: no data
Result:
Method:
Year: GLP:
Test substance:
Result: result: negative
Source: Bayer AG Leverkusen
(64)

Type: other: Inhibition of DNA-synthesis
Species: mouse Sex: male
Strain:
Route of admin.: oral unspecified
Exposure period: single application
Doses: 200 mg/kg b.w.
Result:
Method:
Year: GLP:
Test substance:
Result: no inhibition of testicular DNA-synthesis
Source: Bayer AG Leverkusen
(65)

Type: other: Inhibition of DNA-synthesis
Species: mouse Sex: no data
Strain:
Route of admin.: i.p.
Exposure period: once
Doses: 2-300 mg/kg b.w. (no further data available)
Result:
Method:
Year: GLP:
Test substance:
Remark: 3 mice per dose-level and control group were examined. Autoradio- graphs of nuclei of renal tubular and liver epithelium were examined by visual silver-grain counting, carcinogenic compounds inhibit the nuclear incorporation of 3H-thymidine.
Result: result: negative, no inhibition of DNA-synthesis was found.
Source: Bayer AG Leverkusen
(66) (67)

5.7 Carcinogenicity

Species: rat Sex: male/female
Strain: no data
Route of admin.: oral feed
Exposure period: 83-368 d
Frequency of treatment: daily
Post. obs. period: no data
Doses: 60-90 mg/kg b.w./day
Result:
Control Group: yes
Method:
Year: GLP:
Test substance:
Remark: Diet 1: contained B-group vitamines in quantities lying at or somewhat under the minimum requirement (0.2 mg riboflavin/100 g diet).
Diet 2: see diet 1, but the riboflavin content amounted to 2 mg/100 g diet.
Diet 3: see diet 1, additionally the animals received 2 mg ascorbic acid/day by subcutaneous injection.
Bladder changes:
Grade 0: No pathological changes of the epithelium of the bladder.
Grade 1: Thickening of the epithelium and metaplasia to stratified squamous epithelium with cornification, no proliferation, changes in most cases strictly localized.
Grade 2: Extensive epithelial metaplasia with cornification and proliferation, most often in the form of infolding and down growth of epithelial masses to the submucosa.
Smaller epithelial pearls with cornification may occur. Each group consisted of 12 rats (3 males, 9 females), but not all animals were examined. Average weight of the animals: 167 g, m-toluidine concentration in the diet: 0.1 %, daily average food intake: 10 - 15 g diet/animal, this resulted in a daily average test substance intake of 10 - 15 mg/animal.
Result: histopathological bladder changes:
Diet 1 (107-341 days of application of m-toluidine):
5 out of 9 rats: grade 0
2 out of 9 rats: grade 1
2 out of 9 rats: grade 2
Diet 2 (83-368 days of application of m-toluidine):
5 out of 7 rats: grade 0
1 out of 7 rats: grade 1
1 out of 7 rats: grade 2
Diet 3 (132-339 days of application of m-toluidine):
4 out of 8 rats: grade 0
4 out of 8 rats: grade 2
Control group (fed with diet 1; no duration of feeding given): 5 out of 7 rats: grade 0
2 out of 7 rats: grade 1

(see text)
Source: Bayer AG Leverkusen
(68)

Species: rat Sex: male
Strain: other: Charles River CD
Route of admin.: oral feed
Exposure period: 78 weeks
Frequency of treatment: daily
Post. obs. period: 26 weeks
Doses: 13 w: 8000, 16000; 65 w: 4000, 8000 mg/kg diet (see remarks)
Result:
Control Group: yes
Method:
Year: GLP:
Test substance:
Remark: Dosages (calculation is based on 50 g diet per kg b.w. and day): 13 weeks: 400 and 800 mg/kg b.w./day;
further 65 weeks: 200 and 400 mg/kg b.w./day;
25 male rats per group; histological examination was done on lungs, liver, spleen, kidney, adrenal, heart, bladder, stomach, intestine, reproductive organs and pituitaries.
Testsubstance: m-toluidine-HCl
Result: 400 and 800 mg/kg b.w./day for 13 weeks led to a reduced body weight gain (10 % and more) or death, therefore after 13 weeks the dosages were reduced to 200 and 400 mg/kg b.w./day for the remaining 65 weeks, no tumors were observed.
Source: Bayer AG Leverkusen
(48)

Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure period: 78 weeks
Frequency of treatment: daily
Post. obs. period: 13 weeks
Doses: other (see text)
Result:
Control Group: yes
Method:
Year: GLP:
Test substance:
Remark: Dosages (calculation is based on 150 g diet/kg b.w./day):
22 weeks: 16000 and 32000 mg/kg diet:
2400 and 4800 mg/kg b.w./day;
56 weeks: males 4000 and 8000 mg/kg diet:
600 and 1200 mg/kg b.w./day
females 8000 and 16000 mg/kg diet:
1200 and 2400 mg/kg b.w./day;
25 male and female mice per group; histological examination

was done on lungs, liver, spleen, kidney, adrenal, heart, bladder, stomach, intestine and reproductive organs.
Testsubstance: m-toluidine-HCl

Result: 2400 and 4800 mg/kg b.w./day for 22 weeks led to a reduced body weight gain (10 % and more) or death; after 22 weeks the dosages were reduced for the remaining 56 weeks: males 600 and 1200 mg/kg b.w./day, females 1200 and 2400 mg/kg b.w./day; no tumors were observed except liver tumors in male mice (4 out of 16 examined) at 600 mg/kg b.w./day; simultaneous control 1/18, pooled control 7/99.

Source: Bayer AG Leverkusen

(48)

5.8 Toxicity to Reproduction

-

5.9 Developmental Toxicity/Teratogenicity

-

5.10 Other Relevant Information

Type:

Remark: m-toluidine was detected in the urine (0.3-7.7 ug/24 h) of 2 of 11 smokers and 4 of 9 nonsmokers.

Source: Bayer AG Leverkusen

(69)

Type:

Remark: The mainstream smoke of one US 85 mm cigarette without filter tip contained 13.0 - 19.0 ng m-toluidine per cigarette.

Source: Bayer AG Leverkusen

(70)

Type:

Remark: m-toluidine was detected in the blood of smokers (approx. 1050 pg/g hemoglobin) and nonsmokers (approx. 1140 pg/g hemoglobin) in Turin; in Boston (smokers: approx. 810 pg/g hemoglobin; nonsmokers: approx. 990 pg/g hemoglobin).

Source: Bayer AG Leverkusen

(71)

Type:

Remark: m-toluidine was detected as a hemoglobin adduct in the blood of smokers (blond tobacco: 1097 pg/g hemoglobin; black tobacco 11401 pg/g hemoglobin) and nonsmokers (1141 pg/g hemoglobin) in Turin.

Source: Bayer AG Leverkusen

(72)

Type:
Remark: Hemoglobin examination showed no evidence for different concen- tration of m-toluidine in the blood of smokers (approx. 490 pg/g hemoglobin) and nonsmokers (approx. 680 pg/g hemoglobin).
Source: Bayer AG Leverkusen
(73)

Type:
Remark: Incubation of brown fat cells from adult hamsters with 1 mM (= 107.16 mg/l) m-toluidine for 5 min did not inhibit the noradrenaline induced respiration.
Source: Bayer AG Leverkusen
(74) (75)

Type:
Remark: Incubation of Ascites sarcoma BP8 cells with 1 mM (= 107.16 mg/l) m-toluidine for 48 h did not inhibit the cell growth.
Source: Bayer AG Leverkusen
(74)

Type:
Remark: Incubation of embryo chicken trachea with 5 mM (= 535 mg/l) m-toluidine in ethanol did not inhibit the ciliary activity within 60 minutes.
Source: Bayer AG Leverkusen
(74) (76)

Type:
Remark: 30 min after a single intravenous administration of 0.77 mmol (= 111.1 mg) m-toluidine-HCl/kg b.w. to dogs a maximum concentra- tion of 3.5 ug m-nitrosotoluene/ml blood was reached. 5 hours after the injection the concentration of m-nitrosotoluene was still ca. 1 ug/ml blood.
Source: Bayer AG Leverkusen
(77)

Type:
Remark: An intraveneous injection of 0.25 mmol (= 26.79 mg) m-toluidine- HCl/kg b.w. increased the methemoglobin content in the blood of cats. The maximum was reached after 4 hours, the mean maximum was 60.2 % hemoglobin measured as methemoglobin.
Source: Bayer AG Leverkusen
(78) (79)

Type:
Remark: Intraperitoneal injection of m-toluidine (1-80 mg/kg b.w. in corn oil) led to an increase of methemoglobin in the blood of cats. The effect was dose-dependent, but doses above 30 mg/kg b.w. did not cause any further increase of the methemoglobin level. A dose of 2 mg/kg b.w. caused a formation of Heinz-Ehrlich bodies in 10 % of the erythrocytes, a dose of 80 mg/kg b.w. generated Heinz-Ehrlich bodies in up to 70 % of the erythrocytes. At

high methemoglobin concentrations the cats showed an increased pulmonary respiration; higher dosages of m-toluidine led to a loss of muscle tone with dilated pupil, somnolence, vomiting, incontinence and often severe salivation.
Source: Bayer AG Leverkusen
(80)

Type:
Remark: An application of 700 mg m-toluidine/kg b.w. led to an increase of methemoglobin from 1.3 % up to 32.6 % in the blood of rats.
Source: Bayer AG Leverkusen
(51)

Type:
Remark: An exposure of 40 ppm (176 mg/m3) in the air for 60 minutes produced severe intoxication in persons (no further details available).
Source: Bayer AG Leverkusen
(81)

Type:
Remark: m-toluidine was detected in the blood plasma of rats after dermal application (tail). The plasma levels correlated with the dose- level.
Source: Bayer AG Leverkusen
(82)

Type:
Remark: m-toluidine was detected in the urine of rats after a single oral application (stomach tube) of 20, 100 or 200 mg/kg b.w. High correlation between levels administered and eliminated, was observed (no further details available).
Source: Bayer AG Leverkusen
(83)

Type:
Remark: Methemoglobin concentrations up to 36.4 % were detected in the blood of rats after a single oral application (200 mg/kg b.w.; stomach tube) of m-toluidine. Concentrations up to 40 % were detected after dermal exposure (2.5-12.5 mg/ml) for 2-6 h (no further details available).
Source: Bayer AG Leverkusen
(84)

Type:
Remark: 0.6 mmol (= 64.3 mg)/kg b.w. m-toluidine was orally (gavage) administered to female rats. After 24 h a covalent binding of m-toluidine to hemoglobin was found. The hemoglobin binding index was determined as 4.9 mmol m-toluidine/mol hemoglobin/ dose (mmol/kg b.w.).
Source: Bayer AG Leverkusen
(85)

Type:
Remark: 2.5 % of the administered m-toluidine was recovered as m-toluidine in the 24 h urine from rats after a single oral application of 500 mg m-toluidine/kg b.w. Two urinary metabolites were qualitatively identified: 2-amino-4-methylphenol and 4-amino-2-methylphenol.
Source: Bayer AG Leverkusen
(86)

Type:
Remark: In vitro, the p-hydroxylation of m-toluidine by rabbit liver microsomes was measured with a specific activity of 0.43 nmol/ min and mg microsomal protein.
Source: Bayer AG Leverkusen
(87)

Type:
Remark: After single oral administration (stomach tube) of 3'-Methyl-4- (dimethylamino)azobenzene or 3'-Methyl-4-(methylamino)azobenzene to male rats, m-toluidine was detectable in the enzymatically hydrolyzed bile and urine among other metabolites.
Source: Bayer AG Leverkusen
(88) (89) (90)

Type:
Remark: Incubation of 3'-Methyl-4-(dimethylamino)azobenzene with rat liver slices for 3 h or with rat liver homogenates for 2 h: in extracts from the incubation mixture m-toluidine was identifiable among other metabolites.
Source: Bayer AG Leverkusen
(91)

Type:
Remark: Incubation of human diploid embryonic lung fibroblasts with 25 mM (= 2679 mg/l) m-toluidine for 30 minutes did not damage the membrane.
Source: Bayer AG Leverkusen
(74) (92)

Type:
Remark: 6 hours after a single intravenous administration of 0.77 mmol (= 111.1 mg) m-toluidine-HCl/kg b.w. to dogs the concentration of methemoglobin was ca. 56 %.
Source: Bayer AG Leverkusen
(77)

Type:
Remark: The microsomal oxidation of m-toluidine was described as follows (no further information available):
- with atmospheric oxygen to the corresponding primary hydroxylamine or to the corresponding nitroso compound
- with water to the corresponding p-hydroxy- or o-hydroxyamine
Source: Bayer AG Leverkusen

(93) (94)

5.11 Experience with Human Exposure
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7.1 End Point Summary

-

7.2 Hazard Summary

-

7.3 Risk Assessment

-

I U C L I D

D a t a S e t

Existing Chemical	ID: 106-49-0
CAS No.	106-49-0
EINECS Name	p-toluidine
EINECS No.	203-403-1
TSCA Name	Benzenamine, 4-methyl-
Molecular Formula	C7H9N

Producer Related Part
- Company: Bayer Corporation
- Creation date: 23-SEP-1999

Substance Related Part
- Company: Bayer Corporation
- Creation date: 23-SEP-1999

Memo: Bayer Corporation

Printing date: 28-SEP-2001
Revision date:
Date of last Update: 28-SEP-2001

Number of Pages: 55

Chapter (profile): Chapter: 1, 2, 3, 4, 5, 7
Reliability (profile): Reliability: without reliability, 1, 2, 3, 4
Flags (profile): Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 OECD and Company Information

Type: other: co-sponsoring organization
Name: American Chemistry Council (formerly Chemical Manufacturers Association), Monocyclic Aromatic Amines and Nitro Aromatics (MAANA) HPV Panel
Street: 1300 Wilson Boulevard
Town: 22209 Arlington, VA
Country: United States

25-SEP-2001

Type: cooperating company
Name: Albemarle Corporation
Country: United States

25-SEP-2001

Type: cooperating company
Name: Bayer Corporation
Country: United States

25-SEP-2001

Type: cooperating company
Name: Buffalo Color Corporation
Country: United States

25-SEP-2001

Type: cooperating company
Name: ChemFirst, Inc.
Country: United States

25-SEP-2001

1.0.2 Location of Production Site
-

1.0.3 Identity of Recipients
-

1.1 General Substance Information
-

1.1.0 Details on Template
-

1.1.1 Spectra
-

1.2 Synonyms
-

1.3 Impurities
-

1.4 Additives
-

1.5 Quantity
-

1.6.1 Labelling
-

1.6.2 Classification
-

1.7 Use Pattern
-

1.7.1 Technology Production/Use
-

1.8 Occupational Exposure Limit Values
-

1.9 Source of Exposure
-

1.10.1 Recommendations/Precautionary Measures
-

1.10.2 Emergency Measures
-

1.11 Packaging
-

1.12 Possib. of Rendering Subst. Harmless
-

1.13 Statements Concerning Waste
-

1.14.1 Water Pollution
-

1.14.2 Major Accident Hazards
-

1.14.3 Air Pollution
-

1.15 Additional Remarks
-

1.16 Last Literature Search
-

1.17 Reviews
-

1.18 Listings e.g. Chemical Inventories
-

2.1 Melting Point

Value: 43.7 degree C
Method: other:
Testsubstance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
15-AUG-2001 (1)

Value: >= 43 degree C
Remark: solidification point
15-AUG-2001 (2)

2.2 Boiling Point

Value: 200.4 degree C at 1013 hPa
Method: other:
Testsubstance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
15-AUG-2001 (1)

Value: = 200 degree C at 1013 hPa
15-AUG-2001 (2)

Value: >= 220 degree C
Remark: endotherm decomposition
(Isotherm-Stufen-DTA)
15-AUG-2001 (3)

Value: > 500 degree C at 1013 hPa
Decomposition: yes
Method: other: DTA
Test condition: 10 K/min
15-AUG-2001 (4)

2.3 Density

Type: density
Value: .9619 g/cm3 at 20 degree C
Method: other:
Testsubstance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
15-AUG-2001 (5)

Type: density
Value: = 1.046 g/cm3 at 20 degree C
15-AUG-2001 (2)

Type: density
Value: = 1.05 g/cm3 at 20 degree C
15-AUG-2001 (4)

Type: bulk density
Value: = 700 kg/m3
15-AUG-2001 (4)

2.3.1 Granulometry
-

2.4 Vapour Pressure

Value: .381 hPa at 25 degree C
Method: other (measured)
Testsubstance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Flag: Critical study for SIDS endpoint
28-SEP-2001 (6)

Value: = 1.3 hPa at 43 degree C
15-AUG-2001 (2)

Value: 10 hPa at 77.1 degree C
Method: other (measured)
Testsubstance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
25-SEP-2001 (7)

Value: = .26 hPa at 20 degree C
25-SEP-2001 (8)

2.5 Partition Coefficient

log Pow: 1.623
Method: other (calculated): KOWWIN Program (v1.65)
Year:
GLP: no
Testsubstance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-AUG-2001 (9)

log Pow: 1.39
Method: other (measured): according to Hansch et.al, 1995
Year:
GLP: no data
Testsubstance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Data from Handbook or collection of data
Flag: Critical study for SIDS endpoint
15-AUG-2001 (10)

log Pow: = 1.6
Method: other (calculated): Medchem Software CLOGP3, Release 3.42, Pomona College, Clermont CA
Year: 1986
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-AUG-2001 (11)

2.6.1 Water Solubility

Value: 7.225 g/l at 25 degree C
Method: other: WSKOW (v1.36)
Result: Log Kow (estimated) : 1.62
Log Kow (experimental): 1.39
Cas No: 000106-49-0
Name : p-Toluidine
Refer : Hansch et al; 1995
Log Kow used by Water solubility estimates: 1.39

Equation Used to Make Water Sol estimate:
Log S (mol/L) = 0.796 - 0.854 log Kow - 0.00728 MW

Log Water Solubility (in moles/L) : -1.171
Water Solubility at 25 deg C (mg/L): 7225
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-AUG-2001 (9)

Value: = 11 g/l at 20 degree C
pH: = 7
Flag: Critical study for SIDS endpoint
15-AUG-2001 (4)

Value: = 19 g/l at 60 degree C
15-AUG-2001 (8)

Value: = 24 g/l at 60 degree C
15-AUG-2001 (4)

2.6.2 Surface Tension
-

2.7 Flash Point

Value: = 87 degree C
Type: closed cup
Method: other: DIN 51758
Year:
15-AUG-2001 (8) (4) (12) (2)

2.8 Auto Flammability

Value: ca. 480 degree C
Method: other: DIN 51794
15-AUG-2001 (2)

2.9 Flammability

-

2.10 Explosive Properties

-

2.11 Oxidizing Properties

-

2.12 Additional Remarks

-

3.1.1 Photodegradation

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 1560000 molecule/cm3
Rate constant: .000000000001320953 cm3/(molecule * sec)
Degradation: 50 % after 1 hour(s)
Method: other (calculated): AOP Program v. 1.89
Year: 1999 GLP: no
Test substance: other TS: molecular structure
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-AUG-2001 (9)

Type: air
INDIRECT PHOTOLYSIS
Sensitizer: OH
Conc. of sens.: 500000 molecule/cm3
Rate constant: = .00000000016 cm3/(molecule * sec)
Degradation: = 50 % after .1 day
Method: other (calculated): Atkinson
Year: 1988 GLP:
Test substance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-AUG-2001 (13)

3.1.2 Stability in Water

Type: abiotic
Method: other: from Schultz, T.W. et al. (1989) Bull. Environ. Toxicol. Chem. 42: 192-198.
Year: 1989 GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Result: A solution in distilled water lost 8.8% (+/-0.2) in 48 hours.
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-AUG-2001 (14)

3.1.3 Stability in Soil
-

3.2 Monitoring Data (Environment)
-

3.3.1 Transport between Environmental Compartments

Type: fugacity model level III
Media: other: other: air - water - soil - sediment
Air (Level I):
Water (Level I):
Soil (Level I):
Biota (L.II/III):
Soil (L.II/III):
Method: other: EPIWIN Level III Fugacity Model
Year:
Result:

Media	Distribution (percent)	Half-Life (hr)	Emissions (kg/hr)	Fugacity (atm)
Air	0.352	1.94	1000	6.5e-012
Water	49.8	360	1000	3.8e-011
Soil	49.8	360	1000	7.79e-010
Sediment	0.1	1.44e+003	0	3.08e-011

Persistence Time: 270 hr
Reaction Time: 315 hr
Advection Time: 1.88e+003 hr
Percent Reacted: 85.6
Percent Advected: 14.4

Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-AUG-2001 (9)

3.3.2 Distribution
-

3.4 Mode of Degradation in Actual Use
-

3.5 Biodegradation

Type: aerobic
Inoculum: activated sludge, industrial, non-adapted
Degradation: 94 % after 10 day
Testsubstance: 3 hour(s) 10 - 15 %
5 day 50 %
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: 1986 GLP: no
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
15-AUG-2001 (15)

Type: aerobic
Inoculum: activated sludge, industrial
Degradation: 94 % after 8 day
Method: OECD Guide-line 302 B "Inherent biodegradability: Modified Zahn-Wellens Test"
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
15-AUG-2001 (16)

Type: aerobic
Inoculum: other bacteria: adapted to the test substance
Degradation: ca. 60 %
Method: other: Respirometer test, similar to modified MITI Test
Year: GLP: no
Test substance: no data
Remark: test period not reported
Reliability: (2) valid with restrictions
Comparable to Guideline study with acceptable restrictions
15-AUG-2001 (17) (16)

Type: aerobic
Inoculum: other bacteria: soil bacteria
Degradation: 100 %
Method: other: shake flask test, similar to mod. OECD Screening Test
Year: GLP: no
Test substance: no data
Remark: test period not reported
Reliability: (2) valid with restrictions
Comparable to Guideline study with acceptable restrictions
15-AUG-2001 (18) (16)

3.6 BOD5, COD or BOD5/COD Ratio
-

3.7 Bioaccumulation

Species: other
Exposure period:
Concentration:
BCF: 2.35
Elimination:
Method: other: BCF Program (v2.13)
Year: GLP:
Test substance:
Result: Log Kow (estimated) : 1.62
Log Kow (experimental): 1.39
Log Kow used by BCF estimates: 1.39

Equation Used to Make BCF estimate:
Log BCF = 0.77 log Kow - 0.70

Estimated Log BCF = 0.370 (BCF = 2.346)
Reliability: (2) valid with restrictions
Accepted calculation method
Flag: Critical study for SIDS endpoint
15-AUG-2001 (9)

3.8 Additional Remarks

-

AQUATIC ORGANISMS

4.1 Acute/Prolonged Toxicity to Fish

Type: static
Species: Cyprinodon variegatus (Fish, estuary, marine)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: 60
Method: other: USEPA TSCA Guideline 797.1400
Year: 1985 GLP: yes
Test substance: other TS: p-Toluidine (106-49-0), purity: 99.5%
Remark: The Test Type is Static, Renewal. Test material analysis not done under GLP.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (19)

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: 50
LC50: 100 - 220
LC100: 220
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: 1990 GLP: yes
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
15-AUG-2001 (20)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: 149
EC50 : 137
Method: EPA OPP 72-1
Year: 1985 GLP: no data
Test substance: other TS: other TS: p-toluidine; purity = 99 %
Remark: Analytical monitoring: GLC
LC50, 95 % confidence interval: 135-163 mg/l
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
16-AUG-2001 (21)

Type: flow through
Species: Pimephales promelas (Fish, fresh water)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
LC50: 171
Method: EPA OPP 72-1
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Remark: 95 % confidence interval: 138-213 mg/l
Analytical monitoring: HPLC
Reliability: (1) valid without restriction
Guideline study
15-AUG-2001 (22)

Type: static
Species: Brachydanio rerio (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: 50
LC50: 137
Method: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year: GLP: yes
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
GLP guideline study
15-AUG-2001 (20)

Type: static
Species: Leuciscus idus (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
LC0: 20
Method: other: DIN 38412, Part 15
Year: 1973 GLP: no
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
15-AUG-2001 (23)

Type: static
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 60
Method: other: based on OECD Guideline 203
Year: GLP: no
Test substance: no data
15-AUG-2001 (24)

Type: semistatic
Species: Poecilia reticulata (Fish, fresh water)
Exposure period: 14 day
Unit: mg/l Analytical monitoring: no data
LC50: 10.72
Method: other: 14 day test acc. to Koenemann, H.; Toxicology 19, 209-238 (1981)
Year: GLP: no
Test substance: no data
15-AUG-2001 (25)

Type: static
Species: Oryzias latipes (Fish, fresh water)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
LC50: 42
Method: other: based on OECD Guideline 203
Year: GLP: no
Test substance: no data
15-AUG-2001 (24)

4.2 Acute Toxicity to Aquatic Invertebrates

Type: static
Species: Mysidopsis bahia (Crustacea)
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: yes
EC50: 1.5
NOEC : .63
Method: other: USEPA TSCA Guideline 797.1930
Year: 1985 GLP: yes
Test substance: other TS: p-Toluidine (106-49-0) , purity: . 99.5%.
Remark: Test material analysis not done under GLP.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (26)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no data
EC0: .0002
EC100: 50
Method: other: DIN 38412, Part 11
Year: GLP: no
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
Flag: Critical study for SIDS endpoint
25-SEP-2001 (27)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no data
EC0: 1.6
EC100: 500
Method: other: DIN 38412, Part 11
Year: GLP: no
Test substance: no data
Reliability: (2) valid with restrictions
Meets National standards method (AFNOR/DIN)
25-SEP-2001 (27)

Type:
Species: Daphnia magna (Crustacea)
Exposure period: 48 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: < .6
Method: other: see Authors of this publication
Year: GLP: no
Test substance: no data
15-AUG-2001 (28)

4.3 Toxicity to Aquatic Plants e.g. Algae

Species: Scenedesmus quadricauda (Algae)
Endpoint: other: inhibition of cell multiplication
Exposure period: 96 hour(s)
Unit: mg/l Analytical monitoring: no data
EC0: < 8
Method: other: see Authors of this publication
Year: GLP: no
Test substance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-AUG-2001 (28)

Species: Agmenellum quadruplicatum (Algae)
Endpoint:
Exposure period:
Unit: Analytical monitoring:
Method:
Year: GLP:
Test substance: other TS: p-toluidine; purity not noted
Remark: strain PR 6
The addition of 50 ppb during exponential growth in a liquid culture resulted in a bending of the growth curve to a plateau within 4 hours. Cultures containing 500 ppb did not grow.
15-AUG-2001 (29)

4.4 Toxicity to Microorganisms e.g. Bacteria

Type: aquatic
Species: activated sludge
Exposure period: 3 hour(s)
Unit: mg/l Analytical monitoring: no data
EC50: 100
Method: OECD Guide-line 209 "Activated Sludge, Respiration Inhibition Test"
Year: GLP: no data
Test substance: no data
Reliability: (1) valid without restriction
Guideline study
15-AUG-2001 (30)

Type: aquatic
Species: Escherichia coli (Bacteria)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 1000
Method: other: see Authors of this publication
Year: GLP: no
Test substance: other TS: p-toluidine; purity not noted
15-AUG-2001 (28)

Type: aquatic
Species: Pseudomonas fluorescens (Bacteria)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
EC0: 500
Method: other: Bestimmung der biologischen Schadwirkung toxischer Abwaesser gegen Bakterien. DEV, L 8 (1968) modifiziert
Year: 1973 GLP: no
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
Meets National standards method (AFNOR/DIN)
15-AUG-2001 (23)

Type: aquatic
Species: anaerobic bact. from a domestic water treatment plant
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring: no
TT : 250
Method: ETAD Fermentation tube method "Determination of damage to effluent bacteria by the Fermentation Tube Method"
Year: GLP: no
Test substance: other TS: p-toluidine; purity not noted
Remark: TT = Toxicity Threshold
15-AUG-2001 (15)

Type:
Species: Tetrahymena pyriformis (Protozoa)
Exposure period: 24 hour(s)
Unit: mg/l Analytical monitoring:
EC50: 150
Method:
Year: GLP:
Test substance: other TS: p-toluidine; purity not noted
15-AUG-2001 (30)

4.5 Chronic Toxicity to Aquatic Organisms

4.5.1 Chronic Toxicity to Fish
-

4.5.2 Chronic Toxicity to Aquatic Invertebrates
-

TERRESTRIAL ORGANISMS

4.6.1 Toxicity to Soil Dwelling Organisms
-

4.6.2 Toxicity to Terrestrial Plants
-

4.6.3 Toxicity to other Non-Mamm. Terrestrial Species
-

4.7 Biological Effects Monitoring
-

4.8 Biotransformation and Kinetics
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4.9 Additional Remarks
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5.1 Acute Toxicity

5.1.1 Acute Oral Toxicity

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 620 mg/kg bw
Method: Directive 84/449/EEC, B.1 "Acute toxicity (oral)"
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
15-AUG-2001 (31)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: 656 mg/kg bw
Method: EPA OPP 81-1
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Guideline study without detailed description
Flag: Critical study for SIDS endpoint
15-AUG-2001 (32)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 1285 mg/kg bw
Method: EPA OPP 81-1
Year: GLP: no data
Test substance: other TS: Hydrochloride salt
Reliability: (2) valid with restrictions
Guideline study without detailed description
Flag: Critical study for SIDS endpoint
15-AUG-2001 (32)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 794 mg/kg bw
Method: EPA OPP 81-1
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Guideline study without detailed description
Flag: Critical study for SIDS endpoint
15-AUG-2001 (32)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 760 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
15-AUG-2001 (33)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 2951 mg/kg bw
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
15-AUG-2001 (34)

Type: LD50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 794 mg/kg bw
Method:
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
15-AUG-2001 (35)

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 330 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
15-AUG-2001 (33)

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 270 mg/kg bw
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
15-AUG-2001 (36)

5.1.2 Acute Inhalation Toxicity

Type: LC50
Species: rat
Strain:
Sex:
Number of Animals:
Vehicle:
Exposure time: 1 hour(s)
Value: = .64 mg/l
Method: EPA OPP 81-3
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Guideline study without detailed description
Flag: Critical study for SIDS endpoint
15-AUG-2001 (32)

5.1.3 Acute Dermal Toxicity

Type: LD50
Species: rabbit
Strain:
Sex:
Number of Animals:
Vehicle:
Value: = 890 mg/kg bw
Method: EPA OPP 81-2
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Reliability: (2) valid with restrictions
Guideline study without detailed description
Flag: Critical study for SIDS endpoint
15-AUG-2001 (32)

5.1.4 Acute Toxicity, other Routes

Type: LD50
Species: mouse
Strain:
Sex:
Number of Animals:
Vehicle:
Route of admin.: i.p.
Value: = 50 mg/kg bw
Method: other: no data
Year: GLP: no data
Test substance: no data
15-AUG-2001 (37)

Type: LD50
Species: rat
Strain:
Sex: male
Number of Animals:
Vehicle:
Route of admin.: s.c.
Value: = 1012 mg/kg bw
Method:
Year: GLP: no data
Test substance: no data
15-AUG-2001 (38)

5.2 Corrosiveness and Irritation

5.2.1 Skin Irritation

Species: rabbit
Concentration: other: 0.5 gm/rabbit moistened with water

Exposure: Occlusive
Exposure Time: 4 hour(s)
Number of Animals: 6
PDII: .15
Result: not irritating
EC classificat.:
Method: EPA OTS 798.4470
Year: 1992 GLP: yes
Test substance: other TS: p-toluidine, purity 99.8%
Remark: All rabbits had very slight to well-defined erythema and very slight to slight edema at the 30-60 min scoring interval. All rabbits were free of signs by 72 hr after application.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
28-SEP-2001 (39)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of Animals:
PDII:
Result: not irritating
EC classificat.:
Method: Directive 84/449/EEC, B.4 "Acute toxicity (skin irritation)"
Year: GLP: no data
Test substance: no data
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (40)

Species: rabbit
Concentration:

Exposure:
Exposure Time:
Number of
Animals:
PDII:
Result: not irritating
EC classificat.:
Method: OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year: 1986 GLP: yes
Test substance: other TS: p-toluidine; purity not noted
Remark: Exposure: 4 h; no requirement to classify
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (41)

5.2.2 Eye Irritation

Species: rabbit
Concentration: undiluted
Dose: .1 other: gm
Exposure Time: 24 hour(s)
Comment: rinsed after (see exposure time)
Number of
Animals: 6
Result: moderately irritating
EC classificat.: not irritating
Method: EPA OTS 798.4500
Year: 1992 GLP: yes
Test substance: other TS: p-toluidine, purity 99.8%
Result: Maximum score 27.8/110 at the 24 hr interval.
Corneal opacity, irritation of the iris, conjunctival
erythema, chemosis, and discharge noted.
All rabbits were free of signs by 14 days after application.
FHSA score (24, 48, 72 hr average reading): 21.7/110.
Considered moderately irritating.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
28-SEP-2001 (42)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: irritating
EC classificat.:
Method: OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year: 1986 GLP: yes
Test substance: other TS: p-toluidine; purity not noted
Remark: Exposure: 24 h; R 36 - irritates the eyes
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (43)

Species: rabbit
Concentration:
Dose:
Exposure Time:
Comment:
Number of Animals:
Result: slightly irritating
EC classificat.:
Method: Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (40)

5.3 Sensitization

Type: Open epicutaneous test
Species: human
Number of Animals:
Vehicle:
Result:
Classification:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Positive Reaktion bei 63.8 % der primaer durch PPD (p-Phenylendiamin) sensibilisierten Personen (Gruppensensibilisierung).
15-AUG-2001 (44)

Type: Patch-Test
Species: guinea pig
Concentration: occlusive epicutaneous
Number of Animals:
Vehicle:
Result: sensitizing
Classification:
Method:
Year: GLP: no data
Test substance: no data
Remark: 24 h, occlusive epicutaneous
15-AUG-2001 (45)

5.4 Repeated Dose Toxicity

Species: rat Sex: male
Strain:
Route of admin.: oral feed
Exposure period: 4 weeks
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 165, 825, 1650 ppm (13.8, 66.8, 125.7 mg/kg bw.)
Control Group: yes
NOAEL: 13.8 mg/kg bw
Method: other:
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Remark: 10 animals/group
Result: Reduced body weight development in the highest dose group, as well as increased relative liver weights above 825 ppm.
Reliability: (2) valid with restrictions
Meets generally accepted scientific standards, well documented and acceptable for assessment
Flag: Critical study for SIDS endpoint
15-AUG-2001 (32)

Species: rat Sex: male
Strain: Wistar
Route of admin.: i.p.
Exposure period: 3 consecutive days
Frequency of treatment: once per day
Post. obs. period: no
Doses: 75 mg/kg bw in sunflower oil
Control Group: no data specified
Method: other: Determination of drug metabolizing enzymes
Year: GLP: no data
Test substance: no data
Result: decreased activity of AHH and increased activity of glutathione S-transferase in liver, kidney and lung homogenates
15-AUG-2001 (46)

Species: other: Wild mice Sex:
Strain:
Route of admin.: oral feed
Exposure period: 3 days
Frequency of treatment: daily
Post. obs. period:
Doses: 1025 mg/kg Kgw.
Control Group:
Method: other: no data
Year: GLP: no data
Test substance: no data
Result: Mehr als 50 % der Tiere starben
15-AUG-2001 (47)

5.5 Genetic Toxicity 'in Vitro'

Type: Ames test
System of testing: Salmonella typhimurium TA 102
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: 1988 GLP: yes
Test substance: as prescribed by 1.1 - 1.4
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
16-AUG-2001 (48) (49)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year: GLP: no data
Test substance: other TS: p-toluidine; purity not noted
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
16-AUG-2001 (50) (51) (52)

Type: Cytogenetic assay
System of testing: V79
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Flag: Critical study for SIDS endpoint
16-AUG-2001 (52)

Type: Cytogenetic assay
System of testing: V79
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Flag: Critical study for SIDS endpoint
16-AUG-2001 (53)

Type: Ames test
System of testing: Salmonella typhimurium TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-FEB-1994 (54)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537, TA 1538, G46, C3076, D3052
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-JUN-2000 (55)

Type: Ames test
System of testing: Salmonella typhimurium TA 1535, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-FEB-1994 (56)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-FEB-1994 (57)

Type: Ames test
System of testing: Escherichia coli WP2, WP2uvrA-
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-FEB-1994 (55)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100, TA 1535
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
20-MAY-1994 (58) (59)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Remark: test done in presence of norharman
Source: Bayer AG Leverkusen

20-MAY-1994 (60)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 104
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: ambiguous
Method:
Year: GLP: no data
Test substance: no data
Remark: positive in TA 100
Source: Bayer AG Leverkusen

23-MAY-1994 (61) (62)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

23-MAY-1994 (63)

Type: Ames test
System of testing: Salmonella typhimurium TA 98, TA 100
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen

23-MAY-1994 (64)

Type: Ames test
System of testing: Salmonella typhimurium TA 97, TA 98, TA 100, TA 102, TA 104, TA 1535, TA 1537, TA 1538
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: positive
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Remark: weakly mutagenic
Source: Bayer AG Leverkusen
24-MAY-1994 (65)

Type: Bacterial gene mutation assay
System of testing: Escherichia coli WP2 uvrA
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
24-MAY-1994 (66)

Type: DNA damage and repair assay
System of testing: Escherichia coli polA+/polA-
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-FEB-1994 (56)

Type: DNA damage and repair assay
System of testing: Escherichia coli polA+/polA-
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
23-MAY-1994 (50) (67)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: Saccharomyces cerevisiae
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Remark: mitotische Konversion
Source: Bayer AG Leverkusen
20-MAY-1994 (68)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: Saccharomyces cerevisiae strain D3
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: negative
Method:
Year: GLP: no data
Test substance: other TS: Hydrochlorid
Remark: mitotic crossing over
Source: Bayer AG Leverkusen
20-MAY-1994 (69) (70) (71)

Type: Gene mutation in Saccharomyces cerevisiae
System of testing: strain D3
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
24-MAY-1994 (72) (71)

Type: Unscheduled DNA synthesis
System of testing: primaere Rattenhepatozyten
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result: positive
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-FEB-1994 (55)

Type: other: Alkalische Elution
System of testing: V79-DNA
Concentration:
Cytotoxic Conc.:
Metabolic activation:
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-FEB-1994 (52)

Type: other: DNA binding
System of testing: granulocytes (human)
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method:
Year: GLP: no data
Test substance: no data
Remark: positive following stimulation with phorbol myristate acetate

Source: Bayer AG Leverkusen
24-MAY-1994 (73)

Type: other: DNA damage
System of testing: Chinese hamster fibroblast (V79) cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other: alkaline elution method
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
20-MAY-1994 (74)

Type: other: DNA damage
System of testing: human lung cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: no data
Result: positive
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
20-MAY-1994 (75)

Type: other: DNA damage
System of testing: Escherichia coli PolA-/PolA+
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method:
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
20-MAY-1994 (76)

Type: other: Fluktuationstest
System of testing: Escherichia coli WP2uvrA
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
02-FEB-1994 (77)

Type: other: Inhibition of cell growth
System of testing: Ascites sarcoma B P8 cells
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
20-MAY-1994 (78) (79)

Type: other: Membrane damage
System of testing: Human diploid embryonic lung fibroblasts (line MRC 5)
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
20-MAY-1994 (78) (80)

Type: other: Mitotische Rekombination
System of testing: Saccharomyces cerevisiae D3
Concentration:
Cytotoxic Conc.:
Metabolic activation: with and without
Result: negative
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
23-MAY-1994 (50) (81)

Type: other: alkaline elution
System of testing: DNA from mice liver and kidney
Concentration: 2/3 of LD50
Cytotoxic Conc.:
Metabolic activation:
Result: positive
Method: other: ex vivo testing
Year: GLP: no data
Test substance: other TS: p-toluidine
Source: Bayer AG Leverkusen
06-MAR-1998 (82)

Type: other: formation of DNA adducts by norharman and aromatic amines
System of testing: Salmonella typhimurium TA 98
Concentration: 4 mg testsubstance in 2 ml DMSO and 20 ml S9 mix
Cytotoxic Conc.:
Metabolic activation: with
Result: negative
Method: other: mutation test: pre-incubation method as described by Ames; detection of DNA adducts: 32-P-post-labelling method
Year: GLP: no data
Test substance: other TS: p-toluidine
Source: Bayer AG Leverkusen
06-MAR-1998 (83)

Type: other: inhibition of oxidative metabolism
System of testing: brown fat cells, hamster
Concentration:
Cytotoxic Conc.:
Metabolic activation: without
Result: negative
Method: other
Year: GLP: no data
Test substance: no data
Source: Bayer AG Leverkusen
20-MAY-1994 (78) (84)

5.6 Genetic Toxicity 'in Vivo'

Type: Micronucleus assay
Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: i.p.
Exposure period: single dose
Doses: 43.75, 87.50, 175.0 mg/kg
Result: negative
Method: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year: 1997 GLP: yes
Test substance: other TS: p-Toluidine , purity: .99.80%
Remark: Doses used were 43.75, 87.50, and 175.0 mg/kg. Cells were harvested at 24, 48, and 72 hr (females only at 72 hr, no males remaining). Signs of clinical toxicity and mortality were observed.
Result: Not cytotoxic to the bone marrow (PCE:NCE ratio); no increase in micronuclei in bone marrow polychromatic erythrocytes.
Reliability: (1) valid without restriction
GLP guideline study
Flag: Critical study for SIDS endpoint
16-AUG-2001 (85)

Type: other: DNA binding
Species: rat Sex: male
Strain: Sprague-Dawley
Route of admin.: gavage
Exposure period: single administration
Doses: 500 mg/kg bw given in corn oil
Result: positive
Method:
Year: GLP: no data
Test substance:
Source: Bayer AG Leverkusen
15-AUG-2000 (86) (87)

Type: other: Alkalische Elution
Species: mouse Sex:
Strain:
Route of admin.: i.p.
Exposure period:
Doses: 35 mg/kg Kgw.
Result:
Method: other: keine Daten
Year: GLP: no data
Test substance: no data
Remark: Leber- und Nieren-DNA
Result: Positiv
Source: Bayer AG Leverkusen
25-MAY-1994 (88) (89)

Type: other: Drosophila wing spot test
Species: other: Drosophila melanogaster Sex: no data
Strain: other: multiple wing hairs and flare
Route of admin.: oral feed
Exposure period: from age of 72 h until pupation
Doses: 1.0; 2.0; 5.0 mM
Result:
Method: other: eggs from cross between mwh females and flr3 males, feeding of 72-h old third-instar larvae until pupation, selection of flies of (mwh+/+flr3) genotype
Year: 1995 GLP: no data
Test substance: other TS: p-toluidine
Result: positive at the highest concentration tested
Source: Bayer AG Leverkusen
06-MAR-1998 (90)

Type: other: inhibition of testicular DNA synthesis
Species: mouse Sex: no data
Strain: no data
Route of admin.: oral unspecified
Exposure period:
Doses: 200 mg/kg Kgw
Result:
Method:
Year: GLP: no data
Test substance: no data
Result: positive
Source: Bayer AG Leverkusen
23-MAY-1994 (91)

5.7 Carcinogenicity

Species: rat Sex: male
Strain: other: Charles River CD
Route of admin.: oral feed
Exposure period: 18 Months
Frequency of treatment: daily
Post. obs. period:
Doses: 0, 1000, 2000 ppm
Result:
Control Group: yes
Method: EPA OPP 83-2
Year: GLP: no data
Test substance: other TS: p-toluidine, hydrochloride salt; purity not noted
Remark: 25 animals/Group
Result: Results showed no significant increase in tumor frequency.
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
17-AUG-2001 (92) (93)

Species: mouse Sex: male/female
Strain: CD-1
Route of admin.: oral feed
Exposure period: 18 Months
Frequency of treatment: daily
Post. obs. period: Observation time for all animals was 21 months
Doses: 0, 6 Mon. at 1000, 2000 ppm, then 12 Mon. at 500, 1000 ppm
Result:
Control Group: yes
Method: EPA OPP 83-2
Year: GLP: no data
Test substance: other TS: p-toluidine, hydrochloride salt; purity not noted
Remark: 25 animals/Gender/Group; Matched control; 99 males and 102 females as pooled control.
Result: Among the males in both dosage groups and among the females in the higher dosage group, there occurred a significantly higher rate of liver tumors (adenomas, carcinomas).
Reliability: (1) valid without restriction
Guideline study
Flag: Critical study for SIDS endpoint
25-SEP-2001 (92) (93)

Species: rat Sex: male/female
Strain: Sprague-Dawley
Route of admin.: s.c.
Exposure period: 24 Monate
Frequency of treatment: 1mal/Woche
Post. obs. period: nach Absetzen der Behandlung bis zum spontanen Tod
Doses: 0, 25, 75 mg/kg Kgw in Erdnussoel
Result:
Control Group: yes, concurrent vehicle
Method:
Year: GLP: no data
Test substance: no data
Remark: 30 Tiere/Geschlecht/Gruppe
Result: Koerpergewichtsentwicklung dosisabhaengig reduziert; keine substanzbedingte Mortalitaet; keine klinischen Symptome; benigne Lebertumoren und vermehrt Leberzellnekrosen bei hoher Dosisgruppe; keine erhoehte Inzidenz maligner Tumoren
Source: Bayer AG Leverkusen
20-MAY-1994 (38)

5.8 Toxicity to Reproduction
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5.9 Developmental Toxicity/Teratogenicity
-

5.10 Other Relevant Information

Type: Excretion
Remark: Kaninchen (keine weiteren Angaben); s.c.
Wirkung:
Ausscheidung als N-Glucuronid im Urin
Source: Bayer AG Leverkusen
23-MAY-1994 (94)

Type: Metabolism
Remark: Ratte (Sprague-Dawley), maennlich, 500 mg/kg Kgw, oral, Einzeldosis, 14C-Markierung
Wirkung:
Im 24-h-Urin finden sich als Metabolite Aminomethylphenole, insbesondere 2-Amino-5-methylphenol (keine quantitativen Angaben) und 2.5 % der Dosis als unveraenderte Ausgangs-substanz
Source: Bayer AG Leverkusen
20-MAY-1994 (95)

Type: Metabolism
Remark: Kaninchen (Japanese Albino), maennlich, 100 mg/kg Kgw, Einzeldosis
Ratte (Wistar) und Meerschweinchen (Hartley), keine Geschlechtsangabe, 100 mg/kg Kgw/Tag, 2 Tage
Wirkung:
Nachweis von N-Arylformamid und N-Arylacetamid im Zyto-sol
Source: Bayer AG Leverkusen
23-MAY-1994 (96)

Type: Metabolism
Remark: Reaction of p-toluidine with normal and 18-O-labeled H2O2 in presence of chloroperoxidase and pea seed peroxygenase was found to give quantitative incorporation of 18-O into the nitroso metabolite.
Source: Bayer AG Leverkusen
04-MAR-1998 (97)

Type: other
Remark: Methylsubstitution am Ring verringert die neuromuskulaere Wirkung von Anilinderivaten
Source: Bayer AG Leverkusen
15-AUG-1994 (98)

Type: other
Remark: Untersuchung des Effektes von Detergentien auf Permeation, Absorption und Verteilung von Xenobiotika an Rattendarm-praeparaten und kuenstlichen Lipoidmembranen mit u.a. p-Toluidin als Modellsubstanz
Source: Bayer AG Leverkusen
24-MAY-1994 (99) (100) (101) (102) (103) (104)

Type: other
Remark: review on toxicity
Source: Bayer AG Leverkusen
06-MAR-1998 (105)

Type: other
Remark: review on toxicity
Source: Bayer AG Leverkusen
06-MAR-1998 (106)

Type: other
Remark: review on toxicity
Source: Bayer AG Leverkusen
06-MAR-1998 (107)

Type: other: 50 % inhibition concentration
Remark: I50 (50 % inhibition concentration for viability) fuer p-Toluidin in Balb/3T3 betraegt 0.201 mmol
Source: Bayer AG Leverkusen
24-MAY-1994 (108)

Type: other: Drug Metabolism
Remark: Die Seitenkettenhydroxilierung von p-Toluidin durch die mikrosomale Leberfraktion von Meerschweinchen wird durch Vitamin-C-Mangel um 80 % reduziert
Source: Bayer AG Leverkusen
20-MAY-1994 (109)

Type: other: Drug metabolizing enzymes
Remark: p-Toluidin wird durch die mikrosomale Leberfraktion (Kaninchen) in der Seitenkette zu 4-Hydroxymethylanilin hydroxiliert und anschliessend zum Aldehyd oxidiert
Source: Bayer AG Leverkusen
20-MAY-1994 (110)

Type: other: Haematotoxizitaet
Remark: Ratte (Wistar), 200 mg/kg Kgw., intragastrisch bzw. 0.25, 0.5, 0.75, 1.0 oder 1.25 %, dermal
Wirkung:
Nach p.o.-Gabe 1 h p.a. erhoehte Met-Hb-Bildung (21.7 %), nach dermaler Applikation 2 - 6 h p.a. dosisabhaengig erhoehte Met-Hb-Bildung (bis 40 %)
Source: Bayer AG Leverkusen
02-FEB-1994 (111)

Type: other: Haematotoxizitaet
Remark: Katze, 27 mg/kg Kgw., i.v.
Wirkung:
Erhoehte Met-Hb-Bildung (bis 39.6 %)
Source: Bayer AG Leverkusen
25-MAY-1994 (112) (113)

Type: other: Haematotoxizitaet
Remark: Maus (keine naeheren Angaben), 0.5 mmol (ca.=54.5 mg)/ kg Kgw, Einzeldosis, i.p.
Wirkung:
Met-Hb-Bildung (max. nach 10 min., 6.9 %)
Source: Bayer AG Leverkusen
23-MAY-1994 (114)

Type: other: Hemoglobin binding
Remark: Ratte (Wistar), weiblich, 0.6 mmol/kg Kgw (ca.=64.2 mg/kg Kgw) in 1,2-Propandiol; Schlundsonde
Wirkung: Haemoglobin-Bindungs-Index: 4.3 (mmol/mol Hb/Dosis (mmol/kg))
Source: Bayer AG Leverkusen
20-MAY-1994 (115) (116)

Type: other: MetHb formation
Remark: Assessment of MetHb formation of aniline derivates; in vitro method using rat blood and hepatic metabolic activation system (english abstract from japanese paper only).
Source: Bayer AG Leverkusen
06-MAR-1998 (117)

Type: other: MetHb formation
Remark: After i.v.-administration of 0.025 mM p-toluidine or its corresponding N-hydroxy derivate to rabbits p-toluidine produced much smaller amounts of MetHb.
Source: Bayer AG Leverkusen
06-MAR-1998 (118)

Type: other: N-oxidation in vivo
Remark: Hund (keine naeheren Angaben), 111.1 mg p-Tol-HCl/kg Kgw, i.v. Einzeldosis, 4 Tiere
Wirkung:
Bildung von Methaemoglobin und p-Nitrosotoluol
Source: Bayer AG Leverkusen
20-MAY-1994 (119)

Type: other: N-oxidation of aromatic amines
Remark: The N-hydroxilation of p-toluidine which forms the nitroso derivate of the aromatic amine is paralleled by methemoglobin production in the cat.
Source: Bayer AG Leverkusen
04-MAR-1998 (120)

Type: other: Nephro- and Hepatotoxicity
Remark: p-Toluidin ist im Vergleich zu Anilin weniger nephro-toxisch, aber staerker hepatotoxisch
Source: Bayer AG Leverkusen
20-MAY-1994 (121)

Type: other: Toxicity by cutaneous application
Remark: Albino-Maus (keine naeheren Angaben); keine Dosis-Angabe; Applikation auf Schwanzhaut; Wirkung: nach 6h keine Wirkung auf Atmung oder motorische Reaktion
Source: Bayer AG Leverkusen
20-MAY-1994 (122)

Type: other: aromatase inhibitors
Remark: p-Toluidin besitzt keine Aromatase inhibierende Wirkung.
Source: Bayer AG Leverkusen
24-MAY-1994 (123)

Type: other: dermal absorption
Remark: p-Toluidin wird aus 1 % waessriger Loesung von Ratten durch die Schwanzhaut schneller absorbiert als durch Rueckenhaut
Source: Bayer AG Leverkusen
24-MAY-1994 (124)

Type: other: dermal penetration
Remark: p-Toluidin zeigt in dem Modell nach Potts und Guy (human skin in vitro) eine signifikante dermale Absorption
Source: Bayer AG Leverkusen
20-MAY-1994 (125)

Type: other: hemoglobin binding
Remark: Ratte, (Wistar), weiblich, 0.5 mmol (ca.= 54 mg)/kg Kgw, Schlundsonde, Einzeldosis
Wirkung:
Hemoglobin binding index (HBI): 4.3
Source: Bayer AG Leverkusen
23-MAY-1994 (126)

Type: other: metabolic activation
Remark: p-Toluidine was N-acetylated by recombinant human NAT1 and polymorphic NAT2 acetyltransferases.
Source: Bayer AG Leverkusen
06-MAR-1998 (127)

Type: other: microsomal metabolism
Remark: Die Metabolisierung von p-Toluidin durch die mikrosomale Leberfraktion maennlicher Wistar Ratten wird durch Chlorierung in ortho-Position verlangsamt
Source: Bayer AG Leverkusen
24-MAY-1994 (128)

Type: other: microsomal metabolism
Remark: p-Toluidin wird durch die mikrosomale Leberfraktion von Ratten und Maeusen zu p-Aminobenzoesaeure metabolisiert
Source: Bayer AG Leverkusen
24-MAY-1994 (129)

Type: other: microsomal metabolism
Remark: Die N-Hydroxilierung aromatischer Amine durch die mikrosomale Leberfraktion von Kaninchen ist Cytochrom P-450 abhaengig
Source: Bayer AG Leverkusen
24-MAY-1994 (130)

Type: other: microsomal metabolism
Remark: Die N-Oxidation von p-Toluidin durch die mikrosomale Leberfraktion verlaeuft bei Meerschweinchen, Kaninchen, Hamster, Maus oder Ratte mit unterschiedlicher Aktivitaet
Source: Bayer AG Leverkusen
24-MAY-1994 (131) (132)

Type: other: microsomal metabolism
Remark: Bei Metabolisierung durch mikrosomale Leberfraktion (Ratte) bildet p-Toluidin keine intermediaeren Komplexe mit Cytochrom P-450
Source: Bayer AG Leverkusen
24-MAY-1994 (133)

Type: other: microsomal metabolism
Remark: Bei Pyruvatzusatz wird die Acetylierungsrate von p-Toluidin durch Rattenleberhomogenat (Sprague-Dawley, male) um 15 % gehemmt
Source: Bayer AG Leverkusen
24-MAY-1994 (134) (135)

Type: other: toxicodynamic properties in chronic poisoning
Remark: Aim of study was to assess delayed toxic effects of toluidine isomers during prolonged exposure in female Wistar rats. Isomers were added to food containing 24% protein. Within the dose and exposure-duration ranges used, o-toluidine reached highest blood and urine concentrations (from english abstract of polish publication).
Source: Bayer AG Leverkusen
10-MAR-1998 (136)

Type: other: toxicodynamic properties in chronic poisoning
Remark: Aim of study was to assess delayed toxic effects of toluidine isomers during prolonged exposure in female Wistar rats. Isomers were added to food containing 8% protein. Within the dose and exposure-duration ranges used, o-toluidine reached highest and p-toluidine lowest blood and urine concentrations (from english abstract of polish publication).
Source: Bayer AG Leverkusen
10-MAR-1998 (137)

5.11 Experience with Human Exposure

Remark: Bei Rauchern wird im Vergleich zu Nicht-Rauchern eine- von den Rauchgewohnheiten abhaengige- erhoehte Bildung von Addukten aus Haemoglobin und aromatischen Aminen beobachtet ("blonde- or black-tobacco smoking")
Source: Bayer AG Leverkusen
20-MAY-1994 (138) (139)

Remark: Nachweis von p-Toluidin im Urin von 2/11 Rauchern und 4/9 Nicht-Rauchern
Source: Bayer AG Leverkusen
20-MAY-1994 (140)

Remark: Die unterschiedlich ausgepraegte Bildung von Haemoglobin-Addukten mit aromatischen Aminen bei Rauchern korreliert mit individuellen Stoffwechselunterschieden
Source: Bayer AG Leverkusen
23-MAY-1994 (141)

Remark: Bei Rauchern wurde eine leicht erhoehte Tendenz zur Bildung von Amin-Haemoglobin-Addukten beobachtet; keine strenge Assoziation zwischen Raucher-Status und Haemoglobin-Bildung
Source: Bayer AG Leverkusen
23-MAY-1994 (142)

Remark: Toluidine (Isomerengemisch, keine naeheren Angaben) zeigen die gleichen Vergiftungssymptome wie Anilin, jedoch mit schwaecher ausgepraegter Zyanose. Symptome: Strangurie, Haemoglobinurie, Anaemie
Source: Bayer AG Leverkusen
24-MAY-1994 (143)

Remark: Inhalation von 40 ml/cubic metre (ca.= 176 mg/cubic metre) Toluidin (Isomerengemisch) ueber 60 min fuehrt zu schweren Vergiftungserscheinungen. Bei fortdauernder Exposition treten ab 10 ml/cubic metre (ca.= 44 mg/cubic metre) Symptome auf
Source: Bayer AG Leverkusen
24-MAY-1994 (144)

Remark: Bei der zytoskopischen Untersuchung an 75 von 81 Beschaeftigten einer o/p-Toluidin-Produktion wurden in 2 Faellen Blasenpapillome diagnostiziert
Source: Bayer AG Leverkusen
24-MAY-1994 (145)

Remark: p-Toluidine can be determined simultaneously with numerous other aromatic amines in urine, plasma or erythrocytes.
Source: Bayer AG Leverkusen
04-MAR-1998 (146)

Remark: No correlation could be found between increasing urinary cotinine levels indicating increasing exposure to environmental tobacco smoke and hemoglobin adducts of p-toluidine in nonsmoking pregnant women.
Source: Bayer AG Leverkusen
04-MAR-1998 (147)

Remark: p-Toluidine was detected in the urine of nonsmoking subjects who were not occupationally exposed to arylamines.
Source: Bayer AG Leverkusen
06-MAR-1998 (148)

Remark: The amount of Hb-adducts of p-toluidine in the blood of exposed workers can be quantified by GC-MS.
Source: Bayer AG Leverkusen
04-MAR-1998 (149)

Remark: There were no significant differences in renal excretion of p-toluidine between occupationally exposed and non exposed smokers and nonsmokers.
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7. Risk Assessment

7.1 End Point Summary

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7.2 Hazard Summary

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7.3 Risk Assessment

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